

Antimicrobial Resistance

Dr Nosisa Sipambo - Infectious Diseases



Contents

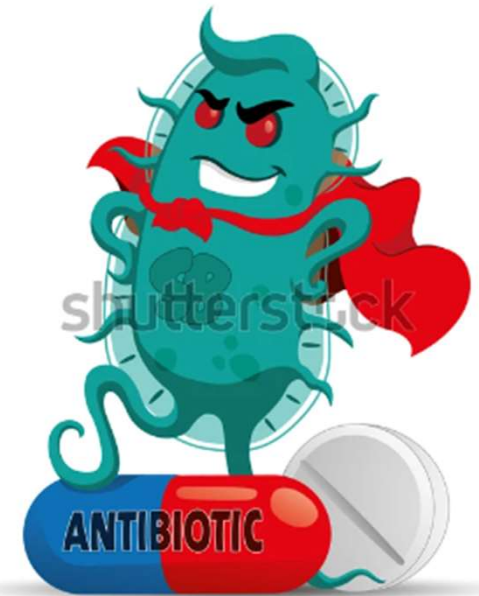
Epidemiology of AMR

- South African picture

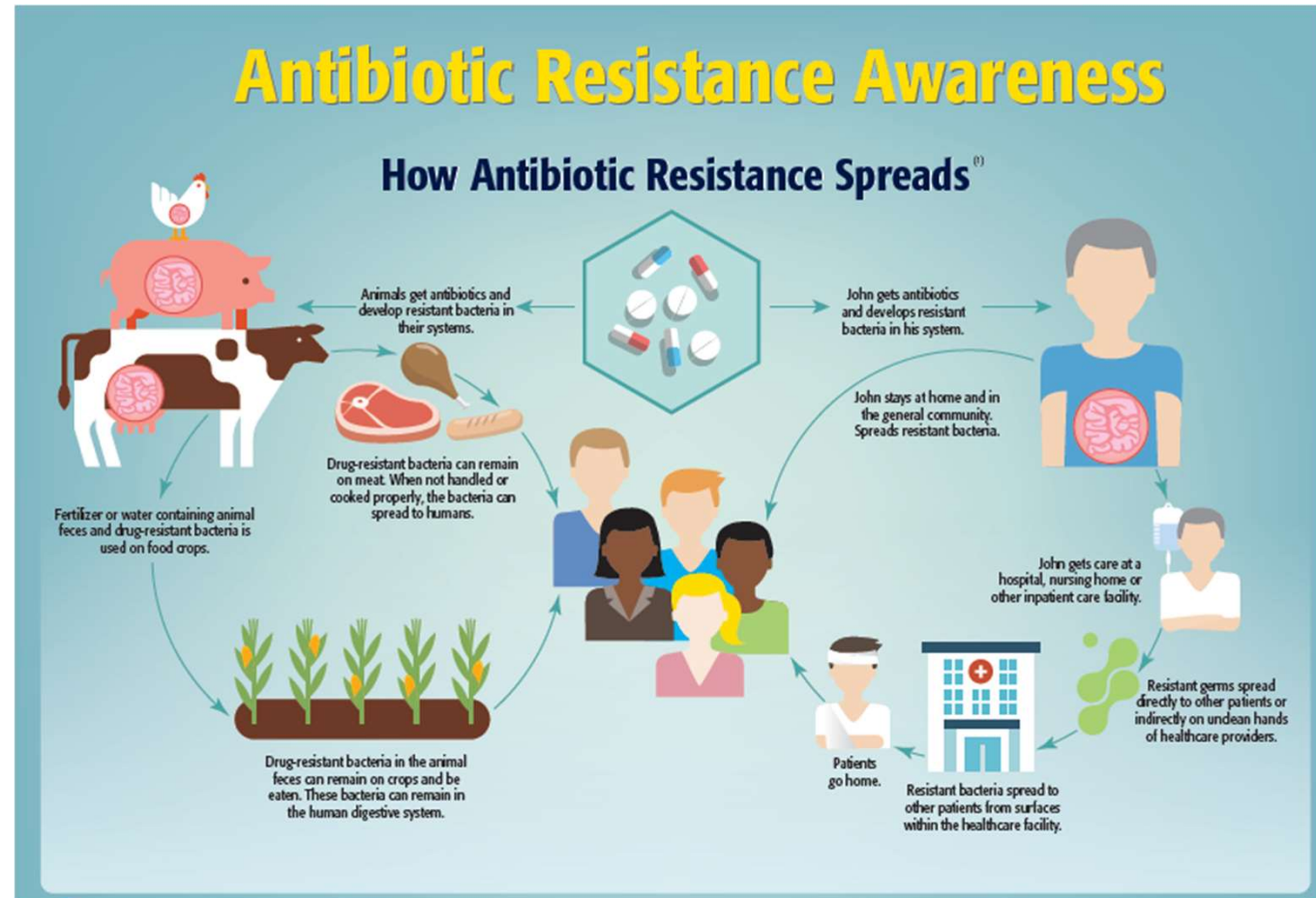
Stock outs

- Amoxicillin-clavulanic acid (Augmentin)
- Piperacillin-tazobactam (Tazocin)
- Penicillin

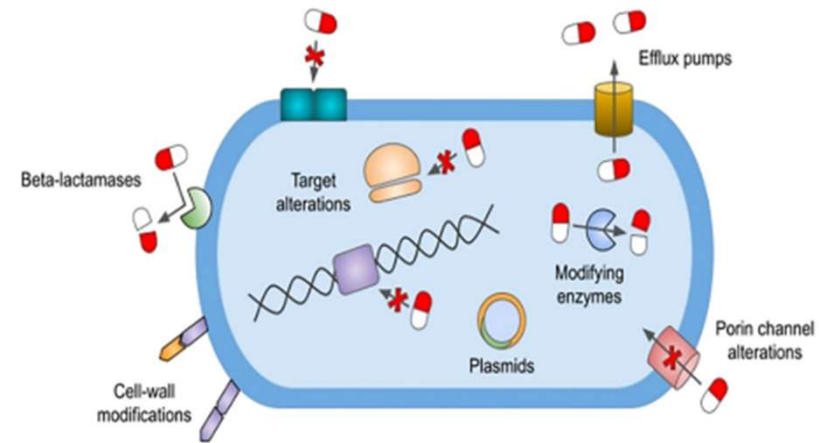
Solutions



One Health



Mechanisms of resistance



Risk factors

- High antibiotic consumption
 - Host factors which increase antibiotic consumption
- Use of broad spectrum antibiotics
- Hospitalisation/health-care association
 - Use of invasive devices/catheters
- Travel or geographic
 - Travel from area with high prevalence of drug resistant MDROs
 - E.g. artemisinin resistance in the Far East

Epidemiology

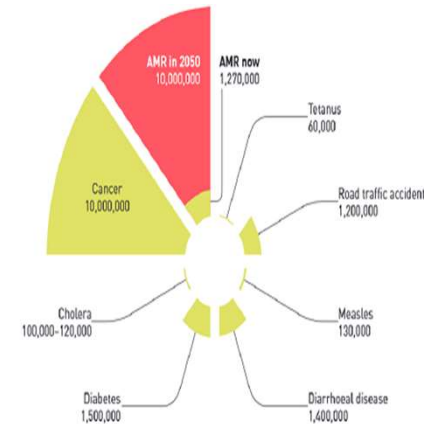
Global

4.95 million deaths associated with bacterial AMR
 1.27 million deaths attributable to AMR

Highest western sub-Saharan Africa at 27.3 deaths per 100 000 population

LRTI 1,5 million AMR associated deaths

World Bank: \$1 trillion additional Healthcare costs by 2050



Predicted mortality from AMR compared to common causes of death today (adapted from O'Neill 2016; Murray et al. 2022)

