SURVEILLANCE FOR ANTIMICROBIAL RESISTANCE AND CONSUMPTION OF ANTIBIOTICS IN SOUTH AFRICA

NOVEMBER 2018

NATIONAL DEPARTMENT OF HEALTH

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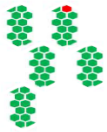
EXECUTIVE SUMMARY

This surveillance report represents the current available information relating to antimicrobial resistance (AMR) in humans and antimicrobial consumption in animals and humans in South Africa over the period 2012 – 2017.

Antimicrobial Resistance in Humans

The AMR surveillance system in humans was built through the collaboration between the public and private sector laboratory services and represents an almost fully comprehensive view of AMR in blood cultures for the ESKAPE[1] pathogens in the country.

Resistance in numbers:

K pneumoniae	*S aureus*	*E coli*	*P aeruginosa*	*A baumanii*	Enterococci	
					E faecium	*E faecalis*
						
1 in 12 BSIs resistant to carbapenems	1 in 4 BSIs resistant to cloxacillin (MRSA)	1 in 4 BSIs resistant to 3rd generation cephalosporins (ESBL)	1 in 4 BSIs resistant to carbapenems	8 in 10 BSIs resistant to carbapenems	1 in 20 BSIs resistant to vancomycin	1 in 50 BSIs resistant to vancomycin

BSI – Blood stream infection

Klebsiella pneumoniae is the commonest isolate from blood in both the public and private sectors followed by *Escherichia coli* and then *Pseudomonas aeruginosa* and *Acinetobacter baumannii.* The prevalence of extended spectrum beta-lactamase producing *K. pneumoniae* has remained between 66-70% over the past 6 years and limits the use of cephalosporins for treatment. The emergence of carbapenem-resistance in *K. pneumoniae* is a growing concern with 1:12 resistant to carbapenems.

E. coli, which is assumed to be a community-acquired infection associated with urinary tract infection (UTI), is showing increasing resistance to quinolones, which are empiric treatment for UTI's. One in four *E coli* is an Extended Spectrum Beta-Lactamase (ESBL) producer, resistant to 3rd generation cephalosporins. *P. aeruginosa* and *A. baumannii,* commonly regarded as healthcare-associated infections, are showing a decline in resistance to piperacillin/tazobactam and carbapenems, which are used as first and

[1] ESKAPE = *Enterococcus faecalis* and *Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa* and *Escherichia coli*

second line treatments respectively. Large variations across the provinces for these two organisms highlights potential differences in empiric treatment between provinces. Carbapenem resistance occurs in a quarter of *P. aeruginosa* isolates, whereas 80% of *A. baumannii* are resistant.

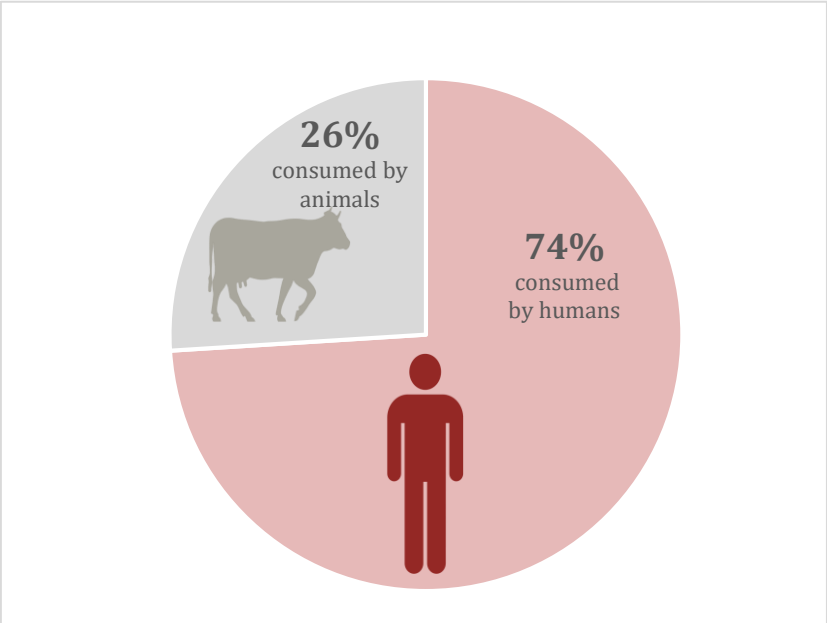
Carbapenem resistance in *A. baumannii* is high at 81%, with consistent findings across the country, as well as increasing levels of resistance over time. This limits treatment options, with only colistin (which is not registered in the country, and requiring a license through the South African Health Products Regulatory Authority (SAHPRA) to procure) being available to treat these resistant infections.

Resistance levels for *Staphylococcus aureus* have declined from 36% to 23% (of which 1 in 4 are methicillin resistant *S.* aureus (MRSA)) over the past 6 years, and resistance varies across the provinces. Ampicillin remains the drug of choice for *Enterococcus faecalis*, however ampicillin resistance of *Enterococcus faecium* is greater than 90% with the added growing concern of vancomycin resistance (a last resort antibiotic), especially in the Free State.

Through the GERMS-SA [2] surveillance program, resistance for *Streptococcus pneumoniae* has been shown to be occur mainly in children under 5 years of age and originates from community-acquired infections.

Antimicrobial Use in South Africa

Import data for antimicrobials between 2014 and 2015 estimates procurement for animal health at 23-36% and for human use at 74-77%. Humans consume the majority of penicillins and streptomycins. This ratio of animal to human use is in contrast to reports from the United States of America (USA), China and India where animal consumption is the far larger proportion.



[2] GERMS-SA is a nationwide network of clinical microbiology laboratories (in the public and private sector) which participate in an active laboratory-based surveillance programme for pathogens of public health importance. Available at http://www.nicd.ac.za/index.php/germs-sa/

Antimicrobial Use in humans

South Africa's antibiotic use in 2015 was 21 149 standard units per 1000/population[3], significantly higher than most other countries in the world. Broad-spectrum penicillin usage was 1.3 to 3.3 time more than that used in other BRICS[4] countries and 0.8 time that used in the United Kingdom or the USA.

The consumption of antimicrobials by humans in the public sector, sourced from procurement data, shows that cotrimoxazole makes up almost ½ of all antibiotics procured with a decreasing trend over time as the contribution of the antiretroviral program starts to take effect and there is a decreased need for *Pneumocystis jiroveci* pneumonia (PJP) prophylaxis. There is minimal use of narrow-spectrum penicillins as compared to broad-spectrum penicillins, however the proportionate consumption of broad-spectrum penicillins has remained between 19,6 to 18,2% between 2016 and 2017.

Antimicrobial Use in Animals

The Department of Agriculture, Forestry and Fisheries (DAFF) in partnership with the South African Animal Health Association (SAAHA) has been reporting antimicrobial consumption in animals against the World Organisation for Animal Health (OIE) requirements. From 2014 to 2015 it appears that the predominant antibiotic group used in animal health are growth promoters (62%), followed by tetracyclines (17%) and macrolides (11%). The growth promoter group includes antibiotics not used in human health such as ionophores, flavophospholipol (flavomycin), olaquindox, zinc bacitracin and tylosin. Only tetracycline and tylosin are registered as antibiotics for growth promotion by The Fertilizers, Farm Feeds, Agricultural Remedies and Stock Remedies Act (Act 36 of 1947) whilst ionophores are classified as antiparasitics but interpreted by the pharmaceutical industry as "growth promoters" and therefore are being reported as such. Efforts are underway to improve the standardised reporting of this category over the next year.

Antimicrobial residues in meat products have been detected in 2.08% of samples analysed through the National Chemical Residue Monitoring Program, which includes penicillins, tetracyclines, sulphonamides and macrolides. This program monitors residues in meat for local and export markets.

[3] IMS Health 2015; 1 standard unit is equivalent to 1 tablet, injection, etc.
[4] BRICS countries: Brazil, Russia, India, China and South Africa

Conclusion

This report presents South Africa's first report on AMR surveillance in the country and, whilst it has attempted to cover the data that is available, there are significant areas where additional data is needed to inform better policy and decision-making abilities in the future.

Introduction

South Africa pledged its commitment to the World Health Assembly resolution "Combating antimicrobial resistance including antibiotic resistance", adopted in May 2014, to develop a National Action Plan on antimicrobial resistance (AMR). By October 2014, the *Antimicrobial Resistance National Strategic Framework, 2014-2024* (AMR Strategic Framework) was developed and launched with the commitment of most of the key stakeholders within the human and animal health, agriculture, as well as science and technology sectors.

The AMR Strategic Framework defines South Africa's approach to manage AMR and limit further increases in resistant microbial infections, and improve patient outcomes and livestock production and health. The vision is ***"to ensure the appropriate use of antimicrobials by healthcare and animal health professionals in all health establishments in South Africa to conserve the efficacy of antimicrobials for the optimal management of infections in human and animal health"***.

The AMR Strategy Framework consists of five interconnected pillars. Strategic objectives to tackle antimicrobial resistance (AMR) are presented in Figure 1.

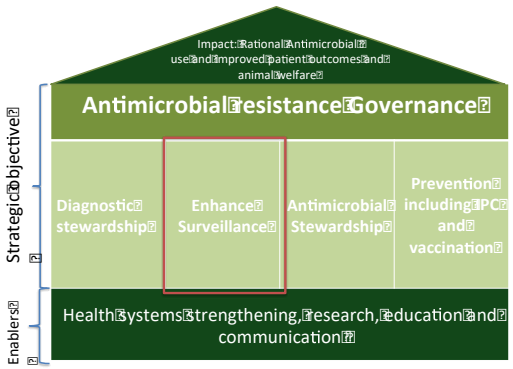


Figure 1 - The South African AMR Strategy Framework with the strategic objectives and key enablers

This report is in fulfilment of one of the main pillars of the AMR Strategic Framework – "Enhance surveillance" with a corresponding objective "*to optimise and report on surveillance of AMR and antimicrobial use in humans and livestock in order to provide reliable data to optimise policy decisions and treatment choice*". The report also seeks to create a consolidated, representative view of AMR and antimicrobial use in South Africa and to monitor trends going forward to evaluate the impact of the AMR Strategy Framework.

A final objective of surveillance is the gathering of data to support research into AMR and other strategic initiatives, policy and planning decisions within the public health realm, as well as to identify data needs and gaps to support policy decision-making.

In drafting this report, the One Health approach has been followed, namely the relationship between human and animal health as it applies to AMR organisms and antimicrobial use has been explored and some significant findings have been made that don't necessarily follow the expectations from international reports.

Abbreviations

AMR	Antimicrobial Resistance
ATCC	Anatomical Therapeutic Chemical Classification
DAFF	Department of Agriculture, Forestry and Fisheries
ESBL	Extended Spectrum Beta-Lactamase
FIDSSA	Federation of Infectious Diseases Societies of Southern Africa
GAP	Global Action Plan
GLASS	Global Antimicrobial Resistance Surveillance System
HAI	Healthcare-Associated Infection
LIS	Laboratory Information System
MAC	Ministerial Advisory Committee
MDRO	Multi-Drug Resistant Organisms
NDoH	National Department of Health
NHLS	National Health Laboratory Service
NICD	National Institute for Communicable Diseases
NMC	Notifiable Medical Conditions
OIE	World Organisation for Animal Health
SASCM	South African Society for Clinical Microbiology
STG	Standard Treatment Guidelines
UTI	Urinary Tract Infection
WHO	World Health Organization

1 Antimicrobial resistance in humans

This section of the report focuses on AMR data derived from blood culture specimens for all public health facilities (including all levels of care, military and prisons) and the majority of private-sector hospitals that are serviced by various private laboratory groups (Lancet Laboratories, Ampath, Vermaak and Partners Pathologists, and PathCare). It is the output of a long-standing collaboration between public and private sector laboratories facilitated through the South African Society for Clinical Microbiology (SASCM) (Figure 2). All AMR data for this report can be viewed on the National AMR Dashboard, available through the National Institute for Communicable Disease (NICD) website, http://www.nicd.ac.za. Further details of the surveillance system and its design can be seen in Annexure A.

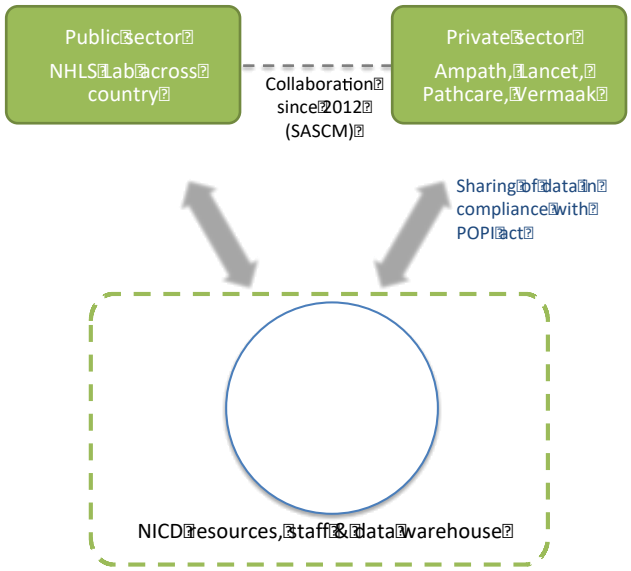


Figure 2 - Partnership between public and private sectors

The acronym ESKAPE is used to describe the organisms that currently form part of the surveillance system, and characterise an internationally accepted group of AMR-priority pathogens. The ESKAPE acronym[5] stands for the following organisms:

- *Enterococcus faecalis* and *Enterococcus faecium*,
- *Staphylococcus aureus*,
- *Klebsiella pneumoniae*,
- *Acinetobacter baumannii*,
- *Pseudomonas aeruginosa*, and
- *Escherichia coli*.

