Antimicrobial Resistance State of the Nation

Marc Mendelson

Chair, Ministerial Advisory Committee on AMR

World Antibiotic Awareness week, 2022


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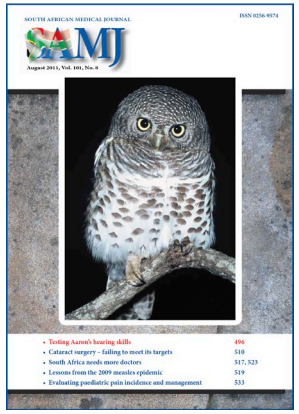
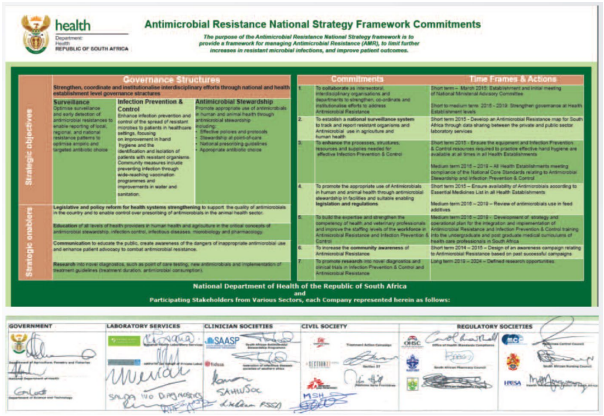
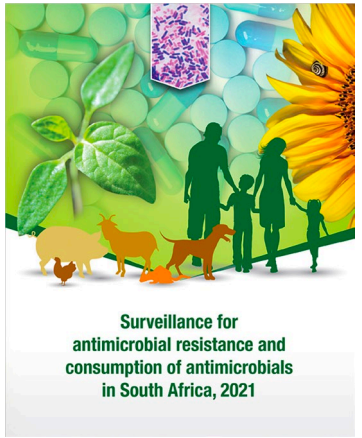




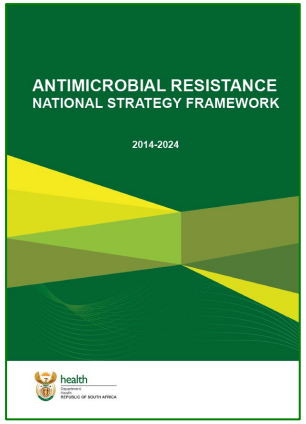


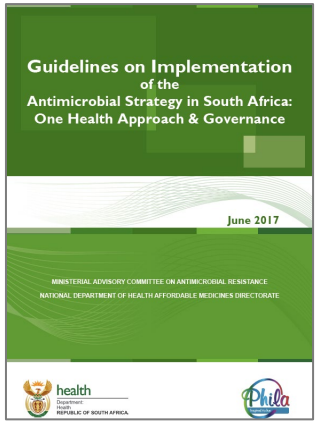
Global Antibiotic Resistance Partnership

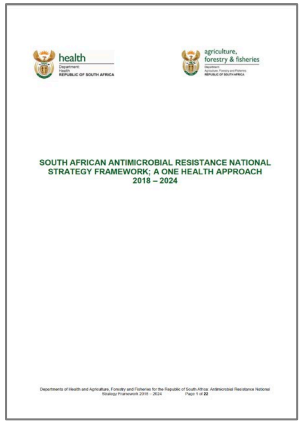
MAC AMR

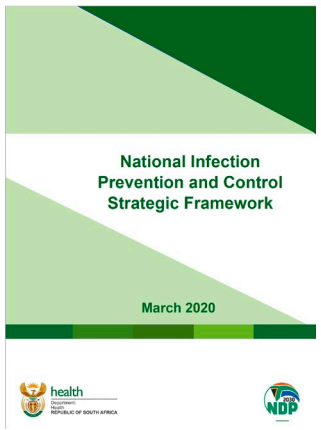
SAASP
SOUTH AFRICAN ANTIBIOTIC STEWARDSHIP PROGRAMME

2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 | 2022



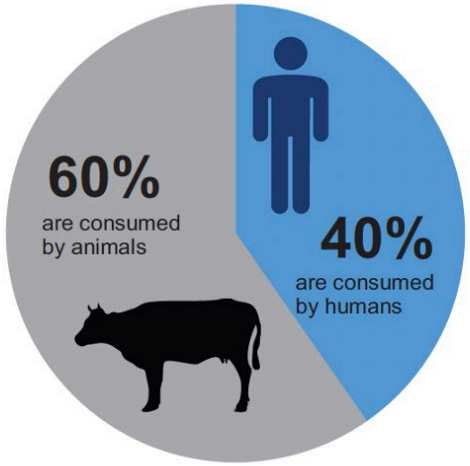


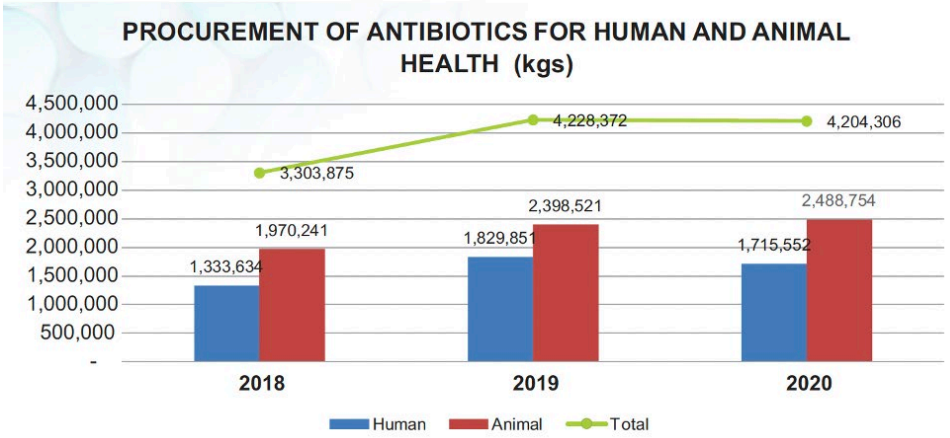




Procurement of antibiotics for use in humans and animals

https://www.knowledgehub.org.za/elibrary/surveillance-antimicrobial-resistance-and-consumption-antimicrobials-south-africa-2021





