# Knowledge, Attitudes and Practices of Veterinarians on Antibiotic Use, Resistance and its Containment in South Africa


**by**

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A dissertation submitted in fulfilment of the requirements for the degree of Master of Medical Science in the School of Health Sciences, University of KwaZulu-Natal, Durban.

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This is a dissertation by manuscript with an overall introduction and final summary.

This is to certify that the content of this dissertation is the original research work of Mr Simbai Allen Maruve, supervised by:

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## DECLARATION

I, Simbai Allen Maruve, declare that

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2. This dissertation has not been submitted to UKZN or other tertiary institution for the purposes of obtaining an academic qualification.

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Signed

[redacted]

Simbai Allen Maruve

On this 12th day of January 2021

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## ABBREVIATIONS AND ACRONYMS

ABR - Antibiotic Resistance

AMR - Antimicrobial Resistance

ANOVA - Analysis of Variance

CIAs - Critically Important Antibiotics

CPD - Continuous Professional Development

DAFF - Department of Agriculture, Land Reform and Rural Development

FAO - Food and Agricultural Organisation of the United Nations

GAP - Global Action Plan

KAP - Knowledge, Attitudes and Practices

NAP - National Action Plan

OIE -World Organisation for Animal Health

SAAHA - South African Animal Health Association

SAALAS - South African Association for Laboratory Animal Science

SAASP - South Africa Antimicrobial Stewardship Programme

SANVAD - South African National Veterinary Surveillance and Monitoring Programme for Resistance to Antimicrobial Drugs

SAVA - South African Veterinary Association

SAVC - South African Veterinary Council

VCIA -Veterinary Critically Important Antimicrobial Agents

VHIA -Veterinary Highly Important Antimicrobial Agents

VIA -Veterinary Important Antimicrobial Agents

VRE -Vancomycin Resistant Enterococci

WAAW -World Antibiotic Awareness Week

WHO - World Health Organisation

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# ABSTRACT

The inappropriate use of antibiotics in the veterinary sector has led to antibiotic resistance (ABR), which negatively impacts animal health and welfare and indirectly on human health. Understanding the knowledge, attitudes, and practices on antibiotic use, ABR, and its containment amongst veterinarians is critical to optimize antibiotic use and contain resistance. A quantitative questionnaire-based online survey was conducted amongst members of professional veterinary associations. The questionnaire consisted of four sections focusing on socio-demographic characteristics, knowledge, attitudes, and practices (KAP) of participants on antibiotic use, ABR, and its containment in the South African veterinary sector. The Independent t-test, analysis of variance (ANOVA), and Chi-square test were used to establish associations among selected socio-demographic variables and selected KAP parameters. A total of 130 responses were received from 2178 animal health professionals, yielding a response rate of 6 %, with 102 complete responses constituting the final sample size. Self-reported knowledge on antibiotic stewardship, antibiotic resistance mechanisms, and pharmacology was good at 96 (94.1%), 91 (89.2%), and 70 (68.6%), respectively. More than half the respondents (60 [58.8%]) were confident that the veterinary training they received prepared them quite a bit/very much on rational antibiotic use. Most respondents (81 [79.4%]) believed that antibiotics were sometimes prescribed for suspected but not confirmed infections. The majority of the respondents (77 [75.5%]) were quite concerned/very concerned about antibiotic resistant infections, compared to 19 (18.7%) of clients expressing the same concern. Veterinary guidelines for appropriate use of antibiotics were sometimes read by respondents (45 [44.1%]). A little more than half of the veterinarians (54 [52.9%]) often/always discussed antibiotic resistance with their clients. Most respondents identified broad-spectrum antibiotics such as amoxicillin-clavulanate and metronidazole as first-line treatment at 62 (60.8%) and 64 (62.7%) respectively. Notably, most of the veterinarians (61 [59.8%]) also lacked an antibiotic stewardship programme at their practice. The cost of diagnostics (90 [88.2%]), time to results of diagnostics (83 [81.4%]), and client expectations of receiving antibiotics (74 [72.5%]) were cited amongst barriers to the implementation of an antibiotic stewardship programme. Place of practice was significantly associated (p=0.004) with possession of knowledge about antibiotic resistance. Veterinarians in urban practice were more knowledgeable about antibiotic resistance than those in rural practice. Place of practice was also significantly associated (p=0.035) with discussions on antibiotic resistance with clients. More veterinarians in rural practice frequently carried out such discussions than their urban counterparts. There is a need for education and training to address gaps in KAP. There is also a need for the development and implementation of antibiotic stewardship programmes in veterinary practice. Cost effective diagnostic tests with shorter turnaround time might assist in achieving such. The programmes might encourage microbiology informed therapy and the use of guidelines for appropriate antibiotic use.

# CHAPTER 1

## INTRODUCTION AND LITERATURE REVIEW

### 1.1 INTRODUCTION

The use of antibiotics in animals has contributed immensely in the fight against infectious diseases. Use has been beneficial in various ways including (1) alleviating pain and suffering, (2) controlling potential epidemics that may cause colossal animal losses, (3) mitigating the spread of zoonotic bacteria, (4) ensuring the sustainability of food animal production and, (5) protecting people's livelihoods and animal resources (Michigan State University, 2011). Antibiotics have been used for therapeutic purposes, prophylaxis, metaphylaxis, and growth promotion. Veterinarians are key stakeholders in containing ABR in animal health. They are trained to diagnose infections and prescribe antibiotics if warranted. Veterinarians ensure that the authorized withdrawal time for antibiotics is adhered to and are key to educating their clients on the rational use of antibiotics and the containment of ABR. Before antibiotics are administered, treatment guidelines that ensure the appropriate use of antibiotics considered to be of critical importance in veterinary medicine and human health should be adhered to (Murphy *et al*., 2017). However, antibiotic misuse and overuse contribute to antibiotic resistance (ABR), a worrying threat to human and animal health the world over (FAO, 2019; OIE, 2016).

The consequences of ABR impact negatively on the welfare of animals. The animals will endure pain and suffering from 'difficult-to-treat" or untreatable infections. The damage to tissues and organs that might occur can be irreversible, and death can occur in some instances. ABR also has a socio-economic and emotional bearing on animal owners due to non-resolving infections in animals. For animal producers, non-resolving infections lead to poor feed conversion, decreased growth, increased mortality, and reduced productivity (Vaarten, 2012). By 2050, an 11% drop in animal productivity is set to occur due to ABR (World Bank, 2017). ABR will also encourage the use of newer, effective antibiotics after the failure of first-line antibiotics, thus broadening the list of ineffective antibiotics. The lack of effective antibiotics will also cause much faster dissemination of zoonotic bacterial organisms and a huge potential for disease outbreaks at a large scale. Such outbreaks will be very costly to control. The lack of advancement of new veterinary antibiotics is of huge concern (Vaarten, 2012), yet, animal production as a contributor to ABR, continues to intensify, thus escalating antibiotic use. Such an escalation is due to a growing demand for animal protein world over (FAO, 2019). Animal health is under threat from the ever increasing ABR (FAO, 2016). To preserve the antibiotics that are still effective and prevent ABR from further worsening in animal health, educators, professional bodies, governments, and animal health stakeholders need to mitigate ABR effectively (O'Neill, 2016).

In a tripartite alliance, the World Organisation for Animal Health (OIE), the Food and Agriculture Organisation (FAO) of the United Nations, and the World Health Organisation (WHO) developed the Global Action Plan (GAP) to address AMR which was adopted in May 2015 by the World Health Assembly (WHO, 2015). The alliance recognises the interrelatedness of human, animal, and environmental health hence the need for such an alliance to effectively control ABR. In support of GAP, the World Organisation for Animal Health (OIE) and the Food and Agriculture Organisation (FAO) of the United Nations have since rolled out their action plans to curb ABR. They both support member states in the development and implementation of strategies to curb ABR in animals and the food and agriculture sectors, respectively (FAO, 2016; OIE, 2016).

Animal health professionals have to possess the necessary knowledge to improve attitudes and practices on antibiotic use, antibiotic resistance, and its containment. Knowledge, attitude and practices are core to behavioural change. Assessing animal health professionals on knowledge, attitudes, and practices on antibiotic use, antibiotic resistance, and its containment is, therefore, necessary in order to inform evidence-based interventions. Such evidence-based interventions could curb the emergence and dissemination of ABR, thereby improving animal welfare, sustaining animal production, and safeguarding the future of veterinary medicine and human medicine.

## 1.2 LITERATURE REVIEW

### 1.2.1 Antibiotics

Antibiotics are substances that are used therapeutically for bacterial infections. They work by inhibiting or killing bacteria (Boolchandani, D'Souza and Dantas, 2019). Antibiotics can be classified based on chemical structure, mechanism of action (Table 1.1) or spectrum of activity (Calderon and Sabundayo, 2007). Based on chemical structure, the common antibiotic classes include β-lactams, aminoglycosides, tetracyclines, quinolones, macrolides, sulphonamides, oxazolidones, amphenicols, rifamycins, streptogramins, polymyxins, pleuromutilins and glycopeptides (Löfmark, Edlund and Nord, 2010; Fair and Tor, 2014; Adzitey, 2015).

Antibiotics can be bactericidal. These kill bacteria, e.g., penicillins, cephalosporins, carbapenems, monobactams, glycopeptides, fluoroquinolones, rifamycins, cyclic lipopeptides, aminoglycosides, and streptogramins. Antibiotics can also be bacteriostatic, e.g., sulfonamides, trimethoprim, tetracyclines, chloramphenicol, and clindamycin. These inhibit bacterial growth. Some classes can be bacteriostatic and bactericidal, e.g., macrolides (Calderon and Sabundayo, 2007). The mechanism of action of an antibiotic influences whether an antibiotic is bactericidal or bacteriostatic. It also determines the mechanism of antibiotic resistance (Boothe, 2015).

**Table 1.1**: Antibiotic classes and their mechanisms of action

| Antibiotic class | Examples | Mechanism of action |
|---|---|---|
| Sulphonamides | sulfadiazine | Inhibit an enzyme crucial to the metabolism of folic acid (dihydropteroate synthetase), leading to suppressed DNA replication. Sulphonamides are bacteriostatic against both aerobic Gram-positive and Gram-negative bacteria (Fair and Tor, 2014). |
| β-lactams | amoxicillin<br>cephalexin<br>imipenem<br>cefazolin<br>ceftazidime | Inhibit cell wall synthesis by attaching to the penicillin-binding protein site transpeptidase (Beauduy and Winston, 2018). Peptide chain cross linkage, which is crucial for peptidoglycan formation, is hindered, leading to the bacterial cell's death (Bush, 2018). |
| Aminoglycosides | amikacin | Causes protein mistranslation by commonly targeting the A site of the 16S ribosomal RNA component of the 30S ribosomal subunit (Fair and Tor, 2014). |
| Amphenicols | chloramphenicol | Affect translation by inhibiting elongation through binding of the 50S ribosomal subunit's peptidyl transferase centre (Fair and Tor, 2014). |
| Macrolides | tulathromycin | Cause premature peptidyl transfer RNA separation from the ribosome, thereby preventing elongation in translation upon binding the 50S ribosomal subunit (Tenson, Lovmar and Ehrenberg, 2003). |
| Tetracyclines | tetracycline<br>doxycycline | Block aminoacyl transfer RNA ribosomal access upon binding to the 30S ribosomal unit. Tetracyclines are bacteriostatic and broad-spectrum in nature (Fair and Tor, 2014). |
| Rifamycins | rifampicin | Inhibit transcription through binding the RNA polymerase β-subunit (Fair and Tor, 2014). |

| Antibiotic class | Examples | Mechanism of action |
|---|---|---|
| Glycopeptides | vancomycin | Binds the peptidoglycan units' terminal dipeptide D-Ala-D-Ala which inhibits their function as transglycosylase and penicillin-binding protein substrates, thereby inhibiting cell wall biogenesis in Gram-positive bacteria (Fair and Tor, 2014). |
| Quinolones | ciprofloxacin | Inhibit DNA synthesis by trapping enzymes responsible for DNA cleavage following the inhibition of topoisomerases II and IV (Drlica *et al*., 2008). Quinolones are bactericidal (Kohanski, Dwyer and Collins, 2010). |
| Streptogramins | dalfopristin<br>quinupristin | They are divided into two classes according to structural basis. Class A streptogramins inhibit translocation and initiation upon binding the 50S ribosomal unit's peptidyl transferase centre. In contrast, class B streptogramins inhibit elongation in translation through binding to the tunnel of peptide exit (Fair and Tor, 2014). Combinations of both classes are usually bactericidal. When used alone, they are bacteriostatic (Kohanski, Dwyer and Collins, 2010). |
| Polymyxins | polymyxin B<br>colistin | Cause a disruptive interlinkage with the Gram-negative lipopolysaccharide outer layer on the cell membrane, resulting in increasing cell membrane permeability, leakage and death of the cells (Evans, Feola and Rapp, 1999). |
| Oxazolidinones | linezolid | Block the formation of the peptide bond by binding to the 50S ribosomal unit peptidyl transferase centre. Oxazolidinones are bacteriostatic against Gram-positive bacteria (Fair and Tor, 2014). |
| Pleuromutilins | tiamulin | Inhibit translation by binding the 50S ribosomal unit peptidyl transferase centre (Fair and Tor, 2014). |
| Nitroimmidazoles | metronidazole | Inhibit the synthesis of DNA, also cause DNA oxidation leading to the degradation of DNA and death of cells (Löfmark, Edlund and Nord, 2010) |
| Phosphonic acid derivatives | fosfomycin | Interfere with a crucial step in bacterial cell wall synthesis by inhibiting an enzymatic reaction. They have bactericidal activity (Skarzynski *et al*., 1996). |

### 1.2.2 Antibiotic resistance

ABR occurs when bacteria continue to survive and grow regardless of the presence and/or pressures posed by antibiotics that were initially effective in managing the infections. In most cases, ABR is encoded genetically in bacteria (Boolchandani, D'Souza and Dantas, 2019). In bacteria, two types of resistance have been observed. These are intrinsic and acquired resistance (Alekshun and Levy, 2007).

Chromosomal genes occurring naturally in a bacterial host mediate intrinsic resistance (Alekshun and Levy, 2007). Intrinsic resistance is usually shared among organisms of the same genus or species (Courvalin, 2008). It often happens via biochemical or structural properties that are characteristic of the organism. Such is the case in many Gram-negative organisms which are resistant to macrolides. The macrolides are excessively large to access their target in the cytoplasm through the outer membrane (Boerlin and White, 2006).

In acquired resistance, a bacterial organism that is usually susceptible to an antibiotic undergoes genetic alteration leading to resistance. Such can occur through mutation in genes responsible for normal cellular structures and physiology or the acquisition of alien resistance genes. A combination of both processes can also lead to antibiotic resistance. The acquisition of foreign DNA that codes for resistance can occur in three processes which are:

1. Transformation, whereby naked DNA in the environment is taken in by bacteria which naturally possess such capacity,
2. Transduction, whereby DNA is transferred between bacteria by bacteriophages, and
3. Conjugation, whereby plasmids are transferred from one bacterium to another via a mating like process (Boerlin and White, 2006).

The movement of genes coding for resistance is also possible within a bacterial cell genome. Various resistance gene combinations can occur through the movement of resistant genes between chromosomes and plasmids with transposons and integrons playing a crucial role. Acquired resistance can present as resistance to the whole antibiotic class, resistance to antibiotics of various classes or resistance to several antibiotics within the same class. In most cases, resistance can be encoded to one or more antibiotics of the same class by a single resistance determinant as observed in fluoroquinolones, β-lactams, or aminoglycosides, e.g., antibiotic inactivating enzymes. It is also possible to have resistance encoded to multiple antibiotic classes by a single resistance determinant, e.g. efflux. A bacterial cell can also simultaneously acquire various resistance determinants leading to multidrug resistance (Boerlin and White, 2006).

Four mechanisms of antibiotic resistance exist, which are (1) active efflux of drug, (2) limited drug uptake, (3) drug target modification, and (4) drug inactivation. The structural variation between Gram-positive and Gram-negative bacteria influences the antibiotic resistance mechanisms. Gram-positive bacteria infrequently employ limited drug uptake due to lack of capacity to carry out some of the efflux mechanisms and lack of a lipopolysaccharide outer membrane. In contrast, Gram-negative bacteria displays all four mechanisms (Reygaert, 2018).

Bacterial cells make use of efflux pumps to maintain normal physiology, which includes expelling toxic waste. Efflux pumps are genetically encoded on the bacterial chromosomes, and efflux pump genes may be expressed in specific environmental conditions such as the presence of antibiotics. Antibiotic efflux enables bacterial survival in conditions of high antibiotic concentration. Efflux pump overexpression is capable of causing antibiotic resistance of clinical relevance in Gram-negative bacteria (Blair, Richmond and Piddock, 2014). Several efflux pump families exist and are classified according to structure and source of energy (Reygaert, 2018). The resistance nodulation division (RND) family is of clinical relevance in Gram-negative bacteria (Blair, Richmond and Piddock, 2014). One example is the AcrAB-TolC efflux pump in *Escherichia coli* capable of transporting β-lactams, fluoroquinolones, erythromycin, tetracycline, linezolid and chloramphenicol, among other compounds (Ma *et al*., 1993; Okusu, Ma and Nikaido, 1996; White *et al*., 1997). Such an ability to transport a wide range of antibiotics allows resistance to different antibiotic classes (Du *et al*., 2014). In Gram-positive bacteria, an example of active efflux pumps is the NorA pump under the major facilitator superfamily (MFS) in *Staphylococcus aureus* responsible for chloramphenicol and flouroquinolone efflux (Reygaert, 2018).

The Gram-negative lipopolysaccharide layer provides a crucial role in limiting drug uptake as it is a barrier for some molecules. It provides intrinsic resistance to some antibiotics (Blair, Richmond and Piddock, 2014). Polar molecules do not easily pass the cell wall in enterococci, thus conferring intrinsic resistance to aminoglycosides. *Mycoplasma* lacks a cell wall, thus limiting the uptake of antibiotics with a cell wall target. Such a structural characteristic confers intrinsic resistance (Bébéar and Pereyre, 2005). Gram-negative bacteria have an outer membrane and use the porin channels which allow the entry of hydrophilic substances (Fernández and Hancock, 2012). However, drug uptake can be limited through mutations that can affect porin selectivity/size, or a reduction in porin numbers can take place (Kumar and

Schweizer, 2005). Bacteria have also been known to form communities on solid surfaces protected by a matrix of polysaccharides. These bacterial communities are termed biofilms. The matrix provides a barrier to antibiotics thus limiting uptake (Mah, 2012).

Bacteria can modify antibiotic targets, thereby conferring resistance (Reygaert, 2018). One example is Gram-positive bacteria's ability to confer resistance to β-lactams by altering penicillin-binding protein numbers and or structure. Penicillin-binding proteins are necessary for peptidoglycan construction. Changes in penicillin-binding protein numbers have a negative impact on the amount of β-lactam binding the target. Structural changes to the target decrease the binding ability of β-lactams. Such changes also have the potential to inhibit β-lactam binding completely. Another example is decreased susceptibility of *S. aureus* to vancomycin following mutations that result in increased thickness of the cell wall, thus limiting vancomycin access to the peptidoglycan target. Gene acquisition (*van* genes) can also cause structural changes in the precursors to the peptidoglycan layer, thus reducing vancomycin binding ability (Beceiro, Tomás and Bou, 2013). Bacteria can also modify ribosomal subunit targets affecting drug binding ability to the ribosome. It can happen either through methylation conferring resistance to lincosamides and macrolides or by mutation, thus conferring resistance to streptogramins and macrolides (Roberts, 2004). Nucleic acid synthesis targets can also be modified through mutation, e.g, genes coding for DNA gyrase and topoisomerase IV (fluoroquinolone targets), affecting drug binding ability confer resistance to fluoroquinolones (Redgrave *et al*., 2014). Enzyme mutation can also affect drugs such as sulphonamides and trimethoprim. Structural alterations in the enzymes interfere with antibiotic binding leading to resistance. Both drugs act as competitive inhibitors by binding to the enzymes dihydropteroate synthase and dihydrofolate reductase, respectively, crucial for folic acid metabolism (Sköld, 2010).

Bacterial cells can carry out antibiotic inactivation either by transferring a chemical group or through antibiotic degradation (Blair *et al*., 2015). Phosphate, adenyl and acetyl groups are among the groups that can be enzymatically transferred to an antibiotic. Antibiotics that can be affected by acetylation include fluoroquinolones, chloramphenicol and aminoglycosides (Robiscek *et al*., 2006; Ramirez and Tolmasky, 2010). Antibiotic degradation can occur through hydrolysis. Both Gram-positive and Gram-negative bacteria are known to produce β-lactamases, a group of enzymes that can hydrolyse the amide bond in β-lactam antibiotics (Bush, 2018). This opens the β-lactam ring making the drug unable to bind to the penicillin-binding protein target (Reygaert, 2018). β-lactamases can be located on the chromosome or acquired through plasmids (Schultsz and Geerlings, 2012).

It is worth noting that several antibiotics appear under two or more resistance mechanisms. One likely explanation for such a scenario is the bacterial evolution that has happened over the years to survive antibiotic effects. Bacterial genome plasticity that enables horizontal gene transfer and mutations has made it possible (Munita and Arias, 2016). Therefore, it is necessary to create new antibiotics putting in mind the versatility shown by bacteria (Reygaert, 2018). Knowledge of antibiotic classifications, mechanisms of action, spectrum of activity and mechanisms of resistance is imperative among veterinarians. Such knowledge will ensure the maintenance of antibiotic efficacy and animal health while simultaneously minimising the risk of antibiotic resistance occurrence.

The risk of antibiotic resistance emergence can be reduced by managing bacterial contaminants, creating a dosing regimen, and de-escalating. Managing bacterial contaminants in the veterinary health facility and the farm environment reduces the dissemination of bacteria with resistance potential. De-escalation involves reducing antibiotic spectrum (Schulz, Osterby and Fox, 2013). Antibiotic use increases selection pressure for antibiotic resistance; therefore, it is necessary to minimise use where possible. Microbial culture and susceptibility testing may help identify a causative agent and its susceptibility profile hence encouraging narrow-spectrum antibiotic use (Weese *et al*., 2015). Education on antibiotic stewardship, assessment of antibiotic prescriptions during therapy and the use of automated clinical decision support tools that assist veterinarians in antibiotic prescribing may facilitate appropriate antibiotic use (Schulz, Osterby and Fox, 2013). Local treatment of abscesses and topical treatment of skin infections should be considered as opposed to systemic antibiotic therapy in such cases. Antibiotic therapy should also be given for the shortest possible duration of therapy. A dosing regimen should be designed so that the choice of antibiotic in an infection eliminates the bacterial inoculum. The causative agent should be identified and characterised, and susceptibility testing should be done to match the drug choice and causative agent effectively. Upon identifying the antibiotics that are effective against the bacterial isolates, the veterinarian should consider host and bacterial responses in choosing the antibiotic that can reach the affected tissue (Boothe, 2015).

### 1.2.3 Antibiotic Resistance and One Health

Antibiotic use and overuse in the animal and human sectors, antibiotic disposal into the environmental sector and the dissemination of resistant organisms and determinants within and between the sectors globally has made ABR a One Health issue. One Health refers to the joint efforts of professions in animal health, human health, and environmental sectors to achieve the best possible health in animals, humans and the environment. The One health approach recognises the interrelatedness of the animal, human and environmental sectors in antibiotic resistance (McEwen and Collignon, 2017).

ABR occurs naturally. However, antibiotic use in agriculture, industries, and human health creates a selection pressure favouring the existence of resistance genes or resistant bacterial strains above the antibiotic susceptible strains. The result is an increased load of resistant organisms in the environment. The ABR emergence rate in humans and animals depends on the antibiotic amounts used together with the exposure frequency and duration (Wall *et al*., 2016).