In addition, resistance data reported to World Health Organisation Global Antibiotic Surveillance System (WHO GLASS) have been included.

[5] Helen W. Boucher, George H. Talbot, John S. Bradley, John E. Edwards, Jr, David Gilbert, Louis B. Rice, Michael Scheld, Brad Spellberg, and John Bartlett. Bad Bugs, No Drugs: No ESKAPE! An Update. From the Infectious Diseases Society of America. IDSA Report on Development Pipeline • CID 2009:48 (1 January)

1.1 Overall burden of ESKAPE organisms in the public sector

The burden of ESKAPE organisms causing bacteraemia in the entire public sector was calculated for 2017 using data from the National Health Laboratory Service (NHLS). In 2017, a total of 284,669 blood specimens were submitted for identification and antibiotic susceptibility testing to NHLS (Figure 3). Twenty-four percent (n=69,352) of blood cultures were positive for bacteria or fungi. The ESKAPE organisms comprised 33% (n=22,788) of all positive cultures and 8% of the total number of all submitted blood cultures.

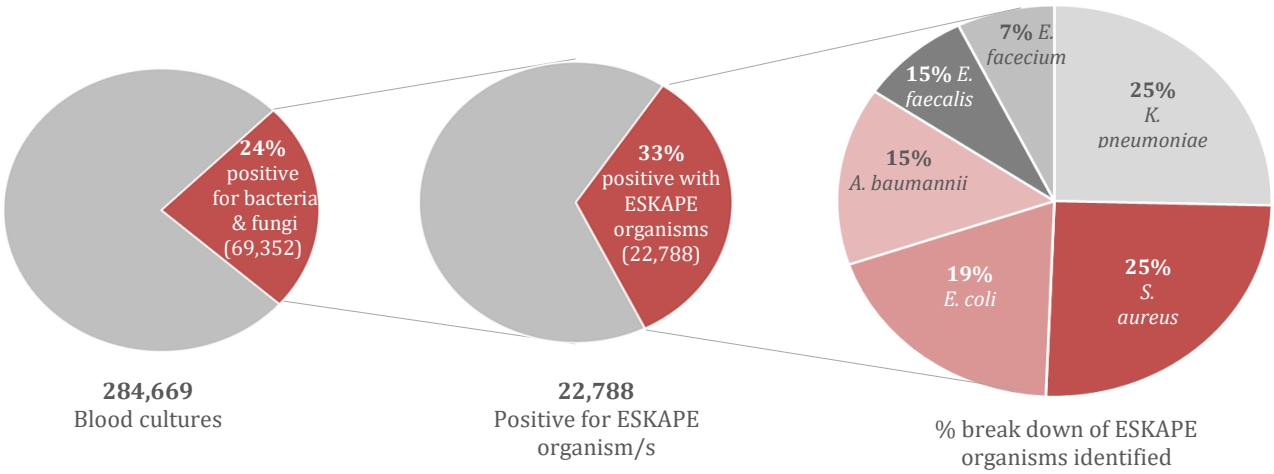


Figure 3 - Burden of ESKAPE pathogens in public sector, 2017

The commonest organisms cultured were *K. pneumoniae*, *S. aureus*, followed by *E. coli* and *A. baumannii* (Figure 214). In this report, the proportion in the private sector could not be calculated.

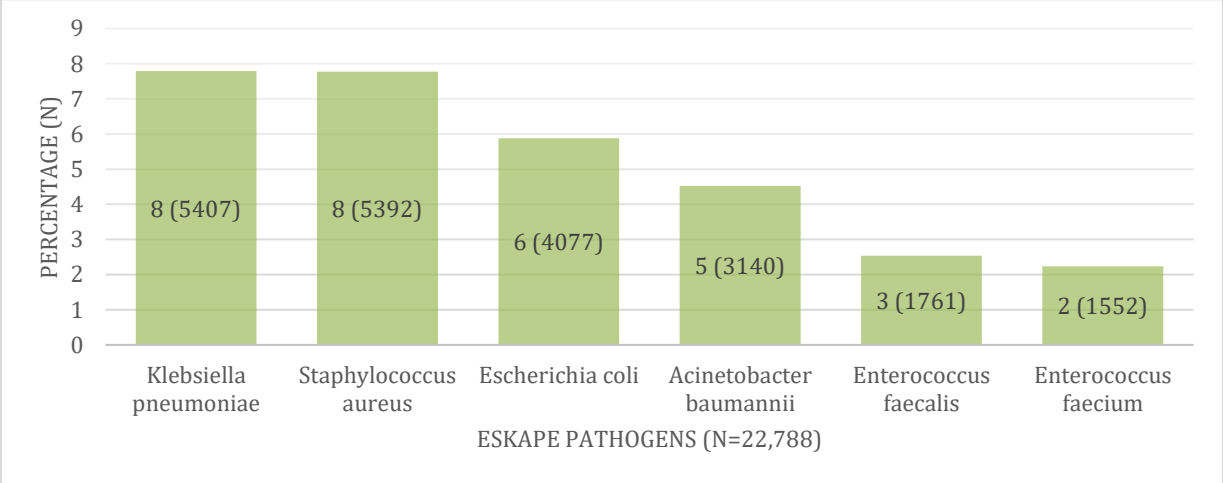
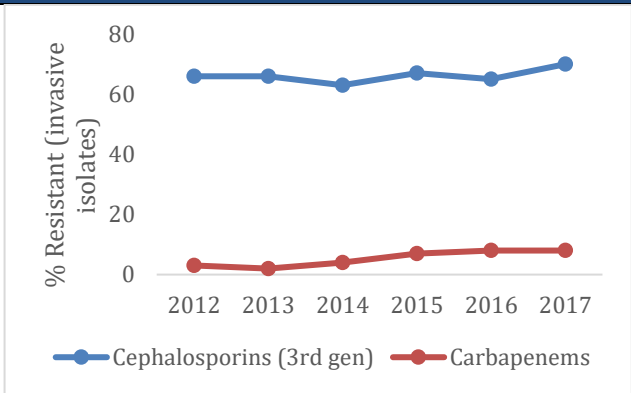
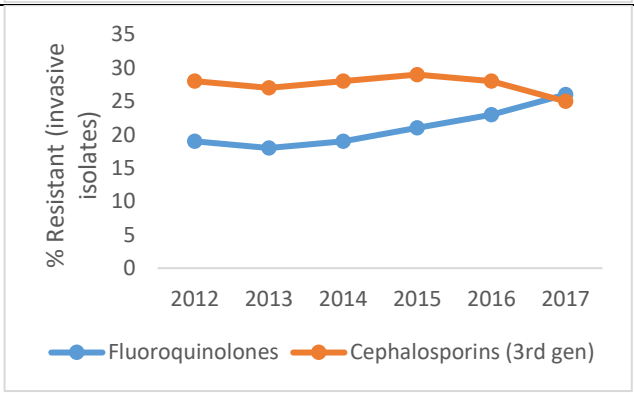
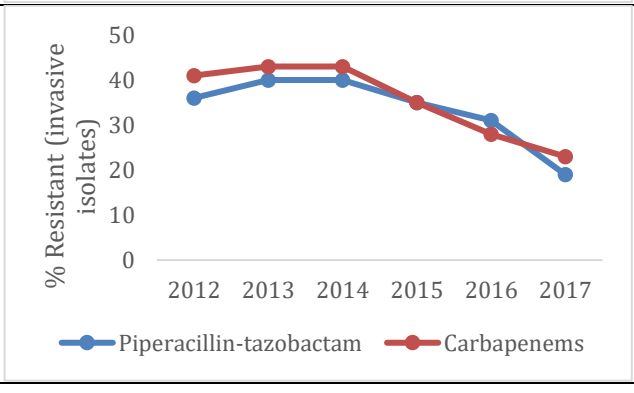


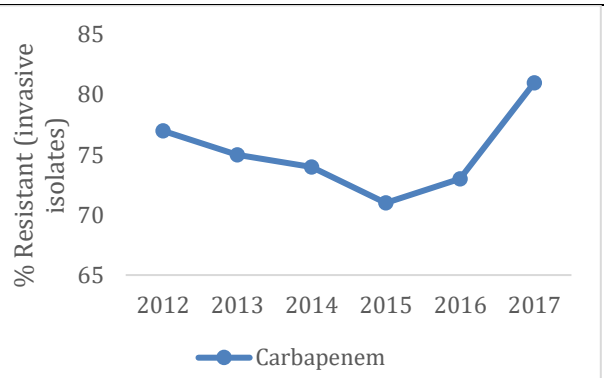
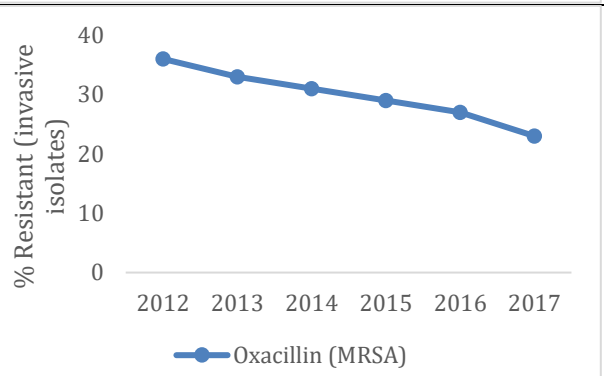
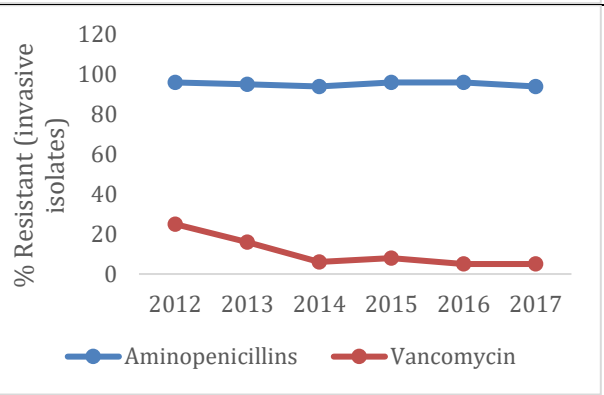
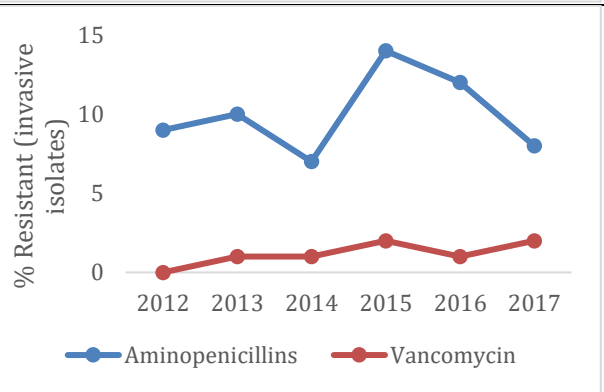
Figure 4 - Proportion of blood culture specimens positive for each ESKAPE bacterial pathogens (n=22,788), 2017

1.2 AMR at a glance (2012 - 2017 data) – Public and Private Sector

The reporting of AMR in humans is focused on certain key drug/bug combinations as illustrated in Table 1, which spans from 2012 to 2017 and includes public and private health sectors. These data represent the organisms and antibiotics commonly used to treat them that are the most critical for monitoring and tracking changes in resistance.

Table 1- AMR trends by organisms group – public and private data 2012 – 2017

Organism	% Non-Susceptible:Drug in 2017		Trend between 2012 - 2017
Klebsiella pneumoniae	**70%** **:** **3rd Generation cephalosporins** (Such as cefotaxime, ceftriaxone)	**8%** **:** **Carbapenems** (Such as ertapenem)	
Escherichia coli	**26%** **:** **Fluoroquinolones** (Such as Ciprofloxacin)	**25%** **:** **3rd Generation cephalosporins** (Such as cefotaxime; ceftriaxone)	
Pseudomonas aeruginosa	**19%** **:** **Piperacillin-tazobactam**	**23%** **:** **Carbapenems** (Such as meropenem)	

Acinetobacter baumannii	**81%** **:** **Carbapenems** (Such as meropenem)	** Due to testing methodology differences between laboratories, colistin resistance is not currently reported*	
Staphylococcus aureus	**23%** **:** **Oxacillin** (i.e. methicillin resistant *S. aureus* (MRSA))		
Enterococcus faecium	**94%** **:** **Ampicillin**	**5%** **:** **Vancomycin**	
Enterococcus faecalis	**8%** **:** **Ampicillin**	**2%** **:** **Vancomycin**	

1.2.1 Klebsiella pneumoniae

K. pneumoniae is one of the commonest isolates from blood in both the private and public sectors in South Africa. The prevalence of extended spectrum beta-lactamase (ESBL)[6] producing *K. pneumoniae* (represented here by cephalosporin 3rd generation non-susceptibility) has remained between 63% - 70% over the past 6 years (2012-17) (Figure 5).