	HUMAN TONNAGE PROCURED			ANIMAL TONNAGE PROCURED			
	2018	2019	2020	2018	2019	2020	
Antimicrobial							
Broad spectrum	542,308	456,803	541,056	6,933	583,367	553,209	
Narrow spectrum	81,872	145,658	263,930	323	13	6	
TOTAL penicillins	**624,180**	**602,461**	**804,987**	**7,256**	**583,381**	**553,214**	
Streptomycins	375	585	425	1,638	46	8	
Tetracyclines	39,552	54,875	57,546	946,715	564,765	782,615	
Amphenicols (Chloramphenicol in humans)	11,788	382	3,837	257	33	116	
Erythromycin	13,090	7,810	6,376	32	2	1	
Macrolides	52,403	49,003	63,807	67,510	93,432	105,278	
Cephalosporins	202	142,667	6,295	2,045	2,394	48	
*Sulfamethoxazole + Trimethoprim**	11,245	914	18,331	1,252	0	1	
*Fluoroquinolones**	890	29,240	15	-	-	-	
Aminoglycosides	984	9,185	1,470	30,615	1	9	
Other beta-lactams	62	325	4	226,243	161,485	273,232	
Other antibiotics	578,864	932,405	752,459	686,678	992,984	774,232	*
TOTAL	**1,333,634**	**1,829,851**	**1,715,552**	**1,970,241**	**2,398,521**	**2,488,754**	

* A complete data set for sulfamethoxazole + trimethoprim and fluoroquinolones were not available at time of publication, and these amounts as they stand are expected to be a great underestimation of actual usage

* Polypeptides and ionophores

Procurement of antibiotics for human health in South Africa based on the WHO AWaRe Index (country target 60% Access)

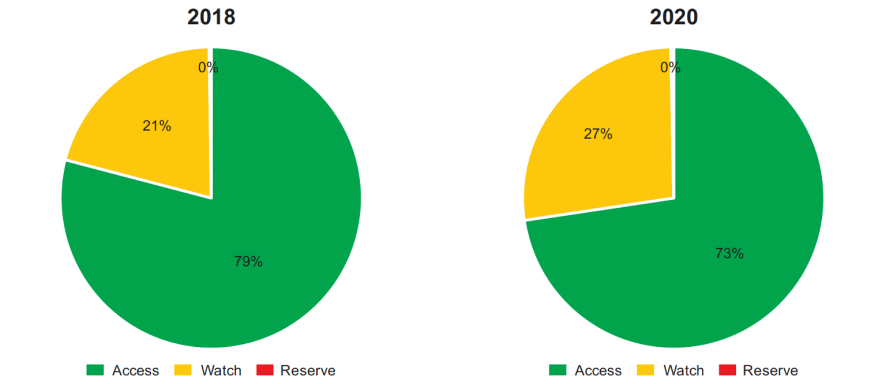
https://www.knowledgehub.org.za/elibrary/surveillance-antimicrobial-resistance-and-consumption-antimicrobials-south-africa-2021

Access	Watch	Reserve
First or second choice empirical treatment. These are the core set of antibiotics that should always be available as they offer the best therapeutic value, minimising potential for resistance	Considered to have a higher toxicity or resistance potential, as either first or second choice antibiotics. These are only indicated for a limited number of disorders and require monitoring due to increased risk of AMR.	These should be considered as a last resort for highly selected patients. These antibiotics are prioritised as key targets for antimicrobial stewardship programmes and require close monitoring.

Some examples include:
(The complete lists can be accessed from: https://list.essentialmeds.org/antibiotics/access)

Access	Watch	Reserve
• Amoxicillin • Amoxicillin + clavulanic acid • Ampicillin • Benzathine benzylpenicillin • Cefalexin • Chloramphenicol • Clindamycin • Cloxacillin • Doxycycline • Flucloxacillin • Gentamicin • Metronidazole • Sulfamethoxazole + trimethoprim	• Azithromycin • Cefaclor • Cefepime • Cefotaxime • Cefoxitin • Ceftazidime • Ceftriaxone • Ciprofloxacin • Clarithromycin • Doripenem • Erythromycin • Kanamycin • Levofloxacin • Neomycin • Piperacillin-tazobactam • Vancomycin	• Colistin* • Fosfomycin (injection) • Linezolid* • Tigecycline* • Cefiderocol • Ceftazidime + avibactam* • Ceftolozane+tazobactam • Daptomycin* • Faropenem • Imipenem + cilastatin + relebactam • Meropenem + vaborbactam • Minocycline* • Polymixin* • Tedizolid

