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ON SAFETY AND QUALITY IN HEALTH CARE

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AUSTRALIAN GROUP ON ANTIMICROBIAL RESISTANCE

Sepsis Outcome Programs

2016 report

AGAR

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Summary

As part of the Antimicrobial Use and Resistance in Australia (AURA) Surveillance System, the Australian Commission on Safety and Quality in Health Care (the Commission) funds the Australian Group on Antimicrobial Resistance (AGAR), a component of the Australian Society for Antimicrobials, to:

- Conduct targeted surveillance of selected pathogens
- Collect demographic, treatment and outcome data, and data on antimicrobial resistance rates
- Analyse and report on these data.

AGAR operates three sepsis outcome programs: the Gram-negative Sepsis Outcome Program, the Australian Enterococcal Sepsis Outcome Program and the Australian Staphylococcal Sepsis Outcome Program. AGAR prepares a detailed annual report on each program for publication on its website (www.agargroup.org).

This report, which includes analyses of the key findings of AGAR 2016 sepsis outcome programs, was commissioned by the AURA National Coordinating Unit (ANCU) to build on the report on AGAR 2015 sepsis outcome programs.

In 2016, AGAR collected data on 11,163 episodes of bacteraemia across Australia. Where the place of onset was known, approximately three-quarters of episodes had their onset in the community.

Key findings from analysis of the 2016 AGAR data include the following:

- *Escherichia coli* is the most common organism causing bacteraemia in Australia, accounting for 36.8% of episodes reported
- AGAR data show a longitudinal trend of increasing *E. coli* non-susceptibility to key anti–gram negative antimicrobial agents such as ceftriaxone and ciprofloxacin; in 2016, extended-spectrum β-lactamase (ESBL) phenotypes were found in 12.7% of *E. coli* and 9.1% of *Klebsiella pneumoniae*
- Increasing fluoroquinolone resistance in *E. coli* is a continuing concern; the percentage of invasive *E. coli* that are fluoroquinolone resistant in Australia is comparable to northern European countries, and is striking in hospital-onset bacteraemia, with a change from 13.7% to 20.2% between 2013 and 2016
- Because fluoroquinolone resistance is often linked to cephalosporin resistance caused by ESBLs of the CTX-M type, it is possible that the high use of oral cephalosporins and penicillins in the community is contributing substantially to this resistance
- When ESBLs first arose, they were more common in hospital-onset infections in *K. pneumoniae*; now, the perception that ESBLs are primarily a hospital problem is not accurate – 11.4% of *E. coli* isolates causing community-onset bacteraemia, which accounted for 83% of all *E. coli* bacteraemia cases, were ceftriaxone resistant
- Compared with ESBLs, plasmid-borne AmpC enzymes still make up only a small proportion (13%) of ceftriaxone resistance
- If the rate of ESBLs continues to rise, it will potentially affect the application of therapeutic guidelines, such as empirical treatment decisions for severe infections; current Australian guidelines recommend third-generation cephalosporins for empirical treatment, partly to avoid even broader-spectrum antibiotic prescribing

- The AGAR data suggest that a greater focus on patient risk assessment may be required in empirical treatment decisions; interestingly, whereas *E. coli* ceftriaxone resistance rates continue to rise in the community (from 7.0% in 2013 to 11.4% in 2016), hospital-onset ceftriaxone resistance has not risen (15.7% in 2013 and 13.3% in 2016), suggesting that ceftriaxone resistance transmission has become a community phenomenon
- The low rates of carbapenemase-producing Enterobacteriaceae (CPE) bacteraemia are encouraging (<0.1% in *E. coli* and 0.3% in *K. pneumoniae*); effective infection control measures, based on the Commission's *Recommendations for the Control of Carbapenemase-Producing Enterobacteriaceae: A guide for acute care health facilities*, are essential to limiting the transmission of CPE
- *Enterococcus faecium* bacteraemia has substantial clinical consequences, including high 30-day all-cause mortality for both community-onset and hospital-onset vancomycin-susceptible or vancomycin-resistant isolates
- Ampicillin resistance and multidrug resistance, including resistance to high-level gentamicin and vancomycin, are common; limited therapeutic options may be a factor in the differing 30-day all-cause mortality between *E. faecium* (27.1%) and *E. faecalis* (12.9%)
- In the 2016 survey, 49.3% of *E. faecium* harboured *vanA* or *vanB* genes or both, and 22% of vancomycin-resistant *Enterococcus* bacteraemias were due to *vanA*; this type of vancomycin resistance has emerged rapidly in the past five years, particularly in New South Wales, where it is now the dominant genotype
- The percentage of *E. faecium* bacteraemia isolates resistant to vancomycin is now much higher in Australia than in almost all European countries
- There is considerable clonal diversity in *E. faecium* across Australia, including vancomycin-resistant strains, with distinct regional differences; this is consistent with the observation that much vancomycin resistance arises through the transmission of the vancomycin resistance gene complexes to susceptible clones, and subsequent amplification locally
- Vancomycin can no longer be recommended as the mainstay of therapy for *E. faecium* bacteraemia, and agents with uncertain less certain efficacy such as linezolid are the alternative; the Commission and AGAR will liaise with expert groups that develop guidelines for treatment of bacteraemia to ensure that they reflect this finding, in addition to the Commission's continued promotion of strict adherence to infection control guidelines
- There is an increasing rate of community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) bacteraemias, and CA-MRSA clones are now the dominant types of MRSA bacteraemia
- EMRSA-15 now outranks the long-established Aus2/3 clone in healthcare-associated MRSA (HA-MRSA) bacteraemia; more EMRSA-15 bacteraemias arise in the community than in hospital, consistent with the prevalence of this clone in long-term care facilities in Australia
- The Queensland clone of CA-MRSA, which harbours the Panton–Valentine leucocidin, has become the dominant CA-MRSA type and is now seen throughout Australia; it is now the most common CA-MRSA clone in Victoria, Queensland and Western Australia

- CA-MRSA is an increasing source of hospital-onset bacteraemia, and now causes a greater frequency of hospital-onset MRSA bacteraemia than HA-MRSA; the rapidly changing picture of MRSA in Australia requires ongoing close monitoring by the Commission and AGAR.

Other highlights from each of the AGAR sepsis outcomes programs are set out below.

Gram-negative species

- A total of 7,565 episodes of gram-negative bacteraemia were reported, including Enterobacteriaceae (89.2%), *Pseudomonas aeruginosa* (9.6%) and *Acinetobacter* species (1.2%)
- Of the Enterobacteriaceae, three genera – *Escherichia* (60.9%), *Klebsiella* (18.2%) and *Enterobacter* (8.2%) – contributed 87.2% of all Enterobacteriaceae bacteraemias
- The all-cause 30-day mortality for gram-negative bacteraemia was 13.3% (11.5% in *E. coli*, 20.7% in *P. aeruginosa*)
- The most frequent source of sepsis or clinical manifestation was urinary tract infection (41.9%)
- Of patients with bacteraemia caused by Enterobacteriaceae, 45.9% had a length of stay following bacteraemia of less than seven days; in contrast, 14.2% of patients with *P. aeruginosa* bacteraemia had a length of stay of more than 30 days
- Although *K. pneumoniae* ESBL phenotypes were significantly more likely to be found among hospital- than community-onset episodes, there was no significant difference in proportions between hospital- and community-onset episodes for *E. coli* ESBL phenotypes
- Most (75.6%) *E. coli* with an ESBL phenotype harboured genes of the CTX-M type; O25b-ST131 accounted for 62.9% of *E. coli* ESBL phenotypes that were ciprofloxacin resistant
- The rate of colistin resistance – when tested for, but excluding species with intrinsic resistance – was 1.4% (11/813); two *E. coli* and one *E. cloacae* harboured *mcr-1*.

Enterococcus species

- A total of 1,058 episodes of enterococcal bacteraemia were reported; the majority (95.3%) of enterococcal bacteraemia episodes were caused by *E. faecalis* or *E. faecium*
- Most *E. faecalis* bacteraemia episodes were community onset (68.6%), whereas 27.8% of *E. faecium* bacteraemia episodes were community onset
- The 30-day all-cause mortality for enterococcal bacteraemia was 19.3%
- There was a significant difference in 30-day all-cause mortality between *E. faecalis* (12.9%) and *E. faecium* (27.2%)
- The most frequent source of sepsis or clinical manifestation for *E. faecalis* was urinary tract infection (26.4%); for *E. faecium*, it was intra-abdominal infection other than that from the biliary tract (21.4%)
- The length of stay following enterococcal bacteraemia was more than 30 days for 21.9% of patients
- There were 48 *E. faecium* multi-locus sequence types, of which M-type 1, ST17, ST796, ST80, ST555, ST203, M-type 3, ST78 and ST262 were the nine most frequently identified
- *vanA* genes were detected in seven sequence types, and *vanB* genes were detected in nine sequence types.

Staphylococcus aureus.

- A total of 2,540 *S. aureus* bacteraemia episodes were reported, of which 19.7% were methicillin resistant
- Of the *S. aureus* bacteraemia episodes, 76.3% were community onset
- The 30-day all-cause mortality for *S. aureus* bacteraemia episodes was 16.7%
- There was a significant difference in 30-day all-cause mortality between MRSA and methicillin-sensitive *S. aureus* (MSSA) – 23.1% and 15.2%, respectively
- There was no significant difference in all-cause mortality between community-onset and hospital-onset *S. aureus* bacteraemia episodes
- Osteomyelitis/septic arthritis (18.5%) and skin and soft tissue infections (18.1%) were the most common principal clinical manifestation for *S. aureus* bacteraemia episodes
- The length of stay was more than 30 days in 26.7% of patients with the *S. aureus* bacteraemia episodes (25.6% for MRSA, 27.0% for MSSA)
- Five HA-MRSA clones were identified; the dominant HA-MRSA clone was ST22-IV (EMRSA-15)
- No HA-MRSA isolates harboured Panton–Valentine leucocidin–associated genes
- Forty CA-MRSA clones were identified; the dominant CA-MRSA clone was ST93-IV (Queensland clone)
- Of CA-MRSA isolates, 40.9% harboured Panton–Valentine leucocidin–associated genes.

AGAR data support informed clinical decisions about antimicrobial therapy and antimicrobial stewardship programs, and improvements to care of patients with sepsis. The data also inform interventions to prevent and control the spread of resistant organisms.

The Commission's ANCU, AGAR and other relevant experts collaborate to identify strategic priorities for surveillance and analysis of antimicrobial resistance. The AURA Surveillance System and the ANCU support the achievement of the objectives of Australia's first National Antimicrobial Resistance Strategy.[1]

The Commission will continue to collaborate with the Australian Society for Antimicrobials to enhance and maintain AGAR as a key element of the AURA Surveillance System, and a key source of data on the emergence of, and trends in, antimicrobial resistance in the human health setting.