Evidence on the link between antibiotic use in animals and ABR in humans has been demonstrated. In the year 2000, the US Food and Drug Administration proposed the withdrawal of fluoroquinolone use following an increase in fluoroquinolone-resistant *Campylobacter* associated human infections linked to poultry consumption. This was then followed by the effective withdrawal of enrofloxacin use in poultry in 2005 in the US. Fluoroquinolones are among the choice for treatment against *Campylobacter* infections in humans, while use is also common in veterinary medicine (Nelson *et al*., 2007). In Denmark, *E. coli* isolates were collected from poultry, pigs, cattle, and meat products and compared to the same isolates from human urinary tract infections and healthy individuals. Upon comparing the virulence genes, pulse-field gel electrophoresis, phylotypes, and antimicrobial susceptibility results, a clonal link was observed between *E. coli* from humans and animals or their meat products (Bager *et al*., 2016). In Canada, a study was carried out to underscore the relationship between ceftiofur-resistant *Salmonella heidelberg* isolated from retail chicken and the occurrence of ceftiofur-resistant *S. heidelberg* human infections. Prior to data analysis with a statistical package, the isolates from retail chicken and humans underwent serotyping, phage typing, and susceptibility testing. A positive correlation between isolates from retail chickens and the incidence of human infections caused by ceftiofur resistant *S. heildelburg* throughout Canada was observed. The study also observed that the ceftiofur resistant patterns in chicken and human *S. heidelberg* were directly linked to the level of ceftiofur usage in broiler chicken hatcheries. Resistant rates for human and chicken isolates diminished after ceftiofur use was interrupted in 2005 and increased after the antibiotic was reintroduced in the hatcheries in 2007 (Dutil *et al*., 2010).

The human demand for animal protein-based diets has been on the rise world over. This has led to a rise in intensive animal production systems that require the frequent use of antibiotics to support productivity and maintain animal health globally. This has a huge potential to increase bacterial selection pressure (Van Boeckel *et al*., 2015). In such establishments, optimal disease prevention measures such as correct vaccination, biosecurity, and proper husbandry measures such as the correct feeding of animals, proper housing, and correct management practices are necessary. Such measures will ensure the minimal use of antibiotics as the likelihood of disease risks will be reduced (Magnusson *et al*., 2019). However, such measures may not be efficiently practised and implemented as they can be very costly.

### 1.2.4 Growth Promotion, Prophylaxis and Metaphylaxis

The use of antibiotics in growth promotion, prophylaxis, metaphylaxis, and therapy has been associated with ABR (Wall *et al*., 2016). Antibiotic use in growth promotion involves administering antibiotics for a prolonged time in healthy livestock. Such a practise aims to boost the capacity in the conversion of feed into body mass thus promoting growth (Doyle *et al*., 2006). Antibiotic growth promoters consist of animal feed with antibiotics in subtherapeutic levels. Regardless of the inconsistent results on whether antibiotic growth promoters lead to the significant enhancement of growth in animals (Lee *et al*., 2012), the application of antibiotic growth promoters in food animal production has been practiced the world over to enhance growth since as early as the 1950s (Wielinga *et al*., 2014). However, it was observed that the use of sub-therapeutic levels of antibiotics in animal feed brings an alteration to the gut microbes of treated animals, which encourages the transmission of resistance into the environment via animal waste (You and Silbergeld, 2014). After concerns were raised on the effects of antibiotic growth promoters on the emergence and dissemination of resistance in livestock, antibiotic growth promoters were banned in the European Union in 2006 (Murphy *et al*., 2017).

Even though antibiotic growth promoters have diminished in some parts of the world, use is still evident in animal production in some countries. According to the third annual OIE report on antibiotics for animal use, data collected between 2015 and 2017 through a data template indicated that 110 of the 155 countries that responded did not use antibiotic growth promoters as of 2017. However, the remaining 29% (45 out of 155) reported the use of antibiotic growth promoters. It was noted that colistin, an antibiotic that is reserved for treatment in serious infections in human beings, was being used in growth promotion in some countries (Gochez *et al*., 2018), thus posing a huge public health risk.

The prophylactic use of antibiotics involves administering antibiotics to healthy, susceptible animals to prevent infectious diseases from occurring. Prophylactic antibiotic use has the potential to produce the same effects as antibiotic growth promoters. Therefore, it is imperative to follow the correct therapeutic dosage which minimally induces resistance in the affected bacteria. However, administering antibiotics to groups of animals via feed and water might create a different picture altogether since the animals exposed and the amounts of antibiotics consumed might vary. In such scenarios, sub-optimal dosing might occur, thereby increasing the risk of ABR emerging (Wall *et al*., 2016).

Metaphylaxis involves administering antibiotics to all animals in a group at therapeutic doses after some of them show signs of an infection. Metaphylaxis acts in both ways, therapeutic for infected animals and preventive for animals who are at risk of contracting an infection in the group. In metaphylaxis, the number of animals that can be exposed to antibiotics can be vast. This creates a huge potential for resistance to emerge as bacteria possessing natural resistance have a high chance of being selected for (Wall *et al*., 2016).

Therapeutic antibiotic use involves the use of antibiotics in the management of an active bacterial infection in one or more animals. The continuous therapeutic use of antibiotics in the case of recurrent infections in an animal increases the chances of ABR emergence in resident bacterial populations in that particular animal (Usui, Uchida and Tamura, 2014). There is a tendency to use broad-spectrum antibiotics in the treatment of animals prior to or as the preference to a confirmed diagnosis (Wall *et al*., 2016), this is known to promote ABR development and spread (Kardos, 2017).

Bacterial resistance that results from veterinary antibiotic use can cause resistance to drugs of the same class used in human medicine, thus contributing to therapeutic failure in humans. Therefore, veterinarians must be knowledgeable about resistance potential in the selection of drug therapy for food animals. Client education is also necessary on the contribution of growth promoters and antibiotic use in intensive production setups to antibiotic resistance (Boothe, 2015).

### 1.2.5 Antibiotic resistance containment strategies

In a tripartite alliance, the World Health Organisation (WHO), the World Organisation for Animal Health (OIE), and the Food and Agriculture Organisation (FAO) of the United Nations developed the Global Action Plan (GAP) on Antimicrobial Resistance (AMR). In May 2015, the World Health Assembly adopted the GAP. The plan supplies the supporting structure for national action plans (NAPs) to curb AMR (WHO, 2015).

#### *1.2.5.1 Selected FAO initiatives from 2012 to date*

The Food and Agriculture Organisation has been involved in various strategies to manage ABR in the food and agriculture sector. The organisation's mandate is to guide global attempts in reducing hunger. Antibiotics are crucial in maintaining the health of food animals. Food animal production sustains livelihoods and the development of economies world over. In 2012, the organisation commemorated World Veterinary Day by renewing a call to appropriate antibiotic use in food animal production to maintain antibiotic efficacy in veterinary and human health (FAO, 2012).

In support of GAP, members of FAO took up Resolution 4/2015 at a FAO conference in June 2015. The resolution is an appeal to the organisation itself and member states to deal with the food and agriculture sectors' contributions to the ABR threat and its impact thereof. The resolution was envisaged to be implemented by way of an action plan which focuses on four key areas (FAO, 2016).

**Key area 1: Improving ABR awareness and its associated threat**

ABR awareness among veterinarians, para-veterinarians, and all other stakeholders in the food chain is necessary for behavioural change. The action plan states that awareness will be improved through the development of communication tools that target veterinary personnel. The FAO will support member countries in developing, adapting, and distributing such communication tools to food and agriculture audiences. Deliberation on ABR will also be consolidated into discussions on policy in food and agriculture through partnering with WHO, OIE, and others in national, regional, and global public awareness events. Published progress reports on Action Plan implementation are also set to contribute to ABR consolidation in policy-level discussions in the food and agriculture sectors (FAO, 2016).

In a bid to raise awareness on ABR among stakeholders in the food and agriculture sectors, health workers, policymakers, and the general public, FAO, OIE and WHO have since 2015 dedicated a week in November of each year to commemorate World Antibiotics Awareness Week (WAAW) the world over. FAO has been involved in supporting member states to foster behaviour change, thus preventing the emergence and dissemination of ABR in the food and agricultural sector, health sector, and the environment (FAO, 2020a). FAO is also involved in projects contributing to raising knowledge and awareness on ABR and its related threats (Table 1.2).

**Key area 2: developing capacity for surveillance and monitoring of ABR and use of antibiotics in food and agriculture sectors**

An understanding of the degree of antibiotic use and level of ABR allows the assessment of progress for measures put in place towards mitigating ABR. In partnership with WHO and OIE, FAO will support countries generating data on antibiotic use and ABR to encourage action locally. Knowledge on the use of antibiotics and ABR is expected to be improved through (1) the development of training materials on antibiotic use, ABR and associated surveillance and monitoring, (2) encouraging research focusing on improving knowledge on antibiotic use, ABR and its transference to humans, and, (3) assisting in the incorporation of antibiotic use and ABR as main foundations in undergraduate, postgraduate and continuing education (FAO, 2016).

In 2017, FAO and the Indian Council of Agriculture Research organised a meeting in India to identify areas for policy formulation and development of programmes to address ABR. With a team of veterinary researchers, human health researchers, and facilitators from USAID and FAO, 25 research topics that were meant to increase knowledge and strengthen ABR mitigation responses were formulated. Among the areas included was identifying behavioural aspects of antibiotic use in animals (FAO, 2017). Knowledge influences behaviour hence the need for KAP studies on antibiotic use and ABR among animal health professionals. Such studies will help inform interventions on education and training of animal health professionals at the undergraduate and postgraduate levels.

**Key area 4: promoting appropriate antibiotic use and good practices in food and agriculture systems**.

This area of focus seeks to support measures that reduce antibiotic use and prevent the dissemination of resistant organisms in the food and agriculture sectors. It also aims to ensure that knowledge on antibiotic use, ABR, and its related threats culminates into better practices among veterinarians, para-veterinarians, and other stakeholders in the food chain. This will be achieved by promoting the use of education and training materials that encourage appropriate antibiotic use, effective infection prevention, proper biosecurity measures, and ABR containment strategies. The use of internationally recognised guidelines and standards that focus on good practices in dealing with ABR will be adopted among member states (FAO, 2016).

In 2018, FAO published the "Antimicrobial resistance policy review and development framework," a guideline for Asia Pacific governments in reviewing, updating, and developing policies on ABR and use of antibiotics in animal production. It aims to identify gaps in national policies on ABR and the use of antibiotics that can be improved by government agencies accordingly. Policy on ABR and antibiotics can be assessed on four areas adopted from the FAO action plan: awareness, practices, governance, and evidence. Governments of the member states should engage with veterinarians, and other animal health workers and evidence-based practices should be used in raising awareness. In this regard, existing policies on education and awareness on ABR need to be evaluated. Aspects that can be evaluated on policies include:

1. The inclusion of ABR topics in undergraduate, graduate, postgraduate and continuing veterinary education,
2. The availability of trainers to educate animal health stakeholders,
3. Clarity, transparency, and accessibility of available policies on education and awareness, and
4. The availability of human resources, teaching materials, and funding among others (FAO, 2018a).

Gaps identified in policies will then provide opportunities for improvement in national actions. Such improvements will foster behaviour change on antibiotic use among animal health professionals and thus help preserve the remaining antibiotics. Effective ABR containment strategies are advocated in veterinary medicine. Animal welfare is maintained, and livelihoods will be safeguarded (FAO, 2018a).

To prevent the emergence of ABR, FAO has also partnered with the Swedish University of Agricultural Sciences to develop a manual that assists veterinarians in Eastern Europe, the Balkans, and Central Asia to improve their practices for appropriate antibiotic use. The partnership will also promote knowledge sharing and international training on ABR (FAO, 2018b). In 2019, a manual entitled "Prudent and efficient use of antimicrobials in pigs and poultry" was then published. Targeting sectors with pronounced antibiotic use, the manual emphasizes on minimising antibiotic use through appropriate use and effective disease prevention. Appropriate antibiotic use involves:

1. Use of the right dosage and duration,
2. The use of an antibiotic following proper diagnosis by qualified animal health personnel where indications are authorised,
3. Preventing the animal use of antibiotics deemed as critically important (CIAs) in human medicine and complying with the list of antibiotics of veterinary importance by the OIE and,
4. Avoiding frequent prophylactic antibiotic use and diminishing antibiotic use in growth promotion.

Effective disease prevention involves appropriate vaccination, biosecurity, and good husbandry practices (Magnusson *et al*., 2019).

**Table 1.2**: Selected FAO initiatives raising knowledge and awareness on ABR and its related threats.

| **Project title** | **Period** | **Target countries** | **Objectives** | **Achievements/ Expected outcomes** | **References** |
|---|---|---|---|---|---|
| "Addressing Antimicrobial Usage in Asia's Livestock, Aquaculture and Crop Production systems." | Oct 2015 to July 2020 | Vietnam, Thailand, Indonesia | Reducing the possibility of AMR occurrence and dissemination through promoting appropriate antibiotic use in livestock, aquaculture, and crop production in Asia. | Awareness on the impact of AMR and best antibiotic use practices is expected to be raised through:<br>• Development of KAP studies.<br>• Data examination of KAP studies among stakeholders in the region to determine trends.<br>• Training of relevant personnel in the communication of behavioural change and KAP study approach.<br>• Creating campaigns and communication materials on AMR.<br>• Celebrating the "World Antibiotic Awareness Week" annually, an event aimed to raise AMR understanding, motivate for appropriate antibiotic use, and good practices among professionals and the public world over.<br>• Promoting regional antibiotic stewardship forums. | (FAO, 2020b) |
| "Developing a national strategy to reduce the threat of AMR in agriculture, fisheries, food, and livestock production as part of the implementation of GAP on AMR in four selected countries." | Jan to Oct 2016 | Cambodia Kenya, Ghana, Zimbabwe | Limiting AMR occurrence and dissemination in the food and agriculture sectors by assisting the targeted countries with the development of NAPs on AMR. | • Awareness on AMR and its associated threats among stakeholder representatives in the food and agriculture sectors was raised.<br>• Insight on the existing knowledge and awareness together with policies and capacities on ABR and antibiotic use were improved in the target countries.<br>• AMR and the use of antimicrobials were improved after being assessed.<br>• Coordination in the implementation of a "One Health" approach in mitigating AMR was improved with this support. | (FAO, 2020c) |

| **Project title** | **Period** | **Target countries** | **Objectives** | **Achievements/ Expected outcomes** | **References** |
|---|---|---|---|---|---|
| "Support the development of NAPs on AMR in Latin America and the Caribbean." | Dec 2016 to May 2018 | Paraguay, Cuba, Bolivia, Dominican Republic, Ecuador, El Salvador, Honduras | Encouraging the food and agriculture sectors in the target countries to assist in developing NAPs on AMR. | • The level of awareness of AMR's threat and impact was raised among key personnel in the food and agriculture sectors.<br>• Stakeholder and institutional technical capability in improving AMR surveillance, prevention, and control were expanded in the food and agriculture sector. | (FAO, 2020d) |
| "Reducing the advance of AMR in food and agriculture." | April 2017 to Nov 2021 | Kazakhstan Belarus, Armenia, Kyrgyz Republic, Tajikistan | Engaging the food and agriculture sector in the target countries to promote the development and application of NAPs on AMR. Among the areas of focus were: advocacy and cross-sectoral coordination for a One Health approach; reinforcing legislation on AMR; reducing antibiotic use through improved practices together with preventing the dissemination of resistant organisms across the food chain; and increasing national laboratory capacity in utilising data on the use of antibiotics, AMR and antibiotic residues. | • Materials that promote awareness on AMR in appropriate antibiotic use, best production practices, governance, antibiotic registration, surveillance, and prevention of disease are expected to be generated.<br>• The World Antibiotic Awareness Week is expected to promote awareness of One Health.<br>• Updated communication tools on AMR that target food and agriculture sector stakeholders are expected to be generated.<br>• An assessment of guidelines and regulations that are in existence, together with data on antibiotic use is expected. Such will aid in the generation of a country situation analysis. | (FAO, 2020e) |

*1.2.5.2 Selected OIE and WHO Initiatives from 2003 to date*

OIE is an organisation with an obligation to better animal health the world over. In curbing ABR, the OIE has been involved in capacity building and setting standards for Veterinary Services, veterinarians, para veterinarians, and other shareholders in animal production (OIE, 2018).

In a bid to avert and decrease ABR selection pressures caused by the use of veterinary antibiotics on bacteria, the OIE developed a list of antibiotics of veterinary importance. The list focuses on antibiotics used in food-producing animals and veterinary medicine. Following the Geneva and Oslo OIE/FAO/WHO Expert Workshops on Non-Human Antimicrobial Usage and Resistance held in 2003 and 2004, respectively, the OIE was requested to develop a list of critically important antibiotics for veterinary use. The WHO formulated a similar list for human medicine. The development of an OIE draft list was then deliberated upon by the member states in 2006 at the 74th General Session of the OIE International committee. After a series of meetings and reviews, the OIE came up with a list approved in May 2013. The list undergoes revision regularly. It underwent revision in 2015 and 2018 (OIE, 2019a). Veterinary antibiotics are categorised into veterinary critically important antimicrobial agents (VCIA), veterinary highly important antimicrobial agents (VHIA), and veterinary important antimicrobial agents (VIA). The classification is based on (1) > 50% of member states categorizing the antibiotic to be of veterinary importance based on a questionnaire and, (2) the availability of antibiotic alternatives for the management of serious disease conditions in animals. The antibiotic class was categorized based on whether it contained compounds considered extremely important in managing specific bacterial conditions coupled with a lack of alternative antibiotics that can be used as alternatives. Antibiotics meeting both benchmarks are categorised as VCIA while those that meet either of the two benchmarks are categorised as VHIA. Antibiotics meeting neither of the benchmarks are categorised as VIA (OIE, 2019a). Knowledge of the OIE list of important antibiotics for veterinary use (Table 1.3) among animal health professionals is necessary to inform practices that preserve antibiotic efficacy. The welfare of animals will thus be maintained.

**Table 1.3**: OIE list of antibiotics of veterinary importance (OIE, 2019a)

| Critically important antibiotics | Highly important antibiotics | Important antibiotics |
|---|---|---|
| Aminocyclitol<br>Aminoglycosides<br>Amphenicols<br>Macrolides<br>Penicillins<br>Quinolones (2nd generation) | Ansamycin – rifamycins<br>Cephalosporins (1st and 2nd generation)<br>Ionophores<br>Lincosamides<br>Phosphonic acid derivatives<br>Pleuromutilins<br>Polypeptides<br>Polymyxins<br>Quinolones (1st generation) | Aminocoumarin<br>Arsenical<br>Bicyclomycin<br>Cephalosporins (3rd and 4th generation)<br>Fusidane<br>Orthosomycins<br>Quinoxalines |

The two OIE/FAO/WHO Expert Workshops on Non-Human Antimicrobial Usage and Resistance held in 2003 and 2004 led to the development of the "WHO CIA List" (OIE, 2019a). From the workshop in 2003, ABR was acknowledged as a concern in both animal and human health the world over. It was also recognised that ABR was influenced by antibiotic use in all sectors, and antibiotics used in therapy, disease prevention, and growth promotion in animals were similar to those available for human medicine. Conclusions that were drawn from the meeting include:

- Resistant bacteria emerging from non-human antibiotic use had unfavourable consequences to human health in the form of high infection and treatment failure cases,
- Non-human antibiotic usage patterns influence the development of antibiotic resistant bacteria in animals and food products and the ultimate dissemination to humans, and,
- ABR effects were severe when bacteria resistant to antibiotics of critical importance to humans were involved (WHO, 2019).

The WHO was then advised to appoint an expert clinical medical group to set down antibiotics regarded to be of critical importance to humans taking into consideration relevant bacteria that can potentially be disseminated to humans from food commodities, environment or animals (WHO, 2019). In 2005, the first list of critically important antibiotics was developed in Canberra, Australia, in the WHO Expert Meeting on Critically Important Antimicrobials for Human Health. The list has since undergone revision in 2007, 2009, 2011, 2013, and 2018 (WHO, 2020). Antibiotic classes currently in use in human medicine are categorised as critically important, highly important and important (Table 1.4), the basis for which is as follows:

- The antibiotic class is the only one or is among the limited options available for the management of severe human bacterial infections, and,
- The antibiotic class is used in the management of human infections due to bacteria that can be disseminated from non human sources to humans or bacteria attaining resistance genes from sources other than humans (WHO, 2019) .

Antibiotics regarded as critically important meet both criteria, whereas those termed highly important meet either one of the criteria. Those antibiotics termed as important meet none of the two criteria. Critically important antibiotics are further categorised into highest priority and high priority antibiotics to help in allotting resources on antibiotics requiring urgent risk management. Three factors are considered in prioritising the critically important antibiotics. The first factor is associated with the people that might require the antibiotic for therapy, the second-factor relates to the antibiotic's frequency and intensity of use that increases the risk of ABR in the human population and the third-factor considers evidence of the dissemination of resistant bacteria or genetic elements of the resistant bacteria (WHO, 2019).

CIAs that do not meet all the three factors fall under high priority CIAs (Table 1.4) (WHO, 2019). CIAs that meet all the three factors fall under highest priority CIAs, as shown in Table 1.5 below.

**Table 1.4**: WHO list of antibiotics of human importance (WHO, 2019).

| Critically important | | Highly important | Important |
|---|---|---|---|
| Highest Priority | High Priority | | |
| Glycopeptides<br>Macrolides and ketolides<br>Quinolones<br>Polymyxins<br>Cephalosporins (3$^{rd}$, 4$^{th}$ and 5$^{th}$ generation) | Oxazolidinones<br>Aminoglycosides<br>Carbapenems and other penems<br>Monobactams<br>Ansamycins<br>Glycylcyclines<br>Phosphonic acid derivatives<br>Penicillins (antipseudomonal, aminopenicillins and aminopenicillins with β-lactamase inhibitors)<br>Lipopeptides | Cephalosporins (1$^{st}$ and 2$^{nd}$ generation) and cephamycins<br>Lincosamides<br>Sulfones<br>Riminofenazines<br>Streptogramins<br>Tetracyclines<br>Steroid antibacterials<br>Sulfonamides, dihydrofolate reductase inhibitors and combinations<br>Pseudomonic acids<br>Penicillins (narrow spectrum, amidinopenicillins and anti-staphylococcal) | Pleuromutilins<br>Cyclic polypeptides<br>Nitroimidazoles<br>Nitrofuran derivatives<br>Aminocyclitols |

**Table 1.5**: Critically important antibiotics of highest priority (WHO, 2019).

| **Antibiotic Class** | **Factors considered in prioritisation** |
|---|---|
| Cephalosporins (3rd and higher generation) | • Select for cephalosporin- resistant *E. coli* and *Salmonella* spp. in animals<br>• Are among the few therapies available for managing severe *E. coli* and *Salmonella* spp infections in children.<br>• The number of severe cases of *E. coli* and *Salmonella* spp infections is significant in humans. |
| Macrolides and Ketolides | • Select for macrolide-resistant *Campylobacter* spp. mainly *Campylobacter jejuni in* poultry.<br>• Are among the few therapies available for managing severe *Campylobacter* infections in children.<br>• The number of severe cases of *Campylobacter* spp infections mainly *C. jejuni* is significant in humans. |
| Polymyxins (e.g., colistin) | • Select for plasmid-mediated polymyxin resistant *E. coli* in animals<br>• Intravenous polymyxins are among the few therapies available for managing severe multiresistant human infections caused by *Pseudomonas aeruginosa* and *Enterobacterales*, mainly in critical care.<br>• The number of severe human cases due to *Enterobacterales* that may require colistin use is considered to be significant in humans. |
| Quinolones | • Select for quinolone-resistant *E. coli* and *Salmonella* spp. in animals<br>• Are among the few therapies available for managing severe *E. coli* and *Salmonella* spp infections.<br>• The number of severe cases of *E. coli* and *Salmonella* spp infections is significant in humans. |
| Glycopeptides | • Select for glycopeptide resistant *Enterococcus* spp. in animals<br>• The use of avorpacin in growth promotion saw the development of vancomycin-resistant enterococci (VRE) in food animals, which were disseminated to humans.<br>• Severe consequences occur as a result of a failure in treatment.<br>• Are among the few therapies at hand in managing severe enterococcal infections. |

Antibiotic use plays a role in the selection of resistant bacteria and the use of antibiotic agents in animal production acts as a driver for the emergence of resistant bacteria that can be disseminated to humans via the food chain. Reducing the use of antibiotics that are of critical importance to human medicine in animal production is crucial to maintain their benefits to the human population. Policymakers, veterinarians, and other animal health stakeholders can use the list in managing risks in food production (WHO, 2020).

