ANTIMICROBIAL RESISTANCE SURVEILLANCE FROM SENTINEL PUBLIC HOSPITALS, SOUTH AFRICA, 2015

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Introduction

Antimicrobial resistance (AMR) is a significant public health concern that threatens effective treatment of severe infections, both locally and globally. Surveillance is conducted to determine the extent and pattern of resistance amongst the most common pathogens causing infections in humans.[1] Integrated data on bacterial resistance are obtained from an electronic database of bacterial antimicrobial susceptibility results generated by public sector diagnostic laboratories in South Africa.

The objectives of the AMR surveillance programme are to determine the number of isolates of selected pathogens reported from selected hospitals by month and to describe antimicrobial susceptibility to the most important treatment regimens by pathogen and by hospital.

Methods

All data for this report were sourced from the National Health Laboratory Service (NHLS) Corporate Data Warehouse (CDW). This is a national repository for laboratories serving all public sector hospitals in South Africa and contains archived data from the Laboratory Information System (LIS).[2]

Bloodstream infections over the period January-December 2015 were extracted for the following ESKAPE pathogens: *Acinetobacter baumannii* complex, *Enterobacter cloacae* complex, *Escherichia coli, Enterococcus faecalis, Enterococcus faecium, Klebsiella pneumoniae, Pseudomonas aeruginosa* and *Staphylococcus aureus.* Routine electronic data were collected from sentinel sites (mostly tertiary academic hospitals) (Table 1).

Antimicrobial susceptibility reporting was based on Clinical Laboratory Standards Institute (CLSI) guidelines.[3] The various laboratory methods used included Microscan, Vitek and disk diffusion. Due to site-specific differences in testing methodologies and data capture on the LIS, extensive cleaning and recoding of data were necessary. This was done within the CDW. The CDW linking algorithm was used to create unique patient identifiers that enabled the generation of patient-level data and de-duplication within a 21-day patient episode, which was initiated from the first occurrence of resistance to a given antibiotic for a given pathogen.

Vancomycin resistance is not reported for *Staphylococcus aureus* due to the lack of confirmatory test methods (pending agreement with the South African Society for Clinical Microbiology (SASCM)). Data were omitted for those sites that tested fewer than 30 organisms for resistance to a particular antibiotic.

Table 1: Hospitals participating in antimicrobial resistance surveillance by province, South Africa, and their characteristics.

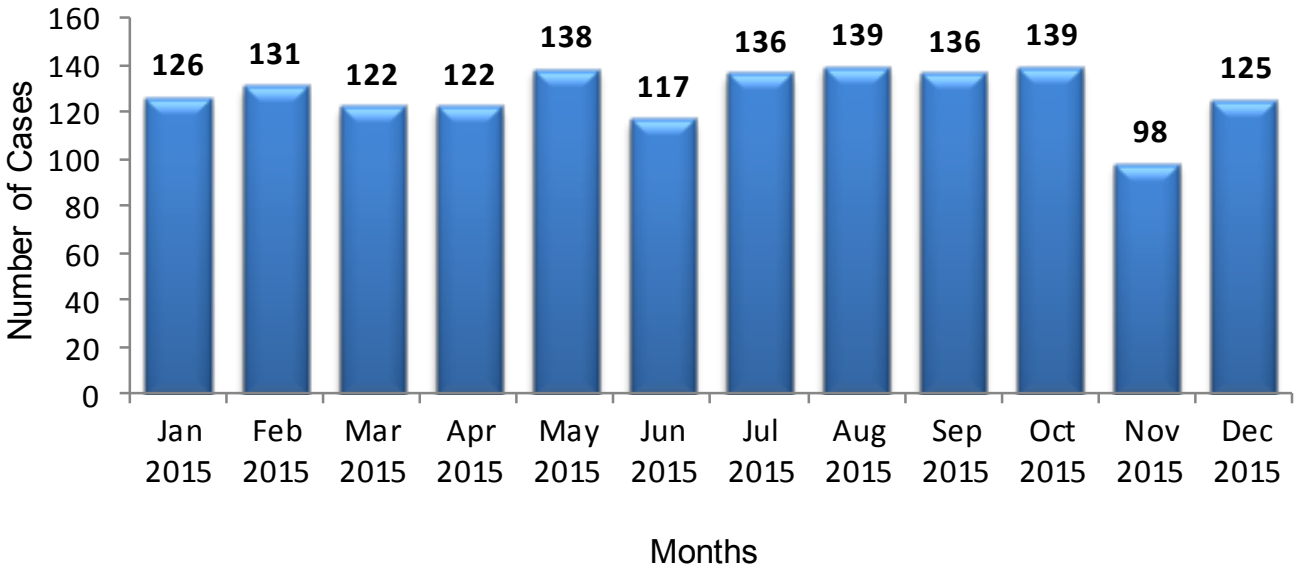
Hospital Site	Province	Academic Hospital	No of beds
Frere Hospital	Eastern Cape	No	916
Livingstone Hospital	Eastern Cape	Yes	616
Nelson Mandela Academic Hospital/Mthatha Tertiary (NMAH)	Eastern Cape	Yes	520
Universitas Hospital (UH)	Free State	Yes	650
Charlotte Maxeke Johannesburg Academic Hospital (CMJAH)	Gauteng	Yes	1088
Chris Hani Baragwanath Hospital (CHBH)	Gauteng	Yes	3200
Dr George Mukhari Hospital (DGMH)	Gauteng	Yes	1200
Steve Biko Academic Hospital (SBAH)	Gauteng	Yes	832
Helen Joseph Hospital (HJH)	Gauteng	Yes	700
Grey's Hospital (GH)	KwaZulu-Natal	Yes	530
Inkosi Albert Luthuli Central Hospital (IALCH)	KwaZulu-Natal	Yes	846
King Edward VIII Hospital (KEH)	KwaZulu-Natal	Yes	922
Mahatma Gandhi Hospital (MGH)	KwaZulu-Natal	No	350
RK Khan Hospital (RKKH)	KwaZulu-Natal	No	543
Tygerberg Hospital (TH)	Western Cape	Yes	1310
Groote Schuur Hospital (GSH)	Western Cape	Yes	893

Results

Data for bloodstream infections and antimicrobial susceptibility tests are summarised for *Acinetobacter baumannii* complex (Figure 1), *Enterobacter cloacae* complex (Figure 2), *Enterococcus faecalis* (Figure 3), *Enterococcus faecium* (Figure 4), *Escherichia coli* (Figure 5), *Klebsiella pneumoniae* (Figure 6), *Pseudomonas aeruginosa* (Figure 7) and *Staphylococcus aureus* (Figure 8). For each organism, the total number of isolates, as well as their susceptibility profiles and percentage susceptibility to selected antimicrobial agents by site were analysed (Figures 1-8).