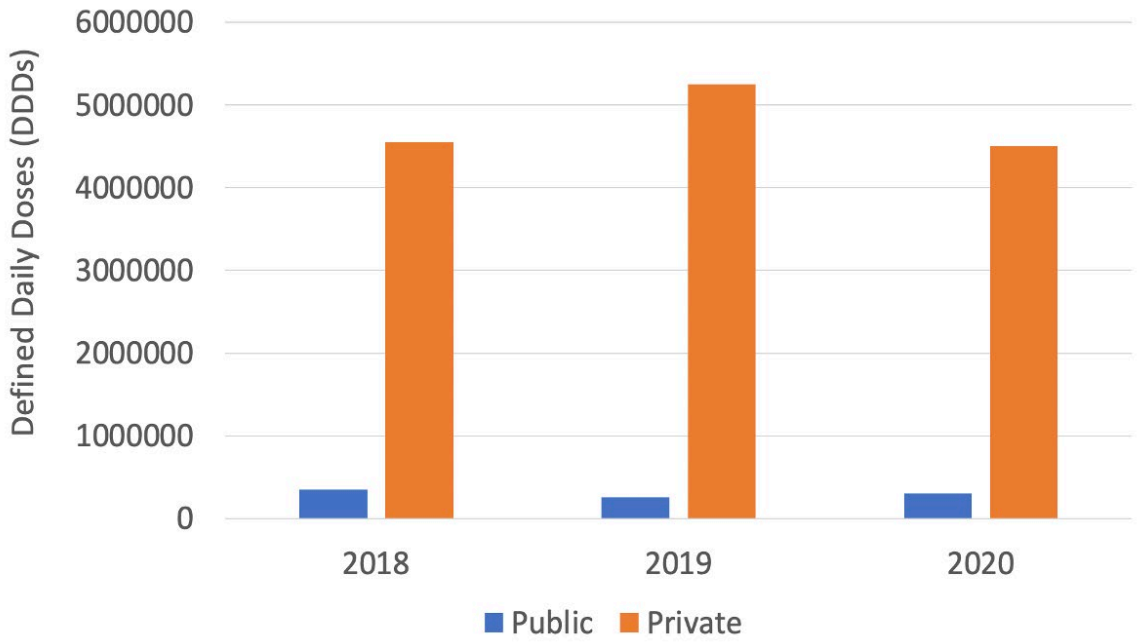
PUBLIC SECTOR – AWaRe PROCUREMENT

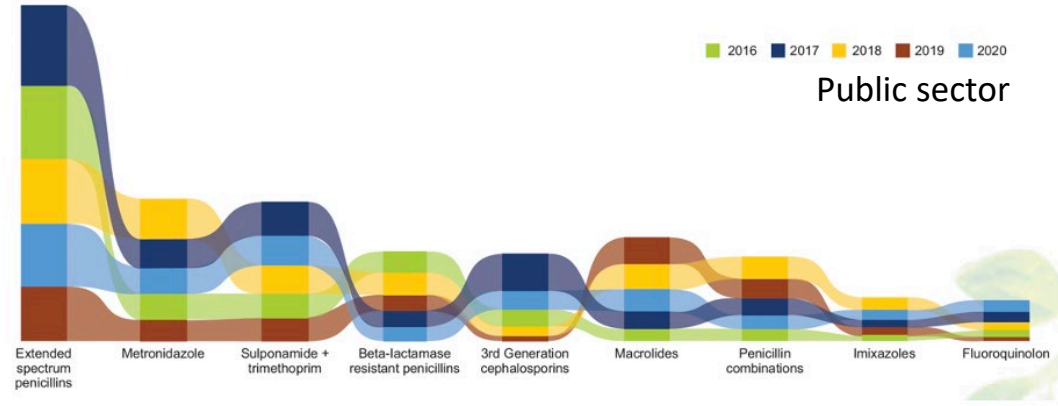


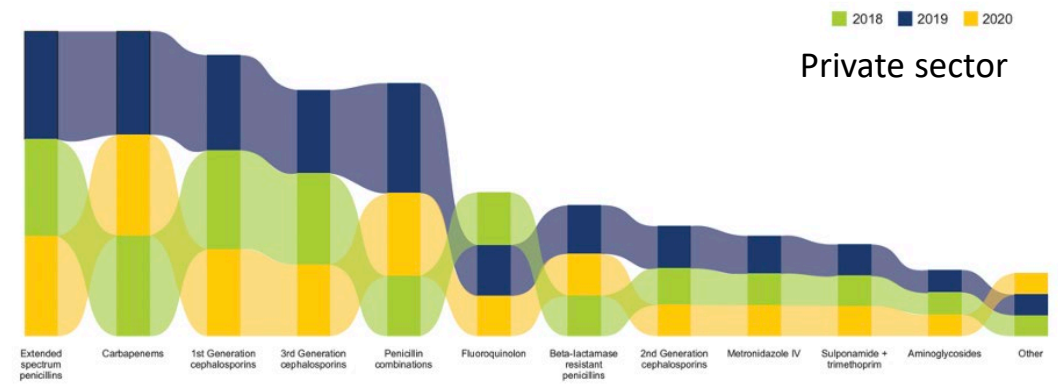
PRIVATE SECTOR – AWaRe PROCUREMENT

Procurement of antibiotics in South Africa based on sector of the health system

https://www.knowledgehub.org.za/elibrary/surveillance-antimicrobial-resistance-and-consumption-antimicrobials-south-africa-2021







Surveillance for antimicrobial resistance and consumption of antimicrobials in South Africa, 2021

Klebsiella pneumoniae

70% BSIs are nonsusceptible to 3rd generation cephalosporins
40% BSIs are nonsusceptible to 1st generation carbapenems

Staphylococcus aureus

17% BSIs are nonsusceptible to cloxacillin (MRSA)

Escherichia coli

25% BSIs nonsuceptible to 3rd generation cephalosporins
33% BSIs are nonsusceptible to ciprofloxacin

Pseudomonas aeruginosa

33% BSIs are nonsusceptible to carbapenems
17% BSIs is nonsusceptible to 3rd and 4th generation cephalosporinds and to piperacillin-tazobactam