OIE supports quality veterinary education (undergraduate, postgraduate, and on the job training) to promote the health and welfare of animals, human beings, and the environment. Upon noting some deficiencies in veterinary education in most of its member states, the "Veterinary Education Core Curriculum OIE Guidelines" was published in 2013 (OIE, 2012; OIE, 2020a). The guidelines are to be used by veterinary institutions in the development of curricula to assure required competency levels for graduating veterinary students in member states. Veterinary institutions may adapt the guidelines to suit their educational requirements. As part of the Veterinary Microbiology course, students have to be taught : (1) bacterial characteristics, classification, isolation, and identification (2) pathogenesis of bacterial infections, (3) clinical signs, available clinical and laboratory tests for diagnosis (4) treatment modalities, (5) ABR development, (6) appropriate antibiotic use and, (7) infection prevention and control (OIE, 2013). Such knowledge, combined with the right attitude, will inform the best practices which prevent ABR emergence and spread.

Following the development of the GAP on AMR by the tripartite alliance of the WHO, OIE, and FAO, the OIE's General Assembly took up Resolution 36 that instructs the OIE to organise its AMR projects into a strategy in 2016. In November 2016, "The OIE strategy on Antimicrobial Resistance and the Prudent Use of Antimicrobials" was published. The OIE's strategy is in line with the GAP and acknowledges the need for a One Health approach in curbing ABR. It provides the OIE's strategies and goals and encourages member states to take ownership and undertake implementation at national level. The strategy contains four objectives which are to:

- "Improve the level of awareness and understanding;
- Reinforce knowledge via research and surveillance;
- Support good governance and capacity building and,
- Encourage the implementation of international standards" (OIE, 2016).

Objective 1 is the focus of this study and is thus discussed in detail here.

**Objective 1: To improve the level of awareness and understanding among animal health professionals**

To achieve this objective, the OIE seeks to assist member states by developing materials targeted at animal health professionals that promote an understanding of AMR and its associated risks. The OIE will also support efforts that decrease antibiotic use and the occurrence and dissemination of antibiotic resistant bacteria in animals. AMR awareness will also be promoted through veterinary education establishments and statutory bodies. Support in organising and conducting symposia, conferences, and workshops that address AMR and appropriate antibiotic use will be rendered. The OIE will also increase its scientific, guidance, and educational material linked to curb the occurrence and dissemination of antibiotic resistant bacteria while encouraging proper husbandry techniques, vaccination programmes, and good biosecurity to avert diseases and the need for antibiotics. OIE will also join forces with the FAO and WHO in policy coordination and alignment on AMR (OIE, 2016).

Concerning improving the level of awareness and understanding among animal health professionals, the OIE has produced standards that are constantly improved and issued in the form of the “Terrestrial Animal Health Code” and the “Aquatic Animal Health Code” among others. The standards lay out methodologies for member states to effectively prevent the risk of occurrence and dissemination of antibiotic resistant bacteria due to antibiotic usage in animal production (OIE, 2020b). The “Terrestrial Animal Health Code” provides information on appropriate antibiotic use in veterinary medicine. The veterinarians are expected to contribute to animal health and welfare and public health through proper practices. A thorough clinical examination of the animal should be done before administering and prescribing antibiotics. The OIE list of antimicrobial agents of veterinary importance should be followed when prescribing and administering antibiotics. Clinical experience and laboratory testing should justify the choice of an antibiotic in the treatment of a disease. Following the failure of first-line antibiotic treatment or in the event of disease recurrence, diagnostic testing should justify second-line antibiotic treatment. However, a different antibiotic class or subclass can be used if diagnostic tests are unavailable. It is also expected that the use of antibiotic combinations is not recommended unless justified . Veterinary schools, research institutes, and professional bodies are advised to offer training on antibiotic usage aimed at preserving antibiotic efficacy (OIE, 2019b).

The “Aquatic Animal Health Code” lays out guidelines on appropriate antibiotic use in aquatic animals. A rigorous clinical assessment should precede antibiotic usage in aquatic species. The veterinarian or any other authorised aquatic animal health professional should utilise a clinical examination, post-mortem examination, bacteriology with culture and sensitivity where possible in order to reach a definitive diagnosis. Poor water quality and other environmental factors are considered sources of infection; therefore, they must be assessed and improved accordingly before antibiotic usage in aquatic species. The standard also recommends training veterinarians, and other aquatic animal health professionals on appropriate antibiotic use by veterinary schools, research institutes and professional bodies (OIE, 2019c). Knowledge of appropriate antibiotic use among animal health professionals will inform good practices, thereby preserving antibiotic efficacy. Such will have a positive impact on animal welfare and public health.

In 2018, the second OIE global conference on AMR and prudent use of antimicrobial agents was held in Marrakesh, Morrocco. It aimed to increase the level of understanding of AMR in animals among professionals, experts, international organisations, donors, policymakers, and OIE delegates. It was also a platform to identify effective ways to assist member states in fulfilling the AMR OIE strategy and the GAP objectives. One of the conference's focus areas was to deliberate on communication materials and strategies leading to behavioural changes in antibiotic use in veterinary medicine (OIE, 2018). It was reported that the OIE, together with the FAO and the WHO, celebrate the World Antibiotic Awareness Week annually. The OIE has also developed communication campaigns that assist national veterinary services in member states with guidelines on developing NAPs. Information resources are also available on the OIE website for veterinarians and other stakeholders as a strategy to improve AMR awareness (Bertrand-Ferrandis and Gabourie, 2018). The need for communication is based on the principle that the information that humans access determines their behaviour. From this reasoning, the importance of communication as a tool for influencing antibiotic use behaviour was born.

Communication has been used the world over as a tool for raising awareness. Using a One Health approach and being led by the Department of Veterinary Services (DVS), experts across the agriculture, health, and academic sectors and non-governmental organisations in Kenya developed a communication strategy on AMR in 2017. The strategy was a course of action on the prevention and containment of AMR in the country. Through education, training, and effective communication, the strategy was meant to enhance AMR awareness and understanding (Njagi, Azegele and Othieno, 2018). It was also reported that the OIE held a set of regional seminars that consisted of behavioural change exercises to reinforce Veterinary Services' capacity on risk communication and behavioural change. The behavioural change initiatives were meant to establish timelines, outputs, barriers, and interventions for desired behaviours in veterinarians, farmers, retailers, consumers, and policymakers. Although the lack of funding and inadequate legislation were identified as common barriers in sustaining the efficacy of antibiotics, there was overwhelming support for strategies that raise awareness on AMR amongst the stakeholders mentioned above (Bertrand-Ferrandis and Gabourie, 2018). Effective communication in education and training on ABR will improve knowledge, thus informing the attitudes and practices of animal health professionals on antibiotic use.

#### *1.2.5.3 Selected containment strategies in South Africa*

Various professional bodies and national departments have been involved in the fight against the global ABR problem by promoting appropriate antibiotic use practices. Collaboration in the form of a One Health approach is necessary for effective ABR containment.

To complement efforts made by the WHO, FAO and OIE to contain ABR from a One Health perspective, the National Department of Health and the then Department of Agriculture, Forestry, and Fisheries (DAFF) developed the National Antimicrobial Resistance Strategy Framework, covering 2018 to 2024. The strategic framework seeks to ameliorate antibiotic use in both the animal and human health sectors to minimise ABR dissemination across the food chain. Its strategic objectives include:

(1) Strengthening, coordinating and institutionalising interdisciplinary and intersectoral efforts by way of governing structures that involve health experts in animal, environmental and medical sectors,
(2) Diagnostic stewardship to refine diagnostic testing, pathogen identification and treatment,
(3) Optimising ABR and antibiotic use surveillance,
(4) Enhancing biosecurity, prevention and control of infections to curb ABR dissemination, and,
(5) Promoting appropriate antibiotic use by way of awareness campaigns on ABR and appropriate antibiotic use, species-specific guidelines for appropriate antibiotic use, antibiotic stewardship programmes and governed antibiotic access.

Educating the animal health profession on antibiotic stewardship, pharmacology, infection prevention and control and microbiology is expected to promote the execution of the strategic objectives. Strategies that effectively improve ABR containment will be integrated into the animal health profession curricula at both the undergraduate and postgraduate levels. KAP studies on antibiotic use and ABR are also expected to provide an evidence base that allows effective execution of the strategic objectives (DoH, 2018).

The South African Veterinary Association (SAVA) is an association representing member interests. The association's membership consists of veterinarians and para-veterinarians. SAVA is also responsible for promoting veterinary science and the veterinary profession (SAVA, 2015). In 2002, the Medicines Committee of the South African Veterinary Association coordinated with the Faculty of Veterinary Science, University of Pretoria, and produced national guidelines on appropriate antibiotic use in veterinary medicine. The guidelines were intended to encourage safe and effective antibiotic use that reduces selection for antibiotic resistant bacteria in animals while maintaining antibiotic efficacy. Such an initiative would prevent the dissemination of resistant bacteria in animals hence maintaining animal health. It would also protect consumers' health as they would consume food of animal origin with high standards of safety. Dissemination of resistant bacteria or resistance genes from animals to human beings would also be minimised thereby maintaining efficacy of antibiotics intended for human health. The guidelines emphasized the need for veterinary institutions, research institutes, and professional bodies to educate and train veterinarians to foster knowledge on ABR and appropriate antibiotic use. The programmes should include: (1) the potential of antibiotics to select antibiotic resistant bacteria in animal production causing problems in animal health and human health, (2) strategies in disease prevention and management in order to minimise antibiotic use, (3) the relevance of bacteriology and susceptibility testing in the process of diagnosis, (4) appropriate information on pharmacokinetics and pharmacodynamics, and (5) the importance of administering antibiotics in livestock farming following the marketing authorisation and or veterinary prescription requirements (SAVA, 2002). Over the years, SAVA has also been involved in providing continuing professional education (CPD) for its members on antibiotics and ABR.

The South African Veterinary Council (SAVC) regulates the veterinary and para-veterinary professions in the country. Among its responsibilities is to ensure that the professions mentioned above are well informed and, hence, incorporate the One Health plan in their curricula. It also ensures ongoing education on antibiotic prescribing and dispensing for their members. The SAVC is linked together with other national organisations in the human health and environmental sector to effectively control ABR through the Antimicrobial Resistance National Strategy Framework (Van Vuuren, 2016). The discovery of plasmid-mediated gene mcr-1 conferring mobilized resistance to colistin an antibiotic of last resort in human beings in 2016, resulted in the SAVC instruction to registered veterinarians and para-veterinarians not to use colistin in food-producing animals unless results from culture and sensitivity justify its usage. Failure to comply is deemed unprofessional conduct (Registrar of Medicines, 2016).

Colistin is currently ranked among the critically important antibiotics of the highest priority on the WHO CIA list. Thus, it should be preserved for human health (WHO, 2019).

The state veterinary services in the then DAFF introduced the South African Veterinary Strategy 2016-2026. The strategy forms the foundation on which the South African government fulfils its responsibilities and commitment to providing safe and sufficient food of animal origin to its citizens. The strategy aims to encourage animal and human well-being by creating mechanisms and systems to deliver efficient state veterinary services involved in effective prevention, detection, containment and the elimination of public and animal health risks. The Veterinary strategy recognises the need for an integrated antimicrobial resistance programme between DAFF and the Department of Health. The OIE and WHO programmes that are in existence are to be used as guides. The following areas address antimicrobial resistance:

- "Clear definition and scope of antimicrobials;
- Use and distribution of veterinary medicines and other antimicrobials;
- Traceability on the use of antimicrobials;
- Surveillance on antimicrobial resistance;
- Use of biosecurity and management practices to limit the use of antimicrobials;
- Prohibition of the use of compounded medicine in food-producing animals;
- Restrict antimicrobial use to therapeutic use only and not prophylactic use;
- Advise end-users on appropriate use of antimicrobials at points of sale;
- Veterinary inspection of cooperatives;
- Accountability of pharmacists for the drugs they dispense;
- Reconsideration of direct sale of pharmaceuticals to farmers by pharmaceutical companies and,
- Compulsory drug registers" (DAFF, 2016)

Antimicrobials can be purchased over the counter as stock remedies or farm feeds. They are regulated by the Fertilizers, Farm Feeds, Agricultural Remedies, and Stock Remedies Act (Act 36/1947) that enables direct farmer access to stock remedies for tick-borne diseases and animal husbandry practices, for example, in cases where veterinarian access was impossible (Eager and Naidoo, 2017). However, from the draft regulations that were published for comment by Act 36/1947 in 2020, the stock remedies are re-classified in such a way that certain antibiotics fall under Group A for access and use by veterinarians only as registered in terms of the Veterinary and Para-veterinary Professions Act 19 of 1982 (Department of Agriculture, Land Reform and Rural Development, 2020).

The South African Animal Health Association (SAAHA) has also been involved in the containment of ABR. The association provides a service to farmers and other veterinary product end-users. It seeks to support and promote an animal health industry that is innovation-driven and viable, thus contributing to a safe, secure, and healthy food supply via a high level of health and welfare of all animals and the environment (SAAHA, 2020). After various bodies mounted pressure for over the counter antibiotic stock remedies to be regulated as scheduled veterinary medicines in Act 101/1965, SAAHA has been involved in a proposal to the Department of Health to motivate for the continued availability of over the counter antimicrobials to farmers to avert adverse outcomes on animal health and welfare. SAAHA drafted a proposal that supported the antibiotics to remain with Act 36/1947 but with greater control over their sales to encourage antibiotic stewardship. The proposal submitted to the Department of Health included:

1. Sales staff wishing to recommend and or dispense antibiotics must be trained on appropriate antibiotic use through a monitored and approved course,
2. Antibiotic sales are to be recorded by the dispenser,
3. A responsible Veterinarian must be available in all intensive operations and is responsible for all medicaments used, including appropriate antibiotic use, and
4. Antibiotics are to be classified based on criteria that will determine their use. Such criteria include free use to no use in veterinary medicine if the antibiotic is only registered for use in humans (Eager and Naidoo, 2017).

Following an OIE appeal to member countries to carry out efforts to set up national programmes for antimicrobial resistance management, the South African National Veterinary Surveillance and Monitoring Programme (SANVAD) for Resistance to Antimicrobial Drugs was created in 2003 in response . to the international standards established by the OIE in May 2002 for animal bacteria antimicrobial resistance detection and quantification. Participating laboratories were set up, and training was provided to the laboratory technologists to utilise the newly published methodologies in the OIE International Standards on Antimicrobial Resistance towards developing and standardizing a surveillance and monitoring program. Following the OIE guidelines, the South African surveillance and monitoring programme was based on pathogenic animal bacteria, zoonotic bacteria, and indicator bacteria. Such basis enabled data production on public health risks and problem identification due to decreased antimicrobial drug efficacy. The VetMic system was used to determine the minimum inhibitory concentrations. According to the 2007 SANVAD report, from the 430 *E. coli* isolates tested, it was observed that 288 (67%) of the isolates were resistant to at least one antibiotic effective against *E. coli*. Resistance was highest to sulphonamides and tetracyclines and lowest to ceftiofur. Poultry *E. coli* isolates were more resistant than those from other animal species. It was also observed that isolates collected from healthy chickens' intestinal tracts from abattoirs recorded higher resistance compared to those from sick birds. Among the zoonotic pathogens, a total of ten isolates of *Salmonella enterica* from pigs were all resistant to sulphonamides, tetracyclines, and chloramphenicol. Among the pathogenic bacteria, ten isolates of *Mannheimia haemolytica* were obtained from cattle. Although resistance was low generally, resistance was high for tetracyclines neomycin and erythromycin (Van Vuuren, Picard and Greyling, 2007). The national surveillance programme was discontinued and is yet to be re-introduced in animal health (DoH, 2018).

The South Africa Antimicrobial Stewardship Programme (SAASP) has veterinary representation. The aims and values of SAASP include to:

- "Provide leadership, advocacy for, and strengthening of, antibiotic stewardship in the public and private sectors of human and animal health in South Africa;
- Direct appropriate training in antibiotic stewardship in all sectors of human and animal health care; and,
- Identify gaps in current knowledge and the necessary operational research/audit that will inform practice. Provide feedback on the results of these studies to stakeholders, so as to implement change" (Eager and Naidoo, 2017).

In 2015, the South African Health Products Regulatory Authority, formally known as the Medicines Control Council, implemented a guideline for antibiotic intramammaries. The guideline required applicants to undertake minimum inhibitory concentration (MIC) tests from local mastitic cultures in South Africa as a requirement to register their intramammaries in order to inform and act accordingly on any ABR trends picked up from these local laboratory tests (MCC, 2013).

### 1.2.6 Knowledge, attitudes, and practices studies on ABR

Knowledge, attitudes, and practices (KAP) studies have contributed to knowledge on ABR. Gaps identified can help mitigate antibiotic resistance. Studies below illustrate some of the common findings identified the world over.

#### *1.2.6.1 Developed countries*

In 2014, a questionnaire-based study was conducted to evaluate behaviours in antibiotic prescribing, attitudes to ABR, and perceptions of appropriate antibiotic use in pigs among veterinarians with a clinical caseload of commercial pigs in Scotland, Wales, and England. The questionnaire comprised open and closed questions and statements on a 5 point Likert scale evaluating prescribing behaviour, ABR perceptions, and what was perceived as appropriate antibiotic use behaviour. The questionnaire was piloted among veterinarians on a farm animal practice in one of the UK's universities. Through the use of the Royal College of Veterinary Surgeons (RCVS) veterinary practise database of 2014, the questionnaire was then distributed via an online mailing list to veterinarians with a clinical caseload of commercial pigs. A paper-based copy was made available to respondents who did not make use of the online platform. From a total of 179 responses, only 61 were usable. A majority of the respondents (≈ 93%) were of the view that the decision on antibiotic prescribing was favoured by the desire to ensure animal welfare, and having confidence in the diagnosis of the type of bacteria causing the infection. Antibiotic use in pigs was considered to have an effect on antibiotic resistance in pigs by 67% of the respondents. Conversely, only 45% of the veterinarians believed antibiotic use in pigs has an effect on antibiotic resistance in humans. It was also observed that antibiotic susceptibility testing was more common with treatment failure (≈20% of the respondents) compared to the initial treatment stages when bacteria was first suspected (≈43% of the respondents). A poor response to treatment was attributed to ABR by less than 10% of the respondents. Antibiotic use behaviours that were regarded as exemplifying appropriate antibiotic use in pigs were assessed for colistin (Coyne *et al*., 2018). Colistin is an antibiotic of last resort in humans that has shown to be effective in managing multidrug- resistant *P. aeruginosa* (Hachem *et al*., 2007), *Enterobacterales* resistant to carbapenems (Gales, Jones and Sader, 2011) and *Acinetobacter baumannii* resistant to carbapenems (Gordon and Warcham, 2010). Colistin use in pigs was perceived as being usually justified by 49% of the respondents. Most respondents (72%) were of the opinion that therapeutic antibiotic use was always justified, whilst only 5% shared the same opinion for prophylactic antibiotic use. Most respondents believed that the veterinarian (>70 %) and the farmer (>40%) are very crucial in monitoring the appropriate use of antibiotics, fewer respondents(< 30%) shared the same sentiments for the European Union, UK government, retailers and farm assurance schemes. It was concluded that a One Health approach is necessary in mitigating antibiotic resistance (Coyne *et al.,* 2018).

In a bid to assess the knowledge, attitudes, and practices on antibiotics and resistance, a cross-sectional multicentre study was carried out among 255 students in 25 universities from the UK in 2016. The study comprised 25 questions with sections assessing knowledge, attitudes, and practices concerning antibiotics, ABR, and antibiotic stewardship awareness. Students received an invitation to participate in the study via email before the survey was made available online. From a sample of 71 students from veterinary medicine, students were assessed whether (1) bacteria and, (2) animals could become resistant to antibiotics. All students agreed that bacteria could become resistant to antibiotics. Only 34% agreed that animals could become resistant to antibiotics. About 11 % of the students suggested the need for more information on how to use antibiotics, while 47% needed more information on antibiotic resistance, 27% on antibiotic prescribing and 69% on the link between human, animal and environmental health. Approximately 67 % of the students had heard about the British Veterinary Association's (BVA) seven point plan that was intended to encourage appropriate antibiotic use in veterinary medicine. It was then concluded that veterinary medicine students in the UK had adequate knowledge of ABR. The misconception on animals becoming resistant to antibiotics could be addressed by more education (Dyar *et al*., 2018).

In 2015, a cross-sectional study was done in Germany to assess the perceptions and attitudes on ABR of veterinarians, pig farmers, general practitioners, hospital physicians, and the general public. Of the 60 veterinary surgeons, 53% perceived their use of antibiotics influenced the occurrence of ABR. Only 40% of the veterinarians considered ABR as important in their daily work. Veterinarians chose three topics on ABR mitigation related to the human sector rather than those in their area of function. Scientific journals (83.3%) and clinical practice guidelines (81.7%) were selected by most veterinarians as important sources of information on antibiotic use. About 67% of veterinarians were in the habit of discussing ABR with their clients in both instances of prescribing and not prescribing antibiotics. It was concluded that a One Health approach is necessary in the development of educational materials for veterinarians to take ownership in mitigating ABR (Schneider *et al*., 2018).

In 2007, a questionnaire-based study was conducted in Ohio, America, to determine the knowledge, beliefs and practices concerning ABR amongst veterinarians on dairy farms. The questionnaire comprised 26 questions on a five point Likert scale, assessing knowledge, beliefs, and practices. A pilot study of the survey was done on four bovine veterinarians prior to survey dissemination. Forty-three out of 168 bovine veterinarians responded to the survey. It was observed that the number of respondents who agreed to ABR affecting animal health negatively (86%) was more than those who agreed to ABR affecting human health negatively (63%). A decrease in antibiotic effectiveness was observed by 37% of the respondents. More than 80% of the respondents were comfortable in responding to questions pertaining to ABR. However, only a minority of them (23%) would regularly initiate ABR discussions with clients. A few respondents (23%) were involved in providing protocols for antibiotic use to the dairy producers. One-on-one meetings were chosen by more than 75% of the respondents as the most effective way to raise awareness on ABR to producers. It was concluded that efforts should be made to encourage the flow of information between bovine veterinarians and their clients to effect the appropriate use of antibiotics (Cattaneo *et al*., 2009).

#### *1.2.6.2 Developing countries*

In order to assess the knowledge, attitudes, and awareness of AMR, an online cross-sectional survey was carried out in Nigeria among veterinary undergraduates (excluding 1st -year students) in 10 of the 12 veterinary schools in 2018. The survey consisted of questions assessing knowledge, attitudes, and awareness on the use of antibiotics and AMR in animals and human beings. From 426 respondents, it was found that AMR knowledge scores were low for 60% of them. About 33.2% of the respondents also recorded low scores on factors contributing to AMR. Students attending clinical years were more knowledgeable about the use of antibiotics and factors contributing to AMR than the other students. AMR control recorded attitudes that were impressively positive; most respondents asserted that antibiotics dispensing over the counter or without prescription should be controlled (90%). Most respondents also asserted that antibiotic prescribing should be controlled closely (91%). This was also true for poor infection control practices as a cause of AMR spread (81%). Conversely, a smaller percentage of the respondents (47.4%) admitted to having adequate knowledge of antibiotic prescription. Additional education and training on AMR to students in clinical years was regarded as a necessity by more than 87% of the respondents. The level of awareness on common AMR terms was low, few of the respondents were familiar with the terms “superbugs” (82.9%), “antimicrobial stewardship” (86.9%), “Global Action plan on AMR” (81.9) and “National Action Plan for AMR, Nigeria” (72.5%). It was concluded that veterinary schools should focus on gaps in knowledge, attitudes, and awareness of the global problem of AMR (Odetokun *et al*., 2019).

A qualitative study was done in the Indian state of Orissa to explore opinions on antibiotic use and resistance development in connection with the environment among registered veterinarians. Using face to face semi-structured interviews, two themes were observed, (1) an interrelationship between antibiotic use, ABR development, and the environment and (2) antibiotic management contributing to the development and dissemination of resistance. Under the first theme, the respondents believed the climate had an influence on antibiotic prescribing. Each season had its disease challenges, which prompted antibiotics to be prescribed. Poor disposal of antibiotics was also thought to contaminate the environment, thereby aiding in the development of antibiotic resistance in bacteria that are disseminated by water. However, some of the respondents believed further scientific investigation was necessary to investigate the link between ABR and the environment. Under the second theme, the veterinarians reported that antibiotics that were commonly in use for humans were also frequently used in poultry and dairy, with some of them being used in growth promotion, and suggested that such use in animals was contributing to ABR in humans. The unavailability of trained personnel and reliable laboratories to carry out susceptibility testing was seen as the reason behind inappropriate antibiotic use in the veterinary sector. It was concluded that environmental changes, human behaviour, and interaction with the environment have an impact on ABR development. Further education, and, implementing, and enforcing proper drug policies were necessary to promote the proper use of antibiotics and prevent environmental contamination with antibiotics (Sahoo *et al*., 2010).