1 Background and objectives

The Australian Group on Antimicrobial Resistance (AGAR) is a longstanding collaboration of clinicians and scientists from major microbiology laboratories around Australia. AGAR tests and gathers information on the level of antimicrobial resistance in bacteria that cause important and life-threatening infections. The group commenced in 1985, when it involved 13 teaching hospitals. It has subsequently grown to involve 32 institutions across Australia, including four private laboratories (Table 1).

Historically, the main focus of the group was antimicrobial resistance in *Staphylococcus aureus*. The scope broadened over time to include studies on *Escherichia coli*, *Enterobacter* species, *Klebsiella* species, *Haemophilus influenzae, Streptococcus pneumoniae* and *Enterococcus* species. Using standardised methods, AGAR has collected ongoing data on the prevalence of antimicrobial resistance in Australia over a long period. AGAR now focuses on bloodstream infections and has three major programs: the Gram-negative Sepsis Outcome Program, the Australian Enterococcal Sepsis Outcome Program and the Australian Staphylococcal Sepsis Outcome Program.

1.1 Gram-negative Sepsis Outcome Program

AGAR began surveillance of the key gram-negative pathogens *E. coli* and *Klebsiella* species in 1992. Surveys were conducted every two years until 2008, when annual surveys commenced, alternating between community-onset and hospital-onset infections.

In 2004, another genus of gram-negative pathogens in which resistance can be of clinical importance – *Enterobacter* – was added. *E. coli* is the most common cause of community-onset urinary tract infection, whereas *Klebsiella* species are less common but are known to harbour important resistances. *Enterobacter* species are less common in the community, but of high importance because of their intrinsic resistance to first-line antimicrobials in the community. Taken together, the three groups of species surveyed are considered to be valuable sentinels for multidrug resistance and emerging resistance in enteric gram-negative bacilli. In 2013, AGAR began the ongoing Enterobacteriaceae Sepsis Outcome Program (EnSOP), which focused on the prospective collection of resistance and demographic data on all isolates from patients with documented bacteraemia. The 2014 survey was the second EnSOP survey. In 2015, *Pseudomonas aeruginosa* and *Acinetobacter* species were added, and the program changed its name to the Gram-negative Sepsis Outcome Program.

Resistances of particular interest include resistance to β-lactams due to β-lactamases, especially ESBLs, which inactivate the third-generation cephalosporins that are normally considered reserve antimicrobials. Other resistances of interest are to agents that are important for treatment of these serious infections, such as gentamicin, and to reserve agents such as ciprofloxacin and meropenem.

The objectives of the 2016 surveillance program were to:

- Monitor resistance in Enterobacteriaceae, *P. aeruginosa* and *Acinetobacter* species isolated from blood cultures taken from patients presenting to the hospital or already in hospital
- Study the extent of co-resistance and multidrug resistance in the major species
- Detect emerging resistance to newer last-line agents such as carbapenems
- Examine the molecular basis of resistance to third-generation cephalosporins, quinolones and carbapenems
- Monitor the epidemiology of *E. coli* sequence type 131.

Table 1: Hospitals that contributed to AGAR, by state and territory, 2016

State or territory	Hospital	
New South Wales	Concord Repatriation General Hospital	Royal Prince Alfred Hospital
	John Hunter Hospital	Westmead Hospital
	Nepean Hospital	Wollongong Hospital
	Royal North Shore Hospital	
Victoria	Alfred Hospital	Royal Women's and Children's Hospital
	Austin Hospital (Austin Health)	St Vincent's Hospital
	Monash Medical Centre (Monash Health)	
Queensland	Cairns Base Hospital	Princess Alexandra Hospital*
	Gold Coast Hospital	Royal Brisbane and Women's Hospital
	Prince Charles Hospital*	Greenslopes Private Hospital†
South Australia	Flinders Medical Centre	Women's and Children's Hospital§
	Royal Adelaide Hospital	
Western Australia	Fiona Stanley Hospital	St John of God Murdoch Hospital
	Joondalup Hospital	Kimberley regional hospitals (Broome, Kununurra, Derby)
	Royal Perth Hospital#	
	Sir Charles Gairdner Hospital	
Tasmania	Launceston General Hospital	Royal Hobart Hospital
Northern Territory	Alice Springs Hospital	Royal Darwin Hospital
Australian Capital Territory	Canberra Hospital	

* Microbiology services provided by Pathology Queensland Central Laboratory
† Microbiology services provided by Sullivan Nicolaides Pathology
§ Microbiology services provided by SA Pathology, Royal Adelaide Hospital
# Microbiology services provided by PathWest Laboratory Medicine WA, Fiona Stanley Hospital

1.2 Australian Enterococcal Sepsis Outcome Program

Globally, enterococci are thought to account for approximately 10% of all bacteraemias. In North America and Europe, they are the fourth and fifth leading cause of sepsis, respectively.[2,3] In the 1970s, healthcare-associated enterococcal infections were primarily due to *Enterococcus faecalis*; since then, the prevalence of *E. faecium* nosocomial infections has steadily increased.[4-6] Worldwide, the increase in nosocomial *E. faecium* infections has primarily been due to the expansion of polyclonal hospital-adapted clonal complex (CC) 17 isolates. *E. faecium* CC17 is innately resistant to many classes of antibiotics and has shown a remarkable capacity to evolve new antimicrobial resistances. In 2009, the Infectious Diseases Society of America highlighted *E. faecium* as one of the key problem bacteria or ESKAPE (*E. faecium*, *S. aureus*, *K. pneumoniae*, *Acinetobacter baumannii*, *P. aeruginosa* and *Enterobacter* species) pathogens requiring new therapies.[7]

AGAR began surveillance of antimicrobial resistance in *Enterococcus* species in 1995.[8] In 2011, AGAR commenced the Australian Enterococcal Sepsis Outcome Programme (AESOP).[9]

The aim of AESOP 2016 was to measure the proportion of *E. faecalis* and *E. faecium* bacteraemia isolates with antimicrobial resistance, with particular emphasis on:

- Assessing susceptibility to ampicillin
- Assessing susceptibility to glycopeptides
- Molecular epidemiology of *E. faecium*.

1.3 Australian Staphylococcal Sepsis Outcome Program

Globally, *S. aureus* is one of the most frequent causes of hospital-acquired and community-acquired bloodstream infections.[10] Although serious invasive infection caused by *S. aureus* has many manifestations, the organism can be detected in blood cultures in the great majority of cases. Therefore, *S. aureus* bacteraemia (SAB) is considered a very useful marker for serious invasive infection.[11]

Although prolonged antimicrobial therapy and prompt source control are used to treat SAB[12], mortality ranges from as low as 2.5% to as high as 40%.[13-15] Mortality rates are known to vary considerably with patient age, clinical manifestation, comorbidities and methicillin resistance.[16,17] A prospective study of SAB conducted by 27 laboratories in Australia and New Zealand found a 30-day all-cause mortality of 20.6%.[18] On univariate analysis, increased mortality was significantly associated with older age, European ethnicity, methicillin resistance, infections not originating from a medical device, sepsis syndrome, pneumonia/empyema and treatment with a glycopeptide or other non-β-lactam antibiotic.

AGAR began surveillance of antimicrobial resistance in *S. aureus* in 1986.[19] In 2013, AGAR commenced the Australian Staphylococcal Sepsis Outcome Program (ASSOP).[9]

The primary aim of ASSOP 2016 was to measure the proportion of SAB isolates with antimicrobial resistance, with particular emphasis on:

- Assessing susceptibility to methicillin
- Molecular epidemiology of methicillin-resistant *S. aureus*.

2 Summary of methods

Thirty-two institutions, in each state and territory of Australia, were enrolled in the 2016 AGAR programs. The AGAR laboratories collected either all isolates or up to 200 isolates of Enterobacteriaceae, *Acinetobacter* species and *P. aeruginosa*, and all isolates of *S. aureus* and *Enterococcus* species from unique patient episodes of bacteraemia from 1 January to 31 December 2016. Approval to conduct the prospective data collection, including de-identified demographic data, was given by the research ethics committees associated with each participating hospital.

In patients with more than one isolate, a new episode was defined as a new positive blood culture more than two weeks after the initial positive culture. An episode was defined as community onset if the first positive blood culture was collected 48 hours or less after admission, and as hospital onset if collected more than 48 hours after admission.

2.1 Data fields

Laboratory data collected for each episode included an accession number, the date the blood culture was collected, the organism isolated (genus and species), and the antimicrobial susceptibility test results (minimum inhibitory concentrations) for each species. The patient's date of birth, sex and postcode of residence were also provided. If the patient was admitted to hospital, the dates of admission and discharge were recorded. Depending on the level of participation, limited clinical and outcome data were also provided. These included the principal clinical manifestation, the outcome at seven and 30 days (including whether the patient died within 30 days), and, if applicable, the date of death (see Appendix A).

2.2 Species identification

Isolates were identified to species level, if possible, using the routine method for each institution. This included the Vitek® and Phoenix™ automated microbiology systems, and, if available, mass spectrometry (MALDI-TOF).

For this report, *Enterobacter cloacae complex comprises E. cloacae, E. asburiae, E. kobei, E. ludwigii, E. hormaechei* and *E. nimipressuralis*; and *Citrobacter freundii* comprises all species of the *C. freundii* complex (*C. freundii, C. braakii, C. gillenii, C. murliniae, C. rodenticum, C. sedlakii, C. werkmanii* and *C. youngae*).

2.3 Susceptibility testing

Susceptibility testing of isolates is described in Appendix B. The analysis used breakpoints from the Clinical and Laboratory Standards Institute (CLSI) M100–A27[20] and the European Committee on Antimicrobial Susceptibility Testing (EUCAST) v7.0.[21]

2.4 Statistical analysis

Confidence intervals of proportions, Fisher's exact test for categorical variables, and chi-square test for trend were calculated, if appropriate, using GraphPad Prism version 7.01 for Windows (GraphPad Software, La Jolla, California).

3 Results

3.1 Isolates recovered

A total of 7,565 gram-negative isolates (64 species, 21 genera) were reported from 32 participating institutions. Enterobacteriaceae accounted for 89.2%, followed by *P. aeruginosa* (9.6%) and *Acinetobacter* species (1.2%). Of the Enterobacteriaceae, three genera – *Escherichia* (60.9%), *Klebsiella* (18.2%) and *Enterobacter* (8.2%) – contributed 87.2% of all isolates. The top 10 species by rank were *E. coli* (54.3%), *K. pneumoniae* (12.6%), *P. aeruginosa* (9.6%), *E.cloacae* complex (5.2%), *K. oxytoca* (3.2%), *Proteus mirabilis* (3.0%), *Serratia marcescens* (2.3%), *E. aerogenes* (1.7%), *Salmonella* species (non-typhoidal) (1.5%) and *C. freundii* (1.0%). These 10 species comprised 94.4% of all isolates (Table 2).