***Acinetobacter baumannii* complex**

Acinetobacter baumannii showed resistance to the majority of antimicrobial agents tested. This was likely due to its ability to encode and upregulate various mechanisms of resistance such as the loss of outer membrane porins and permeability, efflux systems, AmpC β-lactamases and others. The proportions of isolates resistant to imipenem, cefepime and ceftazidime were high at 82%, 81% and 78%, respectively, whereas resistance proportions were 68% to ciprofloxacin, 50% to amikacin and 61% to tobramycin. The extent of resistance to most agents changed in comparison to 2014 i.e. there was a significant decrease in resistance to imipenem (23% in 2014 vs. 18% 2015; $p<0.001$) while resistance to carbapenems, cephalosporins (3rd and 4th generations) and aminoglycosides increased in 2015, with the exception of resistance to colistin which was only 2% in 2015 compared to 5% in 2014. From referral isolates sent to the Antimicrobial Resistance Laboratory (AMRL) of the NICD, no colistin resistance conferred by the *mcr*1 gene was confirmed. Except for these few isolates no confirmation of colistin resistance is performed at the AMRL.



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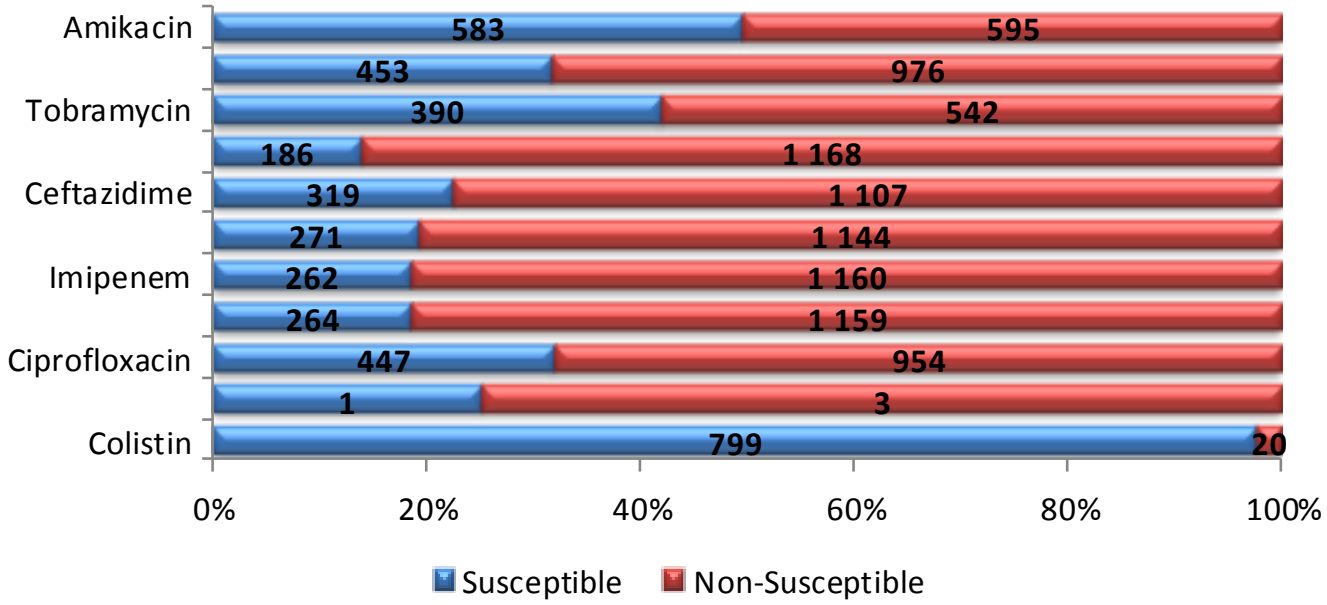

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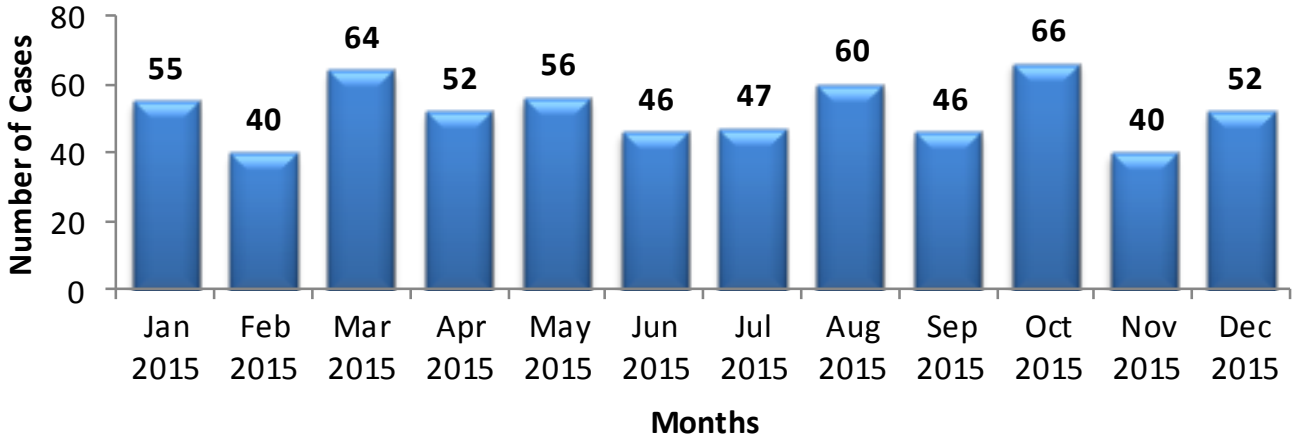
Figure 1: A. *Acinetobacter baumannii* cases by month, and B. Numbers and percentages of susceptible and resistant *A. baumannii* complex isolates from blood cultures at public-sector sentinel sites, 2015. Total number of isolates analyzed = 1529.