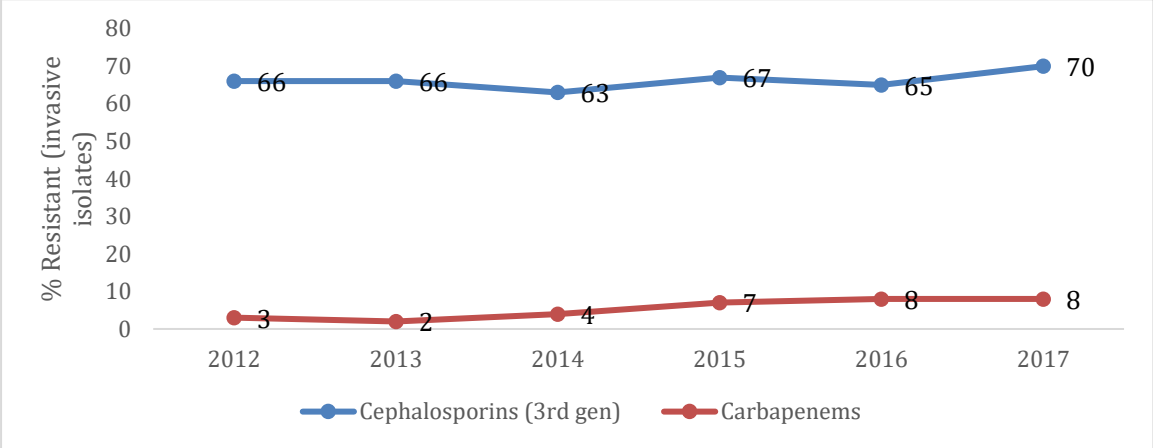


Figure 5 - *K. pneumoniae* % non-susceptible to 3rd generation cephalosporins and carbapenems

The presence of an ESBL affects the susceptibility of *K. pneumoniae* to all cephalosporins, and significantly limits the use of this class of antibiotics as a therapeutic option. These ESBL positive isolates often also display associated quinolone resistance (as it is carried on the same plasmid). This often leaves only the carbapenem group of antibiotics as the only active therapeutic option for one of the commonest blood culture pathogens. The emergence of carbapenem resistance in this group of organisms is a great concern, with 8% of *K. pneumoniae* isolates showing ertapenem resistance in 2017, though with no changes compared to 2016 (Table 1).

Resistance to cephalosporins is similar across most provinces, with a slightly lower incidence in the Western Cape (see Figure 6).

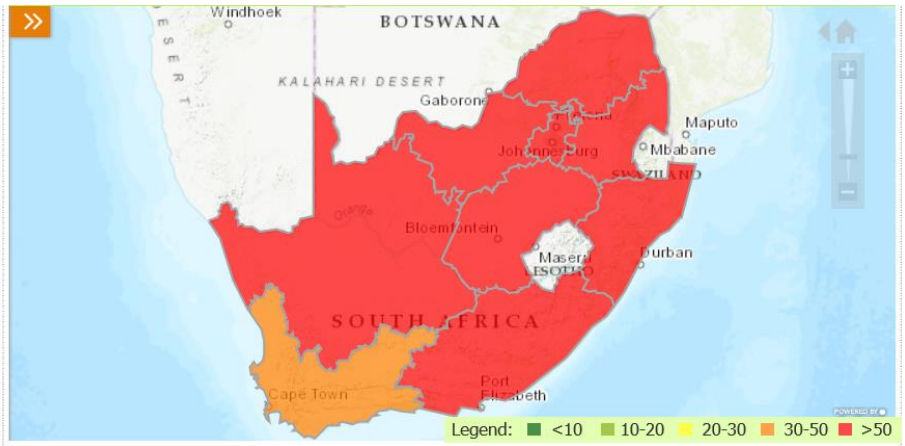


Figure 6 - *K. pneumoniae* % non-susceptible to cephalosporins (3rd generation) by province in South Africa (legend shows % non-susceptible ranges)

[6] ESBLs are enzymes that confer resistance to most beta-lactam antibiotics, including penicillins and cephalosporins. Infections with ESBL-producing organisms have been associated with poor outcomes.

1.2.2 Escherichia coli

E. coli is the second most common Gram-negative pathogen isolated from blood in South Africa. While the data are unable to differentiate community- from healthcare-associated infections, *E. coli* is assumed to reflect community-associated infections, and may be associated with urinary tract infections (UTIs). Isolates show an increase in quinolone resistance (such as ciprofloxacin) from 19% in 2012 to 26% in 2017 (Figure 7), with differences between geographic areas (Figure 8).

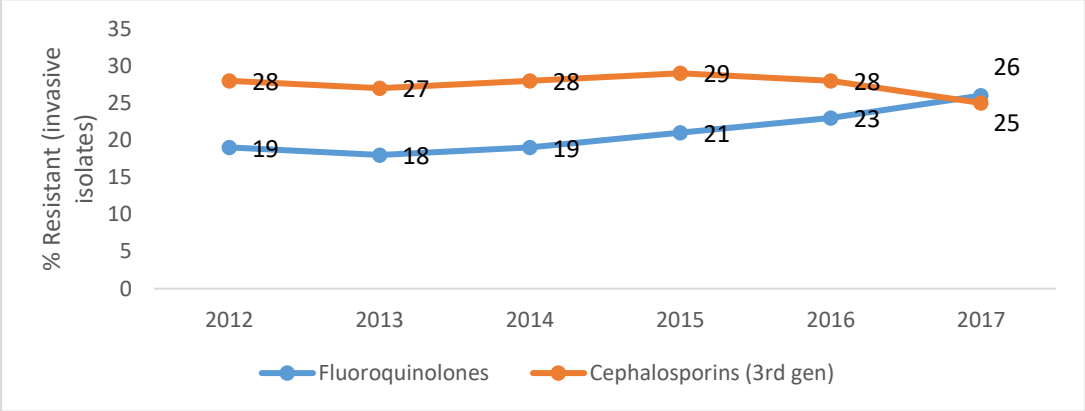


Figure 7 - *E. coli* % non-susceptible to quinolones and cephalosporins

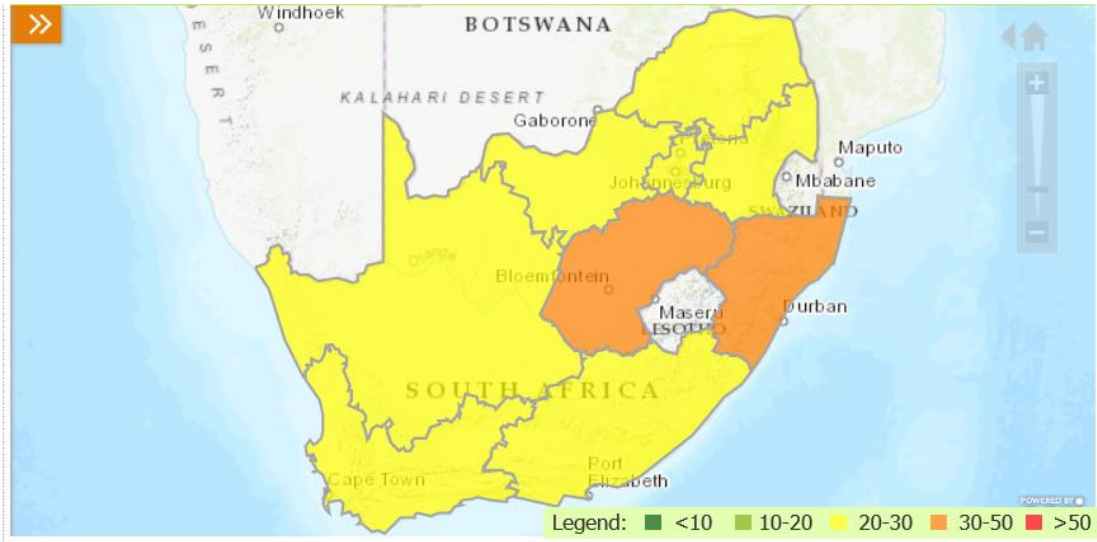


Figure 8 - *E. coli* % non-susceptible to quinolones by province in South Africa (legend shows % non-susceptible ranges)

This high prevalence of resistance is of concern, as quinolones are frequently used as empiric treatment of UTIs. However, the high prevalence of resistance may be affected by selection bias, with a larger proportion of healthcare associated isolates or by specimen collection practices (for example, specimens being taken after a patient has failed therapy, thus increasing the chance of isolating a resistant organism). However, this observed increase in quinolone resistance suggests a need for a prevalence study of community-acquired UTIs.

1.2.3 Pseudomonas aeruginosa and Acinetobacter baumannii

P. aeruginosa and *A. baumannii* are commonly regarded as healthcare-associated pathogens. The 2017 data shows that one-fifth of *Pseudomonas* isolates are resistant to piperacillin/tazobactam, and a quarter are resistant to the carbapenems; these represent first and second line therapeutic options respectively. It is worth noting that there has been a decline in resistance to both agents from 2014 – 2017 (Figure 9 and Figure 10).

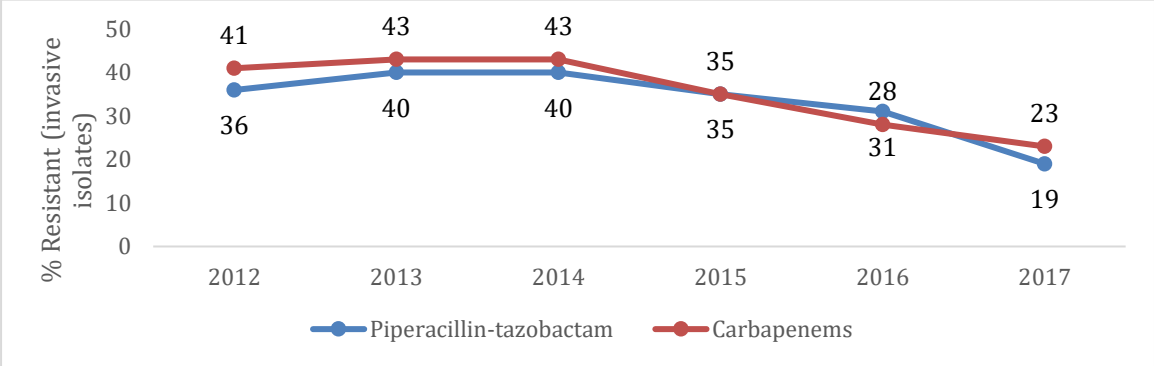


Figure 9 - *Pseudomonas aeruginosa* % non-susceptible to piperacillin/tazobactam and carbapenems

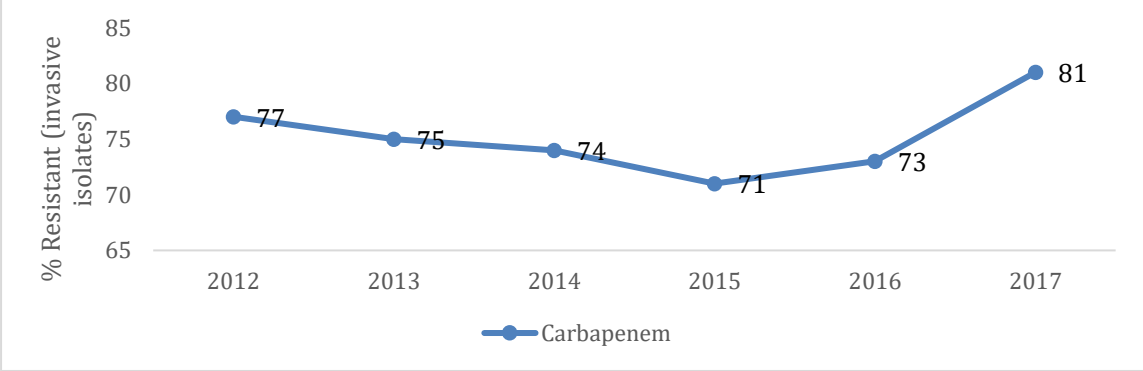


Figure 10 - *Acinetobacter baumannii* % non-susceptible to meropenem

There are also regional variations in susceptibility to both piperacillin-tazobactam (Figure 11) and carbapenems (Figure 12), particularly resistant to piperacillin-tazobactam in the Western Cape, North West and Gauteng; and the Northern Cape, Gauteng and the Free state for carbapenem resistance. This may reflect regional differences in the empirical use of these agents.