In order to determine AMR awareness and knowledge on antibiotics, qualitative studies were carried out between April and November 2017 in Nigeria and India. Semi-structured interviews were carried out among veterinarians involved in prescribing and dispensing antibiotics. The respondents reported that a lack of proper biosecurity measures, proper nutrition, and poor hygiene led to antibiotic prescribing and dispensing, which encouraged the development and dissemination of ABR. Respondents also felt that antibiotic prescribing was also done to avoid unfavourable outcomes, conflicts and legal battles with clients. Difficulties in enforcing drug withdrawal periods due to challenges with economic compensation for the farmer were also reported. Thus, striking a balance between maintaining antibiotic efficacy and reducing the presence of antibiotic residues in animal protein whilst sustaining livelihoods was somewhat difficult. The use of probiotics and vaccines as opposed to antibiotics in disease prevention was suggested to curb ABR. The results show that awareness of ABR was high. However, issues such as the lack of farmer compensation, poor adherence to antibiotic withdrawal periods, and avoiding legal battles with clients would prompt deviation from good practice (Pearson *et al*., 2018).

#### ***1.2.6*.3 South African studies**

A survey was carried out in South Africa to set a point of reference for surveillance and monitoring of antibiotic volumes available for use in food animals. The data generated would assist in the appropriate use of antibiotics, thus preserving their efficacy. Data on antibiotic volumes used and supplied in South Africa between 2002 and 2004 was collected and presented as kg of active ingredient from approximately 32% of the veterinary pharmaceutical companies. Information on antibiotics approved for veterinary use was collected through applications that were done under two Acts controlling antibiotic availability in South Africa (Act 36 of 1947 representing over-the-counter Stock Remedies and Act 101 of 1965 representing drugs in which a veterinary prescription is necessary under the Medicines and Related Sustances Control Act).

A calculation was made for the volume of sold in-feed antibiotics from data supplied by the companies. Two hundred and thirty-four registered antibiotics were accessible for food animal use. Most of these (72%) were registered through Act 36 of 1947, and 28% were registered through Act 101 of 1965. An average of 1 538 443kg of active ingredient was sold between 2002 and 2004. Macrolides and pleuromutilins (42.4%), tetracyclines (16.7%), sulphonamides (12.4%), and penicillins (10.7%) were the commonly used antibiotics. Most antibiotics were administered in-feed (69%) and via the parenteral route (17.5%). Macrolides, lincosamides, and pleuromutilins were the most common in-feed antibiotic classes (61.6%), and glycolipids were the least (0.4%). Penicillins were the most common antibiotic class given via the parenteral route (60%), and aminoglycosides were the least (0.1%). It was concluded that data on antibiotic consumption should be paired with ABR surveillance and monitoring to curb ABR and its associated problems effectively (Eagar, Swan and Van Vuuren, 2012).

A quantitative questionnaire-based study was done in 2014 to determine the level of knowledge and perceptions towards ABR among the University of Pretoria pre-final and final year veterinary students. From the 71 questionnaires that were analysed, all the students considered ABR as a global threat to both humans and animals. Most of the students agreed that antibiotic misuse by veterinarians (84.5%) and farmers (98.6%) contributes significantly to ABR. Most of the students were confident in their knowledge of antibiogram interpretation (62.9%) and identifying the most appropriate route of administration for an antibiotic (58.6%). However, low confidence was observed in knowledge on the side effects, indications and contraindications of antibiotic classes frequently used by veterinarians (17.1%), mechanism of antibiotic resistance (32.9%), choosing an alternative antibiotic secondary to failure in initial treatment (30%) and identifying the appropriate duration in antibiotic therapy (37.1%). The study pointed out knowledge gaps in antibiotic therapy, which can be used when formulating veterinary curricula (Smith *et al*., 2019).

In 2014, a multi-country survey was done among veterinary students from eight veterinary institutions from South Africa, Sudan, and Nigeria to investigate knowledge, attitudes, and perceptions on antimicrobial use. A semi-quantitative questionnaire was used, and pre-final and final year students participated in the survey. From 353 responses that were received, 71 (20.1%) were from South Africa, while 105 (29.7%) were from Nigeria and 177 (50.1%) were from Sudan. Overall, perceptions of antimicrobial stewardship were poor among students. Only 174 (50.7%) of all the respondents agreed to AMR as an increasing global threat to human and animal health. One hundred percent of students from South Africa agreed to the statement compared to 101 (98.1%) and 3 (1.8%) from Nigeria and Sudan, respectively. Only 156 (45.9%)

of all the respondents agreed that providing lay people with education on the importance of antimicrobials as controlled scheduled substances will positively impact decreasing AMR rise. Sixty-two (87.3%) of the students from South Africa were in agreement compared to 85 (84.2%) and 10 (5.8%) of the students in Nigeria and Sudan, respectively. Only 172 (50.1%) of all the respondents agreed that antimicrobial misuse by veterinarians may significantly contribute to AMR. Sixty (84.5%) of the students from South Africa were in agreement compared to 92 (89.3%) and 22 (12.6%) of the students in Nigeria and Sudan, respectively. Only 154 (44.9%) of all the respondents agreed that undergraduate training had prepared them well enough to make informed choices on selecting the ideal antimicrobial for an animal. Fifty-four (76.1%) of the students from South Africa were in agreement compared to 92 (90.2%) and 8 (4.6%) of the students in Nigeria and Sudan, respectively. Significantly high correct responses ($p<0.05$) were recorded in half of the questions on perceptions in the pre-final students than those in the final year. Generally, confidence was recorded among students on knowledge of antimicrobials. Most respondents were confident in making a Gram stain 225 (69.2%), choosing an ideal route for administering a specific antimicrobial 248 (74.7%) and resistance mechanisms 223 (68%). Students from South Africa were the least confident in all the three scenarios, which were 40 (56.3%), 42 (59.2%) and 23 (32.9%) respectively compared to students from Nigeria and Sudan who were 85 (87.6%) and 101 (62.7%); 73 (76%) and 135 (79.9%); 68 (71.6%) and 135 (80.8%) respectively. Overall, few of the respondents were confident in differentiating time-dependent from concentration-dependent antimicrobials 159 (48.1%) with students from South Africa 47 (66.2%) being more confident than those from Nigeria 30 (30.9%) and Sudan 84 (50.3%). In decreasing order, students perceived the abuse of veterinary antibiotics in the following order: tetracyclines, penicillins, sulphonamides, macrolides, aminoglycosides, quinolones, amphenicols, polypeptides, cephalosporins, antimicrobial combinations, and others. It was concluded that identified knowledge gaps in antibiotic stewardship need to be addressed in the curricula of veterinary students (Fasina *et al*., 2020).

In 2014, antibiotic usage patterns of small animal veterinarians were investigated in South Africa. Compliance with appropriate antibiotic use practices was evaluated through a cross-sectional online survey. A population of 1120 veterinarians registered with the SAVC in 2014 was targeted. Of the 181 veterinarians who responded to the survey, a few had practice set protocols for antibiotic treatment 48 (26.52%). Empirical antibiotic use was common among respondents before testing in the laboratory 165 (91.16%). Most respondents encountered a return of patients due to poor antibiotic efficacy 174 (96.14%). The off label use of human registered antibiotics was common in 156 (86.19%) by respondents. Susceptibility records from canine samples submitted for culture and susceptibility testing at the Faculty of Veterinary Science, bacteriology laboratory between 2007 and 2013 were also analysed. The standard Kirby Bauer method was used in determining susceptibility to antibiotics, and resistance prevalence was computed as the number of resistant bacterial isolates as a percentage of the sum of isolates. *E. coli* and Staphylococci were the most commonly isolated bacteria. Resistance to the frequently used antibiotics for Staphylococci was 71.62% for penicillin G, 78.50% for amoxicillin/ampicillin, 18.63% for tylosin, and 19.96% for amikacin. For *E. coli*, resistance was 96.81% for penicillin G, 69.86% for amoxicillin/ampicillin, 93.04% for tylosin, and 34.20% for amikacin. For all isolates, multi-drug resistance (resistance to one or more antibiotics from three or more distinct antibiotic classes) was more than 50%. The study demonstrated the presence of resistant bacteria in small animal practice together with poor implementation of appropriate antibiotic usage guidelines. Treatment guidelines should be incorporated in the veterinary curriculum for undergraduates and in CPD courses for veterinary professionals to curb ABR development and spread (Chipangura *et al*., 2017).

These studies unlock vital information, which, through careful consideration, might assist in mitigating ABR. Therefore, it is necessary to assess the knowledge, attitudes, practices and experiences of animal health professions in the South African veterinary sector. Results from other studies combined with local results from our study will improve ABR containment strategies that fit the local South African setting. The fight against ABR involves many sectors including the veterinary sector hence the need for an integrated approach.

## 1.3 METHODOLOGY

### 1.3.1 Ethical Consideration

Ethical approval was obtained from the Biomedical Research Ethics Committee of the University of Kwa-Zulu Natal (Reference No.: BE033/19) (Appendix 1). Informed voluntary consent was obtained from all the participants in the preamble to the questionnaire.

### 1.3.2 Aim

The aim of the study was to determine the knowledge, attitudes and practices of veterinary/animal health professions on antibiotic use, antibiotic resistance (ABR), and its containment in the South African veterinary sector.

### 1.3.3 Objectives

1. To design a questionnaire using examples of similar studies from the literature.

2. To pilot this questionnaire among veterinarians who did not form part of the final sample population.
3. To identify and obtain gatekeeper permission from the professional associations whose members will be potential participants.
4. To run the online questionnaire survey amongst members of the participating associations.
5. To consolidate the raw data in a manner that facilitates statistical analysis.
6. To correlate socio-demographic data with relevant knowledge attitude and practices parameters using appropriate statistical methods.
7. To make recommendations for interventions based on the results

### 1.3.4 Study Design

This was a quantitative, descriptive study.

***1.3.4.1 Setting***: The study was conducted within South Africa, nationally.

***1.3.4.2 Participants:***

The population comprised of:

All veterinarians, veterinary nurses, animal health technicians, and veterinary technologists who were members of SAVA and South African Association for Laboratory Animal Science (SAALAS).

**Sample Size:**

The sample size was the total number of eligible participants as above.

*1.3.4.3 Data Collection Tool*:

Data was collected using an online self-administered questionnaire (supplementary material). The questionnaire was adapted from four questionnaires used in previous similar studies (University of Colorado Denver, 2018; Hardefeldt *et al*, 2018; Sadiq *et al*, 2018; Ekakoro and Okafor, 2019). The questionnaire was divided into four sections consisting of closed-ended questions (yes or no) and Likert style (strongly agree/agree/neutral/disagree/strongly disagree) questions. Section 1 focused on the socio-demographic characteristics of participants and sections 2-4 dealt with knowledge, attitudes, and practices of participants on antibiotic use, ABR, and its containment in the South African veterinary sector. Two veterinarians were used in the pilot, and the questions were amended as appropriate.

**Timeline:** The survey was open on the 1st of October 2019 till the 31st of October 2019. A reminder was sent two weeks into the opening of the survey. Responses received after the 31st of October were not considered.

*1.3.4.4 Data Collection Process:*

Assistance in distributing the survey to their membership on behalf of the principal investigator was sought from the SAVA and SAALAS. The two associations then distributed the link for the survey to all veterinarians, veterinary nurses, animal health technicians, and laboratory animal technicians on their databases via email.

Upon receiving the link, participants were directed to a specific website containing the questionnaire. Informed voluntary consent was obtained from all the participants in the preamble to the questionnaire. Upon completion of the questionnaires, responses were then recorded automatically.

*1.3.4.5 Data analysis*

Data was entered on the Microsoft Excel spreadsheet and analysed using commercial statistical software (SAS, version 9.4, SAS Institute Inc, Cary, NC). Variables were analysed using descriptive statistics and presented as percentages at 95% confidence intervals. Before analysis, responses to the questions were merged as follows: for knowledge, "very important" and "extremely important" responses were merged into one variable as were "strongly agree" and "agree," "strongly disagree" and "disagree," "not at all" and "a little," and "quite a bit" and "very much"; while for attitudes, "not concerned" and "slightly concerned," "quite concerned" and "very concerned," "strongly disagree" and "disagree" and "agree" and "strongly agree" were merged as one variable. For practices, "very important" and "extremely important" were merged as one variable; this was also true for "never" and "rarely" and "very often" and "always." The merged variables were then statistically analysed. Knowledge-related statements on antibiotic resistance carried a total score of 13 and a 50% score (6.5) was used to classify the respondent as knowledgeable. Correctly identifying contributors to antibiotic resistant infections in people and factors in veterinary medicine leading to antibiotic resistant infections carried a score of 5 and 7 respectively. The Independent t-test (comparing mean values of only two groups) and the analysis of variance (ANOVA) with Tukey multiple comparison (comparing mean values of more than two groups) were then used to establish associations between the knowledge variables and socio-demographics. The criterion for statistical significance was set at a 5% level.

### 1.4 STUDY OUTLINE

This study aimed to determine the knowledge, attitudes and practices of animal health professions on antibiotic use, ABR, and its containment in the South African veterinary sector. The research is presented in three chapters, as follows:

Chapter 1 provides the background, literature review, rationale, aims and objectives for the study and an overview of the study design and research methodology.

Chapter 2 provides results of the KAP study conducted within SA in the form of a manuscript prepared for the Journal of the South African Veterinary Association.

Chapter 3 presents the conclusions, limitations, and recommendations of this study.

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# CHAPTER 2

**This dissertation is in a manuscript format as follows**

Simbai A. Maruve, Nlooto Manimbulu, Sabiha Y. Essack: Knowledge, attitudes and practices of veterinarians on antibiotic use, resistance and its containment in South Africa. (To be submitted to the Journal of the South African Veterinary Association)

Contributions:

- Simbai A. Maruve, as the principal investigator, co-conceptualized the study, undertook data collection and analysis, and drafted the manuscript.
- Professor M. Nlooto, as the co-supervisor, co-designed the study, guided the project proposal and ethical clearance application and undertook a critical revision of the manuscript.
- Professor S.Y. Essack, as the principal supervisor, co-conceptualized the study, guided the ethical clearance application and literature review, supervised data collection and analysis, and undertook a critical revision of the manuscript.

**Knowledge, attitudes and practices of veterinarians on antibiotic use, resistance and its containment in South Africa**

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RUNNING TITLE: KAP of veterinarians on antibiotic use, resistance and its containment.

**Keywords**: antibiotics, antibiotic resistance, antibiotic stewardship, knowledge, attitudes, practices.

# ABSTRACT

The inappropriate use of antibiotics in the veterinary sector has contributed to antibiotic resistance (ABR), which negatively impacts animal health and welfare. Understanding the knowledge, attitudes, and practices on antibiotic use, ABR, and its containment amongst veterinarians is critical to optimize antibiotic use and contain resistance.

A quantitative questionnaire-based online survey was conducted amongst members of professional veterinary associations. The questionnaire consisted of four sections focusing on socio-demographic characteristics, knowledge, attitudes, and practices (KAP) of participants on antibiotic use, ABR, and its containment in the South African veterinary sector. The Independent t-test, analysis of variance (ANOVA), and Chi-square test were used to establish associations among selected socio-demographic variables and selected KAP parameters.

A total of 130 responses were received from 2178 animal health professionals, yielding a response rate of 6 %, with 102 complete responses constituting the final sample size. Self-reported knowledge on antibiotic stewardship, antibiotic resistance mechanisms, and pharmacology was good at 96 (94.1%), 91 (89.2%), and 70 (68.6%), respectively). Most respondents (81 [79.4%]) believed that antibiotics were sometimes prescribed for suspected but not confirmed infections. Veterinary guidelines for appropriate use of antibiotics were sometimes read by most respondents (45 [44.1%]). Notably, most of the veterinarians (61 [59.8%]) also lacked an antibiotic stewardship programme at their practice. Place of practice was significantly associated (p=0.004) with possession of knowledge about antibiotic resistance. Veterinarians in urban practice were more knowledgeable about antibiotic resistance than those in rural practice. Place of practice was also significantly associated (p=0.035) with discussions on antibiotic resistance with clients. More veterinarians in rural practice frequently carried out such discussions than their urban counterparts.

Antibiotic stewardship programmes need to be implemented in veterinary practice. Such programmes might encourage the frequent use of consensus guidelines for the appropriate use of antibiotics and microbiology informed therapy.

## Introduction

Inappropriate antibiotic prescribing and increased antibiotic consumption in animals have contributed to antibiotic resistance (ABR) (Reygaert 2018). Human health is negatively impacted by ABR in animal health as observed in resistance to colistin due to its use in animal production. Colistin is an antibiotic of last resort in humans for the treatment of infections caused by multidrug-resistant Gram-negative bacteria (Rhouma, Beaudry & Letellier 2016). Loss of antibiotic efficacy compromises human therapy (Van Vuuren, Picard & Greyling 2007). Antibiotic use in animal health applies a selective pressure that favours ABR emergence and spread (Chantziaras et al. 2014; Pomba et al. 2017), limiting treatment options for infections in animals and resulting in treatment failure that negatively affect food production, livelihoods, and food security (Food and Agriculture Organisation [FAO] 2019). It is estimated that by 2050, an 11% drop in animal productivity is set to occur due to ABR (World Bank 2017). Loss of antibiotic efficacy due to resistance will also have a negative impact on animal health and welfare. Damage to the tissues and organs canoccur as a result of bacterial infections, and there is a high risk of disease outbreaks and the dissemination of zoonotic bacteria. The problem is further exacerbated by a lack of new antibiotics that are specifically being produced for animal health (Vaarten 2012).

The Global Action Plan (GAP) on Antimicrobial Resistance (AMR) was adopted by the World Health Assembly in 2015 (World Health Organisation [WHO] 2015). This was a joint initiative of the tripartite alliance of the WHO, World Organisation for Animal Health (OIE) and the FAO of the United Nations (WHO 2015). In support of the GAP, the OIE aims to increase awareness and understanding and enhance knowledge via surveillance and research among its strategic objectives. Information materials targeting veterinarians and other stakeholders will be developed to understand ABR risks. A professional culture that ensures appropriate antibiotic use in animal health will be encouraged via veterinary institutions and veterinary governing bodies. OIE guidelines, scientific and educational materials used for reference in mitigating the development and dissemination of antibiotic resistant organisms will be expanded while simultaneously encouraging efficient disease prevention measures to avoid unnecessary antibiotic use in animals (World Organisation for Animal Health [OIE] 2016a). Also in support of GAP, FAO focuses on key areas that include improving the level of awareness on ABR and its associated threats and developing capacity for ABR and antibiotic use surveillance and monitoring in food and agriculture. FAO also focuses on promoting good practices in systems of food and agriculture and appropriate antibiotic use. Knowledge of ABR and antibiotic use will also be improved by developing educational materials, promoting research and contributing to continuing education, professional education, post graduate training and certification (FAO 2016).

Veterinarians are responsible for prescribing and administering antibiotics to animal patients and are critical to appropriate antibiotic use in animal health. We therefore conducted an online questionnaire-based survey to determine the knowledge, attitudes and practices of veterinarians on antibiotic use, resistance, and its containment in South Africa in order to inform interventions to optimize use and contain resistance.

## Materials and Methods

### *Ethical Considerations*

Ethical approval was obtained from the Biomedical Research Ethics Committee of the University of Kwa-Zulu Natal (Reference No.: BE033/19). Informed voluntary consent was obtained from all the participants in the preamble to the questionnaire.

### *Study Design*

A quantitative questionnaire-based online survey was conducted amongst members of the South African Veterinary Association (SAVA) and the South African Association for Laboratory Animal Science (SAALAS) whose members are veterinarians, veterinary nurses, veterinary nurses, animal health technicians and veterinary technologists. SAVA and SAALAS disseminated a link to the questionnaire to their membership via email. The survey was open from the 1st of October 2019 till the 31st of October 2019.

### *Survey instrument*

Data was collected using an online self-administered questionnaire (supplementary material) compiled from four questionnaires used in previous similar studies (University of Colorado Denver 2018; Hardefeldt et al. 2018; Sadiq et al. 2018; Ekakoro & Okafor 2019). The questionnaire was divided into four sections consisting of closed-ended questions (yes or no) and Likert style (strongly agree/agree/neutral/disagree/strongly disagree) questions. Section 1 focused on the socio-demographic characteristics of participants and sections 2-4 dealt with knowledge, attitudes, and practices of participants on antibiotic use, ABR, and its containment in the South African veterinary sector. Two veterinarians were used in the pilot, and the questions were amended as appropriate.

### *Data analysis*

Data was entered on the Microsoft Excel spreadsheet and analysed using commercial statistical software (SAS, version 9.4, SAS Institute Inc, Cary, NC). Variables were analysed using descriptive statistics and presented as percentages at 95% confidence intervals. Before analysis, responses to the questions were merged as follows: for knowledge, "very important" and "extremely important" responses were merged into one variable as were "strongly agree" and "agree," "strongly disagree" and "disagree," "not at all" and "a little," and, "quite a bit" and "very much"; while for attitudes, "not concerned" and "slightly concerned," "quite concerned" and "very concerned," "strongly disagree" and "disagree" and "agree" and "strongly agree" were merged as one variable. For practices, "very important" and "extremely important" were merged as one variable; this was also true for "never" and "rarely" and "very often" and "always." The merged variables were then analysed using the Chi-square test. Knowledge-related statements on antibiotic resistance carried a total score of 13 and a 50% score (6.5) was used to classify the respondent as knowledgeable. Correctly identifying contributors to antibiotic resistant infections in people and factors in veterinary medicine leading to antibiotic resistant infections carried a score of 5 and 7 respectively. The Independent t-test (comparing mean values of only two groups) and the analysis of variance (ANOVA) with Tukey multiple comparison (comparing mean values of more than two groups) were then used to establish associations between the socio-demographic variables and KAP parameter. The criterion for statistical significance was set at 0.05.

## Results

In total, 130 responses were received from 2178 animal health professionals (response rate 6%); all of whom were veterinarians. Among the 130 responses received, only 102 responses were fully complete and constituted the final sample. From the 102 responses that underwent analysis, 49 (48%) were female, and 53 (52%) were male. Seventy (68.6%) of the respondents were more than 40 years in age, while 32 (31.4%) were aged between 20 and 40. Fifty respondents (49%) had more than 20 years of veterinary experience, while 34 (33.3%) had less than 11 years of veterinary experience. Thirty-eight (37.3%) of the respondents were registered as specialists, 64 (62.7%) practised in an urban setting and 38 (37.3%) practised in a rural setting (Table 1). The vast majority of respondents (74.5%) were in general small/mixed animal practice and two-thirds spent 80-100% in clinical practice. Gauteng province had the highest number of respondents at 42 (41.2%) followed by Western Cape with 24 (23.5%) and Kwa-Zulu Natal with 15 (14.7%). Ninety-three (91.2%) of the respondents obtained their veterinary qualifications at the University of Pretoria while 9 (8.8%) attended other universities. Table 1 shows selected socio-demographic data used in statistical analysis with complete socio-demographic data contained in the supplementary table (S1).

**Table 1**: Selected socio-demographics of veterinary participants (n=102).

| Variable | Number (%) of respondents |
|---|---|
| Gender | |
| Female | 49(48) |
| Male | 53(52) |
| Years in veterinary practice | |
| 0-10 years | 34(33.3) |
| 11-20 years | 18(17.6) |
| + 20 years | 50(49.0) |
| Age group | |
| 20-40 years | 32(31.4) |
| +40 years | 70(68.6) |
| Registered as Specialists | 38(37.3) |
| Place of practice | |
| Rural | 38(37.3) |
| Urban | 64(62.7) |

**Knowledge**

Participants had good knowledge of antibiotic resistance (Table 2). Based on a total score of 13, the average score for the respondents was 11.57± 1.33). Veterinarians in urban practice were more knowledgeable about antibiotic resistance (11.86±1.00) compared to those in rural practice (11.08±1.67). The average score on contributors to antibiotic resistant infections in people was low (Based on a total score of 5, the respondents' average score was 1.99±1.13). The average score on selecting factors in veterinary medicine that may play a role in antibiotic resistant infections in people was relatively good (Based on a total score of 7, the average score for the respondents was 3.95±1.17). All the respondents were aware that drug resistant infections could be difficult to treat and they also believed that antibiotics should be prescribed by veterinarians only when necessary. Almost all of the respondents recognised the danger antibiotic resistant infections posed on surgical procedures. About 73% of the respondents recognised antibiotic resistance as one of the biggest problems in livestock production. More than 60% of the respondents recognised that antibiotics should not be stored for later use in animals, i.e., bottles of antibiotic solutions for injection, once opened, need to be discarded after 28 days. Of note was that 6% of the participants believed that antibiotic resistance is not an issue in South Africa.