***Enterobacter cloacae* complex**

The prevalence of presumptive (i.e. no molecular confirmation) resistance of *Enterobacter cloacae* complex to ertapenem of 8% has decreased in comparison to the 2014 resistance prevalence of 11%. Resistance to imipenem and meropenem has remained stable at 2%. Resistance to ceftazidime has decreased since 2014 (p=0.02) while resistance to piperacillin-tazobactam remained stable in 2015. Resistance to cefepime (31%) is suggestive of AmpC hyper-production due to de-repressed AmpC mutants which confer resistance to all cephalosporins. These data may also indicate co-carriage of an extended-spectrum β-lactamase (ESBL).



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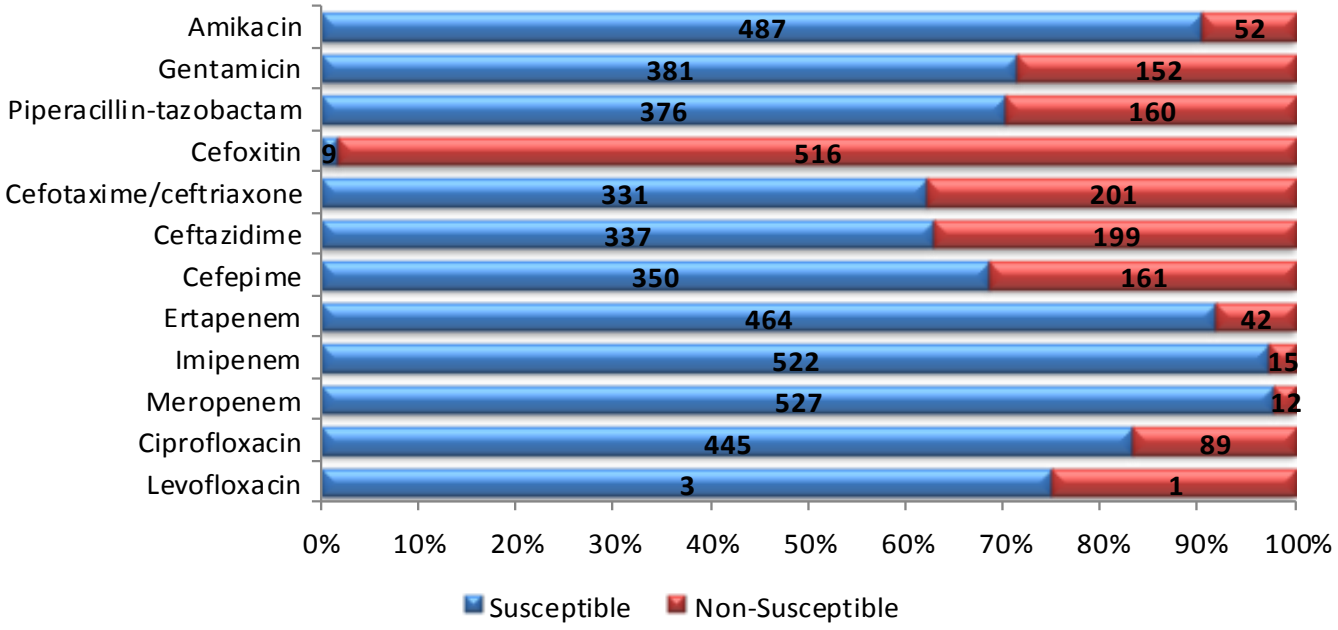

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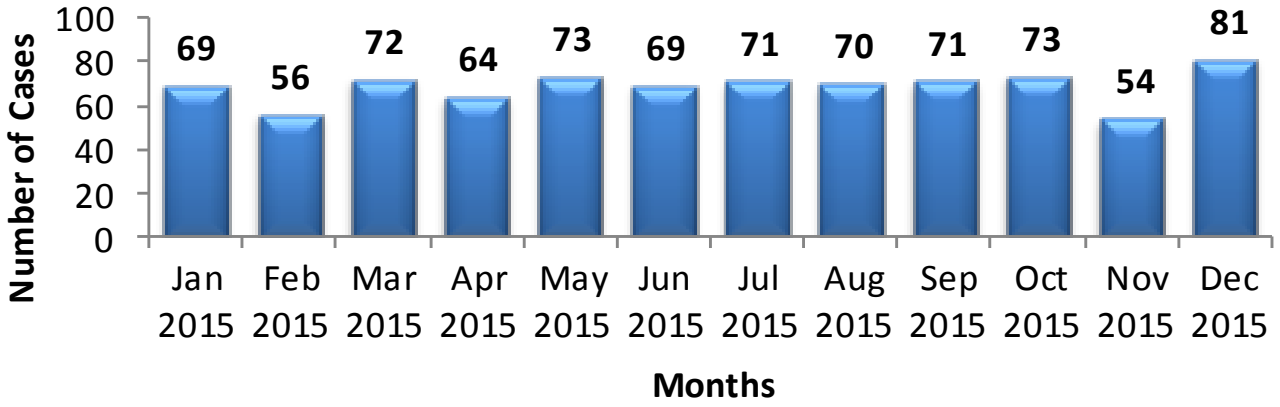
Figure 2: A. *Enterobacter cloacae* cases by month, and B. Numbers and percentages of susceptible and resistant *E. cloacae* complex isolates from blood cultures at public-sector sentinel sites, 2015. Total number of isolates analyzed = 624.