Acinetobacter baumannii

80% BSI are resistant to carbapenems

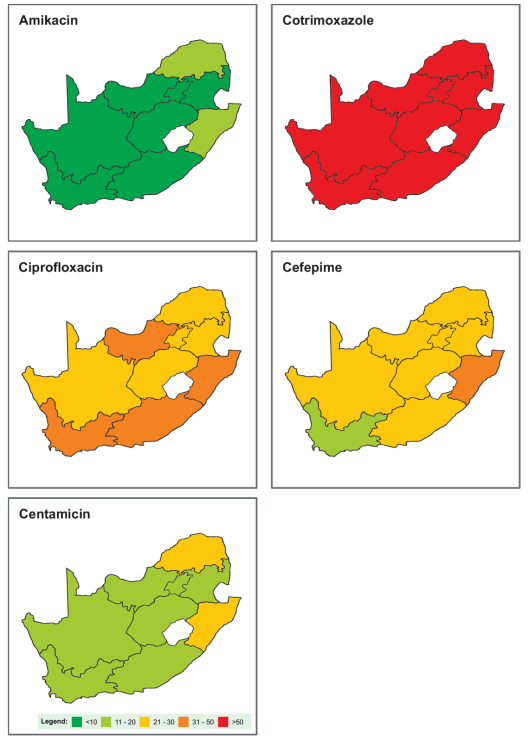
Enterococcus faecium

1.3% BSIs are resistant to vancomycin

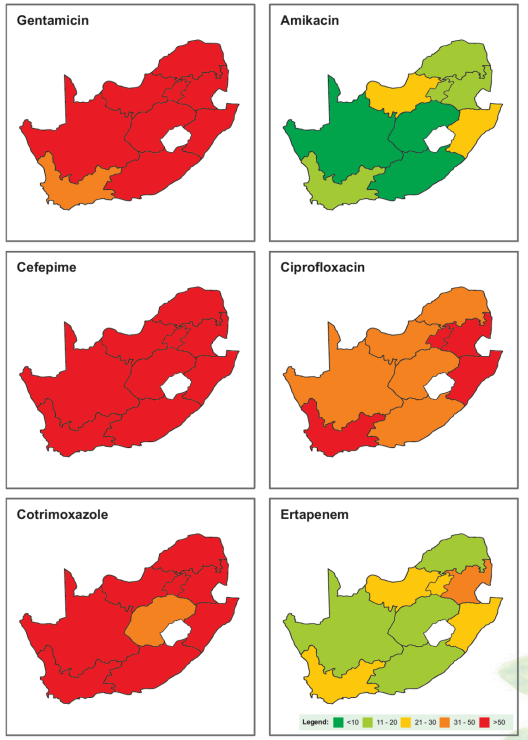
Enterococcus faecalis

1.1% BSIs are resistant to vancomycin

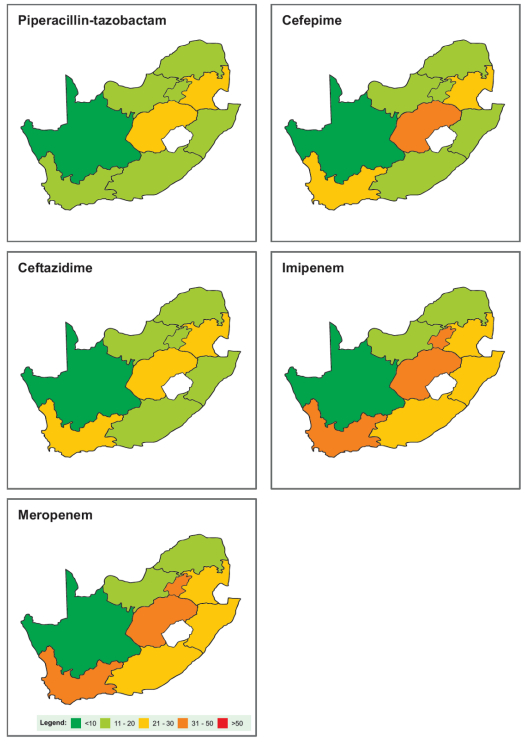
Escherichia coli



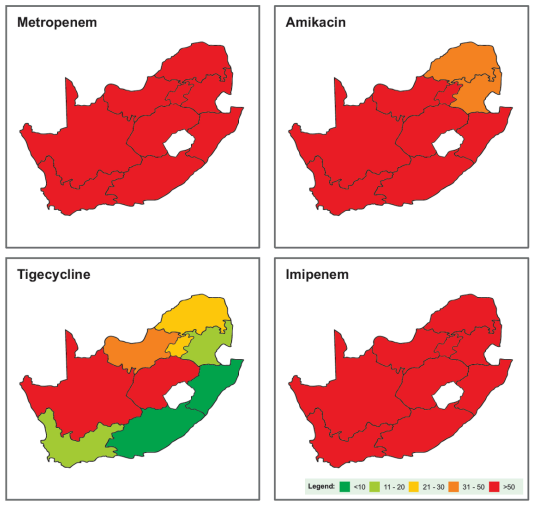
Klebsiella pneumoniae



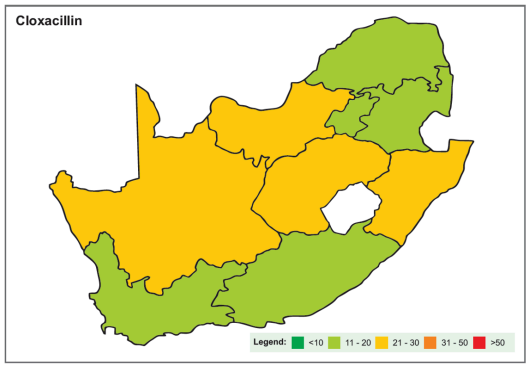
Pseudomanas aeruginosa



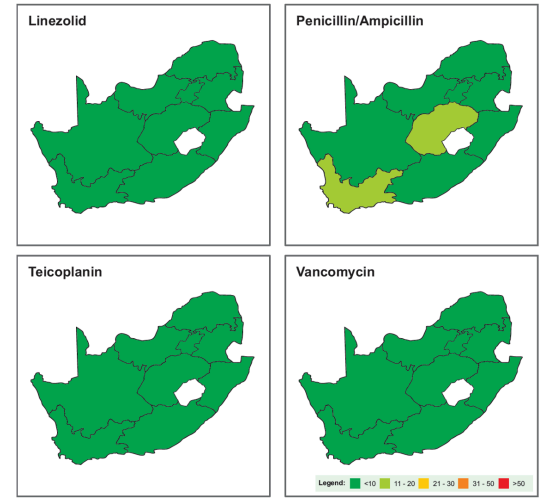
Acinetobacter baumanii



Staphylococcus aureus



Enterococcus faecalis



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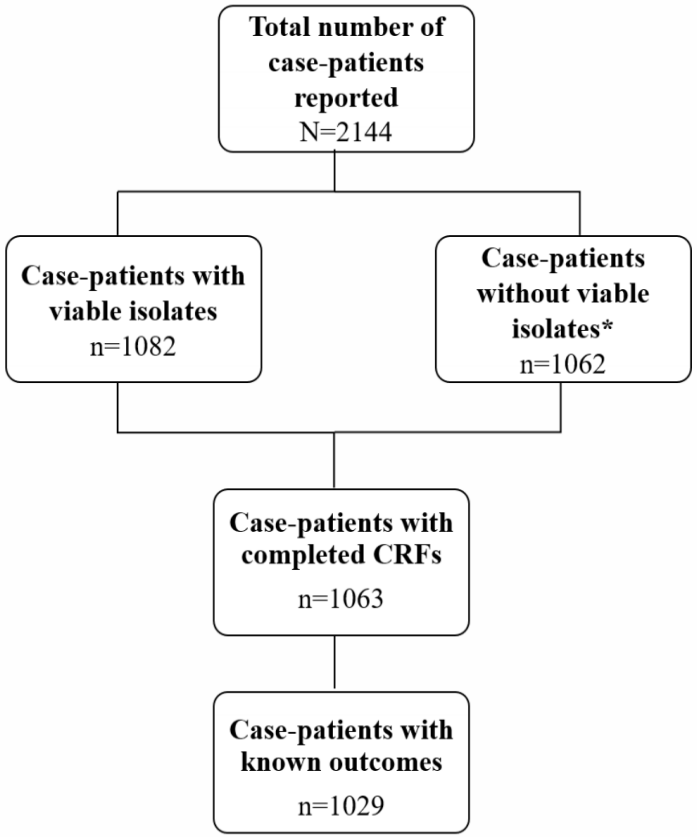
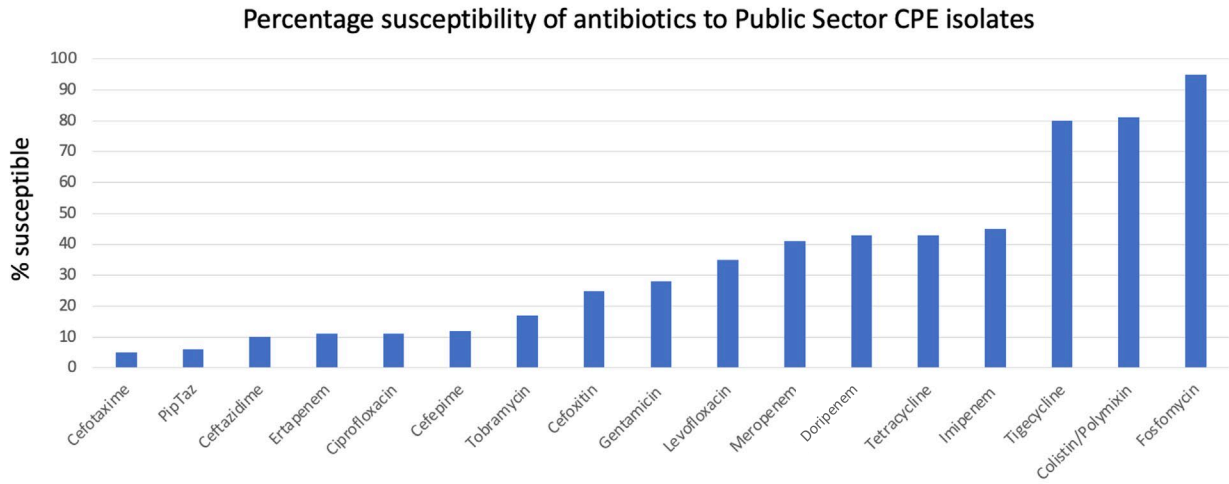
CRE surveillance in South Africa's public sector tertiary academic hospitals, 2019-2020