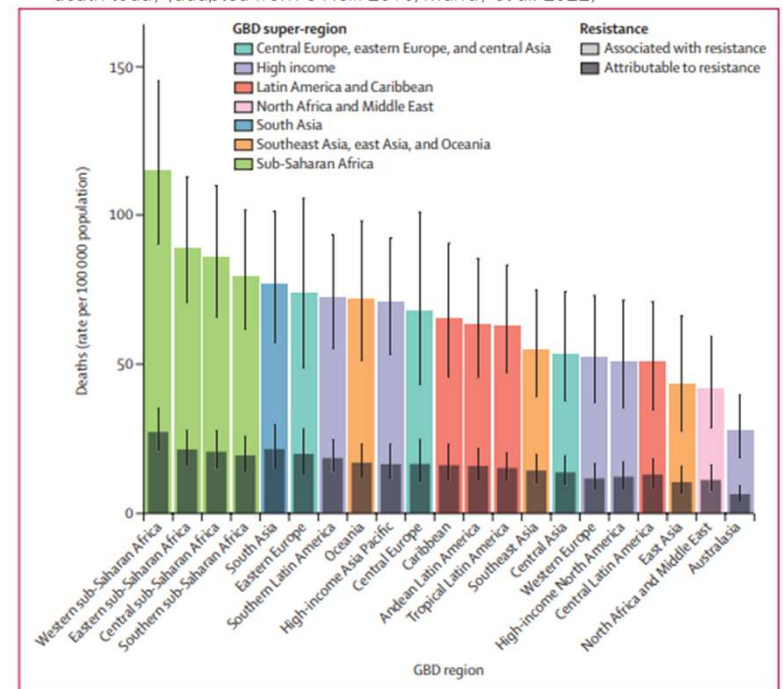


Figure 2: All-age rate of deaths attributable to and associated with bacterial antimicrobial resistance by GBD region, 2019

Epidemiology

South Africa

E
S
K
A
P
E

Klebsiella pneumoniae

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

Staphylococcus aureus

Staphylococcus aureus
17% BSIs are nonsusceptible to cloxacillin (MRSA)

Escherichia coli

25% BSIs nonsusceptible 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 cephalosporins 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

*BSI - Blood Stream Isolate



Surveillance for Antimicrobial Resistance and Consumption of Antibiotics in South Africa 2018-2022

March 2024
National Department of Health



WHO AWaRe



ACCESS	WATCH	RESERVE
<ul style="list-style-type: none">• 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	<ul style="list-style-type: none">• Anti-pseudomonal 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)	<ul style="list-style-type: none">• 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

Figure 19: Total antibiotic consumption and procurement results for South Africa by sector in DDD/100,000 population.