Enterococcus faecalis

Enterococcus faecalis exhibited 14% resistance to penicillins and 1% (non-confirmed) resistance to vancomycin, both of which are slightly reduced from the corresponding prevalences of 2014 (17% to penicillins and 2% to vancomycin). There were no other significant changes in comparison to 2014.



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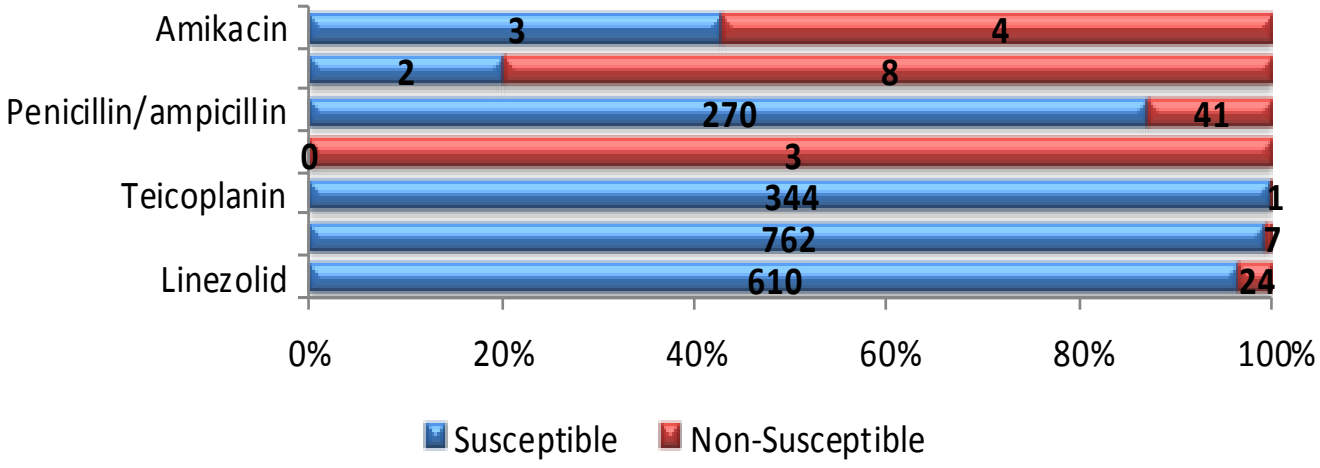

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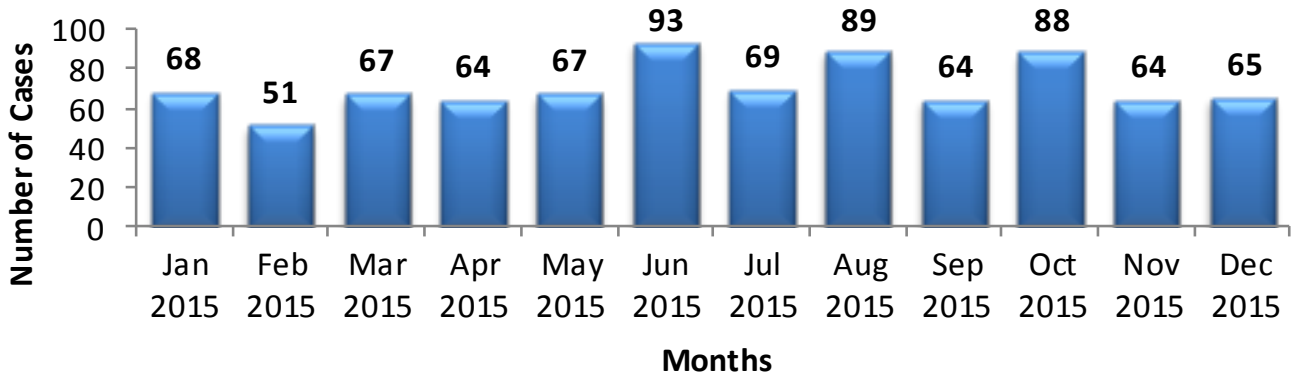
Figure 3: A. *Enterococcus faecalis* cases by month, and B. Numbers and percentages of susceptible and resistant *E. faecalis* isolates from blood cultures at public-sector sentinel sites, 2015. Total number of isolates analyzed = 823.

Enterococcus faecium

Enterococcus faecium is inherently resistant to β-lactam agents. Resistance to vancomycin remained unchanged at 5% in 2015.



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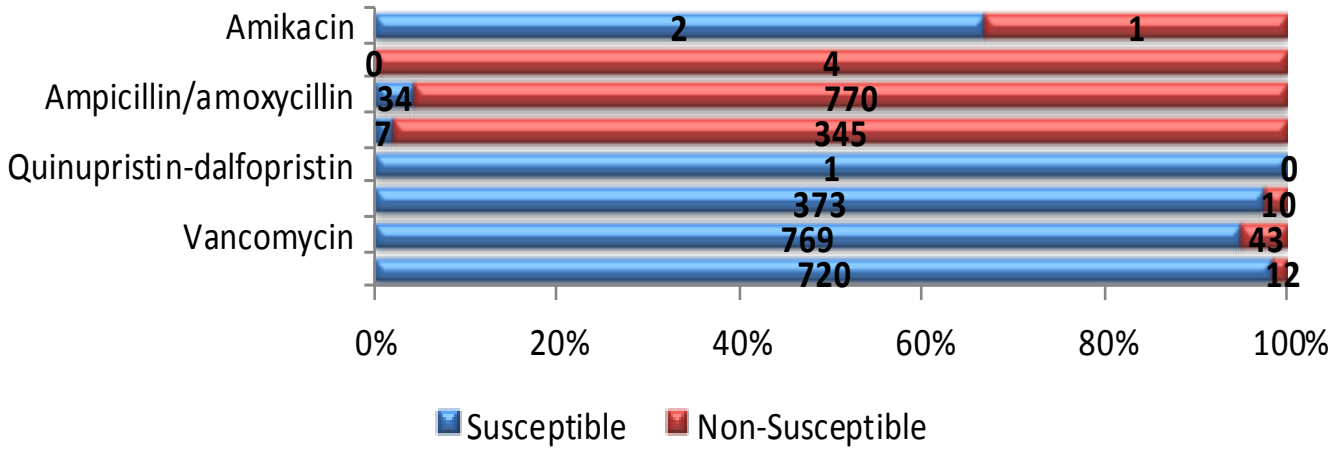