There were 1,058 episodes of enterococcal bacteraemia. *E. faecalis* and *E. faecium* accounted for 95.3% of all enterococcal isolates (Table 2).

Of 2,540 SAB episodes, 500 (19.7%; 95% confidence interval [CI] 18.1–21.2) were methicillin resistant), ranging from 11.0% (95%CI 6.4–18.3) in Tasmania to 45.6% (95%CI 35.7–55.8) in the Northern Territory (Table 2).

Table 2: Number of each species recovered, by state and territory, 2016

Species	NSW	Vic	Qld	SA	WA	Tas	NT	ACT	Total
Gram-negative species*	1,859	1,294	1,577	755	1,214	290	283	293	7,565
Escherichia coli	994	710	812	436	678	169	153	154	4,106
Klebsiella pneumoniae	224	181	189	80	175	35	38	33	955
Pseudomonas aeruginosa	183	100	193	83	93	17	23	31	723
Enterobacter cloacae complex	110	83	87	24	54	13	11	14	396
Klebsiella oxytoca	64	52	37	24	37	14	2	13	243
Proteus mirabilis	62	25	52	23	33	11	12	8	226
Serratia marcescens	56	26	50	11	21	4	1	6	175
Enterobacter aerogenes	32	21	27	10	24	6	2	5	127
Salmonella species (non-typhoidal)	17	18	30	12	12	2	24	1	116
Citrobacter freundii	27	20	9	5	7	2	0	7	77
Morganella morganii	20	6	19	7	11	3	1	2	69
Citrobacter koseri	13	8	11	2	14	0	1	2	51
Acinetobacter baumannii complex	6	8	21	1	3	1	7	1	48
Salmonella species (typhoidal)	4	8	4	0	11	2	1	2	32
Klebsiella variicola	5	0	0	2	6	1	0	5	19
Acinetobacter species	3	1	3	2	5	1	0	1	16
Raoultella ornithinolytica	6	2	1	1	3	0	0	3	16

continued

Table 2: (continued)

Species	NSW	Vic	Qld	SA	WA	Tas	NT	ACT	Total
Enterobacter species	1	0	0	13	0	0	0	0	14
Providencia rettgeri	5	0	2	0	6	0	0	0	13
Other species (*n = 45*)	27	25	30	19	21	9	7	5	143
Enterococcus species	286	247	151	99	151	44	13	67	1,058
Enterococcus faecalis	152	130	100	52	87	27	7	40	595
Percentage vancomycin resistant	0.0	0.8	0.0	1.9	0.0	0.0	–†	0.0	0.3
Enterococcus faecium	124	109	43	43	54	14	4	22	413
Percentage vancomycin resistant	47.6	62.4	30.2	46.5	14.8	42.9	–†	68.2	46.5
Percentage vancomycin susceptible	52.4	37.6	69.8	53.5	85.2	57.1	–†	31.8	53.5
Other enterococcal species	10	8	8	4	10	3	2	5	50
Enterococcus casseliflavus	5	5	5	1	4	1	2	2	25
Enterococcus gallinarum	0	1	3	2	2	1	0	2	11
Enterococcus avium	3	2	0	0	3	0	0	0	8
Enterococcus raffinosus	1	0	0	1	1	0	0	0	3
Enterococcus hirae	1	0	0	0	0	1	0	1	3
Staphylococcus aureus	637	418	494	278	413	109	90	101	2,540
Percentage methicillin resistant	25.3	15.6	13.2	22.3	19.6	11.0	45.6	12.9	19.7
Percentage methicillin susceptible	74.7	84.4	86.8	77.7	80.4	89.0	54.4	87.1	80.3

* Enterobacteriaceae, *Acinetobacter* species and *Pseudomonas aeruginosa*
† Insufficient numbers (<10) to calculate percentage

3.2 Place of onset of bacteraemia

Almost all patients with bacteraemia were admitted to hospital (gram-negative species, 97.3%; *Enterococcus* species, 98.6%; *S. aureus*, 97.6%).

Information on place of onset of bacteraemia was available for 7,440 (98.3%) gram-negative episodes, 1,058 (100%) *Enterococcus* species episodes and 2,540 (100%) *S. aureus* episodes (Table 3).

For gram-negative species, 75.1% of all episodes were community onset, although differences were observed with different species. Episodes involving *E. faecalis* and other *Enterococcus* species were predominantly community onset (68.6%, 95%CI 64.7–72.2 for *E. faecalis*; 76.0%, 95%CI 62.6–85.7 for other *Enterococcus* species); however, *E. faecium* episodes were predominantly hospital onset (72.2%; 95%CI 67.6–76.3). Most SABs were community onset (76.3%; 95%CI 74.6–77.9).

Table 3: Species recovered, by place of onset, 2016

Organism	Community onset (%)	Hospital onset (%)	Total
Gram-negative species*	75.1 (5,589)	24.9 (1,851)	7,440
Escherichia coli	83.1 (3,351)	16.9 (680)	4,031
Klebsiella pneumoniae	70.2 (655)	29.8 (278)	933
Pseudomonas aeruginosa	56.8 (405)	43.2 (308)	713
Enterobacter cloacae complex	52.6 (205)	47.4 (185)	390
Klebsiella oxytoca	65.6 (158)	34.4 (83)	241
Proteus mirabilis	80.4 (181)	19.6 (44)	225
Serratia marcescens	56.6 (99)	43.4 (76)	175
Enterobacter aerogenes	64.0 (80)	36.0 (45)	125
Salmonella species (non-typhoidal)	94.7 (108)	5.3 (6)	114
Citrobacter freundii	66.2 (51)	33.8 (26)	77
Morganella morganii	78.3 (54)	21.7 (15)	69
Citrobacter koseri	62.0 (31)	38.0 (19)	50
Acinetobacter baumannii complex	31.9 (15)	68.1 (32)	47
Salmonella species (typhoidal)	100 (30)	0.0 (0)	30
Klebsiella variicola	57.9 (11)	42.1 (8)	19
Acinetobacter species	75.0 (12)	25.0 (4)	16
Raoultella ornithinolytica	87.5 (14)	12.5 (2)	16
Enterobacter species	78.6 (11)	21.4 (3)	14
Providencia rettgeri	84.6 (11)	15.4 (2)	13
Other gram-negative species (*n* = 45)	75.4 (107)	24.6 (35)	142
Enterococcus species	53.0 (561)	47.0 (497)	1,058
Enterococcus faecalis	68.6 (408)	31.4 (87)	595
Vancomycin resistant	–† (0)	–† (2)	2
Vancomycin susceptible	68.8 (408)	31.2 (185)	593
Enterococcus faecium	27.8 (115)	72.2 (298)	413
Vancomycin resistant	23.4 (45)	76.6 (147)	192
Vancomycin susceptible	31.7 (70)	68.3 (151)	221
Other *Enterococcus* species (*n* = 5)	76.0 (38)	24.0 (12)	50
Staphylococcus aureus	76.3 (1,937)	23.7 (603)	2,540
Methicillin resistant	73.8 (369)	26.2 (131)	500
Methicillin susceptible	76.9 (1,568)	23.1 (472)	2,040

* Enterobacteriaceae, *Acinetobacter* species and *Pseudomonas aeruginosa*

† Insufficient numbers (<10) to calculate percentage

3.3 Onset versus 30-day all-cause mortality

Information on 30-day all-cause mortality, when place of onset was known, was available for 4,758 (62.9%) episodes involving gram-negative species – 917 (86.7%) involving *Enterococcus* species and 2,018 (79.4%) involving *S. aureus*. The only species for which a significant difference was seen in the 30-day all-cause mortality between community-onset and hospital-onset episodes were *E. coli* and *C. koseri* (Table 4).

There was a significant difference in the 30-day all-cause mortality between *E. faecium* (27.2%) and *E. faecalis* (12.9%) episodes (P < 0.0001). However, there was no significant difference in all-cause mortality between vancomycin-resistant and vancomycin-susceptible *E. faecium* episodes.

For *S. aureus*, there was a significant difference in 30-day all-cause mortality between methicillin-susceptible *S. aureus* (MSSA) (15.3%) and methicillin-resistant *S. aureus* (MRSA) (23.1%) episodes (*P* = 0.0003). There was no significant difference in 30-day all-cause mortality between healthcare-associated MRSA (HA-MRSA) and community-associated MRSA (CA-MRSA) clones.

Table 4: Onset setting and 30-day all-cause mortality (blood culture isolates), 2016

	Community onset		Hospital onset		Total		
Organism	**Number**	**Deaths (%)**	**Number**	**Deaths (%)**	**Number**	**Deaths (%)**	**Significance**
Gram-negative species[†]	3,432	12.0 (413)	1,326	16.7 (222)	4,758	13.3 (635)	
Escherichia coli	1,986	10.1 (200)	474	17.3 (82)	2,460	11.5 (282)	P < 0.01
Klebsiella pneumoniae	415	11.3 (47)	193	14.5 (28)	608	12.3 (75)	ns
Pseudomonas aeruginosa	244	23.0 (56)	225	18.2 (41)	469	20.7 (97)	ns
Enterobacter cloacae complex	148	16.2 (24)	144	11.8 (17)	292	14.0 (41)	ns
Klebsiella oxytoca	108	13.0 (14)	58	19.0 (11)	166	15.1 (25)	ns
Proteus mirabilis	119	16.0 (19)	28	10.7 (3)	147	15.0 (22)	ns
Serratia marcescens	69	17.4 (12)	58	15.5 (9)	127	16.5 (21)	ns
Enterobacter aerogenes	52	19.2 (10)	33	12.1 (4)	85	16.5 (14)	ns
Salmonella species (non-typhoidal)	74	4.1 (3)	2	0.0 (0)[§]	76	3.9 (3)	ns
Citrobacter freundii complex	36	22.2 (8)	22	36.4 (8)	58	27.6 (16)	ns
Morganella morganii	34	17.6 (6)	11	9.1 (1)	45	15.6 (7)	ns

continued

Table 4: (continued)