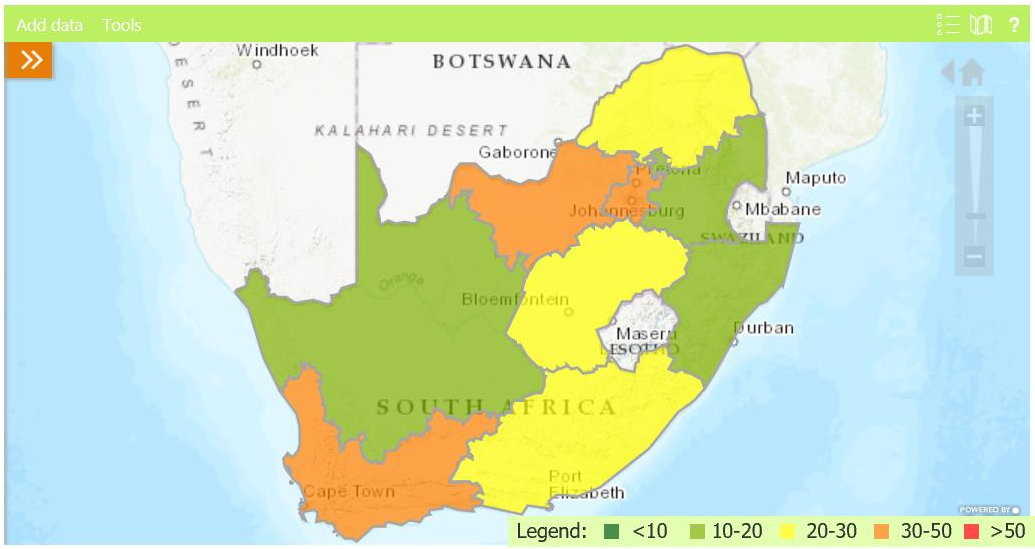


Figure 11 - *Pseudomonas aeruginosa* % non-susceptible to piperacillin/tazobactam by province in South Africa (legend shows % non-susceptible ranges)

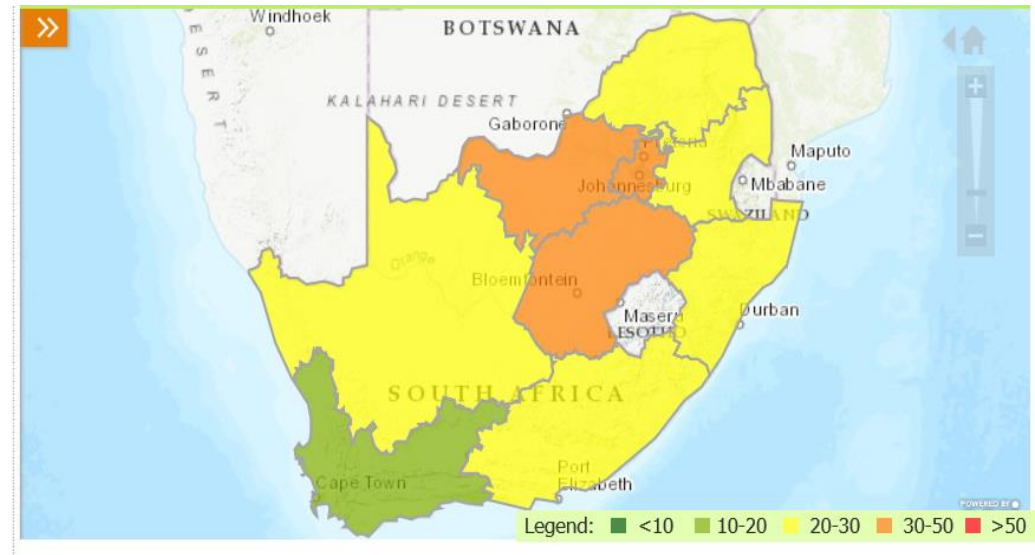


Figure 12 - *Pseudomonas aeruginosa* % non-susceptible to meropenem by province in South Africa (legend shows % non-susceptible ranges)

Carbapenem resistance to *A. baumannii* has been increasing through the years, with resistance observed in 81% of all isolates in 2017 (Table 1). This finding is consistent throughout all the provinces (Figure 13). Treatment options for multi-resistant *A. baumannii* are very limited, and consist of either colistin, tigecycline or combination treatment. Colistin is associated with nephrotoxicity as well as challenges with access (it is not a registered product in South Africa and can only be procured through approval of a Section 21 application by the South African Health Products Regulatory Authority (SAHPRA)). There are also concerns around the clinical outcomes in patients treated with tigecycline as a single agent. Colistin resistance confirmed by mcr1 plasmid has been reported not only in *Acinetobacter*, but in *Klebsiella* and *E. coli*[7] as well.

[7] M Newton-Foot, Y Snyman, M R B Maloba, A Whitelaw; Plasmid-mediated mcr-1 colistin resistance in Escherichia coli and Klebsiella spp. clinical isolates from the Western Cape region of South Africa. Antimicrobial Resistance and Infection control. 3 August 2017

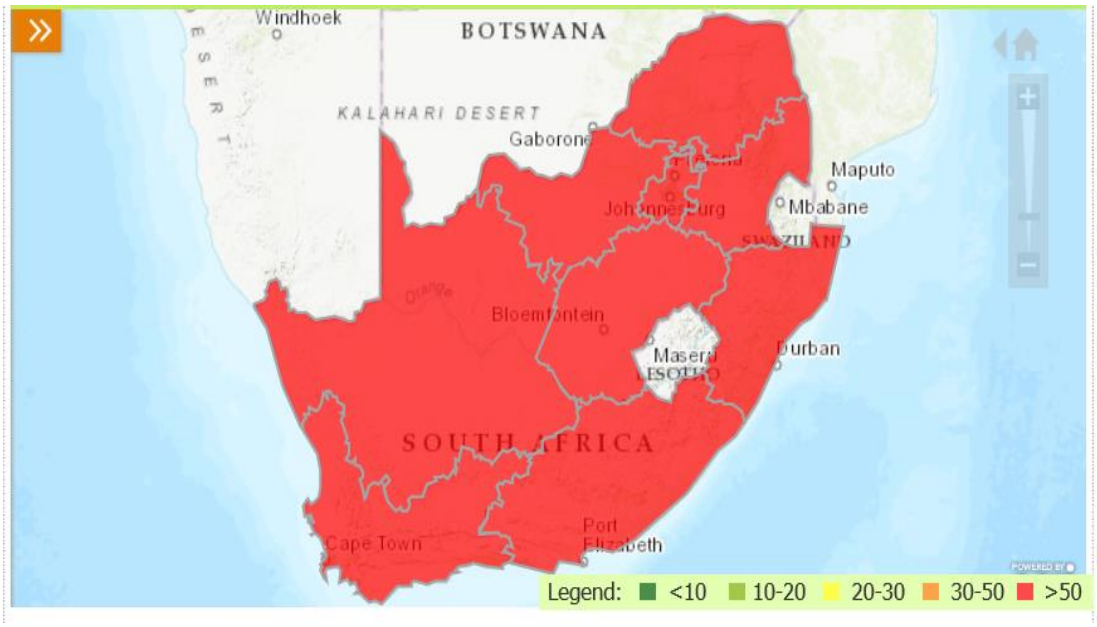


Figure 13 - *Acinetobacter baumannii* % non-susceptible ranges to meropenem by province in South Africa (legend shows % non-susceptible ranges)

1.2.4 Staphylococcus aureus

A consistent decline methicillin resistance in *S. aureus* (MRSA) has been observed, from 36% to 23% over the past six years (Figure 14), with resistance varying across the provinces (Figure 15).

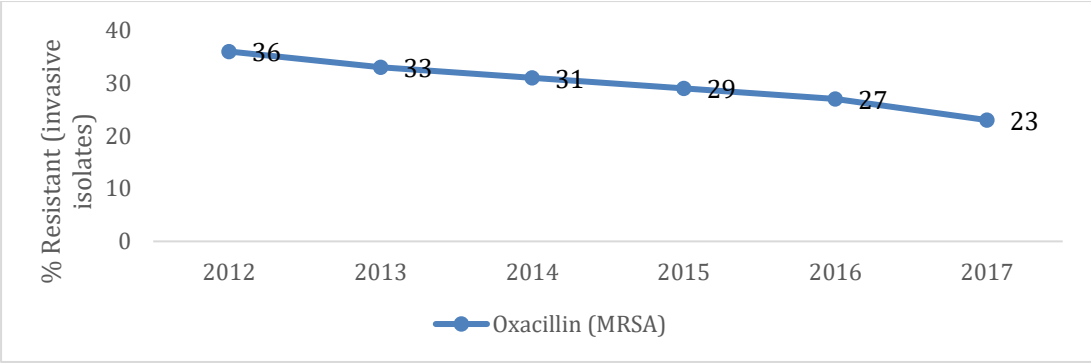


Figure 14 - *Staphylococcus aureus* % non-susceptible to methicillin

Figure 15 - *Staphylococcus aureus* % non-susceptible to methicillin (legend shows % non-susceptible ranges)

Active surveillance in selected sites in two provinces has shown that just under 8% of MRSA bacteraemia is community acquired.[8] This is in contrast to the situation in some other countries where >50% of MRSA originate in the community.

The mainstay of treatment for MRSA remains vancomycin, and vancomycin resistance, while it has been noted in other countries, has not yet been reported in South Africa.

1.2.5 Enterococcus faecalis and Enterococcus faecium

E. faecalis is commonly susceptible to ampicillin (which remains the drug of choice), with resistance of 8% nationally (Figure 16). In contrast, ampicillin resistance in *E. faecium* is seen in more than 90% of isolates in keeping with global distribution (Figure 17). Of concern is the resistance to vancomycin in enterococci. This is a therapeutic challenge as there are limited alternatives to vancomycin, especially in the public sector. Vancomycin resistance in *E. faecalis* was first noted in the 2013 data, and is now present in 2% of blood culture isolates (Figure 16).

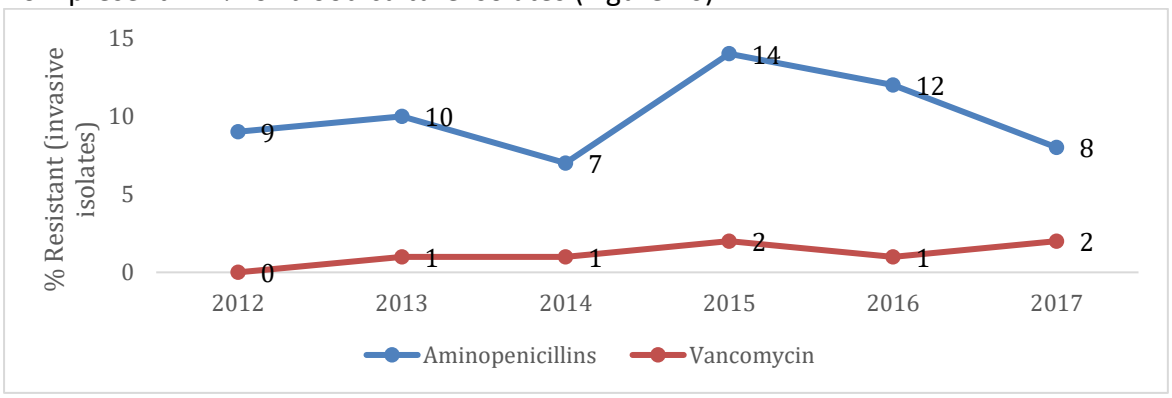


Figure 16 - *Enterococcus faecalis* % non-susceptible to ampicillin and vancomycin

[8] O. Perovic. A Singh-Moodley, N. P. Govender, R. Kularatne, A. Whitelaw, V. Chibabhai, P. Naicker, N. Mbelle, R. Lekalakala, V. Quan, C. Samuel, E. Van Schalkwyk; for GERMS-SA. A small proportion of community-associated methicillin-resistant Staphylococcus aureus bacteraemia, compared to healthcare-associated cases, in two South African provinces, Eur J Clin Microbiol Infect Dis. DOI 10.1007/s10096-017-3096-3; August 2017

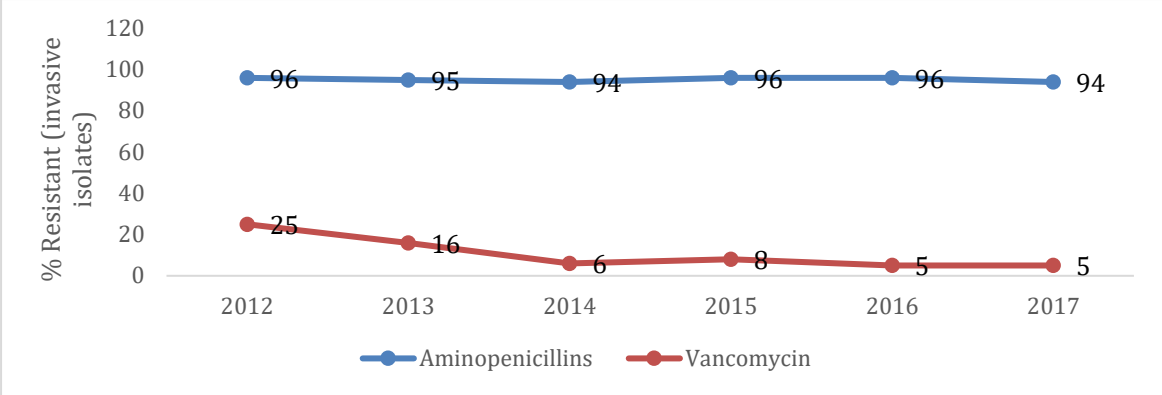


Figure 17 - *Enterococcus faecium* % non-susceptible to vancomycin

While vancomycin resistance remains uncommon in *E. faecalis* (approximately 2% in 2017), it is emerging as a problem in *E. faecium* (Figure 17), although resistance has dropped nationally over the last 5 years to approximately 5% (2016 and 2017).

Table 1One region (Free State) reports higher resistance rates than the others (Figure 18 - E. faecium % non susceptible to vancomycin (legend shows % non-susceptible ranges).