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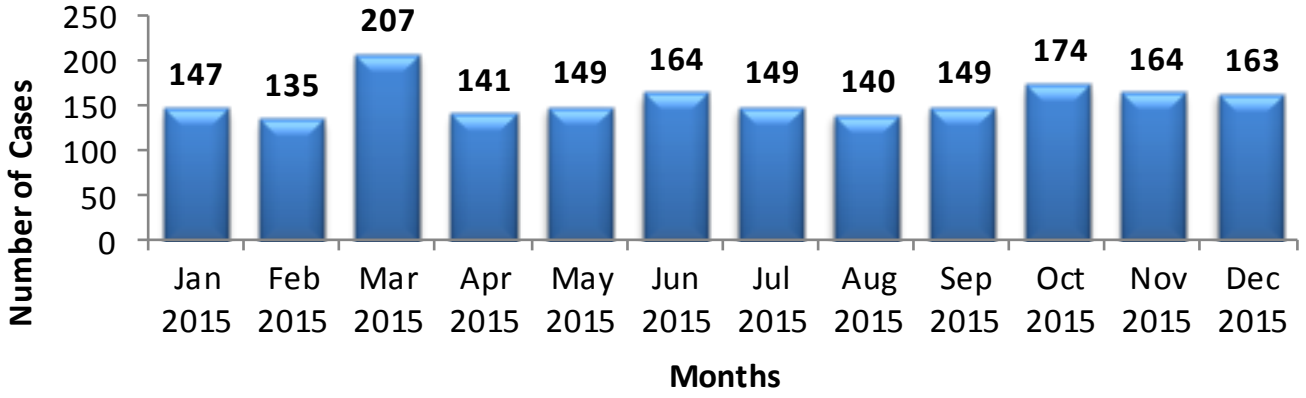
Figure 4: A. *Enterococcus faecium* cases by month, and B. Numbers and percentages of susceptible and resistant *E. faecium* isolates from blood cultures at public-sector sentinel sites, 2015. Total number of isolates analyzed = 849.

Escherichia coli

Escherichia coli showed no change in resistance to piperacillin-tazobactam and ciprofloxacin compared to 2014 and no significant increased resistance to the β-lactam group over a two-year period. Resistance to 3rd generation cephalosporins indicates the presence of extended spectrum β-lactamases (ESBLs) and was recorded in 22% of isolates.



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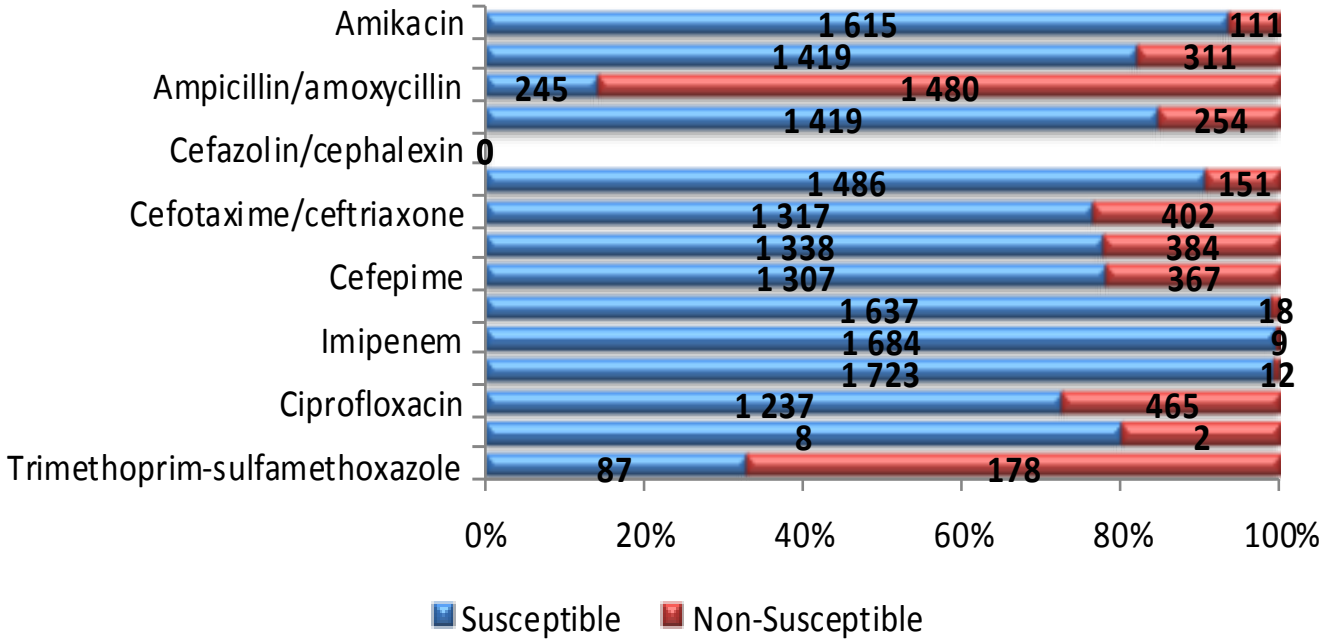