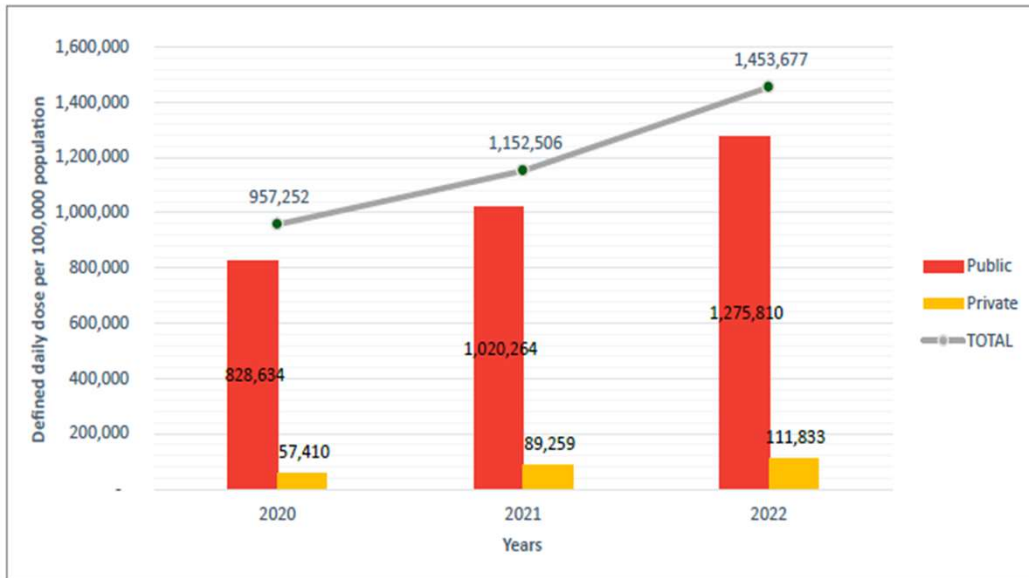
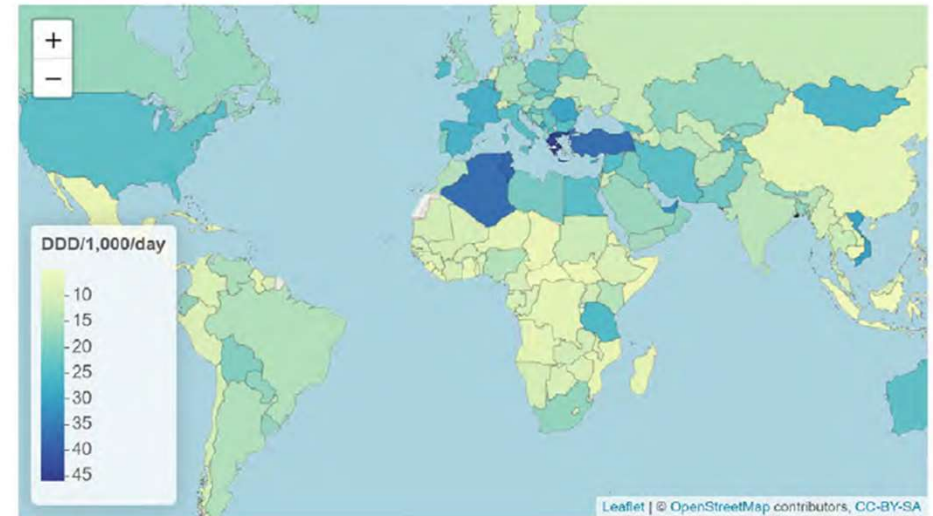


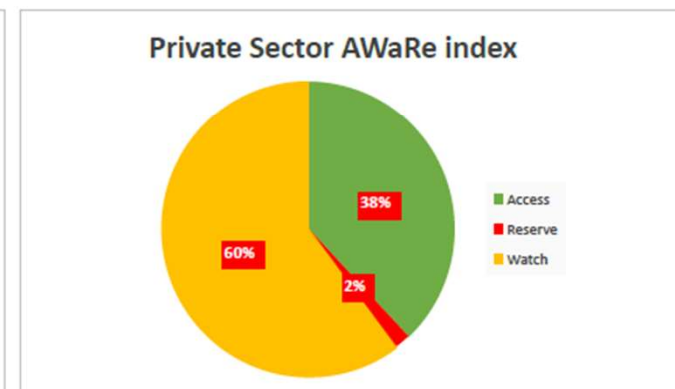
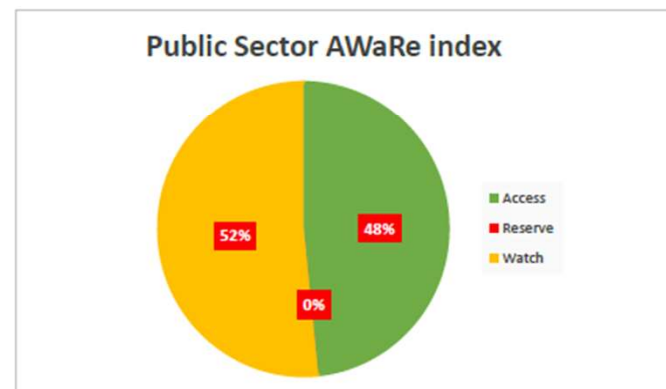
Figure 18: Global antibiotic consumption and usage in humans, 2000 to 2018: a spatial modelling study. *Lancet Planetary Health* 2021.