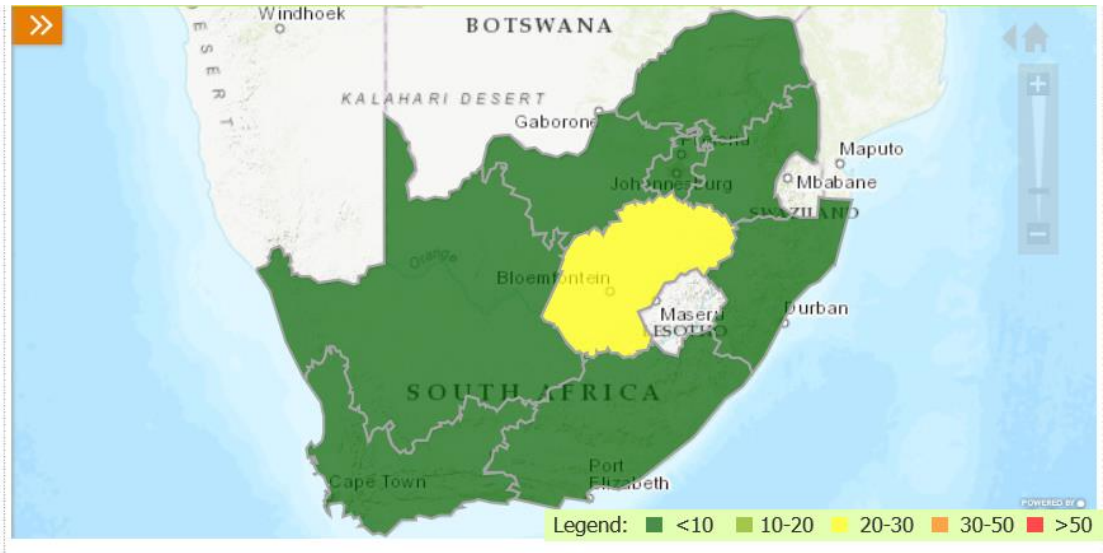


Figure 18 - E. faecium % non susceptible to vancomycin (legend shows % non-susceptible ranges)

1.2.6 Streptococcus pneumoniae report from WHO GLASS submission

S. pneumoniae data are collected through the NICD's GERMS laboratory-based surveillance system (see Annexure A for details). South Africa, through the NICD as the national coordinating centre, also participates in the World Health Organization's (WHO) global surveillance system on AMR - Global Antibiotic Surveillance System (GLASS). These data are obtained from blood culture isolates collected over a 6-year period and includes both public and private sector data. Certain sites perform enhanced surveillance where more details about the patient (e.g. demographics, age, gender, source of specimen, type and infection and site, and patient outcome) are collected.

To fulfil GLASS requirements, tier 1 laboratory-based surveillance is used for AMR data from GERMS[9] and reported for the organism *S. pneumoniae*. Cephalosporin resistance was present in 1% of *S. pneumoniae* isolates, and intermediate resistance in 6% (Figure 19); these resistant isolates originated mainly from community-acquired infections[10]. Resistance to penicillin was 28% with no changes to previous year. The majority of patients with resistant *S. pneumoniae* were under 5-years of age and no difference in resistance was seen between genders (Figure 20).[5]

South Africa, 2017, Blood specimen, Streptococcus pneumoniae pathogen, Origin : All, Gender : All, Age group : All, Batch Id : All, Metric : Proportion excluding Unknown category						
Antibiotic	**Susceptible**	**Intermediate**	**Resistant**	**S+I+R**	**Unknown**	**Total**
Penicillins						
Penicillins	ND	ND	ND	ND	ND	ND
Penicillins						
Penicillin G	338	0	133	471	182	653
	71.8 %	0 %	28.2 %	72.1 %	27.9 %	
Penicilinase-stable beta-lactams						
Oxacillin	ND	ND	ND	ND	ND	ND
Third-generation cephalosporins						
Cefotaxime	ND	ND	ND	ND	ND	ND
Ceftriaxone	ND	ND	ND	ND	ND	ND
Third-generation cephalosporins	437	28	6	471	182	653
	92.8 %	5.9 %	1.3 %	72.1 %	27.9 %	
Sulfonamides and trimethoprim						
Co-trimoxazole	271	45	155	471	182	653
	57.5 %	9.6 %	32.9 %	72.1 %	27.9 %	
Sulfonamides and trimethoprim	ND	ND	ND	ND	ND	ND

Figure 19 - *Streptococcus pneumoniae* susceptibility profile from WHO GLASS submission

AGE GROUPS :	
Subtotal	352
	73.2 %
<1	37
	74 %
01-04	18
	52.9 %

Figure 20 - *Streptococcus pneumoniae* susceptibility profile from WHO GLASS submission: Age group less than 5 years (n=647)

[9] GERMS is a nationwide network of clinical microbiology laboratories (in the public and private sector) which participate in an active laboratory-based surveillance programme for pathogens of public health importance.
[10] Global antimicrobial resistance surveillance system (GLASS) report: early implementation 2016-2017, WHO, July 2017

2 Consumption of antimicrobials in the human and animal sector

2.1 Antimicrobial consumption estimates through import data in South Africa

Import data from 2010 - 2016 showed an average import of 5,66 tons per annum of antibiotics (Figure 21). This was made up of active pharmaceutical ingredients (API), bulk chemicals and fixed dose combination antimicrobials. The largest category of antimicrobial imported was "other" making up about 66% of all imports into the country. Due to the non-specific nature of this "other" category, the NDoH has engaged with the South African Revenue Services (SARS) to break this down into the ATC [11] classes of antimicrobials, with a further split for those used in animals *versus* human use. This will improve reporting details in the future.

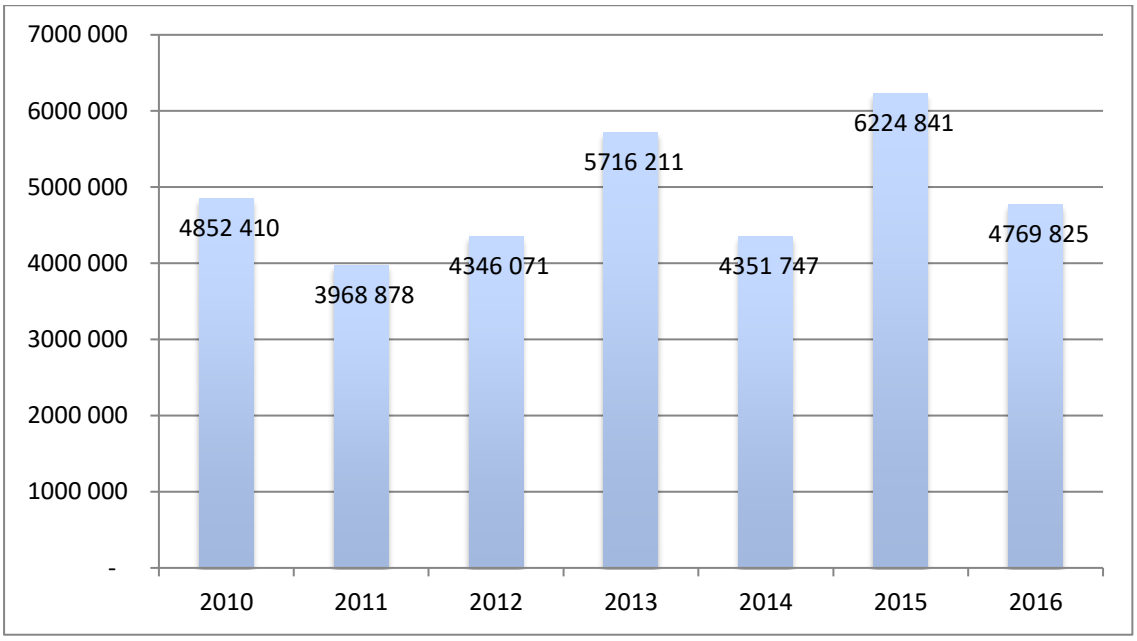


Figure 21 - Total volume of all antibiotics and medicaments imported into South Africa (2010 to 2016, in kilograms)

2.2 Comparative consumption estimates for animals and humans in South Africa

South Africa imported 4,35 tons of antimicrobials into the country in 2014, of which 23% was estimated for animal use, and the remainder (77%) for human use. This is in contrast to the reported USA figures of 70% of consumption being in the animal sector. However, the South Africa estimate is similar to findings in other low-middle income countries (LMICS), excluding India and China.[12] Between 2014 and 2015, there was an increase of 58% in estimated animal imports and 38% in human imports, resulting in a total estimated import of 6,3 tons. The estimated ratio of animal to

[11] Anatomical Therapeutic Chemical (ATC) Classification is used for the classification of active ingredients of drugs according to the organ or system on which they act and their therapeutic, pharmacological and chemical properties.

[12] Tackling Drug Resistant Infections Globally; finaly report and recommendations. The Review on antimicrobial resistance chaired by Jim O Neill, May 2016

human antimicrobial use in 2015 still remains similar to 2014 with 26% being estimated for animal use and 74% for humans (Figure 22).

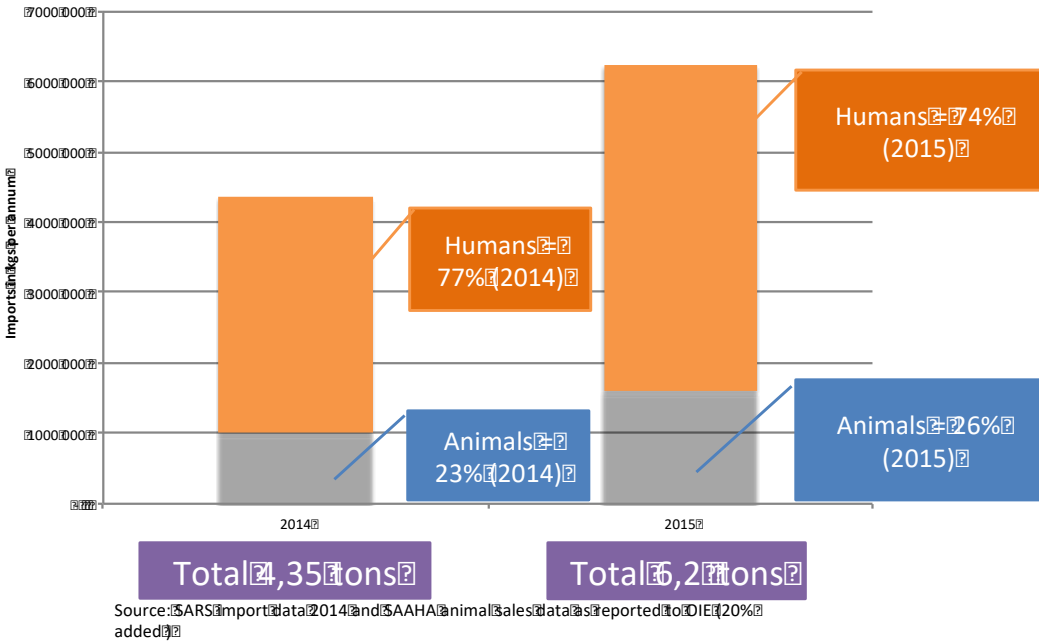


Figure 22 - Comparison between animal and human consumption estimates for 2014 and 2015

Out of the total antimicrobial consumption, humans consume 98% of all penicillin's and streptomycin's imported in the country, and about 69% of the other antibiotics which include tetracycline's, macrolides, cephalosporins, quinolones, etc. (Figure 23).

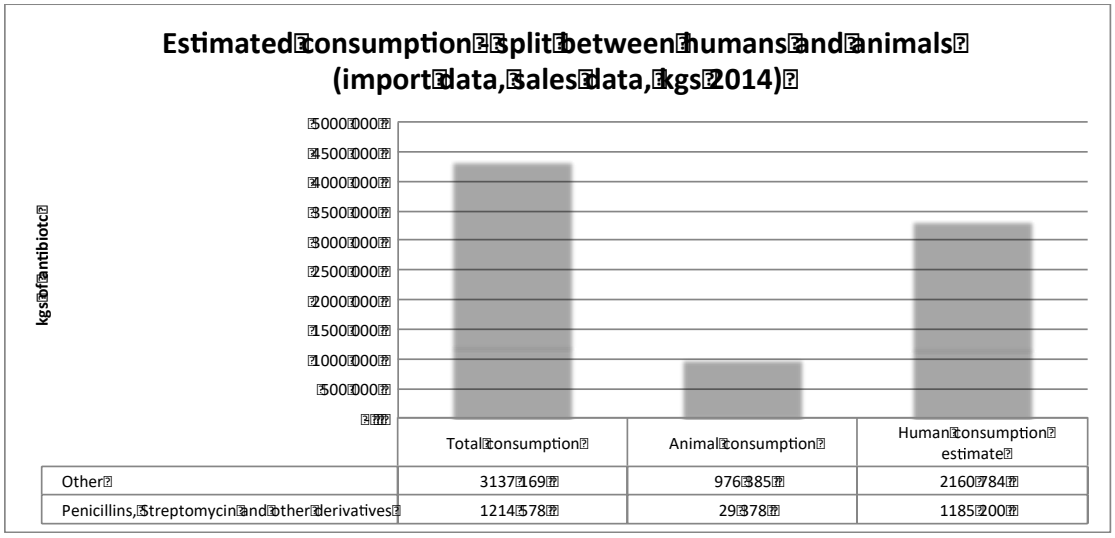


Figure 23 – Estimated consumption – split between humans and animals for penicillins and other antibiotics

2.3 Antibiotics use for Animals that are significant for Humans

The WHO and the OIE have emphasized that it is important for the animal health sector to apply risk management options when considering the use of antibiotics that are critically or highly important for humans. In other words, where humans and animals use shared class antibiotics such as tetracyclines, macrolides, polymyxins and aminoglycosides, the risk management options should allow an appropriate balance between animal, human and public health considerations.[13] Some of these, for example colistin, are regarded as last resort antibiotics for treatment of multi-drug resistant bacterial infections in humans.