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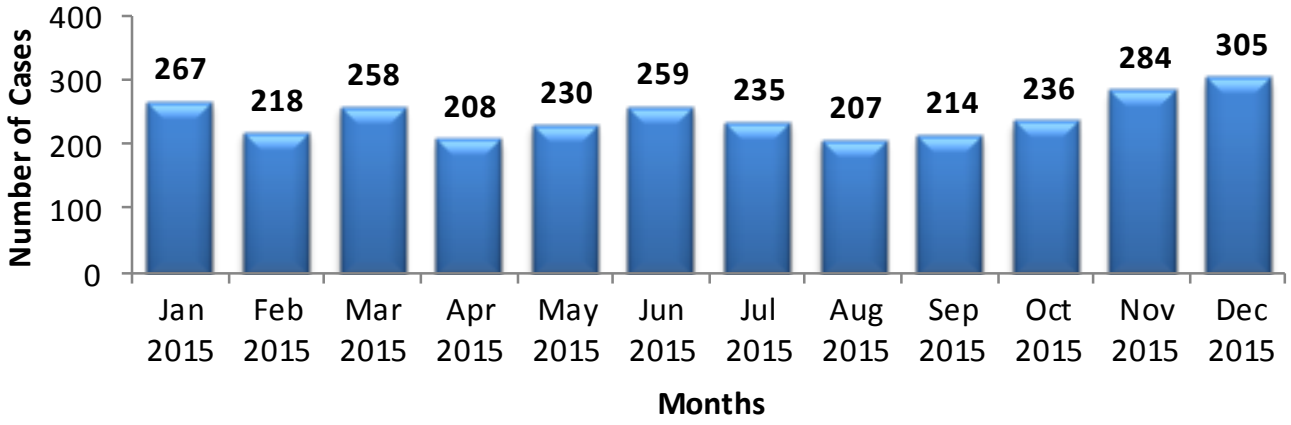
Figure 5: A. *Escherichia coli* cases by month, and B. Numbers and percentages of susceptible and resistant *E. coli* isolates from blood cultures at public-sector sentinel sites, 2015. Total number of isolates analyzed = 1882.

Klebsiella pneumoniae

Klebsiella pneumoniae was resistant to multiple antimicrobials, including 3rd generation cephalosporins that indicate production of ESBLs (69%), ciprofloxacin (33%) and piperacillin-tazobactam (50%). The proportion of isolates resistant to ertapenem (4%) has remained unchanged over a 2-year period. Resistance prevalences to imipenem (6%) and meropenem (6%) showed significant increases compared to 2014 ($p<0.001$). Although resistance to other carbapenems was generally low, the rapid emergence of strains with carbapenemase production threatens the efficacy and use of this vital class of antimicrobials as a therapeutic option. Thus, knowledge of local hospital epidemiology and monitoring of carbapenem resistance is essential.



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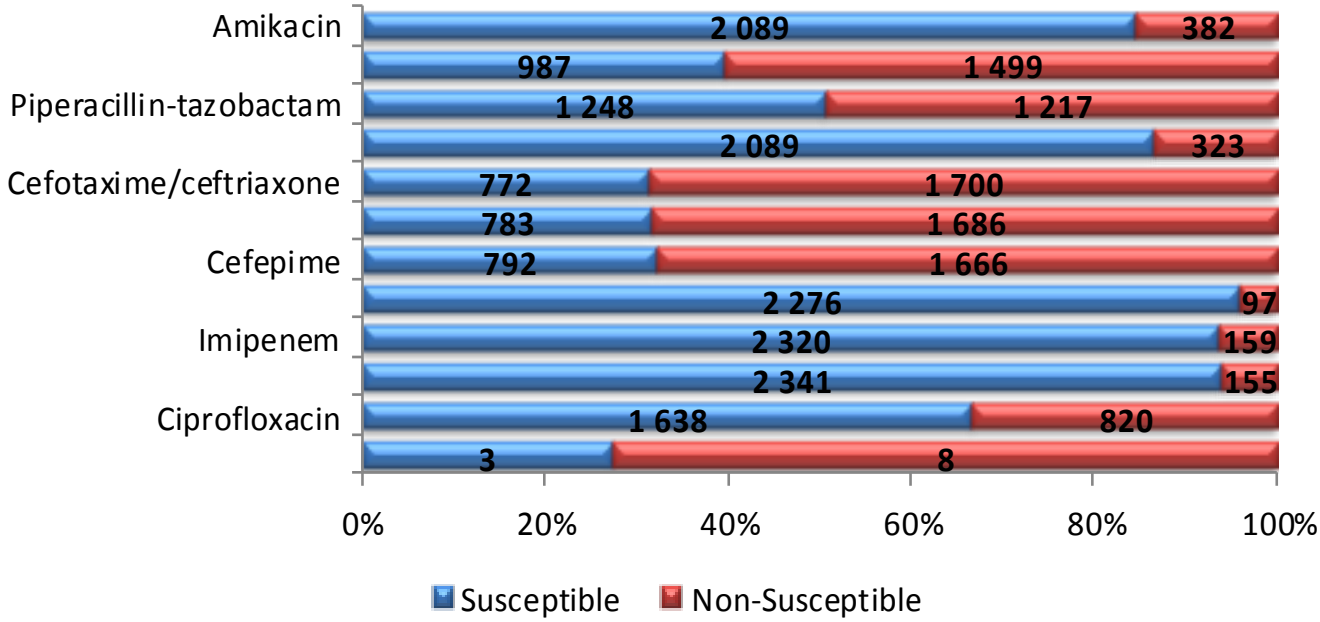