**Table 2**. Knowledge of antibiotic resistance (n=102).

| Item | Number (%) of responses |
|---|---|
| There is an increasing rate of infections resistant to antibiotics in animals | 98(96.1) |
| Infections from antibiotic resistant bacteria could be difficult to treat | 102(100) |
| Antibiotic resistance can greatly affect the animal population | 97(95.1) |
| Antibiotic resistance is not an issue in South Africa | 6(5.9) |
| Antibiotic- resistant bacteria can spread from animal to animal | 95(93.1) |
| Antibiotic resistance in animals can spread to humans | 92(92.9) |
| Infections from antibiotic resistant bacteria can make surgical procedures dangerous | 101(100) |
| Antibiotics should not be stored for later use in animals | 56(67.5) |
| Appropriate antibiotic use can reduce the risk of antibiotic-resistant bacterial infections in animals | 98(96.1) |
| The antibiotic resistance problem can be reduced by good biosecurity | 80(93) |
| Antibiotics should only be administered to animals when prescribed by veterinarians | 99(97.1) |
| Antibiotic resistance is one of the biggest problems in livestock production | 64(72.7) |
| Veterinarians should only prescribe antibiotics when necessary | 102(100) |

Only Yes responses are included in the table

None of the veterinarians thought antibiotics were warranted in ecto-parasite infestation while 80 (78.4%) and 98 (96.1%) thought they were necessary for skin infection and respiratory tract infection respectively. Thirty-one (30.4%) thought they were necessary in diarrhoea and 32 (31.4%) thought the same for fever (Supplementary Table S2). The narrow-spectrum antibiotics amoxicillin and procaine penicillin were identified as first-line treatment by 79 (77.5 %) and 50 (49%) respondents, respectively. Most respondents identified other broad-spectrum antibiotics such as amoxicillin-clavulanate (62 [60.8%]) and metronidazole (64 [62.7%]) as first-line, while a few identified rifampicin (1 [1%]), amikacin (2 [2%]), and marbofloxacin (5 [4.9%]) as first-line (Figure 1a). Penicillins were prescribed most often by most respondents (72 [70.6%]), while aminoglycosides were less-frequently prescribed (46 [45.1%]) (Figure 1b). Notably, a majority never administered or prescribed the antibiotics linezolid (102 [100%]), vancomycin (99 [97.1%]), and imipenem (96 [94.1%]). However, most respondents (72 [70.6%]) had prescribed Polymyxin B (Terra-cortril® and or Surolan®) at some point in time.

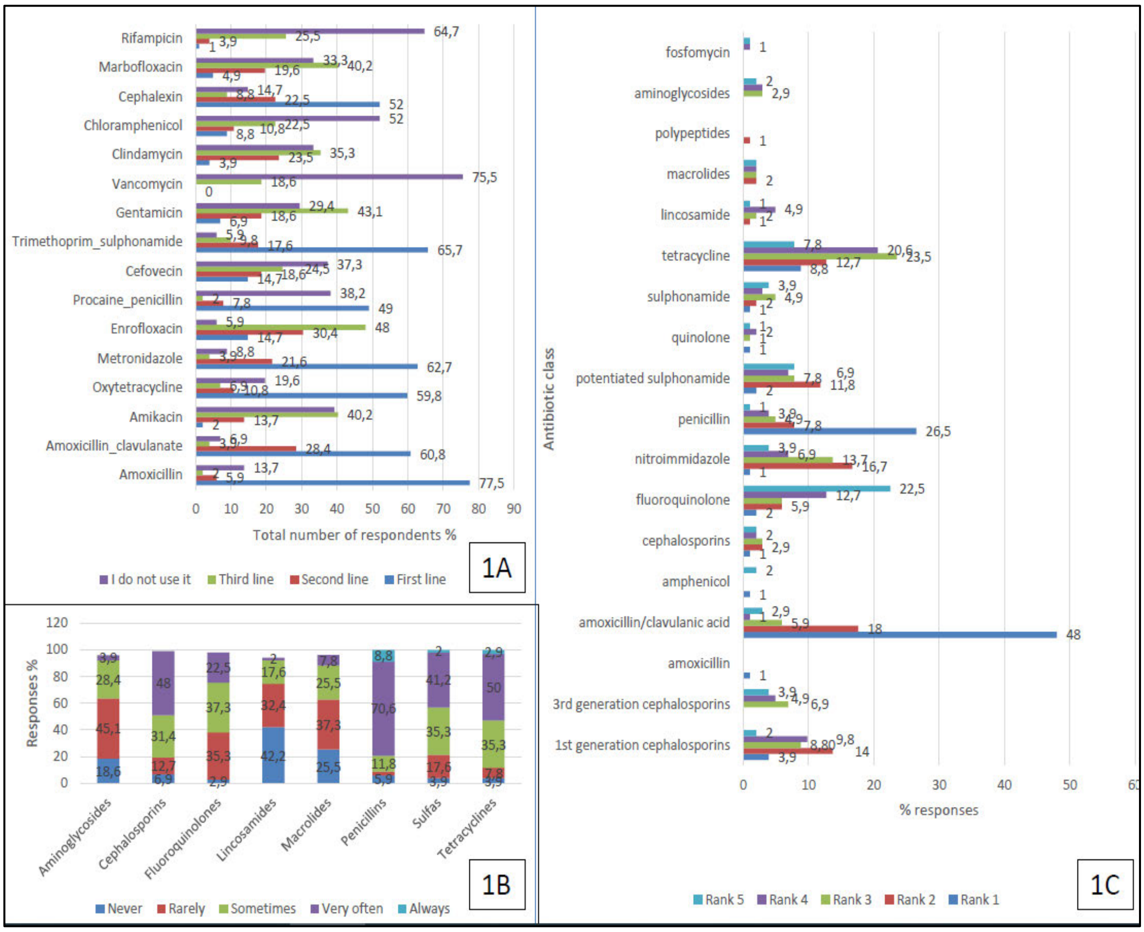


Figure 1: Antibiotic prescribing. 1A: lines of treatment; 1B: frequency of prescribing the major classes of antibiotics; 1C: five most commonly prescribed antibiotics

Generally, the respondents asserted that they had good knowledge of the pharmacology of antibiotics (70 [68.6%]) and appropriate antibiotic use that minimises the development of antibiotic resistance (83 [81.4%]). This was also articulated in relation to understanding antibiotic stewardship (96 [94.1%]) and antibiotic resistance mechanisms (91 [89.2%]) (Supplementary Figure 1). More than half the respondents were confident that their veterinary training equipped them quite a bit/very much (60 [58.8%]) on knowledge on rational antibiotic use. A majority of the respondents (91 [89.2%]) were interested in obtaining continuing professional education on antibiotic use, resistance, or stewardship while a few were not sure (8 [7.8%]). Only three (2.9%) were not interested in obtaining continuing professional education. The veterinary formulary, peer-reviewed scientific literature and textbooks or drug handbooks were considered to be the most important sources of information on antibiotics by 83 (81.4%), 82 (80.4%) and 80(78.5%) of the participants respectively (Supplementary Figure 2).

**Attitudes**

A majority of the respondents (81 [79.4%]) believed that antibiotics were sometimes prescribed for suspected but not confirmed infections. Fifteen (14.7%) believed antibiotics were prescribed based on confirmed infection, while six (5.9%) believed antibiotics were sometimes prescribed based on no documented evidence of infection. A little more than half (56 [54.9%]) the respondents believed that antibiotics were optimally prescribed, 45 (44.1%) believed that antibiotics were overprescribed and one respondent (1%) believed antibiotics were under-prescribed at their practice (Supplementary Figure 3). The concern related to antibiotic resistant infections amongst veterinarians was inverted amongst their clients (Figure 2) with the majority of the respondents (77 [75.5%]) being quite concerned/very concerned about antibiotic resistant infections compared to 19 (18.7%) of clients expressing the same concern (Figure 2).

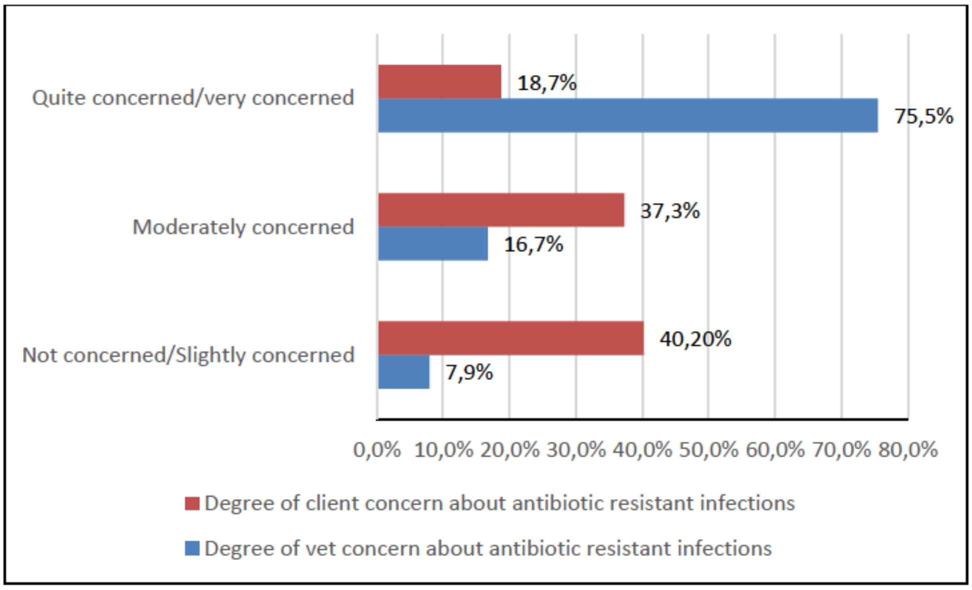


Figure 2. Degree of veterinary and client concern about antibiotic resistant infections.

Only 24 (23.5%) respondents agreed/strongly agreed, while 54 (53%) disagreed/strongly disagreed that the antibiotic classes commonly used in human medicine should not be used in veterinary medicine as they select for antibiotic resistant bacteria. A majority of the respondents (73 [71.5%]) agreed that antibiotic drug use in veterinary practice might lead to antibiotic resistance in pathogens affecting humans (Figure 3).

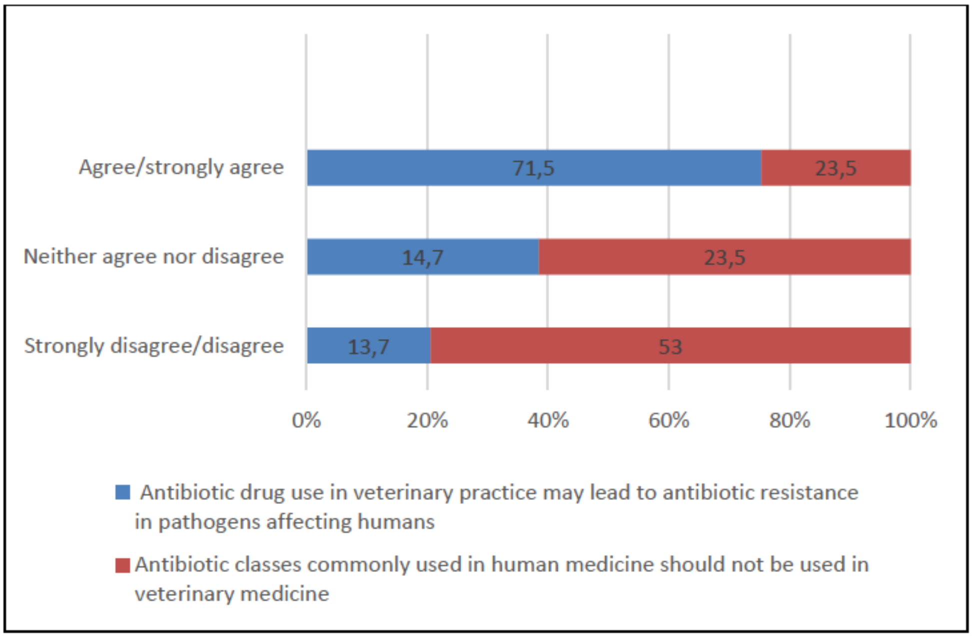


Figure 3. Impact of antibiotic use in veterinary practice on human medicine

The cost of diagnostics (90 [88.2]), time to results of diagnostics (83 [81.4%]), and client expectations of receiving antibiotics (74 [72.5%]) were the most prominent barriers to implementing an antibiotic stewardship plan in their veterinary practices.

**Practices and Experiences**

Persistent infection (89 [87.3%]), recurring infections (73 [71.6%]), and client finances (48 [47.1%]) were the most important factors in influencing the decisions of veterinarians to submit samples for microbial culture and susceptibility testing. Results of bacteriological culture and antibiotic susceptibility (86 [84.3 %]), animal owner compliance to the prescription (77 [75.5%]), clinical signs (75 [73.5%]) and appropriate use guidelines (73 [71.5%]) were considered to be very important in determining the need for and choice of antibiotics while pressure from clients (76 [74.5%]), fear of litigation by the animal owner in the event of an undesirable outcome (72 [70.5%]) and concern about antibiotic resistant infections in humans (33 [32.4%]) were slightly important (Figure 4).

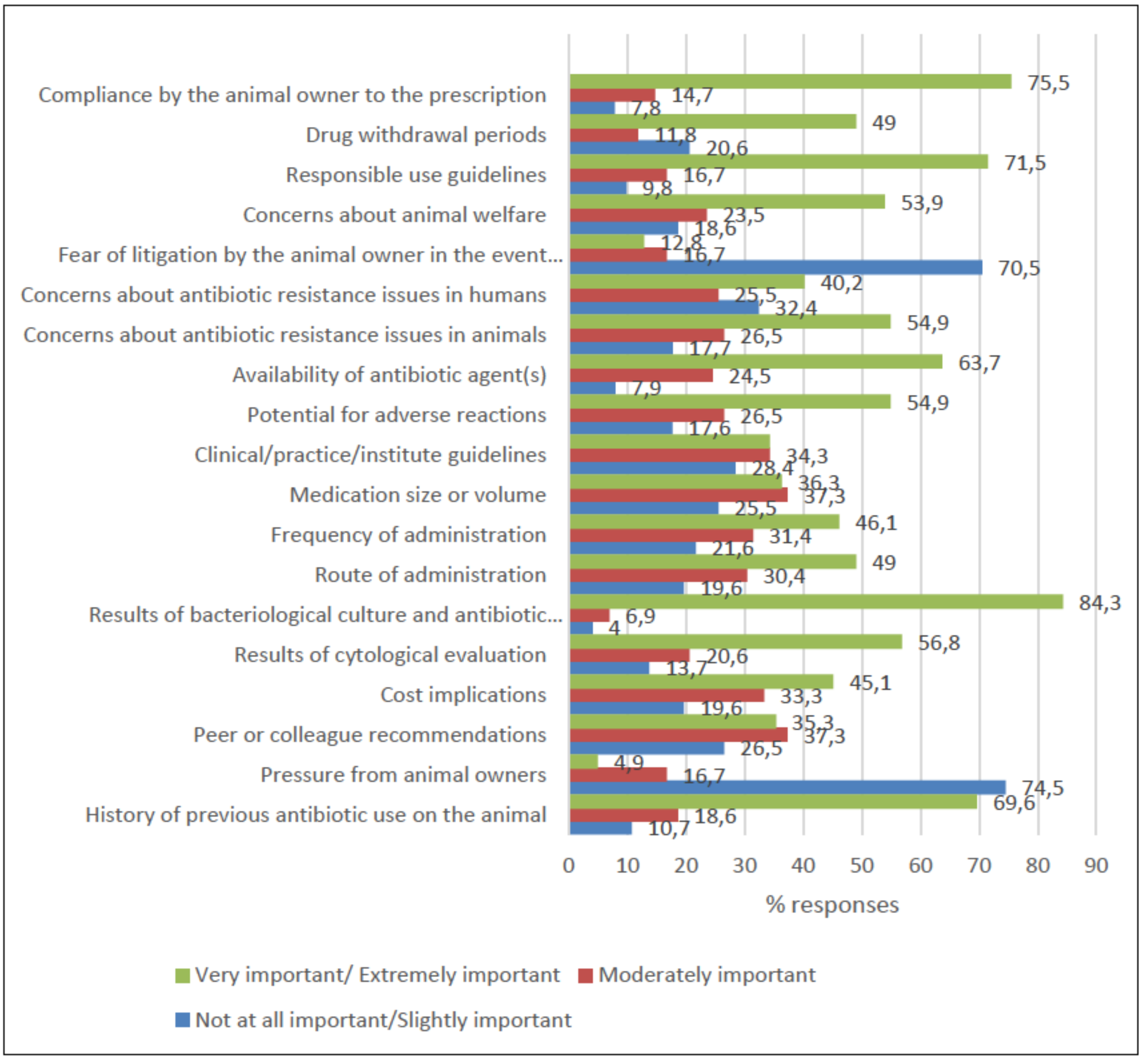


Figure 4. Factors influencing the decision to prescribe antibiotics for clinical use.

Veterinary guidelines for appropriate use of antibiotics was sometimes read by 45 (44.1%) of the respondents, 43 (42.2%) did it very often/always while 13 (12.8%) never/rarely did so. Most veterinarians (41 [40.2%]) prescribed antibiotics for therapeutic purposes three to five times a day while 13 (12.8%) prescribed antibiotics twice a day. There was minimal difference in both pre-operative prophylaxis of infections and post-operative prevention of infections where veterinarians prescribed antibiotics in one to two of every 10 surgical cases (Supplementary Figure 3). Twelve (11.7%) of the veterinarians never/rarely discussed antibiotic resistance with their clients while 54 (52.9%) often/always discussed antibiotic resistance with their clients. A majority of the respondents (61 [59.8%]) did not have an antibiotic stewardship programme at their practice, clinic or institution, only 20 (19.6%) had an antibiotic stewardship programme while 15 (14.7%) were not sure.

**Table 3.** Statistically significant associations between selected socio-demographic factors and selected attitude and practice variables.

| Variables | The extent of agreeing on antibiotic drug use in veterinary practice leading to antibiotic resistance in pathogens affecting humans. | | | | | | Chi-square P-value |
|---|---|---|---|---|---|---|---|
| | Strongly disagree/disagree | | Neither agree nor disagree | | Agree/strongly agree | | |
| | N | % | N | % | N | % | |
| Veterinary experience | | | | | | | |
| 0-10 years | 3 | 8.8 | 5 | 14.7 | 26 | 76.5 | **0.006*** |
| 11-20 years | 4 | 22.2 | 7 | 38.9 | 7 | 38.9 | |
| + 20 years | 7 | 14.0 | 3 | 6.0 | 40 | 80 | |
| Frequency of discussing antibiotic resistance with clients. | | | | | | | |
| | Never/rarely | | Sometimes | | Often/always | | |
| | N | % | N | % | N | % | |
| Place of practice | | | | | | | |
| Rural | 6 | 15.8 | 7 | 18.4 | 25 | 65.8 | **0.035*** |
| Urban | 6 | 9.7 | 27 | 43.5 | 29 | 46.8 | |
| Rating client concerns on antibiotic resistance | | | | | | | |
| | Not concerned/slightly concerned | | Moderately concerned | | Quite concerned/very concerned | | |
| | N | % | N | % | N | % | |
| Gender | | | | | | | |
| Female | 30 | 63.8 | 11 | 23.4 | 6 | 12.8 | **0.000*** |
| Male | 11 | 21.6 | 27 | 52.9 | 13 | 25.5 | |

| Client finances as an influence on the decision to submit samples for culture and sensitivity | | | | | |
|---|---|---|---|---|---|
| | No | | Yes | | |
| | N | % | N | % | |
| Gender | | | | | |
| Female | 18 | 36.7 | 31 | 63.3 | **0.002*** |
| Male | 36 | 67.9 | 17 | 32.1 | |
| Age | | | | | |
| 20-40 | 12 | 37.5 | 20 | 62.5 | **0.035*** |
| +40 | 42 | 60 | 28 | 40 | |
| Veterinary experience | | | | | |
| 0-10 years | 12 | 35.3 | 22 | 64.7 | **0.003*** |
| 11-20 years | 7 | 38.9 | 11 | 61.1 | |
| +20 years | 35 | 70 | 15 | 30 | |

Knowledge on antibiotic resistance was significantly higher amongst veterinarians in urban practice (p=0.004) (Supplementary Table 3). Rating client concerns on antibiotic resistance was significantly associated with gender (p=0.000) (Table 3). The frequency of discussing antibiotic resistance with clients was significantly associated with place of practice (p=0.035) (Table 3). The extent of agreeing on antibiotic drug use in veterinary practice leading to antibiotic resistance in pathogens affecting humans was significantly associated with veterinary experience (p= 0.006) (Table 3). Client finances as an influence on the decision to submit samples for culture and sensitivity was significantly associated with gender (p=0.002), age (p=0.035) and experience (p=0.003) (Table 3).

**Discussion**

A quantitative questionnaire-based online survey was conducted among veterinarians in South Africa. Average knowledge scores on antibiotic use, antibiotic-resistance, and its containment in animal health in South Africa were good. The veterinary training the respondents received appeared to equip the vast majority of respondents with adequate knowledge on the rational use of antibiotics. There was a high degree of concern about antibiotic resistant infections. The veterinarians sometimes consulted veterinary guidelines for appropriate use of antibiotics, and penicillins (procaine penicillin, amoxicillin, amoxicillin-clavulanate) were the most preferred antibiotic class.

Veterinarians in urban practice were more knowledgeable about antibiotic resistance than those in rural practice (p=0.004). This may be due to fewer ABR awareness campaigns targeting the rural areas as compared to urban areas. From the results, a few of the respondents believed that ABR is not an issue in South Africa. ABR is not only a threat in South Africa but worldwide. This is evident in efforts to address ABR in the form of the South African National Strategy Framework (locally) (Department of Health [DoH] 2018) and the FAO and OIE action plans (internationally) (FAO 2016; OIE 2016a). Having a belief that ABR is not a threat might hinder the implementation of antibiotic stewardship programmes in animal health, thus worsening ABR, as was evident in this study where few respondents had antimicrobial stewardship programmes in their practices. Antibiotic stewardship refers to approaches that encompass correct antibiotic usage, dosage, and duration whilst preventing antibiotic resistance. It involves the use of guidelines for appropriate use of antibiotics, culture and sensitivity testing before antibiotic usage, surveillance and monitoring of antibiotic usage, client education, and the implementation of effective infection prevention and control programmes (Guardabassi & Prescott 2015).

Generally, the respondents asserted that they had good knowledge of antibiotics' pharmacology, appropriate antibiotic use that minimises the development of antibiotic resistance, antibiotic stewardship and antibiotic resistance mechanisms. This is in contrast to a study done in 2017 in Nigeria to assess the perceptions, knowledge, and practices of antibiotic stewardship among 280 veterinarians in Enugu state. In the study, few respondents had heard about antibiotic stewardship (17.1%), and overall knowledge on the matter was poor (21.4%) (Anyanwu & Kolade 2017). Such differences in the two studies could be attributed to recent antibiotic stewardship implementation efforts in animal health. Instituting antibiotic stewardship programmes at curricular and practice level will enable appropriate use of antibiotics, thus aiding in minimising ABR emergence and spread. However, effective implementation might be hindered by poor use of microbial culture and susceptibility tests, absence of well-trained veterinary professionals on antibiotic stewardship, gaps in knowledge on current resistance patterns and the lack of evidence-based guidelines (Guardabassi & Prescott 2015).