Perovic et al. 32nd ECCMID: 23-26 April 2022. Abstract number 01010



CRE in the Public Sector (n=1029)	
Median age	35 years
In-hospital mortality	36.6%
Age ≥60 years	aOR 4.53, [95%CI 2.21-9.28], p<0.01
Comorbidities	aOR 1.72, [1.17-2.52], p = 0.006
Altered mental state	aOR 5.36, [3.21-8.92], p<0.001
Previous antibiotic use	aOR 1.88, [1.27-2.77], p = 0.001
Bacteria	*K. pneumoniae* (80%); *E. cloacae* (6%); *S. marcesans* (5%); *E. coli* (4%)
Number of carbapenemase genes	1 (84.6%); 2 (3.5%); 0 (11.9%)
Genes	OXA-48-like (76.8%); NDM (21.1%); VIM (1.3%); GES (0.4%; KPC (0.4%)



Reserve list antibiotics available in South Africa

https://www.who.int/publications/i/item/2021-aware-classification

Registered in South Africa		Not registered	
Used in public sector	**Used in private sector**	**Access via section 21**	**Unavailable**
Linezolid Tigecycline	Linezolid Tigecycline Ceftazidime-avibactam **ZAR 24,667 ($1,372)*** Ceftolozane-tazobactam **ZAR 27,999 ($1,557)*** Daptomycin	Aztreonam Colistin Polymixin	Carumonam Cefiderocol – **ZAR 110,534 ($6149)*** Ceftaroline Ceftobiprole Dalbavancin Dalfopristin + quinupristin Eravacycline Faropenem Iclaprim Imipenem + Cilastin + relebactam Meropenem + vaborbactam Minocycline Oritavancin Plazomicin Tedizolid

*Cost for 7 days of treatment – costs courtesy of Mrs Vanishree Naicker, UCT Pharmacy as of 30th Sept 2022

The increasing reality of Difficult-to-Treat Resistant (DTR) Gram-negative infections in South Africa

Image courtesy of Dr Maritz Laubscher

Acinetobacter baumannii complex (ACIBC)

Comments

Tissue, right knee.

Antibiotic/Culture:	ACIBC
Trimethoprim-sulfamethoxazole	R
Ciprofloxacin	R
Ceftazidime	R
Cefepime	R
Gentamicin	R
Tobramycin	R
Amikacin	R
Piperacillin/tazobactam	R
Imipenem	R
Meropenem	R
Tigecycline	I

S - Sensitive ; I - Intermediate ; R - Resistant

Organism	*Acinetobacter baumannii complex*
Antibiotic	Colistin
MIC	>64 ug/mL
MIC interpretation	Resistant

Epidemiologic Shift in Candidemia Driven by *Candida auris*, South Africa, 2016–2017

Erika van Schalkwyk,[2] Ruth S. Mpembe, Juno Thomas, Liliwe Shuping, Husna Ismail, Warren Lowman, Alan S. Karstaedt, Vindana Chibabhai, Jeannette Wadula, Theunis Avenant, Angeliki Messina, Chetna N. Govind, Krishnee Moodley, Halima Dawood, Praksha Ramjathan, Nelesh P. Govender,[2] for GERMS-SA

Candida auris is an invasive healthcare-associated fungal pathogen. Cases of candidemia, defined as illness in patients with *Candida* cultured from blood, were detected through national laboratory-based surveillance in South Africa during 2016–2017. We identified viable isolates by using mass spectrometry and sequencing. Among 6,669 cases (5,876 with species identification) from 269 hospitals, 794 (14%) were caused by *C. auris*. The incidence risk for all candidemia at 133 hospitals was 83.8 (95% CI 81.2–86.4) cases/100,000 admissions. Prior systemic antifungal drug therapy was associated with a 40% increased adjusted odds of *C. auris* fungemia compared with bloodstream infection caused by other *Candida* species (adjusted odds ratio 1.4 [95% CI 0.8–2.3]). The crude in-hospital case-fatality ratio did not differ between *Candida* species and was 45% for *C. auris* candidemia, compared with 43% for non–*C. auris* candidemia. *C. auris* has caused a major epidemiologic shift in candidemia in South Africa.

Since 2009, when the first case of *Candida auris* infection was identified in South Africa, the number of laboratory-confirmed cases has increased exponentially (*1*). This multidrug-resistant fungal pathogen emerged worldwide, appearing almost simultaneously on 6 continents, causing invasive disease and protracted healthcare-associated outbreaks (*2*–*5*). The reported crude case-fatality ratio among patients with invasive *C. auris* infections is high, although the attributable mortality rate has not been determined (*3*,*6*). *C. auris* persists on surfaces, is transmitted among patients in the healthcare environment, forms biofilms, and resists routinely used environmental cleaning agents (*7*–*10*). *Candida* spp. are a common cause of bloodstream infections and were responsible for 13% (95% CI 6%–26%) of healthcare-associated bloodstream infections according to a 2015 US point-prevalence survey (*11*). *C. parapsilosis* was the dominant species causing candidemia according to a national survey in South Africa conducted during 2009–2010 (*12*). Patients at risk for candidemia in general are the critically ill (especially premature neonates) and those with serious underlying illnesses (e.g., diabetes mellitus and hematologic malignancies), prior or prolonged exposure to broad-spectrum antimicrobial drugs, and invasive medical and surgical interventions (*13*). Previously described characteristics associated with candidemia among adults in South Africa included abdominal surgery, trauma, diabetes mellitus, cancer, and HIV infection (*14*). *C. auris* is thought to occupy a similar niche in the healthcare environment as *C. parapsilosis* because both organisms colonize human skin and adhere to healthcare surfaces and devices. Clinical risk factors for *C. auris* infection would be expected to be similar to those for *C. parapsilosis* infection, but these factors are largely reported from several small case series. Risk factors for *C. auris* candidemia (compared with other species) among patients admitted to 27 intensive care

Author affiliations: National Institute for Communicable Diseases, Johannesburg, South Africa (E. van Schalkwyk, R.S. Mpembe, J. Thomas, L. Shuping, H. Ismail, N.P. Govender); Vermaak & Partners–Pathcare Pathologists, Johannesburg (W. Lowman); Wits Donald Gordon Medical Centre, Johannesburg (W. Lowman); University of the Witwatersrand, Johannesburg (W. Lowman, A.S. Karstaedt, V. Chibabhai, J. Wadula, A. Messina, N.P. Govender); University of Pretoria and Kalafong Provincial Tertiary Hospital, Pretoria, South Africa (T. Avenant); Netcare Hospitals Ltd, Johannesburg (A. Messina); Lancet Laboratories, Durban, South Africa (C.N. Govind, K. Moodley); University of KwaZulu-Natal, Durban (C.N. Govind, H. Dawood, P. Ramjathan); Grey's Hospital, Pietermaritzburg, South Africa (H. Dawood); National Health Laboratory Service, Johannesburg (V. Chibabhai, J. Wadula, P. Ramjathan)

DOI: https://doi.org/10.3201/eid2509.190040

[1]Preliminary results from this study were presented at the Federation of Infectious Diseases Societies of Southern Africa (FIDSSA) conference (oral abstract no. 8,382); November 9–11 2017; Cape Town, South Africa.