Organism	Community onset		Hospital onset		Total		Significance
	Number	Deaths (%)	Number	Deaths (%)	Number	Deaths (%)	
Acinetobacter baumannii complex	10	10.0 (1)	25	12.0 (3)	35	11.4 (4)	ns
Citrobacter koseri	18	5.6 (1)	14	42.9 (6)	32	21.9 (7)	0.01 < P < 0.05
Salmonella species (typhoidal)	21	0.0 (0)	0	0.0 (0)§	21	0.0 (0)	ns
Other gram-negative species (*n* = 46)	98	12.2 (12)	39	23.1 (9)	137	15.3 (21)	
Enterococcus species	462	13.2 (61)	455	25.5 (116)	917	19.3 (177)	0.01 < P < 0.05
Enterococcus faecalis	336	10.4 (35)	161	18.0 (29)	497	12.9 (64)	ns
Enterococcus faecium	96	21.9 (21)	283	29.0 (82)	379	27.2 (103)	ns
Vancomycin resistant	39	23.1 (9)	142	30.3 (43)	181	28.7 (52)	ns
Vancomycin susceptible	57	21.1 (12)	141	27.7 (39)	198	25.8 (51)	ns
Other enterococcal species (*n = 5)*	30	16.7 (5)	11	45.5 (5)	41	24.4 (10)	
Staphylococcus aureus	1,509	16.5 (249)	509	17.5 (89)	2,018	16.7 (338)	ns
Methicillin resistant	277	25.3 (70)	109	17.4 (19)	386	23.1 (89)	ns
CA-MRSA	195	23.6 (46)	58	20.7 (12)	253	22.9 (58)	ns
HA-MRSA	65	29.2 (19)	46	10.9 (5)	111	21.6 (24)	0.01 < P < 0.05
Methicillin susceptible	1,232	14.5 (179)	400	17.5 (70)	1,632	15.3 (249)	ns

CA-MRSA = community-associated methicillin-resistant *Staphylococcus aureus*; HA-MRSA = healthcare-associated methicillin-resistant *S. aureus*; ns = not significant

* Fisher's exact test for difference in mortality between community onset and hospital onset

† Enterobacteriaceae, *Acinetobacter* species and *Pseudomonas aeruginosa*

§ Insufficient numbers (<10) to calculate percentage

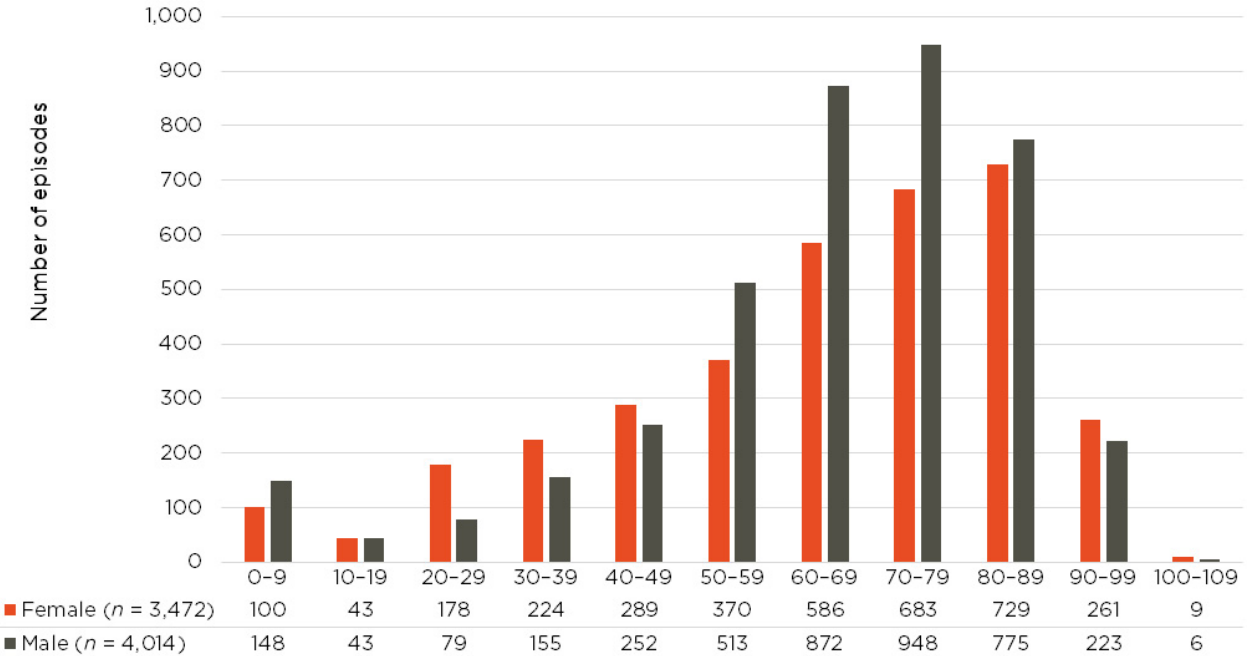
3.4 Patient age and sex

Age and sex were available for 99.0% of patients with gram-negative bacteraemia and for all patients with enterococcal or staphylococcal bacteraemia.

For gram-negative bacteraemia, the proportion of males was 53.6%. For *Enterococcus* species and SAB, 66.3% and 65.4%, respectively, were male.

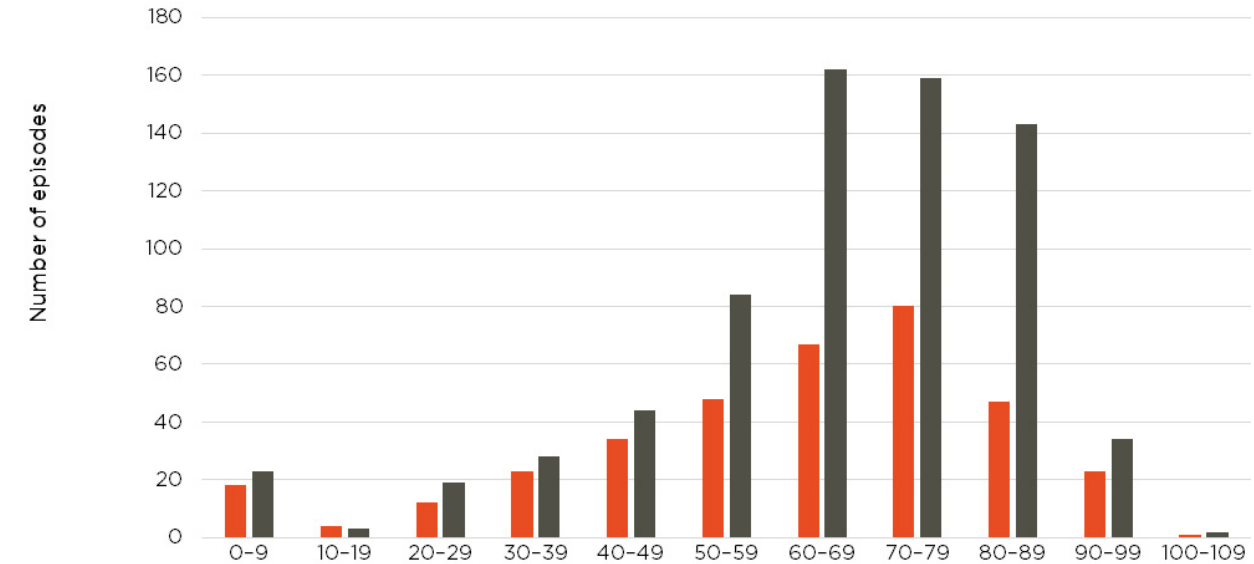
Increasing age was a surrogate risk factor for bacteraemia (Figures 1–3); only 13.0% of gram-negative species episodes, 12.3% of *Enterococcus* species episodes and 21.0% of *S. aureus* episodes were in patients aged less than 40 years.

Figure 1: Number of episodes of bacteraemia due to gram-negative species, by patient decade of life and gender, 2016



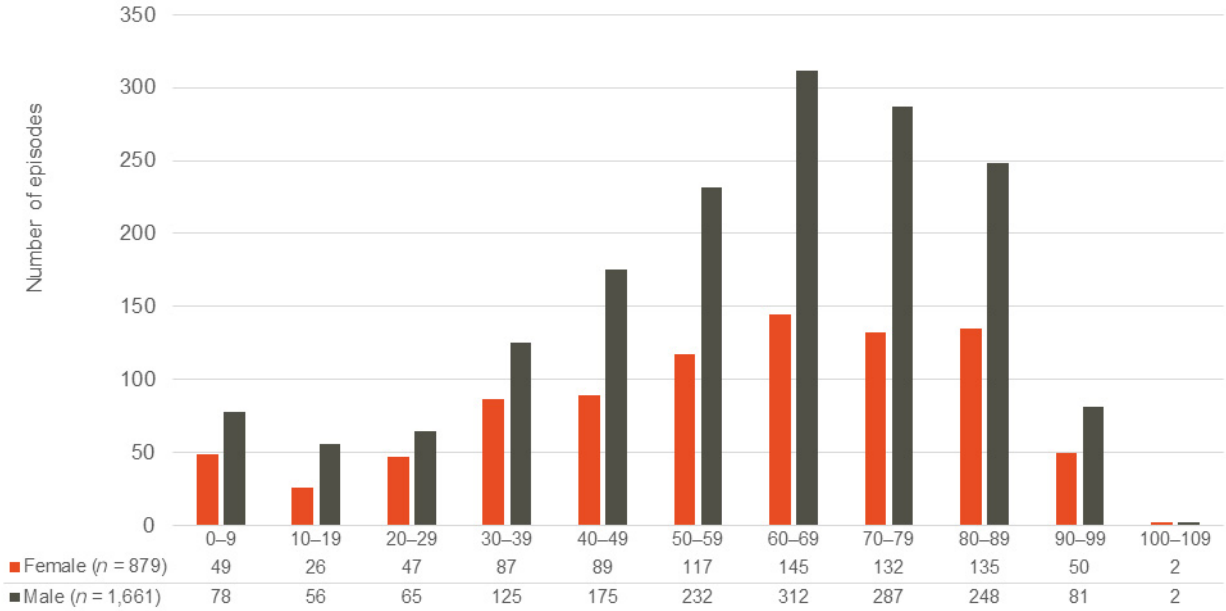
	0–9	10–19	20–29	30–39	40–49	50–59	60–69	70–79	80–89	90–99	100–109
Female (*n* = 3,472)	100	43	178	224	289	370	586	683	729	261	9
Male (*n* = 4,014)	148	43	79	155	252	513	872	948	775	223	6

Figure 2: Number of episodes of bacteraemia due to *Enterococcus* species, by patient decade of life and gender, 2016



	0–9	10–19	20–29	30–39	40–49	50–59	60–69	70–79	80–89	90–99	100–109
Female (*n* = 357)	18	4	12	23	34	48	67	80	47	23	1
Male (*n* = 701)	23	3	19	28	44	84	162	159	143	34	2

Figure 3: Number of episodes of bacteraemia due to *Staphylococcus aureus*, by patient decade of life and gender, 2016



3.5 Principal clinical manifestation

The principal clinical manifestations, which represent the most likely primary site or source for the origin of the bloodstream infection, are described below for patients with gram-negative, enterococcal and staphylococcal bacteraemia.