If you use these modelled estimates on antibiotic consumption and antibiotic usage, please cite this publication as a reference: Browne AJ, Chipeta MG, Haines-Woodhouse G, et al. Global antibiotic consumption and usage in humans, 2000 to 2018: a spatial modelling study. *Lancet Planetary Health* 2021



Figure 24: AWaRe index by sector (2018 - 2022 combined)

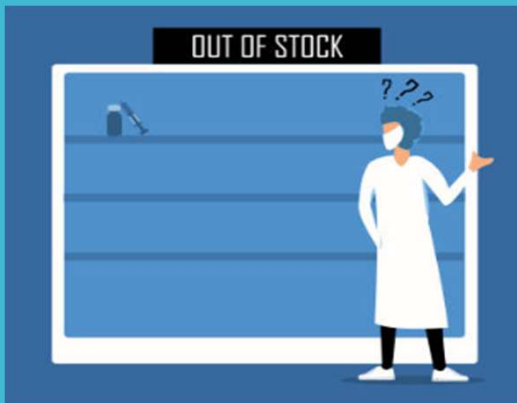


Use of antibiotics

Stock outs



Augmentin



- Gram positive bacteria
- Gram negative bacteria
- Anaerobes
- Anti-staphylococcal
- **Pseudomonas**
- **Atypical organisms**
 - SSTIs
 - **U/LRTIs**
 - UTIs
 - Abdominal infections
- Clinical syndrome
- Likely pathogen
- Antibiotic cover
 - LRTI – high dose amoxicillin?
 - SSTI - cefazolin

Tazocin



Tazocin

- Gram positive bacteria
- Gram negative bacteria
- Anaerobes
- Anti-staphylococcal
- Pseudomonas
- **Atypical organisms**

Cefepime

- Gram positive bacteria
- Gram negative bacteria
- **Anaerobes**
- Anti-staphylococcal
- Pseudomonas
- **Atypical organisms**

Benzyl penicillin (Pen G)



Alternatives for congenital syphilis

Procain Pen G IMI x 10 – 14 days (plus probenecid)

Paediatric challenges

Cover for neuro-syphilis requires drugs that cross BBB

Tests for neuro-syphilis have low sensitivity (high specificity)

Search for evidence → observational data and case reports → meta-analyses →
RTCs:

Neonates: cefotaxime 10- 14 days

Older: ceftriaxone 10 – 14 days

All patients require follow up

Serology

Audiology

neurodevelopment

Southern African HIV Clinicians Society Guideline for the clinical management of syphilis_2024

Stockouts

- Clinical syndrome
 - Antibiotics needed?
- Likely pathogen
- Cover of alternative antibiotic
- Guidelines
- ID specialist
- Microbiologist



Antibiotic pipeline & AMR

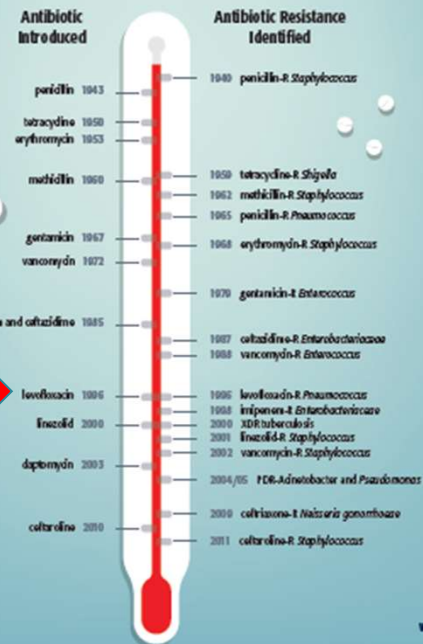
Antibiotic Resistance Awareness

Antibiotic Resistance Timeline

Developing Resistance

Timeline of Key Antibiotic Resistance Events

Dates are based upon early reports of resistance in the literature. In the case of pan drug-resistant (PDR) - Acinetobacter and Pseudomonas, the date is based upon reports of health care transmission or outbreaks. Note: penicillin was in limited use prior to widespread population usage in 1943.¹⁸