[2]These authors contributed equally to this article.

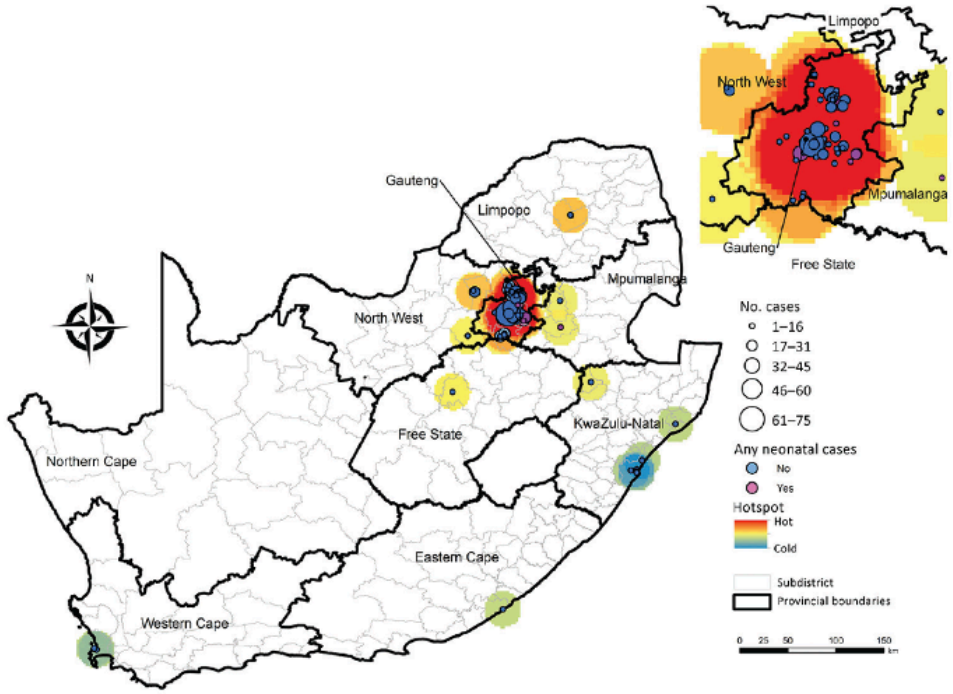


Figure 3. Location and number of 741 *Candida auris* candidemia cases at 79 hospitals, including 7 hospitals with neonatal cases, South Africa, 2016–2017. Location data were missing for 53 cases.

Despite increasing procurement of antibiotics in animals, there has been a reduction in use, 2014-2020

Overall Amount: Growth Promotion + Therapeutic Use	2014	2016	2020
Antimicrobial Class	All animal species (kg)	All animal species (kg)	All animal species (kg)
Aminoglycosides	14 925	18 848	14 078
Amphenicols	3 530	2 958	4 114
Arsenicals	0	0	0
Cephalosporins (all generations)	418	826	297
1-2 gen. cephalosporins	408	248	250
3-4 gen cephalosporins	10	578	47
Fluoroquinolones	0	6 859	2 822
Glycopeptides	0	0	0
Glycophospholipids	0	303	277
Lincosamides	0	159	0
Macrolides	47 757	31 879	15 929
Nitrofurans	0	0	0
Orthosomycins	3 733	1 788	1040
Other quinolones	3 453	0	10 385
Penicillins	16 737	10 055	16 393
Pleuromutilins	7 745	4 481	3 187
Polypeptides	295	140	78
Quinoxalines	3 839	0	31 383
Streptogramins	0	533	0
Sulfonamides (including trimethoprim)	39 264	28 708	35 289
Tetracyclines	231 392	158 519	194 836
Others	469 037	159 451	77 151
Total kg	842 125	425 507	407 428

- Tonnage procured ǂ quantities sold and finally used
- Decline in animal use = phasing out AGPs since 2019
- Multinational pharmaceuticals voluntarily started phasing out claims for prophylaxis and AGP in package inserts
- Registrar of Stock Remedies and SAAHA agreed to remove all claims for antibiotics of prophylaxis and AGP, effectively eliminating medically important antibiotics for growth promotion in South Africa

Limited National Animal ABR Surveillance Reporting

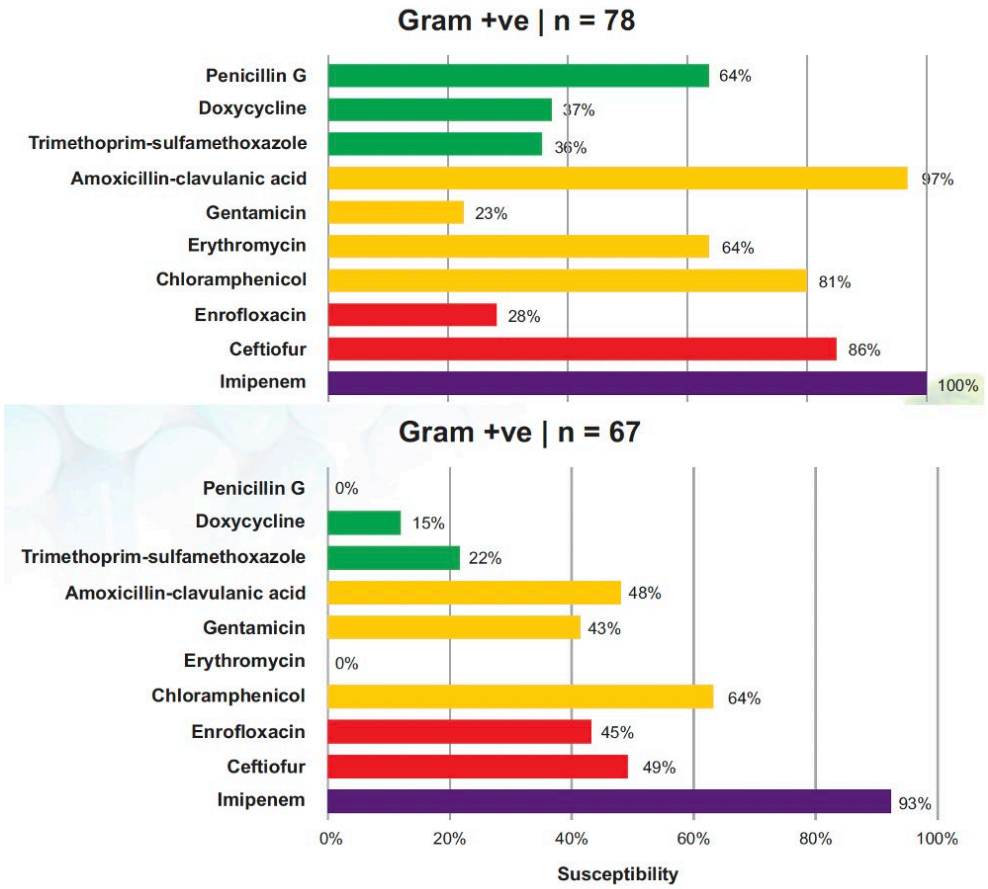
https://www.knowledgehub.org.za/elibrary/surveillance-antimicrobial-resistance-and-consumption-antimicrobials-south-africa-2021