3.5.1 Gram-negative bacteria

The principal clinical manifestation was documented for 6,029 (79.7%) patient episodes of gram-negative bacteraemia. The most frequent clinical manifestations were urinary tract infection (41.9%), biliary tract infection (14.8%) and other intra-abdominal infection (10.7%) (Table 5).

3.5.2 *Enterococcus* species

The principal clinical manifestation was known for 1,004 (94.9%) patient episodes of enterococcal bacteraemia. Overall, the most frequent principal clinical manifestation was urinary tract infection (17.7%), followed by intra-abdominal infection (15.2%) (Table 6). There were no significant differences between the sexes in principle clinical manifestations, but there were more episodes in males.

Of the hospital-onset episodes for which data were available, the most frequent principal clinical manifestation was intra-abdominal infection (20.0%). Of the community-onset episodes for which data were available, the most frequent principal clinical manifestation was urinary tract infection (24.1%).

The principal manifestation was known for 958 of the 1,008 (95.0%) *E. faecalis* and *E. faecium* episodes (Table 7). The most common clinical manifestation for *E. faecalis* was urinary tract infection, whereas for *E. faecium* it was intra-abdominal infection (other than biliary tract). Significant differences were seen between *E. faecalis* and *E. faecium* for a number of clinical manifestations.

3.5.3 *Staphylococcus aureus*

The principal clinical manifestation was known for 2,256 (88.8%) episodes of SAB (Table 8). Overall, the most frequent principal clinical manifestation was osteomyelitis/septic arthritis (18.5%), followed by skin and skin structure infection (18.1%), and device-related infection (17.4%).

Of the hospital-onset SABs for which data were available, the most common principal clinical manifestation was device-related infection (32.9%).

Of the community-onset SABs for which data were available, the most common principal clinical manifestation was osteomyelitis/septic arthritis

Table 5: Principal clinical manifestation for gram-negative* bacteraemia, by patient sex, 2016

Principal clinical manifestation	Female (%)	Male (%)	Total (%)	Significance
Urinary tract infection	49.0 (1,384)	35.7 (1,145)	41.9 (2,529)	P < 0.01
Biliary tract infection (including cholangitis)	12.4 (350)	17.0 (545)	14.8 (895)	P < 0.01
Intra-abdominal infection other than biliary tract	9.7 (274)	11.5 (369)	10.7 (643)	0.01 < P < 0.05
No focus (setting not known)	8.5 (239)	8.9 (286)	8.7 (525)	ns
Febrile neutropenia (when specified)	5.8 (164)	8.5 (274)	7.3 (438)	P < 0.01
Other clinical syndrome	5.0 (141)	6.5 (210)	5.8 (351)	0.01 < P < 0.05
Device-related infection without metastatic focus	5.8 (165)	5.5 (178)	5.7 (343)	ns
Skin and skin structure infection	2.6 (72)	3.9 (125)	3.3 (197)	P < 0.01
Osteomyelitis/septic arthritis	0.3 (9)	1.2 (38)	0.8 (47)	P < 0.01
Device-related infection with metastatic focus	0.4 (12)	0.5 (17)	0.5 (29)	ns
No focus	0.4 (11)	0.6 (21)	0.5 (32)	ns
Total	2,821	3,208	6,029	

ns = not significant

* Enterobacteriaceae, *Acinetobacter* species and *Pseudomonas aeruginosa*

Table 6: Principal clinical manifestation for enterococcal bacteraemia, by patient gender, 2015

Principal clinical manifestation	Female (%)	Male (%)	Total (%)	Significance
Urinary tract infection	14.6 (50)	19.3 (128)	17.7 (178)	ns
Intra-abdominal infection other than biliary tract	16.4 (56)	14.7 (97)	15.2 (153)	ns
Biliary tract infection (including cholangitis)	16.4 (56)	14.0 (93)	14.8 (149)	ns
No focus (setting not known)	15.8 (54)	14.0 (93)	14.6 (147)	ns
Device-related infection without metastatic focus	9.4 (32)	8.9 (59)	9.1 (91)	ns
Febrile neutropenia	7.6 (26)	9.1 (60)	8.6 (86)	ns
Endocarditis, left-sided	5.0 (17)	8.3 (55)	7.2 (72)	ns
Other clinical syndrome	5.6 (19)	5.0 (33)	5.2 (52)	ns
Skin and skin structure	4.4 (15)	3.3 (22)	3.7 (37)	ns
Osteomyelitis/septic arthritis	1.2 (4)	1.8 (12)	1.6 (16)	ns
Device-related infection with metastatic focus	1.8 (6)	0.9 (6)	1.2 (12)	ns
Endocarditis, right-sided	2.0 (7)	0.6 (4)	1.1 (11)	ns
Total	342	662	1,004	

ns = not significant

Table 7: Principal clinical manifestation for enterococcal bacteraemia, by *Enterococcus* species, 2016

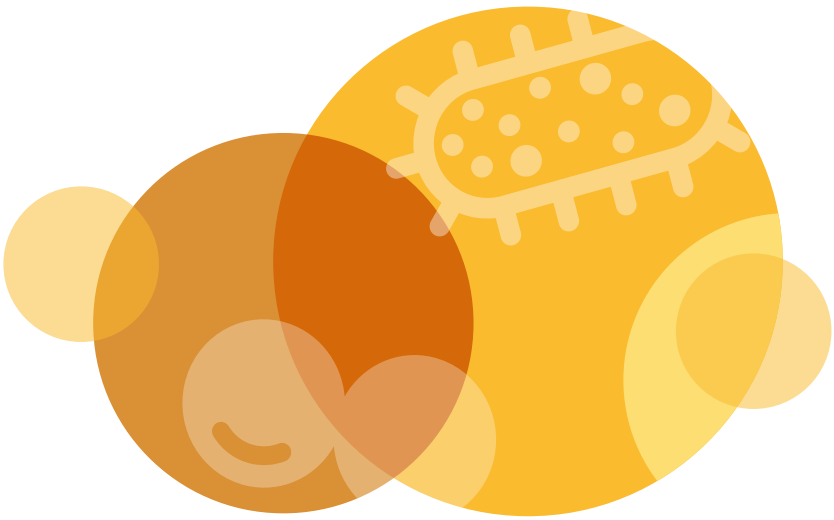
Principal clinical manifestation	*E. faecalis* (%)	*E. faecium* (%)	Total (%)	Significance
Urinary tract infection	26.4 (147)	7.0 (28)	7.0 (28)	P < 0.01
Intra-abdominal infection other than biliary tract	11.3 (63)	21.4 (86)	21.4 (86)	P < 0.01
No focus (setting not known)	14.2 (79)	15.2 (61)	15.2 (61)	ns
Biliary tract infection (including cholangitis)	7.4 (41)	20.9 (84)	20.9 (84)	P < 0.01
Device-related infection without metastatic focus	9.5 (53)	9.0 (36)	9.0 (36)	ns
Febrile neutropenia	3.2 (18)	16.7 (67)	16.7 (67)	P < 0.01
Endocarditis, left-sided	12.1 (67)	1.2 (5)	1.2 (5)	P < 0.01
Other clinical syndrome	5.8 (32)	4.2 (17)	4.2 (17)	ns
Skin and skin structure	4.7 (26)	2.7 (11)	2.7 (11)	ns
Osteomyelitis/septic arthritis	2.2 (12)	0.7 (3)	0.7 (3)	ns
Device-related infection with metastatic focus	1.6 (9)	0.7 (3)	0.7 (3)	ns
Endocarditis, right-sided	1.6 (9)	0.2 (1)	0.2 (1)	ns
Total	556	402	402	

ns = not significant

Table 8: Principal clinical manifestation for *Staphylococcus aureus* bacteraemia, by patient sex, 2016

Principal clinical manifestation	Female (%)	Male (%)	Total (%)	Significance
Osteomyelitis/septic arthritis	17.3 (133)	19.1 (284)	18.5 (417)	ns
Skin and skin structure	17.3 (133)	18.6 (276)	18.1 (409)	ns
Device-related infection without metastatic focus	17.9 (138)	17.1 (254)	17.4 (392)	ns
No focus	17.9 (138)	14.9 (222)	16.0 (360)	ns
Pneumonia/empyema	6.6 (51)	6.1 (90)	6.3 (141)	ns
Other clinical syndrome	5.5 (42)	5.9 (88)	5.8 (130)	ns
Endocarditis, left-sided	4.0 (31)	6.4 (95)	5.6 (126)	0.01 < P < 0.05
Deep abscess(es), excluding those in the CNS	3.1 (24)	3.0 (44)	3.0 (68)	ns
CNS infection (meningitis, abscess[es])	3.4 (26)	2.4 (36)	2.7 (62)	ns
Endocarditis, right-sided	3.2 (25)	2.5 (37)	2.7 (62)	ns
Device-related infection with metastatic focus	1.4 (11)	2.6 (39)	2.2 (50)	ns
Febrile neutropenia	2.2 (17)	1.3 (20)	1.6 (37)	ns
Endocarditis, unspecified	0.1 (1)	0.1 (1)	0.1 (2)	ns
Total	770	1,486	2,256	

CNS = central nervous system;; ns = not significant



3.6 Length of hospital stay following bacteraemic episode

Information on length of stay following bacteraemia was available for 6,383 (85.7%) episodes involving gram-negative species, 998 (94.3%) episodes involving *Enterococcus* species and 2,314 (91.1%) episodes involving *S. aureus*.

The most common length of stay (44.6%) for patients with a gram-negative bacteraemia was less than seven days (Table 9). Overall 21.9% of patients remained in hospital for more than 30 days after enterococcal bacteraemia (Table 10) and 26.7% after staphylococcal bacteraemia (Table 11).