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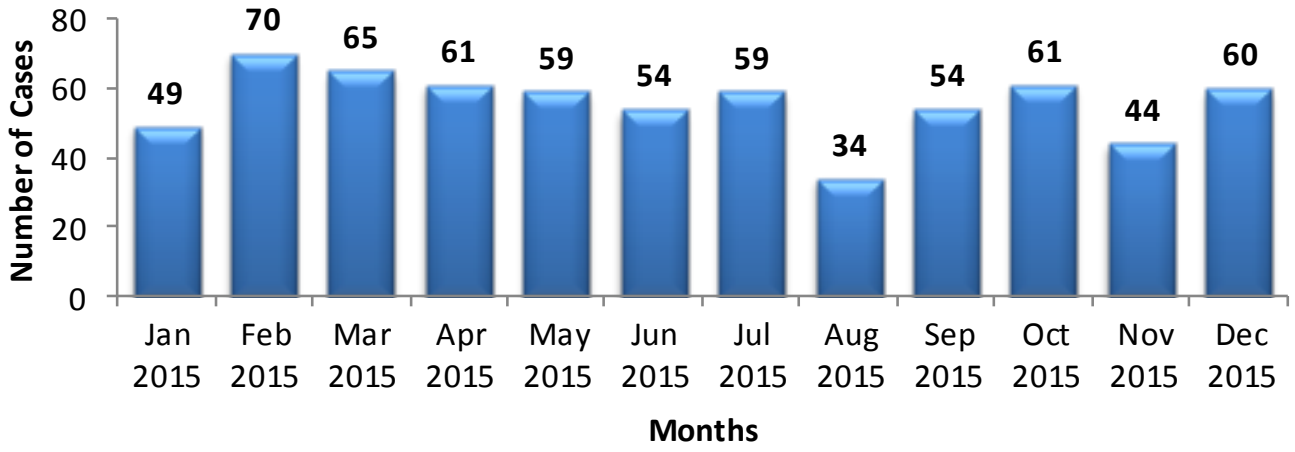
Figure 6: A. *Klebsiella pneumoniae* cases by month, and B. Numbers and percentages of susceptible and resistant *K. pneumoniae* isolates from blood cultures at public-sector sentinel sites, 2015. Total number of isolates analyzed = 2921.

Pseudomonas aeruginosa

Thirty percent of *Pseudomonas aeruginosa* isolates were resistant to piperacillin-tazobactam and 27% were resistant to cefepime. Colistin resistance was low (1%). However, this was not confirmed by reference or molecular methods.



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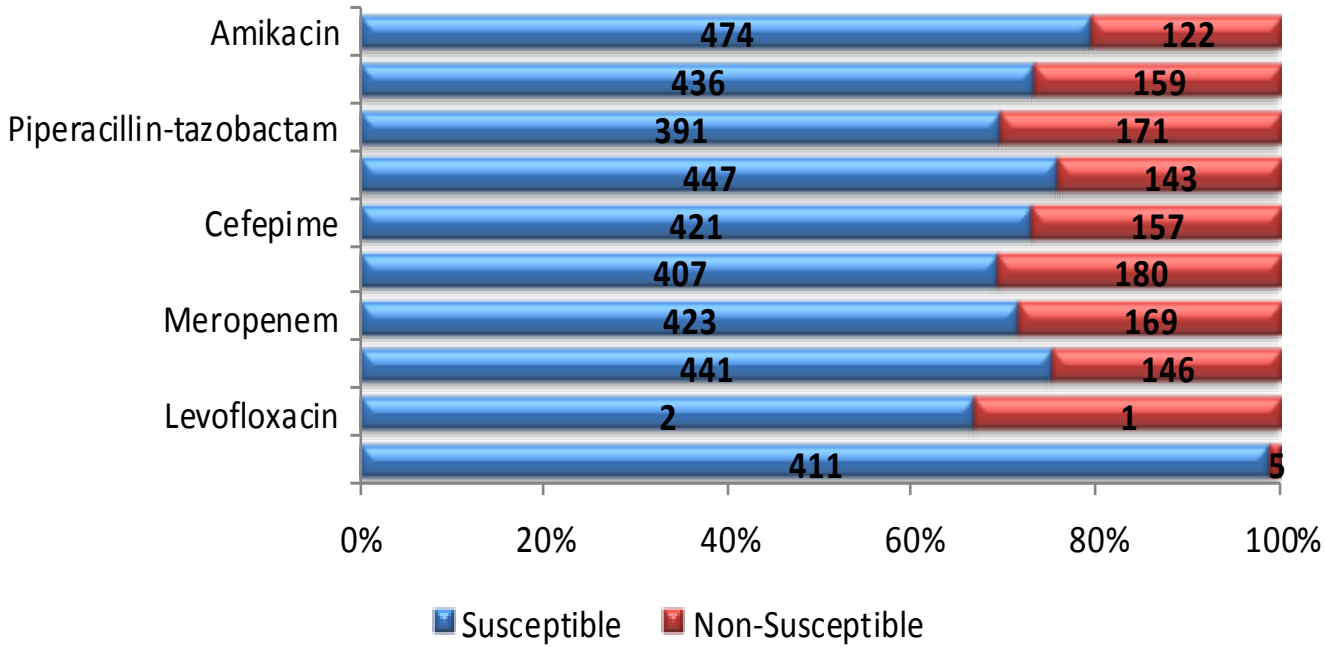

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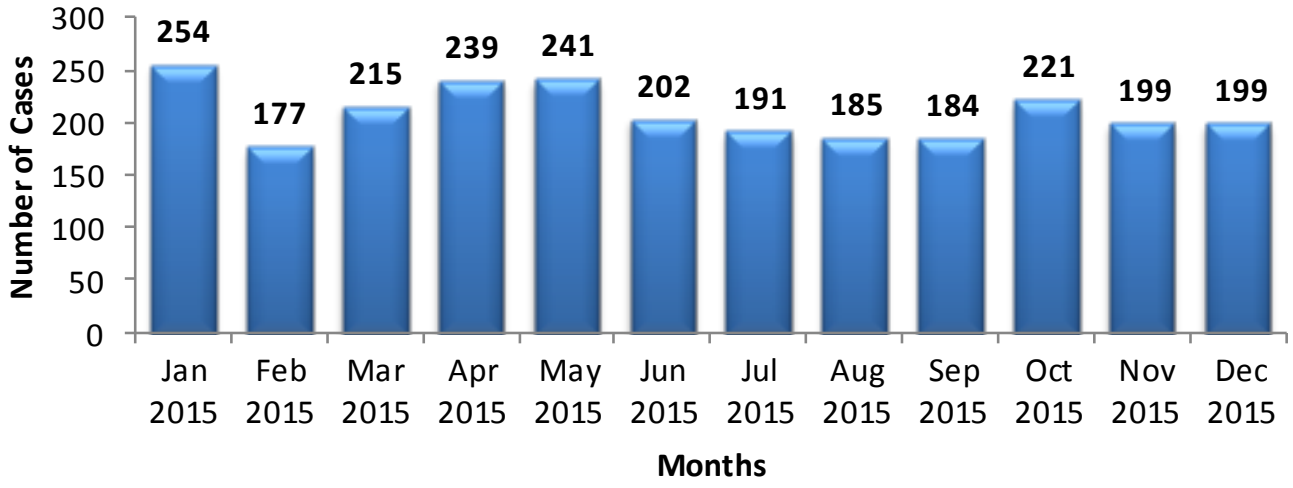
Figure 7: A. *Pseudomonas aeruginosa* cases by month, and B. Numbers and percentages of susceptible and resistant *P. aeruginosa* isolates from blood cultures at public-sector sentinel sites, 2015. Total number of isolates analyzed **=** 670.