	Bovine Respiratory Tract Infections			
	Mannheimia haemolytica	*Pasteurella multocida*	*Histophilus somni*	*Salmonella phimurium*
Penicillin	1/20(5%)		1/21(5%)	2/2
Ampicillin	1/20(5%)		1/21(5%)	
Amoxycillin				
Amoxycillin/ Clavulanic acid				
Cephalosporin 1st gen				2/2
Cephalosporin 2nd gen				2/2
Cephalosporin 3rd gen				
Tetracycline	2/20(10%)	18/32(56%)	7/21(33%)	
Fluoroquinolones				
Erythromycin	6/20(30%)	17/32(53%)	3/21(14%)	2/2
Clindamycin/ lincomycin	20/20(100%)	32/32(100%)	14/21(67%)	2/2
Gentamicin		4/32(13%)	2/21(10%)	2/2
Amikacin	3/20(15%)	12/32(38%)	7/21(33%)	2/2
Kanamycin	3/20(15%)	5/32(16%)	13/21(62%)	2/2
Florfenicol	1/20(5%)	1/32(3%)		
Sulfamethoxazole/ trimethoprim	2/20(10%)	2/32(6%)	3/21(14%)	
Tilmicosin	1/20(5%)	13/32(41%)	2/21(10%)	
Tildipirosin		12/32(38%)	2/21(10%)	
Gamithromycin		12/32(38%)	1/21(5%)	
Ceftiofur				
Cefquinome				

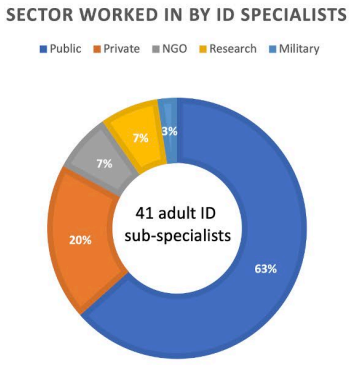
ABR in horses from a single hospital in WC

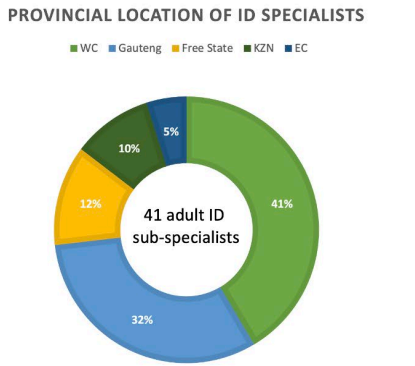
https://www.knowledgehub.org.za/elibrary/surveillance-antimicrobial-resistance-and-consumption-antimicrobials-south-africa-2021

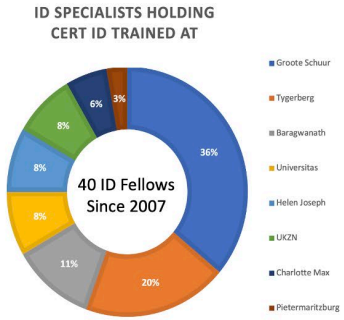
Category	Definitions
Category A - Avoid	• Antibiotics in this category are not authorised as veterinary medicines in South Africa • Should not be used in food-producing animals • May be given to companion animals under exceptional circumstances
Category B - Restrict	• Antibiotics in this category are critically important in human medicine and use in animals should be restricted to mitigate the risk to public health • Should be considered only when there are no antibiotics in Categories C or D that could be clinically effective • Use should be based on antimicrobial susceptibility testing, wherever possible
Category C - Caution	• For antibiotics in this category there are alternatives in human medicine • For some veterinary indications, there are no alternatives belonging to Category D • Should be considered only when there are no antibiotics in Category D that could be clinically effective
Category D - Prudence	• Should be used as first line treatments, whenever possible • As always, should be used prudently, only when medically needed

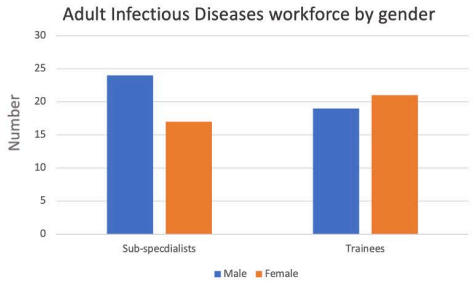


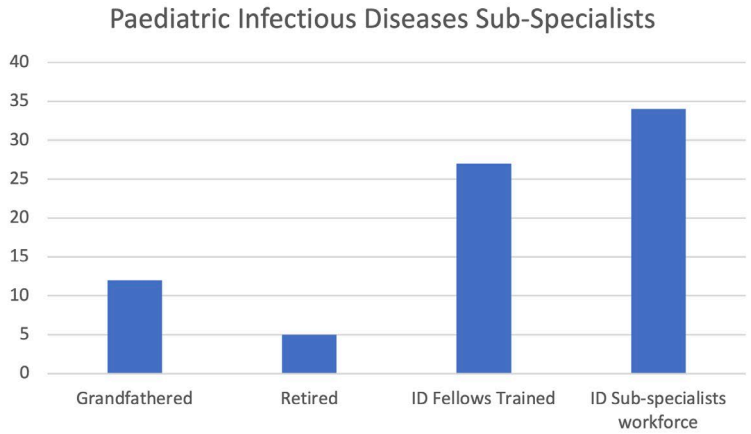
The Infectious Diseases Specialist Human Resources Gap in South Africa