Table 9: Length of stay following gram-negative bacteraemia, by species and place of onset, 2016

Species	Length of stay following bacteraemia (days)				Total
	<7 (%)	7–14 (%)	15–30 (%)	>30 (%)	
Gram-negative species*	44.6 (2,892)	30.0 (1,943)	14.9 (967)	10.5 (681)	6,483
Enterobacteriaceae	45.9 (2,658)	29.8 (1,727)	14.3 (826)	10.0 (577)	5,788
Escherichia coli	51.1 (1,780)	29.3 (1,019)	12.2 (423)	7.4 (259)	3,481
Community onset	56.5 (1,615)	29.0 (828)	9.4 (269)	5.1 (145)	2,857
Hospital onset	26.4 (165)	30.6 (191)	24.7 (154)	18.3 (114)	624
Klebsiella pneumoniae	37.2 (307)	31.4 (259)	19.4 (160)	12.0 (99)	825
Community onset	45.9 (256)	32.1 (179)	15.2 (85)	6.8 (38)	558
Hospital onset	19.1 (51)	30.0 (80)	28.1 (75)	22.8 (61)	267
Enterobacter cloacae complex	27.5 (98)	34.2 (122)	20.2 (72)	18.2 (65)	357
Community onset	39.3 (72)	36.1 (66)	14.2 (26)	10.4 (19)	183
Hospital onset	14.9 (26)	32.2 (56)	26.4 (46)	26.4 (46)	174
Other Enterobacteriaceae (*n* = 49)	42.0 (473)	29.1 (327)	15.2 (171)	13.7 (154)	1,125
Pseudomonas aeruginosa	33.6 (208)	31.2 (193)	21.0 (130)	14.2 (88)	619
Community onset	43.8 (145)	32.3 (107)	18.1 (60)	5.7 (19)	331
Hospital onset	21.9 (63)	29.9 (86)	24.3 (70)	24.0 (69)	288
Acinetobacter baumannii complex	22.7 (10)	27.3 (12)	15.9 (7)	34.1 (15)	44
Community onset	46.2 (6)	30.8 (4)	15.4 (2)	7.7 (1)	13
Hospital onset	12.9 (4)	25.8 (8)	16.1 (5)	45.2 (14)	31

* Enterobacteriaceae, *Acinetobacter* species and *Pseudomonas aeruginosa*. The totals are greater than the sum of the figures for the species listed because some *Acinetobacter* and *Pseudomonas* species that contributed to the totals are not included in the table.

Table 10: Length of stay following *Enterococcus* species bacteraemia, by vancomycin resistance and place of onset, 2016

Species	Length of stay following bacteraemia (days)				Total
	<7 (%)	7–14 (%)	15–30 (%)	>30 (%)	
All species	23.4 (234)	26.5 (264)	28.2 (281)	21.9 (219)	998
E. faecalis	23.3 (128)	28.2 (155)	26.5 (146)	22.0 (121)	550
E. faecium	22.9 (92)	22.7 (91)	31.7 (127)	22.7 (91)	401
Vancomycin susceptible	25.7 (55)	24.8 (53)	28.5 (61)	20.6 (44)	213
Vancomycin resistant	20.0 (38)	20.5 (39)	33.7 (64)	24.7 (47)	188
Other *Enterococcus* species (*n* = 5)	29.8 (14)	38.3 (18)	17.0 (8)	14.9 (7)	47
Community onset					
E. faecalis	26.1 (97)	30.4 (113)	24.5 (91)	19.1 (71)	372
E. faecium	29.9 (32)	31.8 (34)	28.0 (30)	10.3 (11)	107
Vancomycin susceptible	38.5 (25)	26.2 (17)	24.6 (16)	10.8 (7)	65
Vancomycin resistant	16.7 (7)	40.5 (17)	33.3 (14)	9.5 (4)	42
Hospital onset					
E. faecalis	17.4 (31)	23.6 (42)	30.9 (55)	28.1 (50)	178
E. faecium	20.4 (60)	19.4 (57)	33.0 (97)	27.2 (80)	294
Vancomycin susceptible	19.6 (29)	23.6 (35)	31.8 (47)	25.0 (37)	148
Vancomycin resistant	21.2 (31)	15.1 (22)	34.2 (50)	29.5 (43)	146

Table 11: Length of stay following *Staphylococcus aureus* bacteraemia, by methicillin susceptibility and place of onset, 2015

Species	Length of stay following bacteraemia (days)				Total
	<7 (%)	7–14 (%)	15–30 (%)	>30 (%)	
Staphylococcus aureus	18.6 (429)	25.1 (579)	30.0 (691)	26.3 (607)	2,306
Methicillin resistant	23.1 (99)	20.1 (86)	32.7 (140)	24.1 (103)	428
Community onset	26.4 (82)	22.2 (69)	30.5 (95)	20.9 (65)	311
Hospital onset	14.5 (17)	14.5 (17)	38.5 (45)	32.5 (38)	117
Methicillin susceptible	17.6 (330)	26.3 (493)	29.3 (551)	26.8 (504)	1,878
Community onset	18.9 (270)	27.0 (385)	28.7 (410)	25.4 (362)	1,427
Hospital onset	13.3 (60)	23.9 (108)	31.3 (141)	31.5 (142)	451

3.7 Susceptibility testing results

The following sections present the results of susceptibility testing in priority indicator species, and the findings for antimicrobial resistance by place of onset and multidrug resistance.

3.7.1 Percentages of non-susceptibility in national priority indicator species

Overall percentages of resistance or non-susceptibility in the indicator species of national priority, using both CLSI breakpoints and EUCAST breakpoints, are shown in Table 12. Resistance by state and territory can be found in Appendix C.

For some antimicrobials, the concentration range tested did not distinguish between intermediate susceptibility and resistance; the term non-susceptible was used to describe these results. In *Salmonella*, non-resistant refers to isolates that were susceptible or intermediate.

Supplementary data on percentages susceptible, intermediate and resistant for each antimicrobial and all species, and the antimicrobial profiles by state and territory can be found in the 2016 reports for each program on the AGAR website. These reports provide summary susceptibility data (number and percentage for species if more than 10 isolates were tested) using both CLSI and EUCAST interpretive guidelines for all species isolated.

Table 12: Antimicrobial resistances (CLSI and EUCAST), 2016

		CLSI		EUCAST	
Species and antimicrobial	**Number**	**% intermediate (*n*)**	**% resistant (*n*)**	**% intermediate (*n*)**	**% resistant (*n*)**
Acinetobacter baumannii complex					
Piperacillin–tazobactam	34	2.2 (1)	17.4 (8)	–*	–*
Ceftazidime	46	15.2 (7)	17.4 (8)	–*	–*
Cefepime	46	6.5 (3)	17.4 (8)	–*	–*
Gentamicin	47	0.0 (0)	8.5 (4)	–†	8.5 (4)
Tobramycin	47	0.0 (0)	8.5 (4)	–†	8.5 (4)
Amikacin	47	0.0 (0)	0.0 (0)	4.3 (2)	0.0 (0)
Ciprofloxacin	47	0.0 (0)	12.8 (6)	–†	12.8 (6)
Meropenem	47	0.0 (0)	17.0 (8)	0.0 (0)	17.0 (8)
Enterobacter aerogenes					
Piperacillin–tazobactam	124	4.0 (5)	25.0 (31)	4.0 (5)	29.0 (36)
Ceftriaxone	127	0.0 (0)	33.1 (42)	0.0 (0)	33.1 (42)
Ceftazidime	127	0.0 (0)	29.1 (37)	2.4 (3)	29.1 (37)
Cefepime	127	0.0 (0)§	2.4 (3)	2.4 (3)	2.4 (3)
Gentamicin	127	0.0 (0)	1.6 (2)	0.0 (0)	1.6 (2)
Tobramycin	127	0.0 (0)	2.4 (3)	0.0 (0)	2.4 (3)
Amikacin	127	0.0 (0)	0.0 (0)	0.8 (1)	0.0 (0)
Ciprofloxacin	127	0.0 (0)	0.0 (0)	0.0 (0)	1.6 (2)
Meropenem	127	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)
Enterobacter cloacae complex					
Piperacillin–tazobactam	332	2.4 (8)	19.9 (66)	3.0 (10)	22.3 (74)
Ceftriaxone	396	0.8 (3)	26.3 (104)	0.8 (3)	26.3 (104)
Ceftazidime	396	0.8 (3)	23.5 (93)	2.3 (9)	24.2 (96)

continued

Table 12: (continued)

Species and antimicrobial	Number	CLSI		EUCAST	
		% intermediate (*n*)	% resistant (*n*)	% intermediate (*n*)	% resistant (*n*)
Cefepime	394	4.6 (18)	1.5 (6)	9.1 (36)	3.8 (15)
Gentamicin	396	0.0 (0)	5.6 (22)	0.3 (1)	5.6 (22)
Tobramycin	396	2.3 (9)	4.0 (16)	0.0 (0)	6.3 (25)
Amikacin	396	0.3 (1)	0.0 (0)	2.0 (8)	0.3 (1)
Benzylpenicillin	391	–†	88.5 (346)	–§	–§
Ciprofloxacin	373	4.3 (16)	87.9 (328)	–†	74.8 (279)
Enterococcus faecalis					
Ampicillin	592	–†	0.2 (1)	–†	0.2 (1)
Benzylpenicillin	576	–†	1.0 (6)	–*	–*
Ciprofloxacin	559	3.2 (18)	12.2 (68)	–†	8.8 (49)
Daptomycin	564	0.0 (0)	0.5 (3)	–*	–*
Linezolid	591	2.5 (15)	0.3 (2)	–†	0.3 (2)
Teicoplanin	592	0.0 (0)	0.0 (0)	–†	0.0 (0)
Tetracycline	514	0.2 (1)	72.6 (373)	–*	–*
Vancomycin	592	0.2 (1)	0.2 (1)	–†	0.3 (2)
Enterococcus faecium					
Ampicillin	412	0.0 (0)	91.5 (377)	0.0 (0)	91.5 (377)
Benzylpenicillin	409	–†	92.7 (379)	–*	–*
Ciprofloxacin	404	1.7 (7)	90.3 (365)	–†	76.0 (307)
Linezolid	408	0.5 (2)	0.0 (0)	–†	0.0 (0)
Teicoplanin	413	4.4 (18)	13.8 (57)	–†	18.9 (78)
Tetracycline	353	0.0 (0)	66.6 (235)	–*	–*
Vancomycin	413	1.2 (5)	45.3 (187)	–†	46.5 (192)
Escherichia coli					
Ampicillin	4,089	1.6 (67)	53.6 (2,191)	–†	55.2 (2,258)
Amoxicillin–clavulanate	4,060	12.6 (511)	8.3 (337)	–#	–#
Piperacillin–tazobactam	4,083	3.4 (138)	3.1 (127)	1.3 (55)	6.5 (265)
Ceftriaxone	4,096	0.3 (13)	11.5 (470)	0.3 (13)	11.5 (470)
Ceftazidime	4,095	0.4 (18)	6.2 (255)	4.2 (171)	6.7 (273)
Cefepime	4,094	1.9 (79)	3.6 (147)	4.4 (181)	4.7 (193)
Gentamicin	4,095	0.2 (9)	7.4 (303)	0.7 (29)	7.6 (312)
Tobramycin	4,095	5.1 (207)	3.7 (150)	0.7 (29)	8.7 (357)
Amikacin	4,096	0.1 (5)	0.1 (5)	1.8 (74)	0.2 (10)
Ciprofloxacin	4,094	0.1 (5)	12.7 (521)	2.3 (94)	14.0 (573)
Meropenem	4,095	0.0 (2)	0.1 (4)	0.0 (2)	0.0 (2)
Klebsiella oxytoca					
Amoxicillin–clavulanate	242	5.0 (12)	9.9 (24)	–#	–#
Piperacillin–tazobactam	241	0.8 (2)	14.1 (34)	2.9 (7)	14.9 (36)
Ceftriaxone	243	1.6 (4)	9.5 (23)	1.6 (4)	9.5 (23)
Ceftazidime	243	0.0 (0)	1.6 (4)	0.4 (1)	1.6 (4)
Cefepime	243	0.0 (0)	1.2 (3)	1.6 (4)	1.2 (3)

continued

Table 12: (continued)