To a greater extent, the respondents from our study believed the veterinary training they received adequately equipped them with knowledge on rational antibiotic use. One would have expected the recent prioritisation of ABR on the public health agenda to cause disparities between recently graduated veterinarians and their counterparts with more veterinary experience. However, this was not the case in this study. Adequate knowledge of rational antibiotic use combined with the right attitude will enable best practice and effective ABR containment strategies. However, adequate training alone on rational antibiotic use might not translate to appropriate antibiotic use. Gaps might exist in the application of theoretical aspects in practice (Smith et al. 2019). This might have been the case in our study, where respondents identified some broad-spectrum antibiotics as first-line. Knowledge of rational antibiotic use should be among the priority areas in continuing professional development and postgraduate veterinary studies (Smith et al. 2019).

In our study, most respondents were concerned about ABR. It is worth noting that the GAP on AMR was published in 2015 and followed by the OIE and FAO action plans in 2016. Such initiatives could have managed to raise awareness on the implications of antibiotic resistant infections in animal health, thus leading to a high level of concern among veterinarians, concern that is necessary for the effective implementation of antibiotic stewardship programmes and effective ABR containment strategies. Combined with adequate knowledge, it will also favour practices that help preserve the existing finite antibiotic arsenal. Generally, the veterinarians viewed their clients as being slightly concerned over antibiotic resistant infections. This may be due to a low frequency of discussions with clients over the ABR matter. It could have also been due to the lack of clarity when discussions on the matter were held with veterinarians. In our study, veterinarians sometimes discussed antibiotic resistance with their clients. A more significant percentage of veterinarians in rural practice frequently carried out such discussions than their urban counterparts ($p=0.035$). Such disparities might be influenced by an over-reliance on antibiotics in clients from rural areas compared to those in urban areas, hence the need for frequent discussions in those areas. Busy schedules due to high patient loads might hinder such discussions from taking place. Discussing ABR with the clients will assist in raising awareness on the subject. This will help ensure that clients adhere to antibiotic dosages stipulated by veterinarians for their animals, thus, averting client practices that favour ABR emergence and spread.

In our study, most respondents believed that antibiotics were sometimes prescribed for suspected but not confirmed infections regardless of bacteriological culture and antibiotic susceptibility importance. This suggests that an empiric approach to treatment could be preferred compared to a microbiology guided approach in some instances. Microbiology forms an integral part of antibiotic stewardship with microbial culture and susceptibility testing as part of the diagnostic testing (Guardabassi & Prescott 2015). Notably, most respondents indicated the cost of diagnostic testing, time to results of diagnostics and client expectations of receiving antibiotics as barriers to the implementation of antibiotic stewardship programmes. As expected, client finances were among the important factors that could influence the submission of samples for microbiological investigations. All these factors combined could be responsible for such an empiric approach to antibiotic treatment. Microbiology guided treatment would be preferable to empiric treatment. This is because it aids the veterinarian in choosing an ideal antibiotic in an infection, thus preserving the currently available antibiotic arsenal and maintaining animal welfare in the process (Watts, Sweeney & Lubbers 2018).

Most respondents read guidelines for appropriate use of antibiotics. The use of any veterinary formulary, peer-reviewed scientific literature, textbooks or drug handbooks were chosen as the most important sources of information in determining antibiotic choice for clinical use. The results are almost similar to a study done at a veterinary teaching facility in the USA among veterinary clinicians. In that study, the respondents chose peer- reviewed scientific literature (56.5%) and textbook or drug handbook (24.2%) as the most important sources of information (Ekakoro & Okafor 2019). Conversely, in a study done in Australia among veterinarians in companion animal medicine, only 36% of them used peer-reviewed literature as an information source (Hardefeldt et al. 2017). The use of peer-reviewed literature, drug handbooks, and formularies assists in ensuring appropriate antibiotic use. It can also control the use of antibiotics designated to be critically important for both human and veterinary medicines (De Briyne et al. 2014). Consequently, this may assist in curbing the further emergence and dissemination of ABR. One major drawback is that the use of information from such sources may not be based on local resistance surveillance data. Currently, a national antimicrobial surveillance programme is yet to be reintroduced in the South African animal health sector (DoH 2018). The use of local resistance surveillance data is imperative in order to guide in antibiotic prescribing in a manner that minimises ABR dissemination while optimising on antibiotic choice. Notably, antibiotic classes and their respective antibiotic agents which are of clinical importance both in human and veterinary medicine must be included in monitoring programmes to help preserve their efficacy. This entails using the WHO list of critically important antibiotics and the OIE list of antibiotics of veterinary importance (OIE 2015).

Most respondents prescribed antibiotics for pre-operative prophylaxis and the prevention of post-operative infections. Avoiding prophylactic antibiotic use is necessary to minimise the selection of resistant bacteria and possible transfer. However, prophylactic use of antibiotics can be implemented in high infection risk cases and where the infection consequences are grave.

Such cases include surgical procedures with a duration of more than one and a half hours and surgery involving a break in asepsis. Prophylactic antibiotic use is also indicated in surgery of the central nervous system, gastrointestinal tract, and contaminated wounds (Ramsey 2017). Although the cases in which antibiotics were indicated for pre-operative prophylaxis and the prevention of post-operative infections were not assessed in our study, appropriate prophylactic antibiotic use should still be encouraged among veterinarians.

A number of the respondents believed antibiotics were necessary in both diarrhoea and fever cases from our study. Diarrhoea cases do not generally require antibiotic therapy unless the identification of a specific bacterial causative agent has taken place or haemorrhage due to intestinal ulceration is observed (Battersby & Harvey 2006). Antimicrobial stewardship programme implementation might help ensure that proper diagnostic approaches are followed to prevent unnecessary antibiotic use.

Antibiotics that were regarded as the first-line by many respondents were generally the frequently prescribed antibiotics classes. A majority of these antibiotics fall under the OIE list of antibiotics of veterinary importance. These drugs are important in specific infections and have to be preserved because of the few alternatives available (OIE 2019). Impressively, most respondents never prescribed linezolid, vancomycin, and imipenem. These drugs fall under the WHO list of critically important antibiotics. Most respondents had however prescribed polymyxin B at some point in time (WHO 2019).

It should be noted that polymyxin B is structurally similar to colistin and both fall under the polymyxin class of antibiotics. In 2016, the WHO list of critically important antibiotics underwent revision, and polymyxins were re-classified into critically important antimicrobials of the highest priority. The re-classification came after an increase in colistin use in the treatment of severe human infections the world over, the discovery of genes that confer resistance to colistin on plasmids (mcr genes), and the dissemination of colistin-resistant bacteria through the food chain (WHO 2019). OIE thus set the following recommendations on the use of colistin: (1) it should not be used to prevent infection nor be administered through water or feed without clinical signs in the animal(s) proposed to receive treatment, (2) use as a first-line antibiotic should be justified and use as a second-line antibiotic should be based on bacteriological test results, (3) its off label use must be restricted, and, in such instances, it should be used in the absence of alternatives and should be in line with the current national legislation, and (4) use in growth promotion is prohibited (OIE 2019). In our study, many respondents considered the broad-spectrum antibiotics amoxicillin-clavulanate and oxytetracycline to be first-line. Narrow-spectrum antibiotics should be preferred to broad-spectrum antibiotics in first-line treatment because broad-spectrum antibiotics are more likely to promote ABR emergence (Da Silva, Knöbl & Moreno 2013).

Our results are similar to those observed among veterinarians at a USA veterinary teaching facility in a 2017 study where penicillins were frequently prescribed and preferred to other antibiotic classes of medical importance (Ekakoro & Okafor 2019). The OIE has also provided some useful insight in its annual reports on antibiotic usage in animals that have been published since 2016. The reports are intended to create a clear understanding of antibiotic use in animals from a global perspective, which can assist in providing effective containment strategies (OIE 2016b). In these reports, data was collected from OIE and non-OIE members through the use of templates and guidance documents developed by OIE and tested among member countries. The templates determined antibiotic classes sold or used for growth promotion and therapy for all animal species in kgs of active ingredient (OIE 2016b; OIE 2017; OIE 2018). According to data collected between 2012 and 2015 from 34 European OIE member states, penicillins accounted for a third (34%) of all antibiotics used in animals (OIE 2016b). Penicillins constituted almost 30% of all antibiotic classes used in animals from data collected from 107 countries between 2013 and 2016 (OIE 2017). Furthermore, data collected in 116 countries between 2015 and 2017 showed tetracyclines (34.5%) to be the most commonly reported antibiotic class followed by penicillins making up 15.2% of the total proportion of antibiotic classes used in animals (OIE 2018). Penicillins are currently classified under critically important antibiotics by the OIE. They are important in the management of potential life threatening animal conditions such as urinary tract infections and septicaemias, where alternative cost-effective antibiotics are few (OIE 2019). Penicillins are also currently classified under medically important antibiotics in human medicine by the WHO (WHO 2019). Frequent prescribing of penicillins and all other antibiotics exerts selection pressure for resistance development which poses a serious human and animal health risk world over. It is thus vital that veterinary prescribers exercise due diligence when prescribing all antibiotics.

**Conclusion**

From our study, gaps in the knowledge, attitudes, and practices on antibiotic use, antibiotic resistance, and its containment were identified. Knowledge of rational antibiotic use and ABR should be included in continuing professional development programmes to address such gaps in different geographical locations. Antibiotic stewardship programmes need to be implemented in veterinary practice, cost-effective diagnostic tests with shorter turnaround time might assist in achieving such. Antibiotic stewardship programmes might encourage the frequent use of guidelines for the appropriate use of antibiotics and microbiology informed therapy. Client education on ABR is imperative; more discussions between veterinarians and their clients over ABR are necessary to help change client attitudes. There is a need for veterinarians to use narrow-spectrum antibiotics as first-line drugs where possible. Use of the OIE list of veterinary important antibiotics and the WHO list of medically important antibiotics should be encouraged to conserve the antibiotics of critical importance. Veterinarians need to be proactive in reporting adverse antimicrobial drug events together with suspected lack of efficacy antibiotics which may be attributed to ABR to the respective pharmaceutical companies. Such reporting will help the pharmaceutical industry to investigate increasing trends in ABR to their products and act accordingly.

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**Author's Contributions**

S.Y.E., M.N. and S.A co-conceptualized the project. S.A. did the fieldwork and wrote the draft manuscript, and S.Y.E and M.N undertook critical revision of the manuscript.

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**Data availability statement**

Data are available as supplementary material.

**Disclaimer**

Views and opinions presented in this article are those of the authors. They do not reflect the official policy or position of any of the author affiliated agencies.

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# Supplementary Material

## Questionnaire

# SURVEY FOR VETERINARY PERSONNEL

INFORMED CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Dear Colleague,

We kindly request your participation in a survey amongst animal health professionals. The aim is to determine the knowledge, attitudes, practices and experiences of veterinary/animal health professions (veterinarians, veterinary nurses, animal health technicians, veterinary technologists) on antibiotic use, antibiotic resistance (ABR) and its containment in animal health in South Africa.

Antibiotics are substances that either kill or inhibit bacteria. Antibiotic resistance occurs when bacteria are unaffected by the antibiotic agents which were initially effective in curing the infections caused by the bacteria.

The Objectives of the study are;

- To determine the level of knowledge of animal health professionals on antibiotic use, antibiotic resistance (ABR) and its containment in animal health in South Africa.
- To understand the attitudes of animal health professionals on antibiotic use, antibiotic resistance (ABR) and its containment in animal health in South Africa.
- To determine the experiences and practices of antimicrobial stewardship programmes of animal health professionals towards antibiotic resistance containment in South Africa.

Your participation in this study involves answering questions about antibiotics, antibiotic use, antibiotic resistance and antibiotic stewardship. The questions will be open-ended and closed ended. Please be aware that where a question does not apply to a certain profession the option 'not applicable' is available as a response.

Please be advised that;

- No identifying information will be stored or disseminated.
- All answers are anonymous, and all responses will be aggregated before analysis.
- Confidentiality and anonymity are guaranteed by the electronic survey format.
- Your participation is entirely voluntary and, you are free to decline participation.
- There are no known risks in participating in this study.
- This research study has been granted ethical clearance from the UKZN Biomedical Research Ethical Committee (BREC Ref No: BE033/19)

*BREC can be contacted on: BIOMEDICAL RESEARCH ETHICS ADMINISTRATION*
*Research Office, Westville Campus*
*Govan Mbeki Building*
*Private Bag X54001*
*Durban, 4000*
*KwaZulu- Natal, SOUTH AFRICA*
*Telephone: 0027 31 260 2486- Fax: 0027 31 260 0460*
*Email: BREC@ukzn.ac.za*

By proceeding with the survey, you are giving voluntary informed consent.

Thank you in advance for your participation. If you have any questions or queries, please feel free to contact the Researcher: Simbai Allen Maruve, Bachelor of Veterinary Science on 218088135@stu.ukzn.ac.za

We thank you in advance for your participation.

Yours faithfully

Simbai Allen Maruve

There are 44 questions in this survey

# SECTION 1. SOCIO-DEMOGRAPHIC CHARACTERISTICS OF PARTICIPANTS

## What is your gender? *

Please choose **only one** of the following:

- ○ Female
- ○ Male

## What age group do you fall under? *

Please choose **only one** of the following:

- ○ 20-25 years
- ○ 26-30 years
- ○ 31-35 years
- ○ 36-40 years
- ○ 41-45 years
- ○ 46-50 years
- ○ 51-55 years
- ○ 56-60 years
- ○ More than 60 years

## What is your profession? *

Please choose **only one** of the following:

- ◯ Veterinarian
- ◯ Veterinary nurse
- ◯ Animal health technician
- ◯ Veterinary technologist
- ◯ Laboratory animal technologist
- ◯ Animal welfare assistant
- ◯ Veterinary physiotherapist

## What is your qualification? *

Please write your answer here:

## At which university/institution did you obtain the qualification? *

Please choose **only one** of the following:

- ◯ University of Pretoria
- ◯ Medical University of Southern Africa (MEDUNSA)
- ◯ University of South Africa (UNISA)
- ◯ Tshwane University of Technology
- ◯ North West University
- ◯ Tsolo Agricultural and Rural Development Institute (TARDI)
- ◯ Other

## Which of the following describes the period of your graduation from the university/institution mentioned above? *

Please choose **only one** of the following:

- ◯ Prior to 1950
- ◯ 1951 - 1960
- ◯ 1961 - 1970
- ◯ 1971 - 1980
- ◯ 1981 - 1990
- ◯ 1991 - 2000
- ◯ 2001 - 2010
- ◯ 2011 - 2019

## What best describes your current employment setting? *

Please choose **all** that apply:

- ☐ General small animal practice
- ☐ General mixed animal practice
- ☐ Emergency practice
- ☐ Specialty practice
- ☐ Animal welfare
- ☐ Feline only practice
- ☐ Mobile practice
- ☐ Academic teaching hospital
- ☐ Locum
- ☐ Wildlife
- ☐ Retired
- ☐ Unemployed
- ☐ Other (i.e Government Industry)

## Are you registered with the South African Veterinary Council (SAVC) as a specialist? *

Please choose **only one** of the following:

- ◯ Yes
- ◯ No

## Do you have any field of specialization? *

Please choose **only one** of the following:

- ◯ No field of specialization
- ◯ State/ regulatory veterinary medicine
- ◯ General pathology practice
- ◯ Clinical pathology practice
- ◯ Ophthalmology
- ◯ Radiology and veterinary imaging
- ◯ Rehabilitation and physiotherapy
- ◯ Soft tissue surgery
- ◯ Orthopaedic surgery
- ◯ Avian, exotic and zoological medicine
- ◯ Neurology
- ◯ Internal medicine
- ◯ Emergency/critical care/ICU
- ◯ Dermatology
- ◯ Cardiology
- ◯ Anaesthesia
- ◯ Behavioral medicine
- ◯ Dentistry
- ◯ Laboratory diagnostic practice
- ◯ Rural practice - food animal
- ◯ Equine practice

- ◯ In - hospital food animal
- ◯ Theriogenology
- ◯ Other

## How many years have you been in veterinary practice? *

Please choose **only one** of the following:

- ◯ < 1 year
- ◯ 1-5 years
- ◯ 6-10 years
- ◯ 11-15 years
- ◯ 16-20 years
- ◯ 21-25 years
- ◯ 26-30 years
- ◯ > 30 years

## What proportion of your total professional activity is dedicated to clinical practice? *

Please choose **only one** of the following:

- ◯ Less than 20%
- ◯ 20-39%
- ◯ 40-59%
- ◯ 60-79%
- ◯ 80-100%

## Where do you practice? *

Please choose **only one** of the following:

- ◯ Urban
- ◯ Rural

### In which Province do you practice? *

Please choose **only one** of the following:

- ○ Gauteng
- ○ North West
- ○ KwaZulu Natal
- ○ Eastern Cape
- ○ Limpopo
- ○ Free State
- ○ Mpumalanga
- ○ Northern Cape
- ○ Western Cape

# SECTION 2. KNOWLEDGE

### How important are the following sources of antibiotic information in determining your choice of antibiotic for clinical use? *

Please choose the appropriate response for each item:

| | Not at all Important | Slightly important | Moderately important | Very important | Extremely important | Not Applicable |
|---|---|---|---|---|---|---|
| Pharmaceutical company representative | ○ | ○ | ○ | ○ | ○ | ○ |
| Label or package insert | ○ | ○ | ○ | ○ | ○ | ○ |
| Peer-reviewed scientific literature | ○ | ○ | ○ | ○ | ○ | ○ |

| | Not at all Important | Slightly important | Moderately important | Very important | Extremely important | Not Applicable |
|---|---|---|---|---|---|---|
| Peers within my service | ○ | ○ | ○ | ○ | ○ | ○ |
| Peers outside of service (clinician or pharmacist) | ○ | ○ | ○ | ○ | ○ | ○ |
| Veterinary Information Network (VIN) | ○ | ○ | ○ | ○ | ○ | ○ |
| Veterinary formulary | ○ | ○ | ○ | ○ | ○ | ○ |
| Online resource e.g. blog, media post, or web search | ○ | ○ | ○ | ○ | ○ | ○ |
| Textbook or drug handbook | ○ | ○ | ○ | ○ | ○ | ○ |
| Applications on a smartphone or tablet | ○ | ○ | ○ | ○ | ○ | ○ |

## For each of the following antibiotics, please indicate if they are used as first, second or third line agents. *

Please choose the appropriate response for each item:

| | First line | Second Line | Third Line | I do not use it | Not Applicable |
|---|---|---|---|---|---|
| Amoxicillin | ○ | ○ | ○ | ○ | ○ |
| Amoxicillin clavulanate | ○ | ○ | ○ | ○ | ○ |
| Amikacin | ○ | ○ | ○ | ○ | ○ |
| Oxytetracycline | ○ | ○ | ○ | ○ | ○ |
| Metronidazole | ○ | ○ | ○ | ○ | ○ |
| Enrofloxacin | ○ | ○ | ○ | ○ | ○ |
| Procaine penicillin | ○ | ○ | ○ | ○ | ○ |
| Cefovecin | ○ | ○ | ○ | ○ | ○ |
| Trimethoprim sulphonamide | ○ | ○ | ○ | ○ | ○ |
| Gentamicin | ○ | ○ | ○ | ○ | ○ |
| Vancomycin | ○ | ○ | ○ | ○ | ○ |
| Clindamycin | ○ | ○ | ○ | ○ | ○ |
| Chloramphenicol | ○ | ○ | ○ | ○ | ○ |
| Cephalexin | ○ | ○ | ○ | ○ | ○ |
| Marbofloxacin | ○ | ○ | ○ | ○ | ○ |
| Rifampicin | ○ | ○ | ○ | ○ | ○ |

## Do the following conditions require antibiotic therapy? *

Please choose the appropriate response for each item:

| | Yes | No | Not Applicable |
|---|---|---|---|
| Diarrhea? | ○ | ○ | ○ |
| Fever? | ○ | ○ | ○ |
| Urinary tract infection? | ○ | ○ | ○ |
| Skin infection? | ○ | ○ | ○ |
| Respiratory infection? | ○ | ○ | ○ |
| Ecto-parasite infestation? | ○ | ○ | ○ |

| | Yes | No | Not Applicable |
|---|---|---|---|
| Parasitic-gastroenteritis? | ○ | ○ | ○ |

## Which of these is true about antibiotic resistance? *

Please choose the appropriate response for each item:

| | TRUE | FALSE | NOT APPLICABLE |
|---|---|---|---|
| There is an increasing rate of infections resistant to antibiotics in animals | ○ | ○ | ○ |
| Infections from antibiotic resistant bacteria could be difficult to treat | ○ | ○ | ○ |
| Antibiotic resistance can greatly affect the animal population | ○ | ○ | ○ |
| Antibiotic resistance is not an issue in South Africa | ○ | ○ | ○ |
| Antibiotic resistant bacteria can spread from animal to animal | ○ | ○ | ○ |
| Antibiotic resistance in animals can spread to humans | ○ | ○ | ○ |

| | TRUE | FALSE | NOT APPLICABLE |
|---|---|---|---|
| Infections from antibiotic resistant bacteria can make surgical procedures dangerous | ○ | ○ | ○ |
| Antibiotics should not be stored for later use in animals | ○ | ○ | ○ |
| Appropriate antibiotic use can reduce the risk of antibiotic resistant bacterial infections in animals | ○ | ○ | ○ |
| The antibiotic resistance problem can be reduced by good farm security | ○ | ○ | ○ |
| Antibiotics should only be administered to animals when prescribed by veterinarians | ○ | ○ | ○ |
| Antibiotic resistance is one of the biggest problems in livestock production | ○ | ○ | ○ |

| | TRUE | FALSE | NOT APPLICABLE |
|---|---|---|---|
| Veterinarians should only prescribe antibiotics when necessary | ○ | ○ | ○ |

## In your opinion, which of the following contributes to antibiotic resistant infections in people? *

Please choose **all** that apply:

- ☐ Antibiotic use in human medicine
- ☐ Antibiotic use in small animal veterinary medicine
- ☐ Antibiotic use in food animal veterinary medicine
- ☐ Environmental pressure
- ☐ Random genetic mutations
- ☐ Not Applicable
- ☐Other:

## Select any of the following factors in veterinary medicine that you believe may play a role in antibiotic resistant infections in people *

Please choose **all** that apply:

- ☐ Client non-compliance when giving antibiotics to their animals
- ☐ Clients' expectation of receiving antibiotics for their animals
- ☐ Over prescribing of antibiotics to animals
- ☐ Inadequate dose, frequency or duration of antibiotics prescribed to animals
- ☐ The use of medically important antibiotics (i.e. those used in human medicine) in veterinary medicine.
- ☐ Antibiotic use in veterinary medicine does not contribute to antibiotic resistant infections in people.

- ☐ Not enough evidence to link antibiotic use in veterinary medicine and antibiotic resistance in people
- ☐ Not Applicable
- ☐ Other:

### Please indicate how strongly you agree with each of the following statements *

Please choose the appropriate response for each item:

| | Strongly agree | Agree | Neither agree nor disagree | Disagree | Strongly disagree | Not Applicable |
|---|---|---|---|---|---|---|
| I understand what antibiotic stewardship is | ○ | ○ | ○ | ○ | ○ | ○ |
| I understand antibiotic resistance mechanisms | ○ | ○ | ○ | ○ | ○ | ○ |
| I have a good knowledge of the pharmacology of antibiotics | ○ | ○ | ○ | ○ | ○ | ○ |
| I know how to use antibiotics to minimize the risk of antibiotic resistance developing | ○ | ○ | ○ | ○ | ○ | ○ |

## To what extent did your veterinary training alone, adequately equip you with knowledge on rational use of antibiotics? *

Please choose **only one** of the following:

- Not at all
- A little
- Somewhat
- Quite a bit
- Very much
- Not Applicable

## Would you be interested in obtaining continuing professional education (CPD) pertaining to antibiotic use/resistance or stewardship?