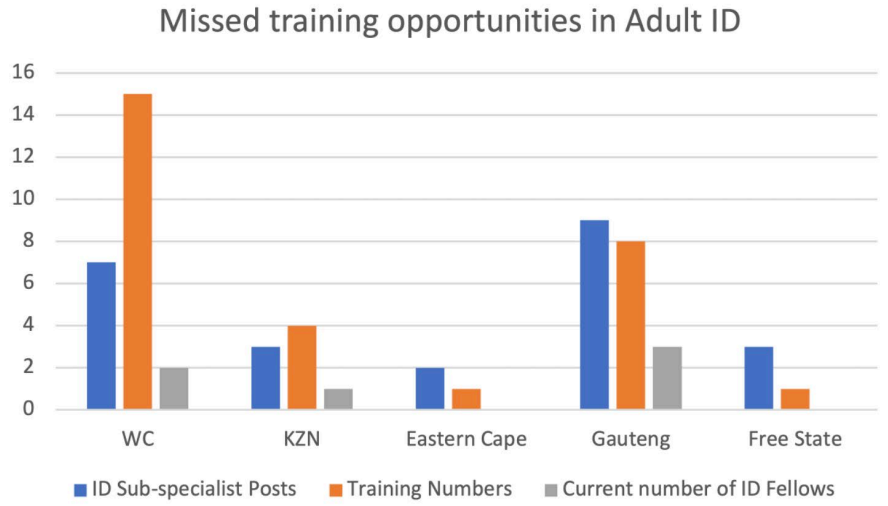


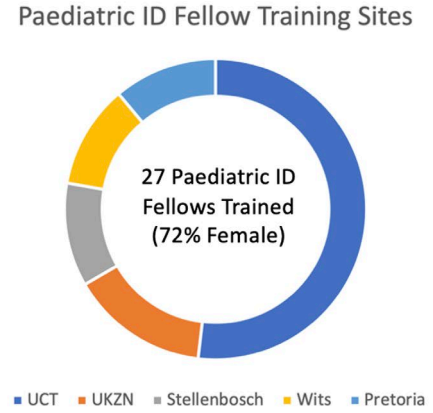






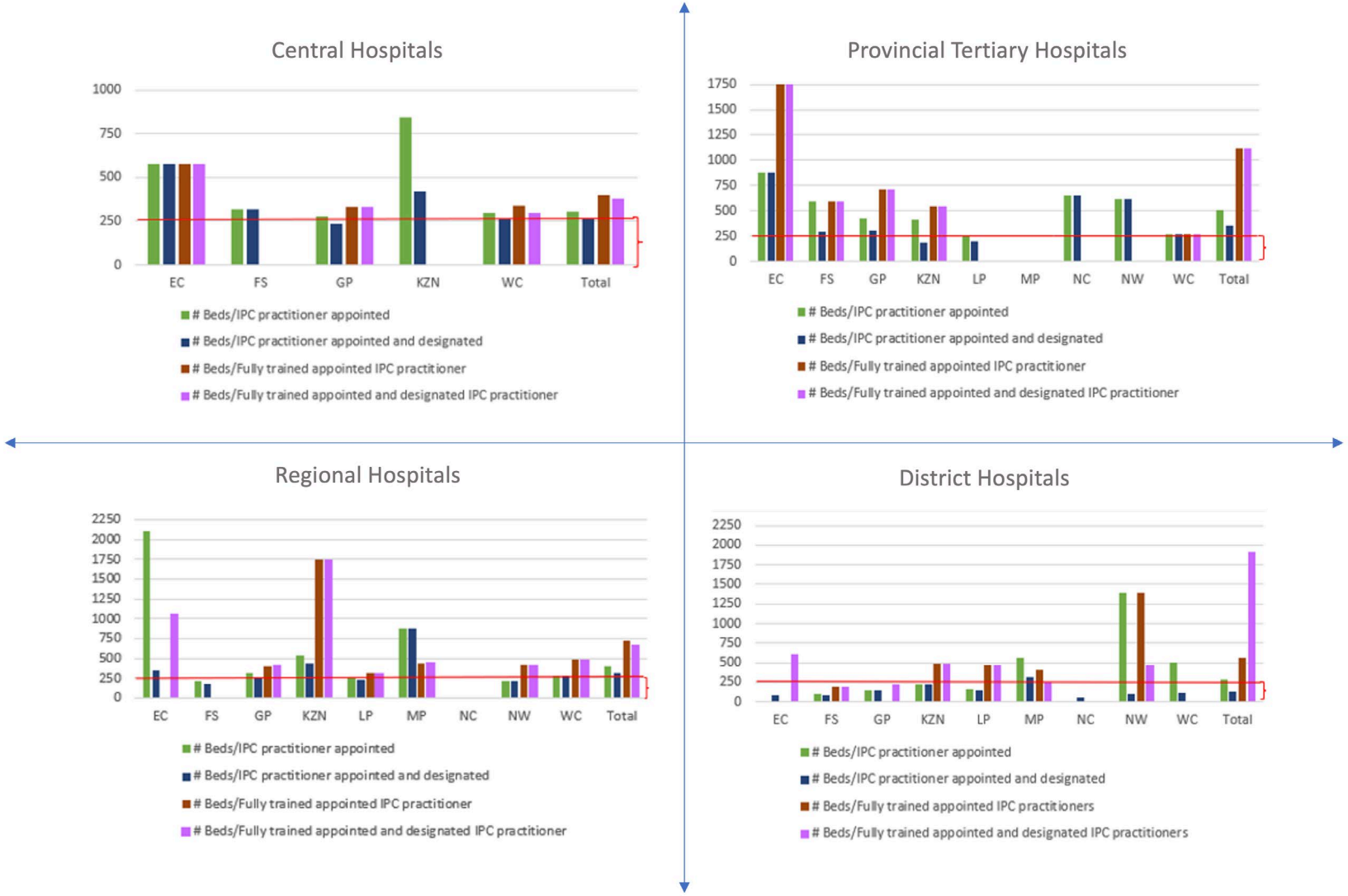






The Infection Prevention Control Human Resources Gap in the South African Public Sector

Data courtesy of Sr Yolanda van Zyl



Lack of Resilience of South Africa's AMR Response

- The commitments made by stakeholders at the Ministerial Summit to combat AMR in 2014 have largely not been met
- South Africa's National Action Plan remains unfunded
- The workforce required to deliver the national AMR implementation plan (& pandemic preparedness) is deficient across the board
- Our response in human health remains too hospital-based and has not strengthened a community response
- Surveillance of AMR in food production systems (risking food security) and in companion animals, is weak
- The MAC-AMR members are acting as advisors and supporters of implementation – requires de-coupling

Thank you to the countless healthcare professionals in South Africa who support the country’s response to AMR on a daily basis