Species and antimicrobial	Number	CLSI		EUCAST	
		% intermediate (*n*)	% resistant (*n*)	% intermediate (*n*)	% resistant (*n*)
Gentamicin	243	0.0 (0)	1.2 (3)	1.2 (3)	1.2 (3)
Tobramycin	243	1.6 (4)	0.0 (0)	0.8 (2)	1.6 (4)
Amikacin	243	0.0 (0)	0.0 (0)	0.8 (2)	0.0 (0)
Ciprofloxacin	243	0.4 (1)	0.4 (1)	0.4 (1)	1.6 (4)
Meropenem	243	0.0 (0)	0.4 (1)	0.0 (0)	0.4 (1)
Klebsiella pneumoniae					
Amoxicillin–clavulanate	947	4.6 (44)	4.9 (46)	–#	–#
Piperacillin–tazobactam	948	3.5 (33)	3.6 (34)	5.5 (52)	7.1 (67)
Ceftriaxone	953	0.8 (8)	6.8 (65)	0.8 (8)	6.8 (65)
Ceftazidime	953	0.8 (8)	4.5 (43)	2.6 (25)	5.4 (51)
Cefepime	953	0.7 (7)	2.5 (24)	3.3 (31)	2.8 (27)
Gentamicin	953	0.0 (0)	4.3 (41)	0.1 (1)	4.3 (41)
Tobramycin	953	1.9 (18)	3.7 (35)	0.1 (1)	5.6 (53)
Amikacin	953	0.0 (0)	0.2 (2)	0.4 (4)	0.2 (2)
Ciprofloxacin	953	1.2 (11)	2.6 (25)	2.3 (22)	6.7 (64)
Meropenem	953	0.1 (1)	0.4 (4)	0.3 (3)	0.1 (1)
Proteus mirabilis					
Ampicillin	225	1.3 (3)	16.9 (38)	–†	18.2 (41)
Amoxicillin–clavulanate	219	6.4 (14)	2.7 (6)	–#	–#
Piperacillin–tazobactam	225	0.9 (2)	0.0 (0)	0.0 (0)	0.9 (2)
Ceftriaxone	225	0.0 (0)	0.4 (1)	0.0 (0)	0.4 (1)
Ceftazidime	224	0.0 (0)	0.0 (0)	0.4 (1)	0.0 (0)
Cefepime	225	0.4 (1)	0.0 (0)	0.4 (1)	0.0 (0)
Gentamicin	225	1.8 (4)	0.4 (1)	2.7 (6)	2.2 (5)
Tobramycin	225	1.8 (4)	0.4 (1)	1.8 (4)	2.2 (5)
Amikacin	224	0.0 (0)	0.0 (0)	0.4 (1)	0.0 (0)
Ciprofloxacin	225	0.4 (1)	1.3 (3)	0.4 (1)	3.1 (7)
Meropenem	225	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)
Pseudomonas aeruginosa					
Piperacillin–tazobactam	710	6.6 (47)	5.2 (37)	–†	11.8 (84)
Ceftazidime	713	3.2 (23)	4.6 (33)	–†	7.9 (56)
Cefepime	714	3.2 (23)	2.9 (21)	–†	6.2 (44)
Gentamicin	714	2.5 (18)	1.7 (12)	–†	4.2 (30)
Tobramycin	714	0.0 (0)	1.5 (11)	–†	1.5 (11)
Amikacin	714	0.6 (4)	0.6 (4)	3.1 (22)	1.1 (8)
Ciprofloxacin	715	1.7 (12)	3.8 (27)	0.0 (0)	9.4 (67)
Meropenem	710	4.1 (29)	3.9 (28)	5.6 (40)	2.4 (17)
Salmonella species (non-typhoidal)					
Ampicillin	114	0.0 (0)	4.4 (5)	–†	4.4 (5)
Amoxicillin–clavulanate	112	1.8 (2)	0.0 (0)	–#	–#

continued

Table 12: (continued)

Species and antimicrobial	Number	CLSI		EUCAST	
		% intermediate (*n*)	% resistant (*n*)	% intermediate (*n*)	% resistant (*n*)
Piperacillin–tazobactam	114	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)
Ceftriaxone	114	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)
Ceftazidime	114	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)
Cefepime	114	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)
Ciprofloxacin	112	–**	1.8 (2)	–**	1.8 (2)
Meropenem	114	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)
Serratia marcescens					
Piperacillin–tazobactam	138	–‡	–‡	–‡	–‡
Ceftriaxone	174	0.0 (0)	4.6 (8)	0.0 (0)	4.6 (8)
Ceftazidime	174	0.6 (1)	2.3 (4)	0.6 (1)	2.9 (5)
Cefepime	174	1.1 (2)	1.1 (2)	0.6 (1)	2.3 (4)
Gentamicin	174	0.0 (0)	2.3 (4)	0.6 (1)	2.3 (4)
Tobramycin	174	18.4 (32)	2.3 (4)	17.2 (30)	20.7 (36)
Amikacin	174	0.0 (0)	0.0 (0)	0.6 (1)	0.0 (0)
Ciprofloxacin	174	0.6 (1)	0.6 (1)	2.3 (4)	5.7 (10)
Meropenem	174	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)
Staphylococcus aureus					
Benzylpenicillin	2,535	–†	82.6 (2,095)	–†	82.6 (2,095)
Ciprofloxacin	2,535	0.7 (19)	10.1 (257)	–†	10.9 (276)
Clindamycin	2,540	0.0 (0)	3.4 (86)	0.1 (3)	3.5 (89)
Daptomycin	2,537	0.3 (8)§§	–†	–†	0.3 (8)
Erythromycin	2,532	3.0 (77)	14.5 (367)	0.2 (6)	15.8 (399)
Gentamicin	2,538	0.6 (16)	2.6 (66)	–†	3.7 (95)
Linezolid	2,538	0.0 (0)	0.0 (0)	–†	0.0 (0)
Oxacillin	2,537	–*	19.3 (489)	–†	19.3 (489)
Rifampicin	2,479	<0.1 (1)	0.6 (15)	–##	0.6 (16)
Trimethoprim–sulfamethoxazole	2,538	–	4.1 (105)	0.2 (5)	3.9 (100)
Teicoplanin	2,537	0.0 (0)	0.0 (0)	0.0 (0)	<0.1 (1)
Tetracycline	2,231	0.0 (0)	4.6 (103)	0.4 (10)	4.6 (103)
Vancomycin	2,535	<0.1 (1)	0.0 (0)	–*	<0.1 (1)

CLSI = Clinical and Laboratory Standards Institute; EUCAST = European Committee on Antimicrobial Susceptibility Testing

* No guidelines for indicated species

† No category defined

§ Includes sensitive dose dependent category for CLSI

For susceptibility testing purposes, EUCAST fixes the concentration of clavulanate at 2 mg/L, rather than the 2:1 ratio used in CLSI guidelines. All cards used in this study have a 2:1 ratio; therefore, no EUCAST categories can be determined.

** The ciprofloxacin concentration range available on the cards used restricts the ability to accurately identify susceptible (CLSI/EUCAST) and intermediate (CLSI) categories for *Salmonella* species.

‡ Not indicated on susceptibility testing cards

§§ Non-susceptible; resistance not defined

The rifampicin concentration range on cards restricts category interpretation to non-resistant or resistant.

3.7.2 Antimicrobial resistance by place of onset

Antimicrobial resistances (CLSI and EUCAST) in indicator species by place of onset, if known, are shown in Table 13.

Table 13: Antimicrobial resistances (CLSI, EUCAST), by place of onset, 2016

		Community onset		Hospital onset	
Species and antimicrobial	**Number**	**% intermediate**	**% resistant**	**% intermediate**	**% resistant**
Acinetobacter baumannii complex					
Piperacillin–tazobactam	34	0.0, –*	10.0, –*	4.2, –*	25.0, –*
Ceftriaxone	45	92.3, –*	0.0, –*	53.1, –*	28.1, –*
Ceftazidime	46	35.7, –*	0.0, –*	6.3, –*	25.0, –*
Cefepime	46	0.0, –*	0.0, –*	0.0, –*	25.0, –*
Gentamicin	47	0.0, –†	0.0, 0.0	0.0, –†	12.5, 12.5
Tobramycin	47	0.0, –†	0.0, 0.0	0.0, –†	12.5, 12.5
Amikacin	47	0.0, 0.0	0.0, 0.0	0.0, 6.3	0.0, 0.0
Ciprofloxacin	47	0.0, –†	0.0, 0.0	0.0, –†	18.8, 18.8
Meropenem	47	0.0, 0.0	0.0, 0.0	0.0, 0.0	25.0, 25.0
Enterobacter aerogenes					
Piperacillin–tazobactam	122	5.2, 3.9	20.8, 26.0	2.2, 4.4	31.1, 33.3
Ceftriaxone	125	0.0, 0.0	32.5, 32.5	0.0, 0.0	33.3, 33.3
Ceftazidime	125	0.0, 2.5	28.8, 28.8	0.0, 2.2	31.1, 31.1
Cefepime	125	0.0, 1.3§	2.5, 2.5	0.0, 4.4§	2.2, 2.2
Gentamicin	125	0.0, 0.0	1.3, 1.3	0.0, 0.0	2.2, 2.2
Tobramycin	125	0.0, 0.0	2.5, 2.5	0.0, 0.0	2.2, 2.2
Amikacin	125	0.0, 1.3	0.0, 0.0	0.0, 0.0	0.0, 0.0
Ciprofloxacin	125	0.0, 0.0	0.0, 1.3	0.0, 0.0	0.0, 2.2
Meropenem	125	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0
Enterobacter cloacae complex					
Piperacillin–tazobactam	328	3.6, 3.0	14.5, 18.2	1.2, 3.1	25.2, 26.4
Ceftriaxone	390	1.0, 1.0	22.0, 22.0	0.5, 0.5	31.4, 31.4
Ceftazidime	390	1.0, 2.4	19.0, 20.0	0.5, 2.2	28.6, 29.2
Cefepime	388	5.4, 6.8§	1.5, 3.4	3.3, 12.0§	1.6, 3.8
Gentamicin	390	0.0, 0.0	7.3, 7.3	0.0, 0.5	3.8, 3.8
Tobramycin	390	2.9, 0.0	5.4, 8.3	1.6, 0.0	2.7, 4.3
Amikacin	390	0.0, 2.4	0.0, 0.0	0.5, 1.6	0.0, 0.5
Ciprofloxacin	390	1.5, 2.0	1.0, 4.4	0.5, 2.7	0.5, 2.2
Meropenem	390	0.5, 1.5	2.9, 1.5	0.0, 0.5	1.6, 1.1
Enterococcus faecalis					
Ampicillin	592	–†, 0.0	0.0, 0.0	–†, 0.0	0.5, 0.5
Benzylpenicillin	576	–†, –*	0.8, –*	–†, –*	1.6, –*
Ciprofloxacin	559	3.2, –†	10.8, 7.7	3.3, –†	15.0, 11.1

continued

Table 13: (continued)