In South Africa's efforts to collect data on antimicrobial consumption against the OIE reporting requirements, DAFF has collaborated with the South African Animal Health Association (SAAHA), which represents about 80% of the pharmaceutical industry in the country. The OIE reporting template requires that "growth promoters" are reported, however these are not defined nor are the classes of antibiotics that constitute this defined, leaving it up to the discretion of the pharmaceutical industry to categorise antibiotics as growth promoters or not. Therefore, from the 2014 and 2015 reports it appears that the predominant antibiotic group used in animal health are growth promoters. Growth promoters[14] made up more than 55% (in 2014) and 62% (in 2015) of all antimicrobials sold in animal health. This group contains antibiotics not used in human health such as ionophores (monensin sodium and salinomycin), flavophospholipol (flavomycin), olaquindox, zinc bacitracin and tylosin.

Only tetracycline and tylosin are registered as antibiotics for growth promotion by the Fertilizers, Farm Feeds, Agricultural Remedies and Stock Remedies Act (Act 36 of 1947). In addition, ionophores are classified as antiparasitics, but interpreted by the industry as "growth promoters". Efforts are underway to improve the standardised reporting of this category over the next year.

Estimated consumption by animals of tetracyclines makes up about 27% of total antimicrobial sales (see Figure 24), compared to the OIE reported 63% for most African countries over the same period.[15,16] This possibly demonstrates that South Africa's farming practices vary from those of other African countries, however this data does not reflect the use of colistin, which until 2017 was a commonly used antibiotic especially in the poultry sector.

[13] WHO Critically Important Antimicrobials for Human Medicine, 5th Revision, 2016

[14] *The growth promoters used most commonly include flavophospholipol (flavomycin), olaquindox, zinc bacitracin, tylosin phosphate and ionophores such as monensin sodium and salinomycin.*

[15] OIE Annual report on the use of antimicrobial agents in animals; Better understanding of the global situation, December 2016

[16] OIE Annual report on the use of antimicrobial agents in animals; Better understanding of the global situation, Second report, December 2017

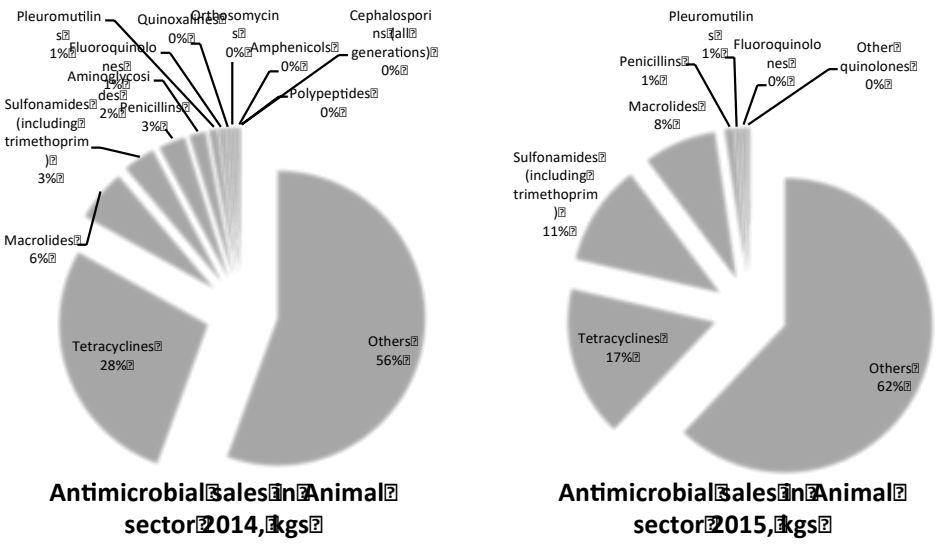


Figure 24 –pie chart showing split of antimicrobial sales by class for animals in 2014 and 2015 (*Data provided by the South African Animal Health Association and reported as part of OIE report* [9,10])

Of concern is the increase in certain antibiotics between 2014 and 2015 (see Table 2) especially “growth promoters” (78%), sulfonamides (398%), macrolides (120%). There has been a significant decrease in the use of penicillins (-49%) and fluoroquinolones (-26%).

Table 2 –Comparison between 2014 and 2015 reported antimicrobial used in animals in South Africa

Overall antibiotic sales amounts 2014 - 2015: growth promotion + therapeutic use			
Antibiotic Class	**2014**	**2015**	**Variation**
	All animal species (kg)	**All animal species (kg)**	
Growth promoters category	558 614	980 782	76%
Tetracyclines	277 670	262 232	-6%
Sulfonamides (including trimethoprim)	35 117	175 049	398%
Macrolides	57 308	125 899	120%
Penicillins	29 378	15 016	-49%
Aminoglycosides	17 910	1 318	-93%
Pleuromutilins	9 294	8 562	-8%
Fluoroquinolones	6 304	6 907	10%
Other quinolones		6 259	
Orthosomycins		5 376	
Amphenicols	4 236	3 742	-12%
Quinoxalines	4 607		
Orthosomycins	4 480		
Cephalosporins (all generations)	502	922	84%
Lincosamides		433	
Polypeptides	343	347	1%
Total (kg)	**1 005 763**	**1 592 842**	**58%**

Tylosin, a macrolide, is an important drug for both therapy and prophylaxis in animals, but macrolides as a class are also used to treat some human bacterial infections. Resistance in animal bacteria to the macrolide-group has consequences for both animal and human health, the latter when resistance genes or resistant bacteria are transmitted via the food chain. Tylosin is closely associated with the streptogramins and lincosamides by virtue of their mode of action. The most common mechanism of acquired resistance to tylosin (and all other lincosamides and streptogramins) is alteration of the bacterial ribosomal target.

Pleuromutilins have been used in veterinary medicine since the late 1970s, especially against mycoplasma infections in bird and pig species. It has only been used for topical therapy in humans. The carbapenems are not registered for use in animal husbandry in South Africa.

Colistin is included in the 2014 surveillance data, but was prohibited from further use by veterinarians from the beginning of 2016, and will not feature in future annual reports for antibiotic use in animals.

2.4 Human consumption in South Africa compared to global levels

South Africa's antimicrobial use is 21 149 standard units[17] per 1000/population, significantly higher than most other countries in the world however similar to that of other BRICS [18] countries where access to antibiotics has increased through improvements to primary health care facilities and health systems strengthening of the pharmaceutical management system.

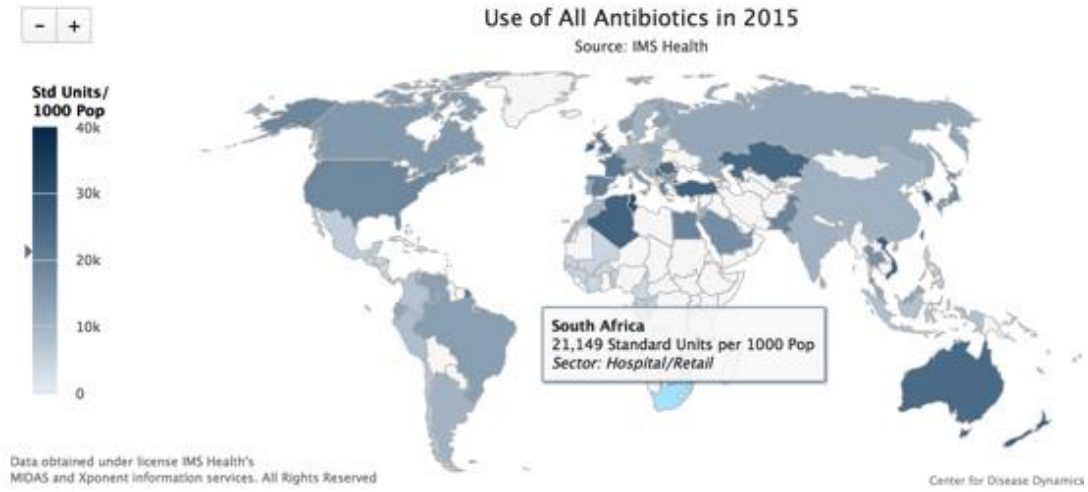
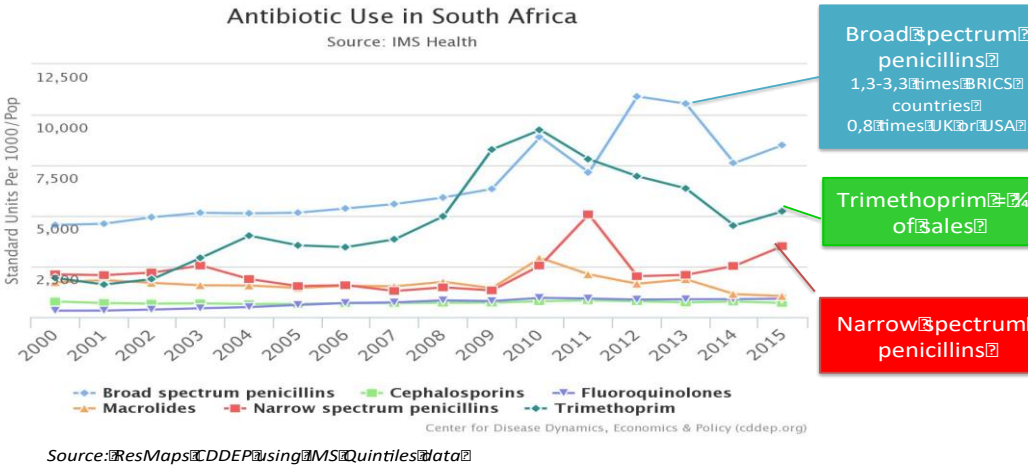


Figure 25 - use of antibiotics across the world 2015 (*IMS Quintiles data as presented by ResMaps (CDDEP). Limitations to the data; see Annexure A for further information***).**

About one quarter of this antimicrobial use is composed of trimethoprim, which is a component of co-trimoxazole and is used as prophylaxis against *Pneumocystis jiroveci* pneumonia in HIV positive people with low CD4 counts (*South Africa has the largest ARV programme in the world*). The consumption of trimethoprim is reducing over time as the antiretroviral therapy program is being rolled out, resulting in less people requiring this prophylaxis. In its place, broad-spectrum penicillin's are showing a steady increase.



Source: ResMaps CDDEP using IMS Quintiles data

Figure 26 - Antibiotics use in South Africa since 2000 – 2015 (*IMS data as supplied by ResMaps (CDDEP) Limitations to the data; see Annexure A for further information)*

[17] Standard units in this instance indicates each unit of medication (e.g. vial, tablet, etc…)

[18] BRICS is the acronym for an association of five major emerging national economies: Brazil, Russia, India, China and South Africa.

In fact broad spectrum penicillin usage is 1.3 to 3.3 times more than usage in other BRICS countries and 0.8 times more than in the United Kingdom (UK) or USA, as can be seen in the below comparison graphs.

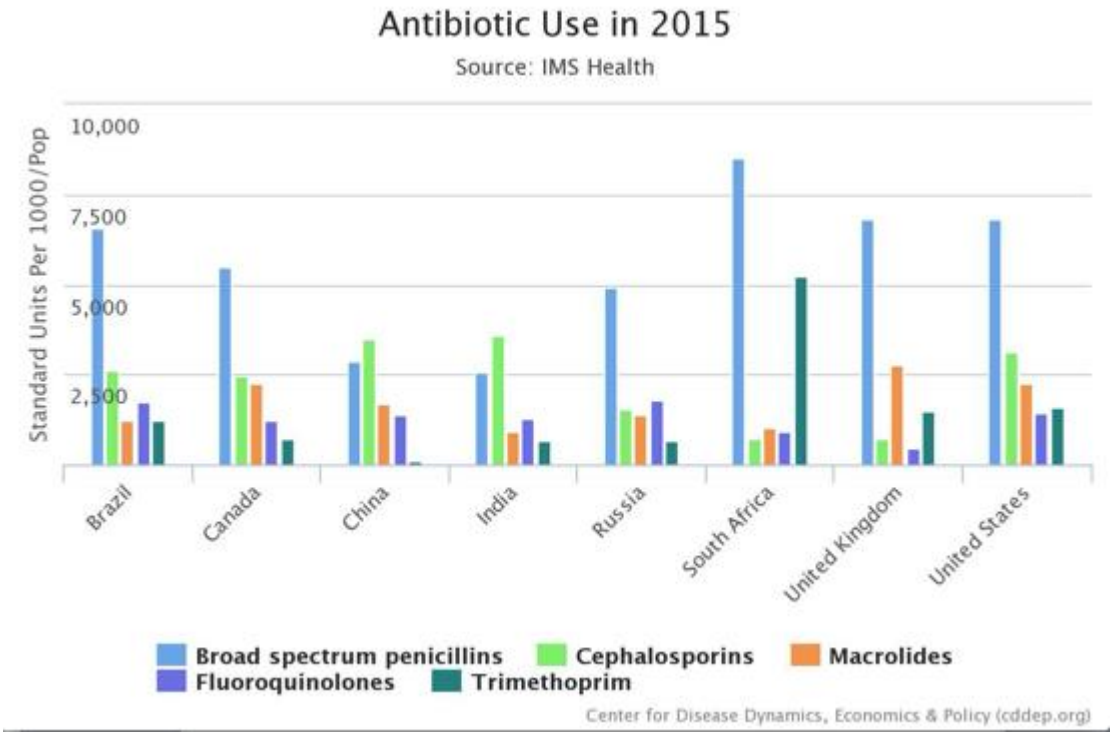


Figure 27 - Antibiotics use comparison of South Africa compared to BRICS, US and UK ((*IMS data as supplied by ResMaps (CDDEP)* *Limitations to the data; see Annexure A for further information)*

2.5 Human consumption in South Africa's public health care sector

Antibiotic consumption was analysed using data extracted from the RSA Pharma database and expressed as defined daily doses (DDDs) per 1000 inhabitants per day.[19] DDDs were taken from the World Health Organisation definitions (available from www.whocc.no/atc_ddd_index/), using the 2018 DDD values.