Staphylococcus aureus

No *S. aureus* isolates were reported to be vancomycin resistant in 2015. Resistance to methicillin/oxacillin and all other β-lactams showed a minor increase compared to 2014. Cefoxitin resistance was indicative of methicillin resistance (MRSA). Resistance rates to erythromycin and clindamycin remained unchanged.



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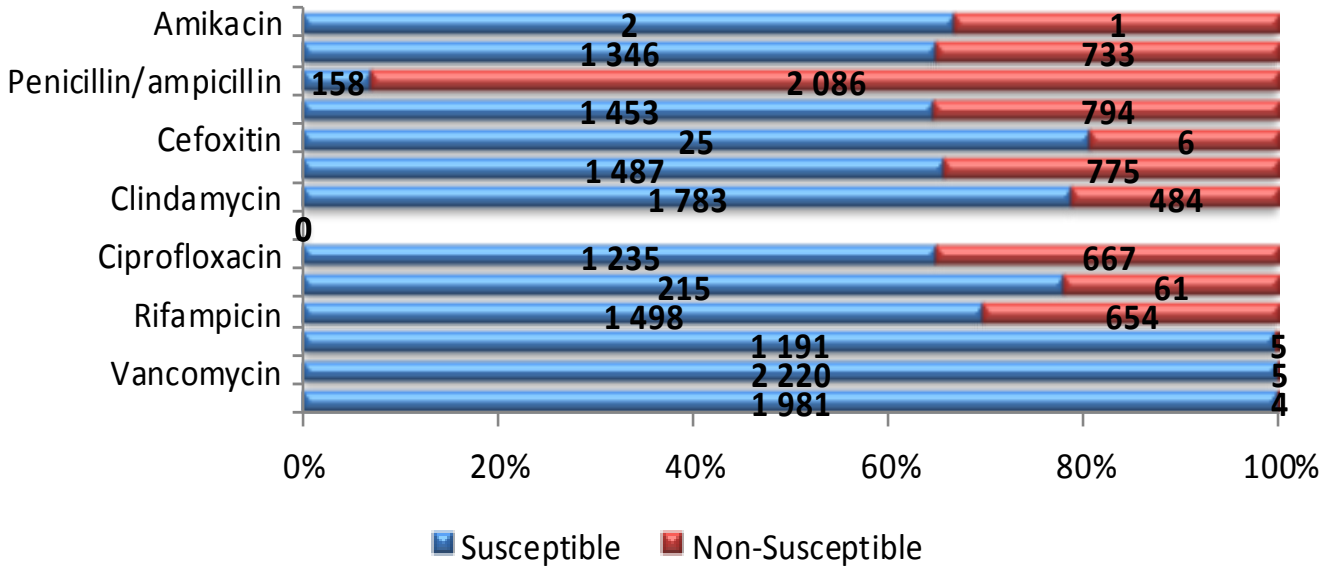

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Figure 8: A. *Staphylococcus aureus* cases by month, and B. Numbers and percentages of susceptible and resistant *S. aureus* isolates from blood cultures at public-sector sentinel sites, 2015. Total number of isolates analyzed = 2507.

Carbapenemase-producing Enterobacteriaceae (CPE)

The Antimicrobial Resistance Laboratory confirmed the presence of carbapenemase genes in Enterobacteriaceae isolates that were referred from public laboratories following phenotypic confirmation of carbapenem resistance (Table 2). Few organisms presented with more than one CPE gene.

Table 2: Numbers of confirmed carbapenemase-producing *Enterobactericeae* by species and genoptype

Carbapenemases producing Enterobacteriaceae	**No. of isolates**
Species	
Citrobacter freundii	19
Enterobacter aerogenes	8
Enterobacter asburiae	3
Enterobacter cloacae	114
Enterobacter kobei	2
Enterobacter spp.	2
Escherichia coli	64
Klebsiella oxytoca	20
Klebsiella pneumoniae	552
Klebsiella spp.	3
Morganella morganii	10
Proteus mirabilis	2
Proteus spp.	1
Providencia rettgeri	23
Providencia vermicola	1
Raoutella ornithinolytica	1
Serratia marcescens	55
Genotype	
OXA-48$_{like}$	234
VIM	55
NDM	438
GES	12
KPC	11
IMP	8

Discussion and conclusion

Certain limitations are inherent in the data presented. Data may be incomplete due to missing cases not captured on the LIS or non-standardised coding of pathogens and antibiotics. Testing methods and microbiological practice vary between sites and this could account for variation in the results presented. Confirmatory antimicrobial susceptibility test (AST) methods were not performed for any of these organisms and results presented here are reported as captured on the LIS. Thus, while some results may suggest the occurrence of an outbreak, it is not possible to confirm this. For certain sites, not all organisms are represented. This may be due to organisms not being identified at a particular site for 2015.

Surveillance for CPEs is currently being conducted at 14 national sites. Due to the limitations mentioned above

there is a continuous need for improvement in the quality of data obtained by electronic surveillance. The data presented in this report nevertheless highlight the importance of surveillance for antimicrobial resistance patterns.

Disclaimer

Data are reported as received through the CDW. No demographic, epidemiological, clinical or molecular data were available to distinguish between hospital-associated and community-acquired infections.

Acknowledgements

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