## *

Please choose **only one** of the following:

- Yes
- No
- Not sure
- Not Applicable

# SECTION 3. ATTITUDES

## Which one of the following best represents your opinion about antibiotic use at your clinic/practice/institute? *

Please choose **only one** of the following:

- ○ Antibiotics are sometimes prescribed based on no documented evidence of infection.
- ○ Antibiotics are sometimes prescribed for suspected (but not confirmed) infections.
- ○ Antibiotics are prescribed based only on confirmed infection.
- ○ Not sure
- ○ Not Applicable

## Which one of the following best represents your opinion about antibiotic prescription at your practice/clinic/institute? *

Please choose **only one** of the following:

- ○ Antibiotics are under prescribed
- ○ Antibiotics are optimally prescribed
- ○ Antibiotics are over-prescribed
- ○ Not Applicable

## How do you rate your degree of concern about antibiotic resistant infections? *

Please choose **only one** of the following:

- ○ Not concerned
- ○ Slightly concerned
- ○ Moderately concerned
- ○ Quite concerned
- ○ Very concerned
- ○ Not Applicable

## To what extent do you agree or disagree with the following statement? “Antibiotic classes commonly used in human medicine should not be used in veterinary medicine because their use in veterinary medicine selects for antibiotic resistance in bacteria that can cause infections in humans. *

Please choose **only one** of the following:

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Neither disagree nor agree
- ◯ Agree
- ◯ Strongly Agree
- ◯ Not Applicable

## To what extent do you agree or disagree with the following statement? "Antibiotic drug use in veterinary practice may lead to antibiotic resistance in pathogens affecting humans."

## *

Please choose **only one** of the following:

- ◯ Strongly disagree
- ◯ Disagree
- ◯ Neither disagree nor agree
- ◯ Agree
- ◯ Strongly agree
- ◯ Not Applicable

## Which of the following factors in veterinary medicine pose a challenge to implementing and using an antibiotic stewardship plan (i.e., a protocol for judicious antibiotic use)? (Select all that apply) *

Please choose **all** that apply:

- ☐ Client expectations of receiving antibiotics
- ☐ Time required for adequate client education
- ☐ Practice culture
- ☐ Cost of diagnostics (i.e. bacterial culture/sensitivity)
- ☐ Time to results of diagnostics (i.e. bacterial culture/sensitivity)
- ☐ Current low rates of antibiotic prescribing
- ☐ Antibiotic stewardship plans are not needed in veterinary medicine
- ☐ There are no barriers to antibiotic stewardship plans in veterinary medicine
- ☐ Not Applicable
- ☐ Other:

## How often do you discuss antibiotic resistance with your clients? *

Please choose **only one** of the following:

- ○ Never
- ○ Rarely
- ○ Sometimes
- ○ Often
- ○ Always
- ○ Not Applicable

## How do you rate the majority of your clients' concerns about antibiotic resistance? *

Please choose **only one** of the following:

- ○ Not concerned
- ○ Slightly concerned
- ○ Moderately concerned
- ○ Quite concerned
- ○ Very concerned

- ○ Not Applicable

# SECTION 4. PRACTICES AND EXPERIENCES

## What are the 3 most important factors that would influence your decision to submit samples for culture and sensitivity testing? *

Please choose **all** that apply:

- ☐ Location of the infection
- ☐ Ease of obtaining a sample
- ☐ Persistent infection
- ☐ Severe infection
- ☐ Client finances
- ☐ Unusual infection
- ☐ Atypical cytology
- ☐ To confirm a diagnosis
- ☐ Herd problems
- ☐ Recurring infections
- ☐ Not applicable
- ☐ Other:

## How important are the following factors in determining your choice of antibiotic for clinical use? *

Please choose the appropriate response for each item:

| | Not at all important | Slightly important | Moderately important | Very important | Extremely important | Not Applicable |
|---|---|---|---|---|---|---|
| Clinical signs | ○ | ○ | ○ | ○ | ○ | ○ |
| History of previous antibiotic use on the animal | ○ | ○ | ○ | ○ | ○ | ○ |
| Pressure from clients/producers | ○ | ○ | ○ | ○ | ○ | ○ |
| Peer or colleague recommendations | ○ | ○ | ○ | ○ | ○ | ○ |
| Cost implications | ○ | ○ | ○ | ○ | ○ | ○ |
| Results of cytological evaluation | ○ | ○ | ○ | ○ | ○ | ○ |
| Results of bacteriological culture and antibiotic susceptibility testing | ○ | ○ | ○ | ○ | ○ | ○ |
| Route of administration | ○ | ○ | ○ | ○ | ○ | ○ |
| Frequency of administration | ○ | ○ | ○ | ○ | ○ | ○ |
| Medication size or volume | ○ | ○ | ○ | ○ | ○ | ○ |
| Clinical/practice/institute guidelines | ○ | ○ | ○ | ○ | ○ | ○ |
| Potential for adverse reactions | ○ | ○ | ○ | ○ | ○ | ○ |

| | Not at all impor tant | Slight ly impor tant | Moder ately import ant | Very impor tant | Extre mely impor tant | Not Applic able |
|---|---|---|---|---|---|---|
| Availability of antibiotic agent(s) | ○ | ○ | ○ | ○ | ○ | ○ |
| Concerns about antibiotic resistance issues in animals | ○ | ○ | ○ | ○ | ○ | ○ |
| Concerns about antibiotic resistance issues in humans | ○ | ○ | ○ | ○ | ○ | ○ |
| Fear of litigation by the client/producer in the event of an undesirable clinical outcome | ○ | ○ | ○ | ○ | ○ | ○ |
| Concerns about animal welfare | ○ | ○ | ○ | ○ | ○ | ○ |
| Prudent use guidelines | ○ | ○ | ○ | ○ | ○ | ○ |
| Drug withdrawal periods | ○ | ○ | ○ | ○ | ○ | ○ |
| Compliance by the client/producer to the prescription | ○ | ○ | ○ | ○ | ○ | ○ |

## How frequently do you read veterinary guidelines for judicious use of antibiotics? *

Please choose **only one** of the following:

- ◯ Never
- ◯ Rarely
- ◯ Sometimes
- ◯ Very often
- ◯ Always
- ◯ Not Applicable

## How often do you prescribe antibiotics for therapeutic treatment of infectious diseases in your clinical setting? *

Please choose **only one** of the following:

- ◯ Never
- ◯ Once a day
- ◯ 2 times a day
- ◯ 3 - 5 times a day
- ◯ > 5 times a day
- ◯ Not Applicable

## How often do you prescribe antibiotics for metaphylaxis? *

Please choose **only one** of the following:

- ◯ Never
- ◯ Once a day
- ◯ 2 times a day
- ◯ 3 - 5 times a day
- ◯ > 5 times a day
- ◯ Not Applicable

## How often do you prescribe antibiotics for prophylaxis of infectious diseases? *

Please choose **only one** of the following:

- Never
- Once a day
- 2 times a day
- 3 - 5 times a day
- > 5 times a day
- Not Applicable

## How often do you prescribe antibiotics for pre-operative prophylaxis of infections? *

Please choose **only one** of the following:

- Never
- 1 - 2 cases out of every 10 surgical patients
- 3 - 5 cases out of every 10 surgical patients
- 6 - 8 cases out of every 10 surgical patients
- > 8 cases out of every 10 surgical patients
- Not Applicable

## How often do you prescribe antibiotics to prevent post-operative infections? *

Please choose **only one** of the following:

- Never
- 1 - 2 cases out of every 10 surgical patients
- 3 - 5 cases out of every 10 surgical patients
- 6 - 8 cases out of every 10 surgical patients
- > 8 cases out of every 10 surgical patients
- Not Applicable

## How often do you prescribe the following classes of antibiotics? *

Please choose the appropriate response for each item:

| | Never | Rarely | Sometimes | Very often | Always | Not Applicable |
|---|---|---|---|---|---|---|
| Aminoglycosides | ○ | ○ | ○ | ○ | ○ | ○ |
| Cephalosporins | ○ | ○ | ○ | ○ | ○ | ○ |
| Fluoroquinolones | ○ | ○ | ○ | ○ | ○ | ○ |
| Lincosamides | ○ | ○ | ○ | ○ | ○ | ○ |
| Macrolides | ○ | ○ | ○ | ○ | ○ | ○ |
| Penicillins | ○ | ○ | ○ | ○ | ○ | ○ |
| Sulfas | ○ | ○ | ○ | ○ | ○ | ○ |
| Tetracyclines | ○ | ○ | ○ | ○ | ○ | ○ |

## Have you ever prescribed or administered any of the following antibiotics (Select all that apply)? *

Please choose **all** that apply:

- ☐ Imipenem
- ☐ Linezolid
- ☐ Polymyxin B (Terra-cortril® and or Surolan®)
- ☐ Vancomycin
- ☐ No, I have not prescribed or administered any of these antibiotics
- ☐ Unsure
- ☐ Not Applicable

## What are the 5 antibiotic drugs that you commonly prescribe? (Rank from the most to the least.)

## (*If the question doesn't apply, please indicate with "Not Applicable"*)

## *

Please write your answer here:

## For each of the following scenarios please indicate the level of biosecurity you would take for examination and performing procedures. *

Please choose the appropriate response for each item:

| | None | Handwash after contact | Gloves only | Apron only | Gloves and apron | Not Applicable |
|---|---|---|---|---|---|---|
| Routine examination of a dog or cat | ○ | ○ | ○ | ○ | ○ | ○ |
| Routine examination of a horse | ○ | ○ | ○ | ○ | ○ | ○ |
| Routine examination of a cow | ○ | ○ | ○ | ○ | ○ | ○ |
| Horse with fever of unknown origin and neurological signs | ○ | ○ | ○ | ○ | ○ | ○ |
| Horse with acute watery diarrhoea | ○ | ○ | ○ | ○ | ○ | ○ |
| Cow with acute watery diarrhoea | ○ | ○ | ○ | ○ | ○ | ○ |
| Respiratory signs of 4 days duration in an otherwise healthy cat | ○ | ○ | ○ | ○ | ○ | ○ |
| Postmortem examination of a cow | ○ | ○ | ○ | ○ | ○ | ○ |
| Postmortem examination of a horse | ○ | ○ | ○ | ○ | ○ | ○ |
| Aborted foetal material from a horse | ○ | ○ | ○ | ○ | ○ | ○ |
| Routine dental prophylaxis in a dog | ○ | ○ | ○ | ○ | ○ | ○ |

| | None | Handwash after contact | Gloves only | Apron only | Gloves and apron | Not Applicable |
|---|---|---|---|---|---|---|
| Cow with dystocia | ○ | ○ | ○ | ○ | ○ | ○ |
| Goats with poor conception rates | ○ | ○ | ○ | ○ | ○ | ○ |
| Mare with dystocia | ○ | ○ | ○ | ○ | ○ | ○ |
| Methicillin resistant *Staphylococcus pseudintermedius dermatitis* | ○ | ○ | ○ | ○ | ○ | ○ |
| An animal with a multi-drug resistant urinary tract infection | ○ | ○ | ○ | ○ | ○ | ○ |
| When entering a pig farm | ○ | ○ | ○ | ○ | ○ | ○ |

**Antibiotic stewardship programmes are coordinated interventions designed to improve and measure the appropriate use of antibiotics by promoting the selection of optimal antibiotic regimens, dose, and duration of therapy and route of administration. Does your practice/clinic/institute have an antibiotic stewardship program? ***

Please choose **only one** of the following:

- ○ No
- ○ Not sure
- ○ Yes
- ○ Not Applicable

## If your answer was no above, do you think that your practice should develop and implement an antibiotic stewardship program?

Please choose **only one** of the following:

- ○ Yes
- ○ No
- ○ Not sure
- ○ Not Applicable

Thank you for your participation.
11-04-2019 – 12:08

Submit your survey.
Thank you for completing this survey.

**Supplementary Data**

**Table S1**. Socio-demographic characteristics of the veterinary participants.

| Variable | Number (%) of respondents |
|---|---|
| **Gender** | |
| **Female** | 49(48) |
| **Male** | 53(52) |
| **Years in veterinary practice** | |
| **0-10 years** | 34(33.3) |
| **11-20 years** | 18(17.6) |
| **+ 20 years** | 50(49) |
| **Age group** | |
| **20-40 years** | 32(31.4) |
| **+40 years** | 70(68.6) |
| **Qualification** | |
| **BVSc only** | 68(66.7) |
| **BVSc and other** | 28(27.5) |
| **Other** | 6(5.9) |
| **University attended** | |
| **University of Pretoria** | 93(91.2) |
| **Other** | 9(8.8) |
| **Current employment setting** | |
| **General small animal practice** | 56(54.9) |

| | |
|---|---|
| **General mixed animal practice** | 20(19.6) |
| **Emergency practice** | 4(3.9) |
| **Specialty practice** | 11(10.8) |
| **Animal welfare** | 6(5.9) |
| **Feline only practice** | 0(0) |
| **Mobile practice** | 7(6.9) |
| **Academic teaching hospital** | 6(5.9) |
| **Locum** | 10(9.8) |
| **Wildlife** | 7(6.9) |
| **Retired** | 0(0) |
| **Unemployed** | 1(1) |
| **Other i.e. Government industry** | 14(13.7) |
| **Registered as Specialists** | 38(37.3) |
| **Proportion of total professional activity dedicated to clinical practice** | |
| **Less than 20%** | 9(8.8) |
| **20-39%** | 8(7.8) |
| **40-59%** | 9(8.8) |
| **60-79%** | 8(7.8) |
| **80-100%** | 68(66.7) |
| **Place of practice** | |
| **Rural** | 38(37.3) |
| **Urban** | 64(62.7) |
| **Province of Practice** | |
| **Gauteng** | 42(41.2) |
| **Free state** | 5(4.9) |
| **North West** | 6(5.9) |
| **Mpumalanga** | 3(2.9) |
| **KwaZulu Natal** | 15(14.7) |
| **Northern Cape** | 3(2.9) |
| **Eastern Cape** | 3(2.9) |

| | |
|---|---|
| **Western Cape** | 24(23.5) |
| **Limpopo** | 1(1.0) |

**Table S2**: Opinion on conditions requiring antibiotic therapy

| Condition | Number(%) of respondents |
|---|---|
| **Diarrhoea** | 31(30.4) |
| **Fever** | 32(31.4) |
| **Urinary tract infection** | 89(87.3) |
| **Skin infection** | 80(78.4) |
| **Respiratory infection** | 98(96.1) |
| **Ectoparasite infestation** | 99(97.1) |
| **Parasitic gastroenteritis** | 6(5.9) |

**Table S3A.** Association between socio-demographic factors and selected knowledge variables.

| Factor | Knowledge of antibiotic resistance | | Opinion on contributors to antibiotic resistant infections in people. | | Selection of factors in veterinary medicine playing a role in antibiotic resistant infections in people | |
|---|---|---|---|---|---|---|
| | Mean (+/- SD) | Independent t-test/ANOVA P value | Mean (+/- SD) | Independent t-test/ANOVA P value | Mean (+/- SD) | Independent t-test/ANOVA P value |
| Gender | | | | | | |
| Female | 11.67(1.42) | [I]0.447 | 1.94(1.25) | [I]0.661 | 3.78(1.33) | [I]0.147 |
| Male | 11.47(1.25) | | 2.04(1.02) | | 4.11(0.99) | |
| Age | | | | | | |
| 20-40 years | 11.81(1.00) | [I]0.213 | 1.75(1.08) | [I]0.148 | 3.97(1.20) | [I]0.918 |
| +40 years | 11.46(1.45) | | 2.10(1.14) | | 3.94(1.17) | |
| Veterinary experience | | | | | | |
| 0-10years | 11.82(1.00) | [A]0.235 | 1.74(1.05) | [A]0.206 | 3.94(1.18) | [A]0.157 |
| 11-20years | 11.17(1.69) | | 1.94(1.30) | | 3.50(1.25) | |
| + 20years | 11.54(1.37) | | 2.18(1.10) | | 4.12(1.12) | |
| | | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Place of practice | | | | | | |
| Rural | 11.08(1.67) | [I]**0.004*** | 2.13(1.12) | [I]0.333 | 3.76(1.28) | [I]0.214 |
| Urban | 11.86(1.00) | | 1.91(1.14) | | 4.06(1.10) | |

**Table S3B:** Association between socio-demographic factors and selected knowledge variables.

| Factor | Importance of sources of antibiotic information in determining choice of antibiotic for clinical use | | Knowledge of antibiotic stewardship, antibiotic resistance mechanisms, and pharmacology. | |
|---|---|---|---|---|
| | Mean (+/- SD) | Independent t-test/ANOVA P value | Mean (+/- SD) | Independent t-test/ANOVA P value |
| Gender | | [I]0.524 | | [I]0.478 |
| Female | 5.37(2.21) | | 3.27(0.93) | |
| Male | 5.62(1.81) | | 3.40(0.93) | |
| Age | | [I]0.833 | | [I]0.125 |
| 20-40 years | 5.44(2.11) | | 3.13(1.10) | |
| +40 years | 5.53(1.98) | | 3.43(0.83) | |
| Veterinary experience | | [A]0.112 | | [A]0.136 |
| 0-10years | 5.47(2.06) | | 3.15(1.08) | |
| 11-20years | 4.67(2.25) | | 3.17(1.10) | |
| + 20years | 5.82(1.83) | | 3.52(0.71) | |
| | | | | |

| | | | | |
|---|---|---|---|---|
| Place of practice | | | | |
| Rural | 5.45(1.97) | [I]0.804 | 3.24(1.00) | [I]0.420 |
| Urban | 5.53(2.05) | | 3.39(0.88) | |

**Table S3C.** Association between socio-demographic factors and selected knowledge variables.

| Variables | The extent to which veterinary training alone adequately equipped veterinarians with knowledge on the rational use of antibiotics. | | | | | | Chi-square P-value |
|---|---|---|---|---|---|---|---|
| | Not at all/a little | | Somewhat | | Quite a bit/very much | | |
| | N | % | N | % | N | % | |
| Gender | | | | | | | |
| Female | 2 | 5.9 | 8 | 23.5 | 24 | 70.6 | 0.103 |
| Male | 1 | 2.5 | 3 | 7.5 | 36 | 90 | |
| Age | | | | | | | |
| 20-40 | 0 | 0 | 2 | 11.1 | 16 | 88.9 | 0.504 |
| +40 | 3 | 5.4 | 9 | 16.1 | 44 | 78.6 | |
| Veterinary experience | | | | | | | |
| 0-10 years | 0 | 0 | 2 | 11.1 | 16 | 88.9 | 0.498 |
| 11-20 years | 0 | 0 | 2 | 12.5 | 14 | 87.5 | |
| + 20 years | 3 | 7.5 | 7 | 17.5 | 30 | 75 | |
| Place of practice | | | | | | | |
| Rural | 0 | 0 | 3 | 12.5 | 21 | 87.5 | 0.416 |
| Urban | 3 | 6 | 8 | 16.0 | 39 | 78 | |

**Table S4.** Association between socio-demographic factors and selected attitude variables.

| Variables | Opinion about antibiotic use at the clinic/practice/institute. | | | | | | Chi-square P-value |
|---|---|---|---|---|---|---|---|
| | Antibiotics are sometimes prescribed for suspected but not confirmed infections | | Antibiotics are prescribed based only on confirmed infection | | Antibiotics are sometimes prescribed based on no documented evidence of infection | | |
| | N | % | N | % | N | % | |
| Gender | | | | | | | |
| Female | 37 | 75.5 | 8 | 16.3 | 4 | 8.2 | 0.553 |
| Male | 44 | 83 | 7 | 13.2 | 2 | 3.8 | |
| Age | | | | | | | |
| 20-40 | 27 | 84.4 | 4 | 12.5 | 1 | 3.1 | 0.637 |
| +40 | 54 | 77.1 | 11 | 15.7 | 5 | 7.1 | |
| | | | | | | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Veterinary experience | | | | | | | |
| 0-10 years | 29 | 85.3 | 4 | 11.8 | 1 | 2.9 | 0.682 |
| 11-20 years | 14 | 77.8 | 2 | 11.1 | 2 | 11.1 | |
| +20 years | 38 | 76 | 9 | 18 | 3 | 6 | |
| Place of practice | | | | | | | |
| Rural | 29 | 76.3 | 8 | 21.1 | 1 | 2.6 | 0.244 |
| Urban | 52 | 81.3 | 7 | 10.9 | 5 | 7.8 | |
| | Opinion about antibiotic prescription at clinic/practice/institute | | | | | | |
| | Antibiotics are overprescribed | | Antibiotics are under prescribed | | Antibiotics are optimally prescribed | | |
| | N | % | N | % | N | % | |
| Gender | | | | | | | |
| Female | 24 | 49 | 1 | 2 | 24 | 49 | 0.335 |
| Male | 21 | 39.6 | 0 | 0 | 32 | 60.4 | |
| | | | | | | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Age | | | | | | | |
| 20-40 | 15 | 46.9 | 0 | 0 | 17 | 53.1 | 0.754 |
| +40 | 30 | 42.9 | 1 | 1.4 | 39 | 55.7 | |
| Veterinary experience | | | | | | | |
| 0-10 years | 15 | 44.1 | 0 | 0 | 19 | 55.9 | 0.312 |
| 11-20 years | 8 | 44.4 | 1 | 5.6 | 9 | 50 | |
| +20 years | 22 | 44 | 0 | 0 | 28 | 56 | |
| Place of practice | | | | | | | 0.252 |
| Rural | 14 | 36.8 | 1 | 2.6 | 23 | 60.5 | |
| Urban | 31 | 48.4 | 0 | 0 | 33 | 51.6 | |
| | The extent of agreeing on antibiotic use in veterinary practice leading to antibiotic resistance in pathogens affecting humans | | | | | | |
| | Strongly disagree/disagree | | Neither agree nor disagree | | Agree/strongly agree | | |
| | N | % | N | % | N | % | |
| | | | | | | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Gender | | | | | | | |
| Female | 6 | 12.2 | 7 | 14.3 | 36 | 73.5 | 0.901 |
| Male | 8 | 15.1 | 8 | 15.1 | 37 | 69.8 | |
| Age | | | | | | | |
| 20-40 | 3 | 9.4 | 5 | 15.6 | 24 | 75 | 0.688 |
| +40 | 11 | 15.7 | 10 | 14.3 | 49 | 70 | |
| Place of practice | | | | | | | |
| Rural | 6 | 15.8 | 5 | 13.2 | 27 | 71.1 | 0.865 |
| Urban | 8 | 12.5 | 10 | 15.6 | 46 | 71.9 | |
| | Rating the degree of concern about antibiotic resistant infections | | | | | | |
| | Not concerned/Slightly concerned | | Moderately concerned | | Quite concerned/Very concerned | | |
| Gender | | | | | | | |
| Female | 1 | 4.2 | 3 | 12.5 | 20 | 83.3 | 0.563 |
| Male | 0 | 0 | 4 | 17.4 | 19 | 82.6 | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Age | | | | | | | |
| 20-40 | 0 | 0 | 1 | 6.7 | 14 | 93.3 | 0.416 |
| +40 | 1 | 3.1 | 6 | 18.8 | 25 | 78.1 | |
| Veterinary experience | | | | | | | |
| 0-10 years | 0 | 0 | 1 | 6.3 | 15 | 93.8 | 0.053 |
| 11-20 | 0 | 0 | 5 | 38.5 | 8 | 61.5 | |
| +20 years | 1 | 5.6 | 1 | 5.6 | 16 | 88.9 | |
| | | | | | | | |
| Place of practice | | | | | | | |
| Rural | 1 | 5.9 | 2 | 11.8 | 14 | 82.4 | 0.379 |
| Urban | 0 | 0 | 5 | 16.7 | 25 | 83.3 | |
| | Rating client concerns on antibiotic resistance | | | | | | |
| | Not concerned/slightly concerned | | Moderately concerned | | Quite concerned/very concerned | | |
| | N | % | N | % | N | % | |
| | | | | | | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Veterinary experience | | | | | | | |
| 0-10 years | 18 | 54.5 | 10 | 30.3 | 5 | 15.2 | 0.332 |
| 11-20 years | 8 | 47.1 | 6 | 35.3 | 3 | 17.6 | |
| +20 years | 15 | 31.3 | 22 | 45.8 | 11 | 22.9 | |
| Age | | | | | | | |
| 20-40 | 16 | 51.6 | 10 | 32.3 | 5 | 16.1 | 0.410 |
| +40 | 25 | 37.3 | 28 | 41.8 | 14 | 20.9 | |
| Place of practice | | | | | | | |
| Rural | 17 | 45.9 | 12 | 32.4 | 8 | 21.6 | 0.604 |
| Urban | 24 | 39.3 | 26 | 42.6 | 11 | 18 | |
| | The extent of agreeing on the statement "Antibiotic classes commonly used in human medicine should not be used in veterinary medicine because veterinary use selects for antibiotic resistance in bacteria." | | | | | | |
| | Strongly disagree/disagree | | Neither disagree nor agree | | Strongly agree/agree | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Gender | | | | | | | |
| Female | 8 | 26.7 | 13 | 43.3 | 9 | 30 | 0.509 |
| Male | 9 | 25.7 | 11 | 31.4 | 15 | 42.9 | |
| Age | | | | | | | |
| 20-40 | 3 | 13.6 | 10 | 45.5 | 9 | 40.9 | 0.248 |
| +40 | 14 | 32.6 | 14 | 32.6 | 15 | 34.9 | |
| Veterinary experience | | | | | | | |
| 0-10 years | 4 | 16.7 | 11 | 45.8 | 9 | 37.5 | 0.078 |
| 11-20 years | 3 | 37 | 5 | 62.5 | 0 | 0 | |
| +20 years | 10 | 30.3 | 8 | 24.2 | 15 | 45.5 | |
| Place of practice | | | | | | | |
| Rural | 7 | 25 | 9 | 32.1 | 12 | 42.9 | 0.671 |
| Urban | 10 | 27 | 15 | 40.5 | 12 | 32.4 | |