[19] Guidelines on Implementation of the Antimicrobial Strategy in South Africa: One Health Approach and Governance. National Department of Health, June 2017

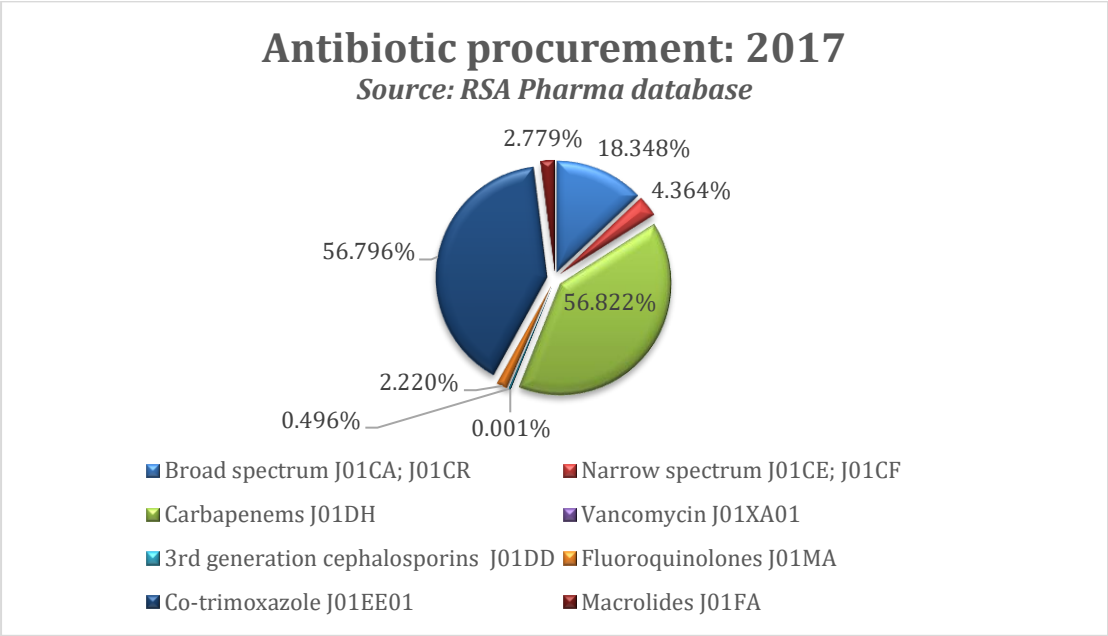


Figure 23 – Antibiotic procurement in South Africa's public health care sector (percentage of DDD per thousand patient days per population)

More than half of the procurement of antibiotics within the J01 ATC class in the public health care sector for 2017 consisted of co-trimoxazole (57%); this value has been decreasing slowly over time (see Figure 24). This decline can possibly be attributed to the large antiretroviral programme run by the public health care system of South Africa reducing the need for co-trimoxazole prophylaxis in this cohort of patients.

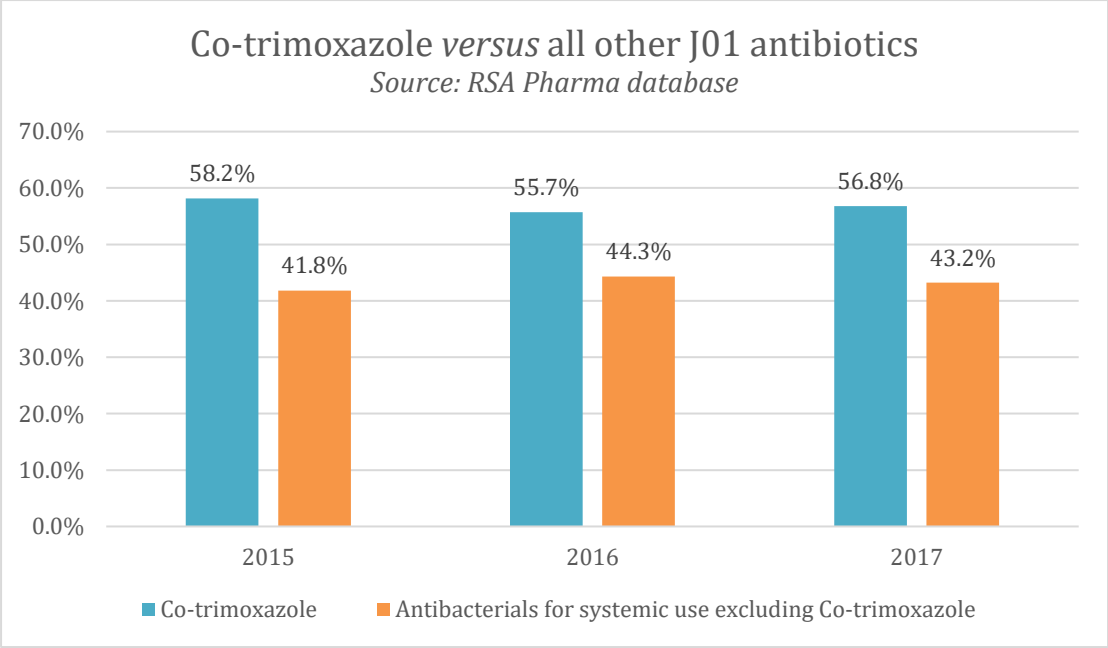


Figure 24: Co-trimoxazole *versus* other antibiotics in South Africa's public health care sector (as a percentage of DDDs per 1000 patient days per population)

The procurement of broad-spectrum penicillin's have remained stable, decreasing slightly from 89.9% in 2016 to 80.8% in 2017.

Concurrently, the ratio of narrow-spectrum penicillins procured compared to broad-spectrum penicillins has increased from 10.2% in 2015 to 19.2% in 2017. Due to the international shortages of narrow spectrum penicillin since 2015, [20] the NDoH has set up alternative procurement methods outside of the normal channels (i.e. through international procurement, requiring approval through SAHPRA). These quantities are reflected in Figure 26. However, complementary procurement outside these channels by the provinces or facilities are not reflected.

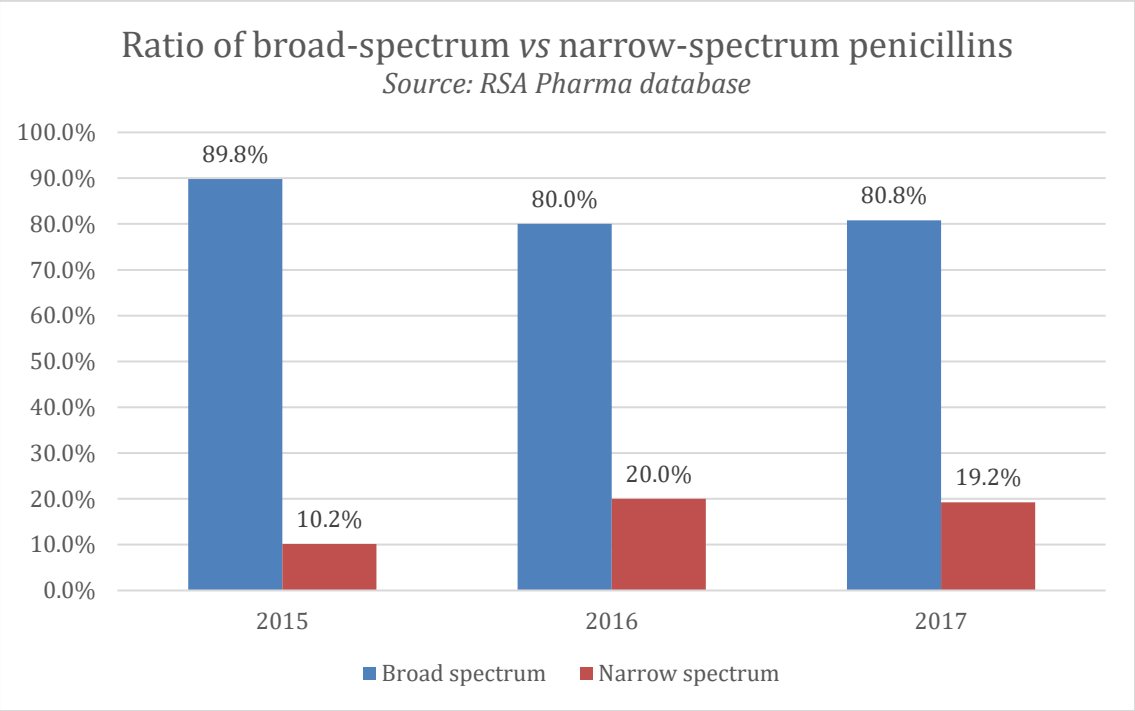


Figure 26: Ratio of broad-spectrum penicillin versus narrow spectrum penicillin use in South Africa's public health care sector (as a percentage of DDDs per 1000 patient days per population)

2.6 Access, Watch and Reserve (AWaRe) Index

The World Health Organisation (WHO) reviewed the antibiotics on the Essential Medicines List (EML) for the 2017 update. The Expert Committee identified options for first- and second-choice antibiotics for each type of infection, and categorised them into 3 groups: Access, Watch and Reserve (see Table 3).[21]

The Access group antibiotics are identified to be first or second choice empirical treatment for 21 common or severe clinical syndromes. These antibiotics are the core set of antibiotics that should always be available. The Watch group antibiotics are considered to have a higher toxicity or resistance potential. The Reserve group are

[20] Notice: Updated recommended therapeutic alternatives for benzathine benzylpenicilln injection; Reference: EDP032018/04. Available from http://www.health.gov.za/index.php/circulars

[21] Sharland M, et. al. Classifying antibiotics in the WHO Essential Medicines List for optimal use – be AWaRE. Lancet. 2018. Vol 18

antibiotics that should be considered as a last resort and prioritised as key targets for antimicrobial stewardship programmes.[21]

Table 3: Antibiotics categorised into Access, Watch and Reserve groups[21]

ACCESS	WATCH	RESERVE
• Amoxicillin • Amoxicillin and clavulanic acid • Ampicillin • Benzathine benzylpenicillin • Benzylpenicillin • Cefalexin, cefazolin • Chloramphenicol • Clindamycin • Cloxacillin • Doxycycline • Gentamicin, amikacin • Metronidazole • Nitrofurantoin • Phenoxymethylpenicillin • Procaine benzylpenicillin • Spectinomycin • Sulfamethoxazole and trimethoprim	• Anti-psuedomonal penicillins with beta-lactamase inhibitor (e.g. piperacillin and tazobactam) • Carbapenems and penems (e.g. imipenem and cilastatin, meropenem) • Third generation cephalosporins with or without beta-lactamase inhibitor (e.g. cefixime, cefotaxime, ceftazidime, ceftriaxone) • Glycopeptides (e.g. teicoplanin, vancomycin) • Macrolides (e.g. azithromycin, clarithromycin, erythromycin) • Quinolones and fluoroquinolones (e.g. ciprofloxacin, levofloxacin, moxifloxacin)	• Aztreonam • Fourth generation cephalosporins (e.g. cefepime) • Fifth generation cephalosporins (e.g. ceftaroline) • Daptomycin • Fosfomycin (intravenous) • Oxazolidinones (e.g. linezolid) • Polymixins (e.g. colistin) • Tigecycline

The ratio of each categorisation of antibiotic was calculated (see Figure 27). The most commonly used antibiotics fall into the Access group (over 90% from 2015 to 2017). The use of the Watch group of antibiotics has also remained steady over the years (from 8% in 2015, 5% in 2016 and 6% in 2017). The use of antibiotics in the Reserve group has been less than 0.1% throughout.