Prevention of AMR

Prevent all infections

- Vaccination
- IPC
- Care Bundles for HAIs (e.g. CLABSI, VAP, CAUTI)

Diagnostic stewardship

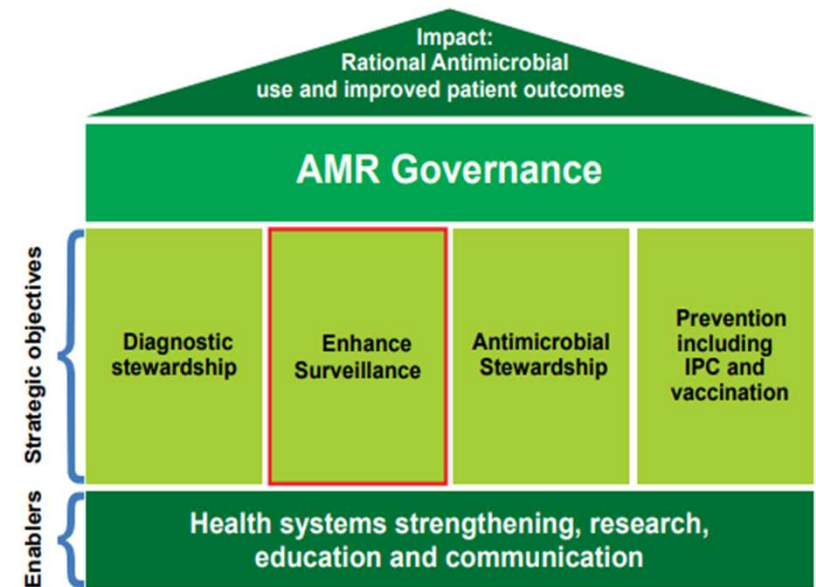
Rational use of antibiotics

- Guidelines
- WHO AWaRe

Novel

- Faecal transplant
- Oral probiotics
- bacteriophages

Surveillance



Prevent all infections

HIB vaccine introduced in 1999

Hussey et al (1994) incidence per 100 000

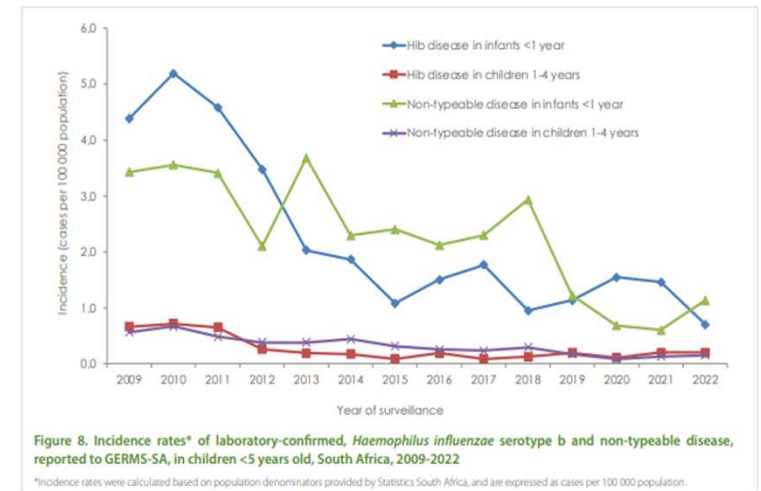
- 169 in < 1 year
- 47 in < 5 years

Gottberg et al (2006) incidence per 100 000

- 5.7 in < 1 year
- Ampicillin resistance 31 %
- MDR 19 %

GERMS-SA 2022

Ampicillin resistance 8 %



Thank you