**Table S5A:** Association between socio-demographic factors and selected practice variables.

| Factor | Frequency of prescribing classes of antibiotics | | Frequency of prescribing antibiotics for therapeutic treatment of infectious diseases in the clinical setting | | Importance of factors in determining choice of antibiotic for clinical use | |
|---|---|---|---|---|---|---|
| | Mean (+/- SD) | Independent t-test/ANOVA P value | Mean (+/- SD | Independent t-test/ANOVA P value | Mean (+/- SD | Independent t-test/ANOVA P value |
| Gender | | [I]0.487 | | | | |
| Female | 2.51(1.17) | | 2.63(1.02) | [I]0.838 | 10.33(4.13) | [I]0.610 |
| Male | 2.68(1.27) | | 2.58(1.05) | | 9.92(3.81) | |
| Age | | [I]0.844 | | | | |
| 20-40 years | 2.56(1.01) | | 2.62(0.98) | [I]0.919 | 9.88(3.89) | [I]0.677 |
| +40 years | 2.61(1.31) | | 2.60(1.06) | | 10.23(4.00) | |
| Veterinary experience | | [A]0.112 | | | | |
| 0-10years | 5.47(2.06) | | 2.65(0.99) | [A]0.707 | 9.74(3.91) | [A]0.315 |
| 11-20years | 4.67(2.25) | | 2.40(0.99) | | 9.22(4.76) | |
| + 20years | 5.82(1.83) | | 2.64(1.09) | | 10.70(3.64) | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Place of practice | | | | | | |
| Rural | 2.68(1.25) | [I]0.585 | 2.42(1.15) | [I]0.211 | 10.11(3.28) | [I]0.981 |
| Urban | 2.55(1.21) | | 2.71(0.96) | | 10.13(4.32) | |

**Table S5B:** Association between socio-demographic factors and selected practice variables

| Variables | Frequency of reading veterinary guidelines for appropriate use of antibiotics | | | | | | Chi-square P value |
|---|---|---|---|---|---|---|---|
| | Never/rarely | | Sometimes | | Very often/always | | |
| Gender | | | | | | | |
| Female | 9 | 18.8 | 23 | 47.9 | 16 | 33.3 | 0.104 |
| Male | 4 | 7.5 | 22 | 41.5 | 27 | 50.9 | |
| Age | | | | | | | |
| 20-40 | 6 | 18.8 | 16 | 50 | 10 | 31.3 | 0.225 |
| +40 | 7 | 10.1 | 29 | 42 | 33 | 47.8 | |
| Veterinary experience | | | | | | | |
| 0-10 years | 6 | 17.6 | 16 | 47.1 | 12 | 35.3 | 0.252 |
| 11-20 years | 2 | 11.1 | 11 | 61.1 | 5 | 27.8 | |
| +20 years | 5 | 10.2 | 18 | 36.7 | 26 | 53.1 | |
| Place of practice | | | | | | | |
| Rural | 5 | 13.2 | 17 | 44.7 | 16 | 42.1 | 0.996 |
| Urban | 8 | 12.7 | 28 | 44.4 | 27 | 42.9 | |
| | Frequency of discussing antibiotic resistance with clients | | | | | | |
| | Never/rarely | | Sometimes | | Often/always | | |
| Gender | | | | | | | |
| Female | 8 | 16.7 | 15 | 31.3 | 25 | 52.1 | 0.378 |
| Male | 4 | 7.7 | 19 | 36.5 | 29 | 55.8 | |
| Age | | | | | | | |
| 20-40 | 4 | 12.5 | 9 | 28.1 | 19 | 59.4 | 0.691 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| +40 | 8 | 11.8 | 25 | 36.8 | 35 | 51.5 | |
| Veterinary experience | | | | | | | |
| 0-10 years | 4 | 11.8 | 10 | 29.4 | 20 | 58.8 | 0.555 |
| 11-20 years | 4 | 22.2 | 10 | 55.6 | 4 | 22.2 | |
| +20 years | 4 | 8.3 | 14 | 29.2 | 30 | 62.5 | |

| | | | | | |
|---|---|---|---|---|---|
| | Client finances as an influence on the decision to submit samples for culture and sensitivity | | | | |
| | No | | Yes | | |
| | N | % | N | % | |
| Place of practice | | | | | |
| Rural | 19 | 50 | 19 | 50 | 0.647 |
| Urban | 35 | 54.7 | 29 | 45.3 | |
| | Recurring infections as an influence on the decision to submit samples for culture and sensitivity | | | | |
| | No | | Yes | | |
| Gender | | | | | |
| Female | 13 | 26.5 | 36 | 73.5 | 0.682 |
| Male | 16 | 30.2 | 37 | 69.8 | |
| | | | | | |
| Age | | | | | |
| 20-40 | 5 | 15.6 | 27 | 84.4 | 0.053 |
| +40 | 24 | 34.3 | 46 | 65.7 | |
| Veterinary experience | | | | | |
| 0-10 years | 5 | 14.7 | 29 | 85.3 | 0.057 |
| 11-20 years | 8 | 44.4 | 10 | 55.6 | |

| | | | | | |
|---|---|---|---|---|---|
| +20 years | 16 | 32 | 34 | 68 | |
| Place of practice | | | | | |
| Rural | 9 | 23.7 | 29 | 76.3 | 0.413 |
| Urban | 20 | 31.3 | 44 | 68.8 | |
| | Persistent infection as an influence on the decision to submit samples for culture and sensitivity | | | | |
| | No | | Yes | | |
| Gender | | | | | |
| Female | 5 | 10.2 | 44 | 89.8 | 0.459 |
| Male | 8 | 15.1 | 45 | 84.9 | |
| | | | | | |
| Age | | | | | |
| 20-40 | 4 | 12.5 | 28 | 87.5 | 0.960 |
| +40 | 9 | 12.9 | 61 | 87.1 | |
| Veterinary experience | | | | | |
| 0-10 years | 4 | 11.8 | 30 | 88.2 | 0.511 |
| 11-20 years | 1 | 5.6 | 17 | 94.4 | |
| +20 years | 8 | 16 | 42 | 84 | |
| Place of practice | | | | | |
| Rural | 8 | 21.1 | 30 | 78.9 | 0.053 |
| Urban | 5 | 7.8 | 59 | 92.2 | |

**Figure S1:** Knowledge on pharmacology, antibiotic resistance and antibiotic stewardship.

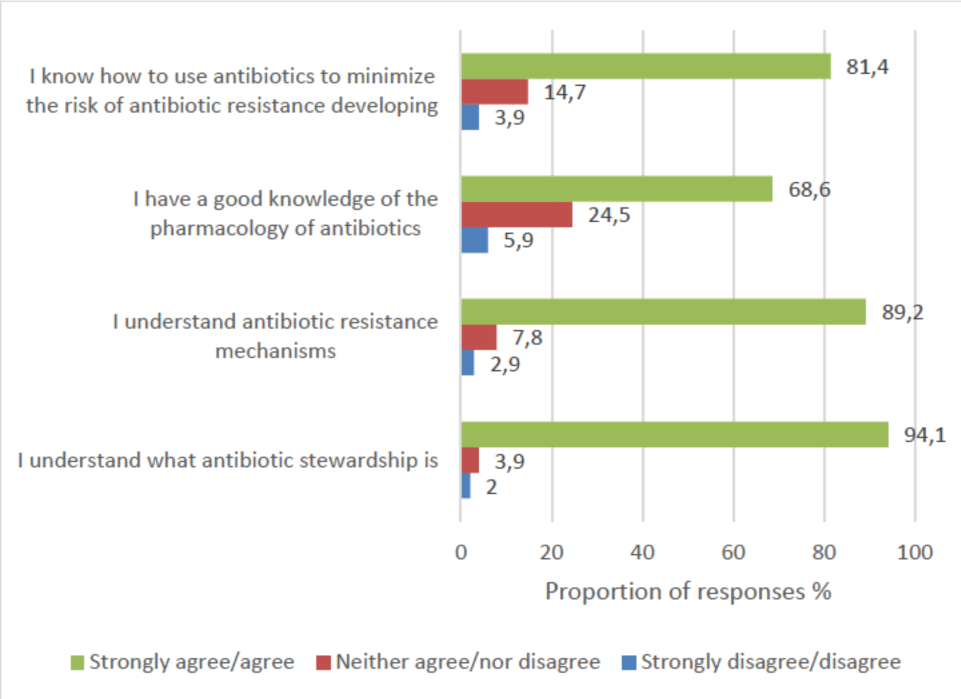



**Figure S2:** Sources of information on choice of antibiotic.

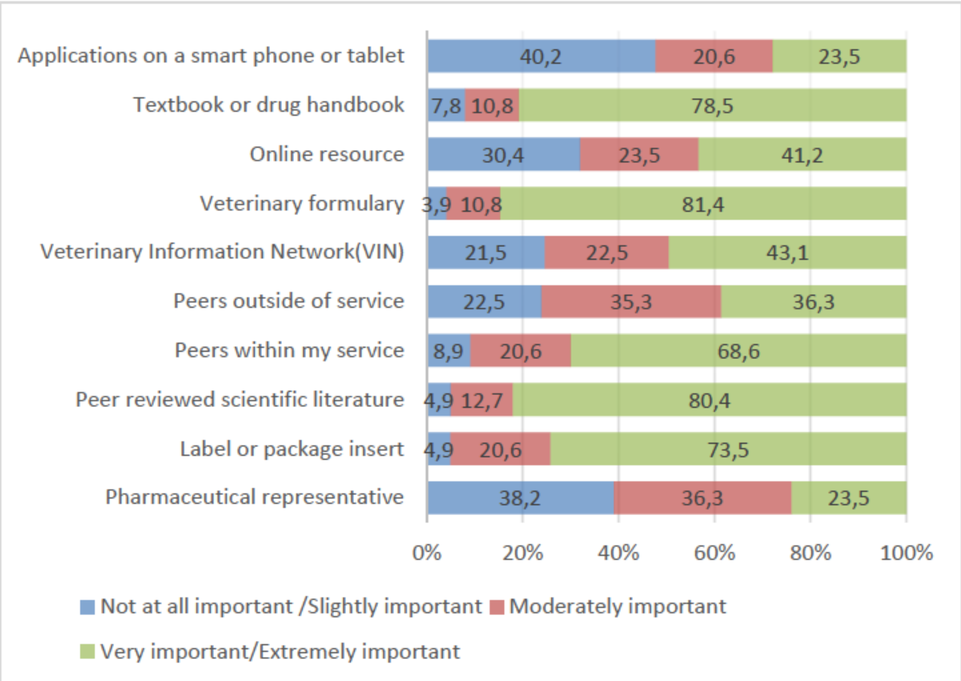
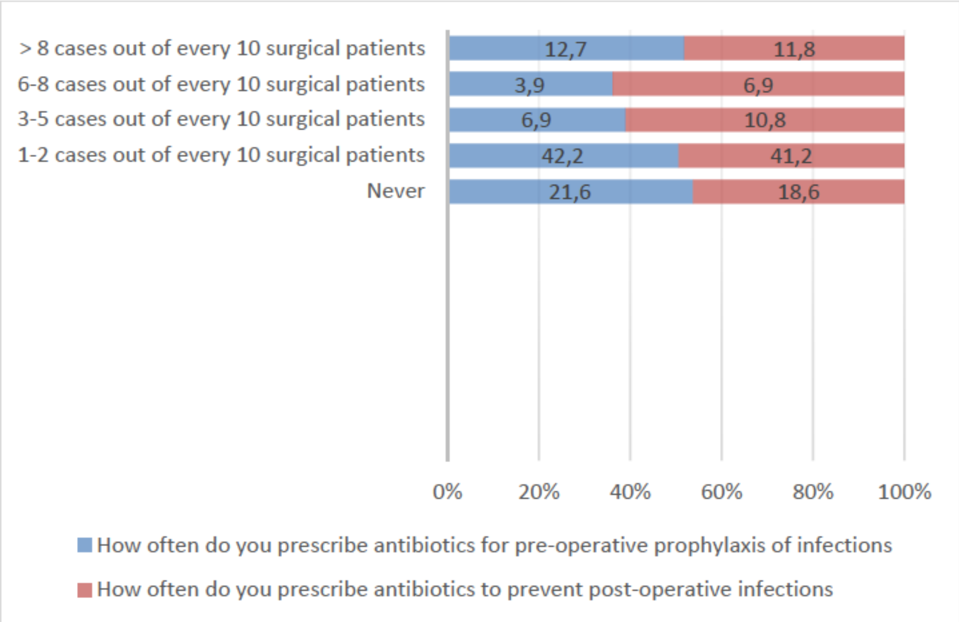


**Figure S3**: Frequency of prescribing antibiotics for surgical patients



# CHAPTER 3

## CONCLUSIONS, LIMITATIONS, AND RECOMMENDATIONS

### 3.1 CONCLUSIONS

A quantitative questionnaire-based online survey was conducted to determine the knowledge, attitudes and practices of veterinarians on antibiotic use, ABR, and its containment in the South African veterinary sector.

#### 3.1.1 Knowledge

Concerning knowledge on antibiotic use, ABR, and its containment, the following conclusions were drawn. From the results, the average scores on knowledge on antibiotic resistance were very good. Based on a total score of 13, the average score for the respondents was 11.57± 1.33). Veterinarians in urban practice were more knowledgeable about antibiotic resistance (11.86±1.00) compared to those in rural practice (11.08±1.67). The average score on contributors to antibiotic resistant infections in people was low (Based on a total score of 5, the respondents' average score was 1.99±1.13). The average score on selecting factors in veterinary medicine that may play a role in antibiotic resistant infections in people was good (Based on a total score of 7, the average score for the respondents was 3.95±1.17). Self-reported knowledge on antibiotic stewardship, antibiotic resistance mechanisms, and pharmacology was good (96 (94.1%), 91 (89.2%), and 70 (68.6%), respectively). To a greater extent, veterinary training alone adequately equipped veterinarians with knowledge of antibiotics' rational use (More than half the respondents 60 (58.8%) were confident that veterinary training prepared them quite a bit/very much). The veterinary formulary, peer-reviewed scientific literature, and textbooks or drug handbooks were considered to be the most important sources of information on antibiotics (83 (81.4%), 82 (80.4%), and 80 (78.5%) respectively). A majority of veterinarians identified the narrow-spectrum antibiotics amoxicillin and procaine penicillin as first-line treatment (79 (77.5 %) and 50 (49%) respectively). Some respondents also identified broad-spectrum antibiotics such as amoxicillin-clavulanate and metronidazole as first-line treatment (62 (60.8%) and 64 (62.7%) respectively). Penicillins were often prescribed (70.6%), with amoxicillin-clavulanate and procaine penicillin being the preferred antibiotics in that class (49 (48%) and 27 (26.5%), respectively).

#### 3.1.2 Attitudes

Notably, most of the respondents believed that antibiotics were sometimes prescribed for suspected but not confirmed infections 81 (79.4%). A little more than half of the respondents believed that antibiotics were optimally prescribed 56 (54.9%). The concern related to antibiotic resistant infections amongst veterinarians was inverted amongst their clients. The majority of the respondents were quite concerned/very concerned about antibiotic resistant infections 77 (75.5%) compared to 19 (18.7%) of clients expressing the same concern. Impressively, most of the respondents agreed/strongly agreed that antibiotic drug use in veterinary practice might lead to antibiotic resistance in pathogens affecting humans 73 (71.5%). In contrast, only 24 (23.5%) agreed/strongly agreed that the antibiotic classes commonly used in human medicine should not be used in veterinary medicine as they select for antibiotic resistant bacteria. The cost of diagnostics (90 [88.2]), time to results of diagnostics (83 [81.4%]), and client expectations of receiving antibiotics (74 [72.5%]) were cited the most as barriers to the implementation and use of an antibiotic stewardship plan in veterinary medicine.

### 3.1.3 Practices

Some respondents (45 [44.1%)] sometimes read veterinary guidelines for appropriate use of antibiotics while 43 (42.2%) did it very often/always. A little more than half the veterinarians (54 [52.9%]) often/always discussed antibiotic resistance with their clients, with those in rural practice frequently doing so compared to their urban counterparts (p value=0.035). Persistent infection (89 [87.3%]), recurring infections (73 [71.6%]), and client finances (48 [47.1%]) were the most important factors in influencing the decisions of veterinarians to submit samples for microbial culture and susceptibility testing. Most veterinarians (61 [59.8%]) lacked antibiotic stewardship programmes at their practices.

### 3.1.4 Overall Conclusion

From our study, gaps in the knowledge, attitudes, and practices on antibiotic use, antibiotic resistance, and its containment were identified. Knowledge of rational antibiotic use and ABR should be included in continuing professional development programmes to address such gaps in different geographical location. Antibiotic stewardship programmes need to be implemented in veterinary practice, cost-effective diagnostic tests with shorter turnaround time might assist in achieving such. Antibiotic stewardship programmes might encourage the frequent use of guidelines for the appropriate use of antibiotics and microbiology informed therapy. Client education on ABR is imperative; more discussions between veterinarians and their clients over ABR might help change client attitudes. There is a need for veterinarians to use narrow-spectrum antibiotics as first-line drugs . Use of the OIE list of veterinary important antibiotics and the WHO list of medically important antibiotics should be encouraged to conserve the antibiotics of critical importance.

## 3.2 LIMITATIONS

- The South African Veterinary Council was unable to assist in sending out the survey to their registered members because of compliance with the Protection of Personal Information Act which might have affected the response rate.
- The response rate was abysmal (6%) compared to other studies of a similar nature elsewhere. Therefore, the results of the study may not be generalised to the whole veterinary profession. However, the study managed to unlock areas that require

further attention amongst veterinarians.

- The survey was made available only for a month (1st of October 2019 till the 31st of October 2019). This might have affected the response rate.
- Only veterinarians participated in the survey. Results could have been more comprehensive if the other animal health professions had participated.

**3.3 RECOMMENDATIONS**

- Professional veterinary bodies could help in encouraging animal health professionals to participate in research to produce an evidence base that can efficiently inform interventions.
- Awareness should be raised on the importance of the OIE list of veterinary important antibiotics and the WHO list of medically important antibiotics and the need to conserve them for the treatment of infections in humans and animals.
- The use of diagnostic tests that are more cost-effective and with a shorter turnaround time could encourage culture and susceptibility testing and might assist in implementing antibiotic stewardship programmes.
- Continuing professional development programmes should encompass rational antibiotic use and ABR to improve knowledge among veterinarians.
- Veterinarians must be encouraged to raise awareness on ABR through engaging in frequent discussions with clients on the ABR matter.
- Veterinarians also need to be proactive in reporting adverse antimicrobial drug events together with suspected lack of efficacy of antibiotics which may be related to ABR to the respective pharmaceutical companies. This will favour the analysis of possible ABR trends thus informing interventions thereof.

# APPENDICES

## Appendix 1: Gatekeeper permission

South African Veterinary Association
Suid-Afrikaanse Veterinêre Vereniging

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Reg 1903/002020/08

P O Box 25033
Monument Park
Pretoria, 0105
47 Gemsbok Avenue
Monument Park, 0181

4 September 2019

Professor Sabiha Essack
College of Health Sciences
University of KwaZulu-Natal
Private Bag X54001
Durban
4000
Email: essacks@ukzn.ac.za

**RE: PERMISSION TO SEND SURVEY OUT TO SAVA MEMBERS**

The South African Veterinary Association (SAVA) agrees to send out the survey (as relates to the research protocol listed below) to our membership.

**Research Title:** Animal health professionals' knowledge, practices, attitudes and experiences to antibiotic resistance and its containment using a one health approach in the public and private sectors in South Africa. BREC Ref No: BE033/19
**Researcher:** Dr SA Maruve
**Supervisor:** Dr Manimbulu Nlooto
**Co-supervisor:** Prof Sabiha Essack
**Institution:** Pharmaceutical Sciences, College of Health Sciences, University of KwaZulu-Natal

Regards,

[redacted]

Gert Steyn

Managing Director

saalas
south african association for laboratory animal science

**President: Dr Tamsyn Fourie** BVSc, MMedVet (LAS),
president@saalas.org | Tel: +27 82 368 0666
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Professor Sabiha Essack
College of Health Sciences
University of KwaZulu-Natal
Private Bag X54001
Durban
4000
Email: essacks@ukzn.ac.za

26 August 2019

Dear Professor Essack,

**RE: Permission to send survey out to SAALAS members**

The South African Association for Laboratory Animal Science's (SAALAS) Executive committee agrees to send out the survey (as relates to the research protocol listed below) to our membership.

**Research Title:** Animal health professionals' knowledge, practices, attitudes and experiences to antibiotic resistance and its containment using a one health approach in the public and private sectors in South Africa. BREC Ref No: BE033/19
**Researcher:** Dr SA Maruve
**Supervisor:** Dr Manimbulu Nlooto
**Co-supervisor:** Prof Sabiha Essack
**Institution:** Pharmaceutical Sciences, College of Health Sciences, University of KwaZulu-Natal

Kind regards,

[redacted]

Tamsyn Fourie
SAALAS President

## Appendix 2: Ethical Approval Certificate

UNIVERSITY OF ™
KWAZULU-NATAL
INYUVESI
YAKWAZULU-NATALI

23 September 2019

Dr SA Maruve (218088135)
School of Health Science
College of Health Sciences
simbaiallenmaruve@gmail.com

Dear Dr Maruve

**Protocol: Animal Health professionals' knowledge, practices, attitudes and experiences to antibiotic resistance and its containment using a one health approach in the public and private sectors in South Africa.** **Degree: MMedSc**
**BREC Ref No: BE033/19**

**EXPEDITED APPLICATION: APPROVAL LETTER**

A sub-committee of the Biomedical Research Ethics Committee has considered and noted your application received on 21 January 2019.

The study was provisionally approved pending appropriate responses to queries raised. Your response received on 05 September 2019 to BREC letter dated 24 July 2019 has been noted by a sub-committee of the Biomedical Research Ethics Committee. The conditions have been met and the study is given **full ethics approval** and may begin as from 23 September 2019. **Please ensure that outstanding site permissions are obtained and forwarded to BREC for approval before commencing research at a site.**

This approval is valid for one year from **23 September 2019.** To ensure uninterrupted approval of this study beyond the approval expiry date, an application for recertification must be submitted to BREC on the appropriate BREC form 2-3 months before the expiry date.

Any amendments to this study, unless urgently required to ensure safety of participants, must be approved by BREC prior to implementation.

Your acceptance of this approval denotes your compliance with South African National Research Ethics Guidelines (2015), South African National Good Clinical Practice Guidelines (2006) (if applicable) and with UKZN BREC ethics requirements as contained in the UKZN BREC Terms of Reference and Standard Operating Procedures, all available at http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx.

BREC is registered with the South African National Health Research Ethics Council (REC-290408-009). BREC has US Office for Human Research Protections (OHRP) Federal-wide Assurance (FWA 678).

The sub-committee's decision will be noted by a full Committee at its next meeting taking place on **12 November 2019.**

Yours sincerely

[redacted]

**Prof V Rambiritch**
**Chair: Biomedical Research Ethics Committee**

cc: nenep1@ukzn.ac.za Nlooto@ukzn.ac.za essacks@ukzn.ac.za

**Biomedical Research Ethics Committee**
**Professor V Rambiritch (Chair)**
**Westville Campus, Govan Mbeki Building**
**Postal Address:** Private Bag X54001, Durban 4000
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**Website:** http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx

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