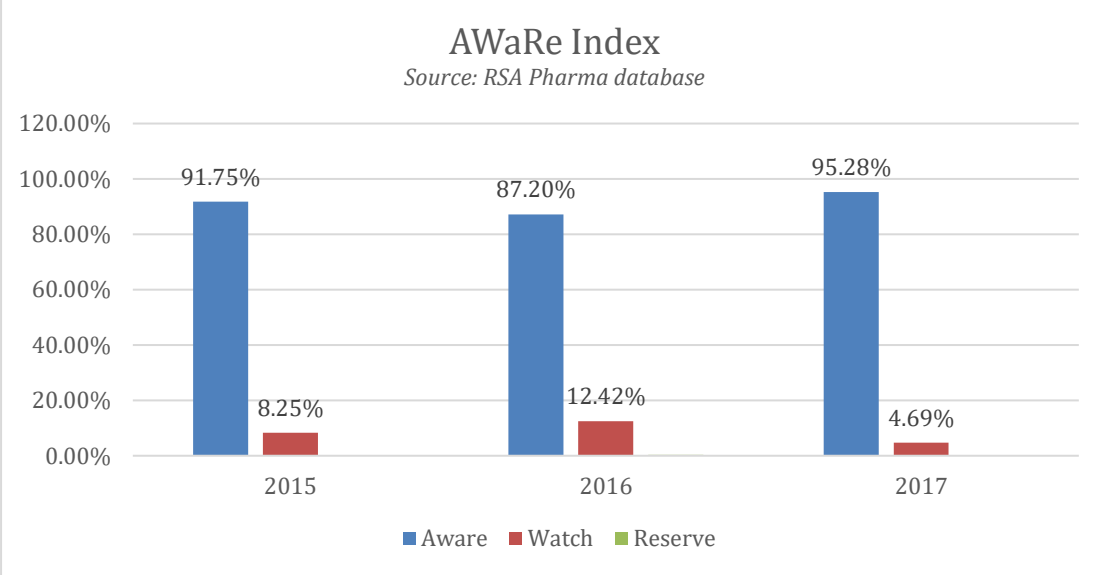


Figure 27: Ratio of Access, Watch and Reserve antibiotics, using the sum of issued product as DDDs

3 Antimicrobial residues from National Chemical Residues Monitoring program in Animal Health

Residue testing in South Africa is conducted under the Directorate of Veterinary Public Health within DAFF, and consists of two national programmes:

- The National Chemical Residue Monitoring Programme (NCRMP) covers meat from abattoirs in South Africa destined for local consumption as well as export to non-EU countries. The maximum residue levels used are based upon Codex and South African legislation.
- The National Chemical Residue Control Programme (NCRCP) is a parallel programme targeting farms and establishments specifically registered for export to the EU. The analyses and maximum residue levels for the NCRCP are based on EU legislation, which includes other prohibited substances such as steroids and growth promoters (e.g. antibiotic and others).

3.1 National Chemical Residue Monitoring Programme

The NCRMP is coordinated and funded by the DAFF under the Meat Safety Act (Act no 40 of 2000). The objectives of the program are to verify that official controls are in place at farms and abattoirs and collate data on chemical residues in food products of animal origin for local and export consumption.

Meat samples of kidneys from beef, mutton/lamb, poultry and port are sampled with 0,014% of the red meat production of the country being sampled and in poultry, 3 in 10 million birds slaughtered. Results represent 1163 samples taken over the period May 2016 – February 2017 tested against 14 antibiotic classes, depending on the species.

Of the total meat samples collected, seventy percent (70,2%) received by the laboratory were analysed (see Figure 28).

Meat products	Beef	Lamb/mutton	Pork	Poultry	Total
Sampled	479	318	199	167	1163
Analysed	329	221	138	129	817
	40%	**27%**	**17%**	**16%**	**70%**

Figure 28 – Number of samples collected by species type and number analysed

Antimicrobial residues were detected in 2.08% (17 out of 817) of samples analysed, which involved penicillins, tetracyclines, sulphonamides and macrolides. Higher detection was observed with tetracyclines in pig kidney samples (7.97%). No antimicrobials were detected in samples from sheep.

Samples	Level of Action (ppb)*	Beef	Lamb/ mutton	Pork	Poultry	Total	%
		n = 329	n=221	n=138	n=129	n=817	
Tetracyclines	600	1	0	10	0	11	1%
Penicillins	50	0	0	1	0	1	0%
Sulphonamides	100	0	0	0	1	1	0%
Macrolides	200	2	0	0	2	4	0%
Total		3	0	11	3	17	
		1%	0%	8%	2%	2%	
**** MRLS are based on the EU legislation, which are almost exactly aligned to Codex guidelines. Where differences exist between Codex and EU, DAFF is aligned to the EU levels***							

Figure 29 – Number of resistant specimens by species type

The contamination of commercially produced meat in South Africa and exposure of consumers to antimicrobial residues from these products appears to be low. It is possible that the results are an underestimation of the situation in the country due to gross under sampling, largely due to a lack of available funds and capacity constraints within the provincial veterinary public health structures to sample, monitor and follow up establishments with non-compliances.

4 Future plans for surveillance

This report presents South Africa's first report on AMR and antimicrobial use surveillance in the country and, whilst it has attempted to cover the data that is available, there are significant areas where additional data is needed to inform better policy and decision making abilities.

The following plans are being put in place for future surveillance reporting:

- A national veterinary surveillance programme for microbiology resistance to antibiotics testing is being developed in collaboration with the NICD through a One Health approach. Bacterial isolates collected via the veterinary food safety surveillance programme will be tested with the same laboratory methodology used by the NICD for human specimens. It will also serve as part of a capacity building exercise for laboratory technologists from the Onderstepoort Veterinary Research Institute who will manage an independent and dedicated veterinary programme in future and continue collaboration with National Reference Laboratory (NRL) at NICD.
- The OIE surveillance programme for quantities of antibiotics used in livestock is an incremental programme that includes more detailed information as Member States make use of the more advanced options for reporting. The objective is to comply with the most advanced reporting option, that includes quantities of antibiotics used in kg per antibiotic class, therapeutic and growth

promotion use, use per animal species/farming enterprise, and the routes of administration of antibiotics.

- The antimicrobial residue monitoring programme will be transitioning to a risk based sampling plan which reflects testing for antimicrobial of interest by species and includes some veterinary compounds that are registered but not previously tested. The maximum residue limits will be amended to the updated Codex Alimentarius Commission guidelines and the program expanded to represent meat production in the country including rural farming operations.
- Human AMR surveillance will continue improving data quality for surveillance purposes and expand surveillance to other specimen types, such as urine.
- Human antimicrobial use data collection systems are being developed to improve the accuracy of use data and provide DDD comparisons between antibiotic classes.

5 Acknowledgements

This report has been compiled by the Surveillance Technical Working Group of the Ministerial Advisory Committee on AMR in collaboration with the National Institute for Communicable Diseases, private sector laboratories, the Department of Agriculture, Forestry and Fisheries, South African Animal Health Association, the World Organisation for Animal Health (OIE) and the World Health Organization (WHO).

ANNEXURE A - Background to the existing surveillance system

- **Design of AMR Surveillance System**

Surveillance for AMR is a key public health priority in South Africa. The NICD is the responsible entity, which coordinates, collates, and analyses AMR surveillance data. Since 2016, this has become a unified process between the public (NHLS) and private sector laboratories where previously these reports were released individually by the South African Society for Clinical Microbiology (SASCM).

There are two tiers of surveillance:

1. Laboratory based antimicrobial resistance surveillance (LARS) which collects laboratory and clinical data from a selection of sentinel sites consisting primarily of academic and large referral laboratories in the public sector;
2. Electronic surveillance (ES) which uses data from the NHLS Laboratory Information System as well as from major private laboratories, reported in the form of resistance heat maps.

In addition, data was included from sentinel sites from public sector hospitals as listed: Charlotte Maxeke Johannesburg Academic Hospital, Chris Hani Baragwanath Hospital, Dr George Mukhari Hospital , Frere Hospital, Grey's Hospital , Groote Schuur Hospital, Helen Joseph Hospital, Inkosi Albert Luthuli Central Hospital, King Edward VIII Hospital, Livingstone Hospital, Mahatma Gandhi Hospital, Nelson Mandela Academic Hospital/Mthatha Tertiary RK Khan Hospital, Steve Biko Academic Hospital, Tygerberg Hospital, and Universitas Hospital.

For the analysis of ESKAPE pathogens, results of antimicrobial susceptibility testing (AST) were interpreted in accordance with the Clinical and Laboratory Standards Institute (CLSI) 2016 guidelines and were categorised as susceptible (S) and non-susceptible [which includes intermediate (I) and resistant (R)]. All laboratories have an External Quality Assurance program for quality checks and all private laboratories and the majority of NHLS laboratories are SANAS (South African National Accreditation Society) accredited.

Data were omitted for those hospitals that tested less than 30 ESKAPE pathogens for a particular antimicrobial agent.

- **Case definitions used:**

Patients with blood stream infections who cultured ESKAPE organisms were included. Once the data was uploaded into the central data warehouse a linking algorithm was used to create unique patient identifiers, which enabled the de-duplication of results within a 21-day patient episode (the start of the 21 days being defined as the first occurrence of resistance to a given antibiotic for a given pathogen for that unique patient). This same case definition was implemented for public and private laboratory groups.

The results of this report should be interpreted with caution. A number of factors might have introduced bias, resulting in either an overestimation or underestimation of AST reporting.

- **Limitations to the data source**

Some key limitations to the data include:

- ◊ Lack of standardization in the collection of specimens at health facilities. This includes insufficient information provided by healthcare professionals requesting tests, of the indication for blood culture. This in turn means that the organisms isolated cannot be linked to a primary source of infection (e.g. respiratory tract, urinary tract, central nervous system, etc.) and cannot be differentiated as either hospital or community acquired.
- ◊ Limited access to microbiology laboratory services in some health facilities (either due to logistic constraints or financial constraints), resulting in limited blood cultures being requested.
- ◊ The syndromic approaches to certain diseases whereby health professionals treat empirically without ordering diagnostics tests as first line. If specimens are collected they may only be collected if empiric treatment fails, and may result in an over-representation of resistant pathogens.
- ◊ Differences in testing methodologies and data capture between laboratories in the public sector and between the public and private sector.
- ◊ Data may have been incomplete due to missing cases not captured on the LIS or non-standardised coding of ESKAPE pathogens and antimicrobial agents at diagnostic laboratories.
- ◊ For some sentinel hospitals, not all ESKAPE pathogens may have been represented. This may be due to ESKAPE pathogens not being isolated at a particular sentinel hospital in 2016.

• World Health Organisation Global Antibiotic Surveillance System (WHO GLASS)

South Africa, through the NICD as the national coordinating centre, also participates in the WHO global surveillance system on AMR, called the WHO Global Antibiotic Surveillance System (GLASS). WHO GLASS is reliant upon countries to conduct their own national surveillance and then report it to a central database which allows international collaboration and sharing of progress on AMR situation.

One of the aims of GLASS is to promote national surveillance systems with harmonized global standards. Data sets required by GLASS are requested with a more comprehensive approach to surveillance standards.

To fulfil GLASS requirements, tier 1 laboratory-based surveillance is used for AMR data from GERMS [22] , and reported for two organisms: *Staphylococcus aureus* and *Streptococcus pneumonia* for a 5 year period from blood specimens. *S. aureus* surveillance was performed at 5 sentinel sites in two provinces and *S. pneumonia*

[22] GERMS-SA is a nationwide network of clinical microbiology laboratories (in the public and private sector) which participate in an active laboratory-based surveillance programme for pathogens of public health importance. Available at http://www.nicd.ac.za/index.php/germs-sa/

surveillance is conducted nationally. Both organisms were part of an enhanced surveillance program where by additional information was obtained about the patients including demographic, clinical, laboratory, origin of the specimen (hospital and community), source of bacteraemia, clinical signs and symptoms and outcome data.

The additional information is important for better planning of treatment approaches in different patient groups and determining the origination of MRSA. The additional information for *S. pneumonia* was important to allow the follow up of the immunisation program implementation phases, including the determination of the impact of the pneumococcal conjugate vaccine. These data reflect resistance of *S. pneumoniae* amongst blood isolates and not from throat, nose or ear specimens where antibiotic treatment is not recommended.

- **Human Antimicrobial Use Data Sources**

There are three existing sources of antimicrobial use data in South Africa. Each of the data sources currently available have some minor gaps in the completeness of information to allow a comprehensive view of antimicrobial use to be formulated:

- South African Revenue Services (SARS) import data, which contains the volume of antimicrobials (in kgs) and rand value imported into the country (as either the final product or as the Active Pharmaceutical Ingredient). This data does not distinguish between antimicrobials for use in humans or animals due to the current limitations on the tariff coding system. They also exclude any antimicrobials produced in South Africa and those procured in terms of Section 21 of the Medicines and Related Substance Act 101 of 1965.
- Quintiles IMS/IQVIA (formally known as IMS Health) contains standard units per 1000 population of antimicrobials supplied by the pharmaceutical manufacturers in the country to both the public and private sectors. It provides insights into the usage patterns by antimicrobial class for both sectors, and tracks usage from previous years as far back as 2000. However, the public sector data only represents 4 provinces and therefore is insufficient to analyse for the purposes of evaluating usage.
- The RSA Pharma database, and in the future the ABC analysis of this data, reflects procurement data from the public sector. It consists of deliveries data to facilities from the relevant suppliers against contracts awarded by the NDoH since 2015. This data reflects provincial usage patterns but does not distinguish between hospital and community levels, and excludes the non-contract purchases (buy-outs) and Section 21 purchases made by provinces and institutions.

- **Animal Antimicrobial Use Data**

A process was started by the OIE in 2012 that required all Member States to provide antibiotic use data on an annual basis. The first year of reporting was 2013 in which South Africa could not comply with. At the request of DAFF, the South African Animal Health Association SAAHA, which represents 80% of all pharmaceutical companies that provide antimicrobials in the animal health domain, agreed to provide use data in volumes per antibiotic class for 2014.

The data was submitted to the OIE, which included it in its annual report that was published on the OIE website in August 2017. Collection of the 2015 data is now in progress as the OIE surveillance programme reports 2 years retrospectively. An underestimation of 20% was calculated based on the number of companies that are not members of SAAHA, including a number of compounding pharmacies.