Species and antimicrobial	Number	Community onset		Hospital onset	
		% intermediate	% resistant	% intermediate	% resistant
Daptomycin	564	0.5#, –*	–†, –*	0.6#, –*	–†, –*
Linezolid	591	2.7, –†	0.5, 0.5	2.2, –†	0.0, 0.0
Teicoplanin	592	0.0, –†	0.0, 0.0	0.0, –†	0.0, 0.0
Tetracycline	514	0.3, –†	70.9, –*	0.0, –†	76.2, –*
Vancomycin	592	0.0, –†	0.0, 0.0	0.5, –†	0.5, 1.1
Enterococcus faecium					
Ampicillin	411	–†, 0.0	78.3, 78.3	–†, 0.0	96.6, 96.6
Benzylpenicillin	408	–†, –*	79.6, –*	–†, –*	97.6, –*
Ciprofloxacin	403	4.5, –†	75.9, 62.5	0.7, –†	95.9, 81.2
Linezolid	407	1.8, –†	0.0, 0.0	0.0, –†	0.0, 0.0
Teicoplanin	412	0.9, –†	13.9, 14.8	5.7, –†	13.8, 20.5
Tetracycline	352	0.0, –†	58.2, –*	0.0, –†	69.8, –*
Vancomycin	412	0.9, –†	38.3, 39.1	1.3, –†	48.0, 49.3
Escherichia coli					
Ampicillin	4,018	1.7, –†	52.5, 54.2	1.5, –†	58.0, 59.4
Amoxicillin–clavulanate	3,989	12.6, –**	7.5, –**	12.1, –**	12.3, –**
Piperacillin–tazobactam	4,012	3.0, 1.4	2.3, 5.2	5.2, 1.0	7.1, 12.3
Ceftriaxone	4,025	0.3, 0.3	11.1, 11.1	0.3, 0.3	13.0, 13.0
Ceftazidime	4,024	0.4, 4.2	5.6, 6.1	0.4, 4.0	8.8, 9.3
Cefepime	4,023	1.9§, 4.4	3.2, 4.3	2.1§, 4.6	5.5, 6.6
Gentamicin	4,024	0.2, 0.6	7.1, 7.3	0.4, 1.0	8.3, 8.7
Tobramycin	4,024	4.9, 0.7	3.4, 8.3	5.8, 1.0	4.1, 9.9
Amikacin	4,025	0.0, 1.7	0.1, 0.1	0.7, 1.9	0.3, 1.0
Ciprofloxacin	4,023	0.1, 2.3	11.9, 13.1	0.1, 2.2	16.5, 18.0
Meropenem	4,024	0.0, <0.1	<0.1, 0.0	0.3, 0.1	0.4, 0.3
Klebsiella pneumoniae					
Amoxicillin–clavulanate	926	4.2, –**	3.5, –**	5.8, –**	8.3, –**
Piperacillin–tazobactam	927	4.0, 4.1	1.7, 5.7	2.5, 8.7	8.3, 10.9
Ceftriaxone	932	1.1, 1.1	6.1, 6.1	0.4, 0.4	9.0, 9.0
Ceftazidime	932	0.5, 2.0	4.0, 4.4	1.8, 4.3	6.1, 7.9
Cefepime	932	0.6§, 2.6	2.3, 2.4	1.1§, 5.0	3.2, 4.0
Gentamicin	932	0.0, 0.0	3.8, 3.8	0.0, 0.4	5.8, 5.8
Tobramycin	932	2.0, 0.2	3.1, 5.0	1.8, 0.0	5.4, 7.2
Amikacin	932	0.0, 0.6	0.2, 0.2	0.0, 0.0	0.4, 0.4
Ciprofloxacin	932	1.1, 2.8	2.3, 6.1	1.4, 1.5	3.6, 8.3
Meropenem	932	0.0, 0.3	0.3, 0.0	0.4, 0.4	0.7, 0.4
Klebsiella oxytoca					
Amoxicillin–clavulanate	240	4.5, –**	4.5, –**	6.0, –**	20.5, –**
Piperacillin–tazobactam	239	0.6, 3.8	7.6, 8.3	1.2, 1.2	26.8, 28.0
Ceftriaxone	241	0.6, 0.6	5.1, 5.1	3.6, 3.6	18.1, 18.1
Ceftazidime	241	0.0, 0.6	0.6, 0.6	0.0, 0.0	3.6, 3.6

continued

Table 13: (continued)

Species and antimicrobial	Number	Community onset		Hospital onset	
		% intermediate	% resistant	% intermediate	% resistant
Cefepime	241	0.0§, 0.6	1.3, 1.3	0.0, 3.6	1.2, 1.2
Gentamicin	241	0.0, 1.3	0.6, 0.6	0.0, 1.2	2.4, 2.4
Tobramycin	241	1.3, 0.6	0.0, 1.3	2.4, 1.2	0.0, 2.4
Amikacin	241	0.0, 1.3	0.0, 0.0	0.0, 0.0	0.0, 0.0
Ciprofloxacin	241	0.0, 0.0	0.0, 0.6	1.2, 1.2	1.2, 3.6
Meropenem	241	0.0, 0.0	0.0, 0.0	0.0, 0.0	1.2, 1.2
Proteus mirabilis					
Ampicillin	224	0.6, –†	14.4, 14.9	4.7, –†	25.6, 30.2
Amoxicillin–clavulanate	218	5.7, –**	1.1, –**	9.5, –**	7.1, –**
Piperacillin–tazobactam	224	1.1, 0.0	0.0, 1.1	0.0, 0.0	0.0, 0.0
Ceftriaxone	224	0.0, 0.0	0.6, 0.6	0.0, 0.0	0.0, 0.0
Ceftazidime	223	0.0, 0.0	0.0, 0.0	0.0, 2.3	0.0, 0.0
Cefepime	224	0.6§, 0.6	0.0, 0.0	0.0, 0.0	0.0, 0.0
Gentamicin	224	1.7, 2.2	0.0, 1.7	2.3, 4.7	2.3, 4.7
Tobramycin	224	1.1, 1.7	0.0, 1.1	4.7, 2.3	2.4, 7.0
Amikacin	223	0.0, 0.6	0.0, 0.0	0.0, 0.0	0.0, 0.0
Ciprofloxacin	224	0.0, 0.6	1.1, 2.8	2.3, 0.0	2.3, 4.7
Meropenem	224	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0
Pseudomonas aeruginosa					
Piperacillin–tazobactam	700	6.3, –†	2.0, 8.3	7.3, –†	9.2, 16.5
Ceftazidime	703	2.0, –†	1.8, 3.8	4.9, –†	8.2, 13.1
Cefepime	704	0.0, –†	1.5, 3.5	0.0, –†	4.9, 9.8
Gentamicin	704	2.0, –†	1.0, 3.0	3.3, –†	2.6, 5.9
Tobramycin	704	0.0, –†	1.0, 1.0	0.0, –†	2.3, 2.3
Amikacin	704	0.0, 2.8	0.3, 0.3	1.3, 3.6	1.0, 2.3
Ciprofloxacin	705	2.0, 0.0	4.3, 10.5	1.3, 0.0	3.3, 8.2
Meropenem	700	2.5, 3.5	2.3, 1.3	6.0, 8.3	6.0, 3.6
Salmonella species (non-typhoidal)					
Ampicillin	112	0.0, –†	3.8, 3.8	0.0, –†	16.7, 16.7
Amoxicillin–clavulanate	110	1.0, –**	0.0, –**	16.7, –**	0.0, –**
Piperacillin–tazobactam	112	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0
Ceftriaxone	112	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0
Ceftazidime	112	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0
Cefepime	112	0.0§, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0
Ciprofloxacin	112	–‡	1.9, 1.9	–‡	0.0, 0.0
Meropenem	112	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0
Serratia marcescens					
Ampicillin	160	46.0, –†	29.9, 75.9	47.9, –†	39.7, 87.7
Amoxicillin–clavulanate	173	13.3, –†	58.2, –†	25.3, –†	62.7, –†
Piperacillin–tazobactam	138	–§§	–§§	–§§	–§§
Ceftriaxone	174	0.0, 0.0	2.0, 2.0	0.0, 0.0	7.9, 7.9

continued

Table 13: (continued)

Species and antimicrobial	Number	Community onset		Hospital onset	
		% intermediate	% resistant	% intermediate	% resistant
Ceftazidime	174	0.0, 1.0	1.0, 1.0	1.3, 0.0	3.9, 5.3
Cefepime	174	0.0*, 1.0	1.0, 1.0	2.6, 0.0	1.3, 3.9
Gentamicin	174	0.0, 1.0	0.0, 0.0	0.0, 0.0	5.3, 5.3
Tobramycin	174	16.3, 17.3	1.0, 17.3	21.1, 17.1	3.9, 25.0
Amikacin	174	0.0, 1.0	0.0, 0.0	0.0, 0.0	0.0, 0.0
Ciprofloxacin	174	1.0, 2.0	1.0, 7.1	0.0, 2.6	0.0, 3.9
Meropenem	174	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0
Staphylococcus aureus					
Benzylpenicillin	2,535	–†, –†	82.1, 82.1	–†, –†	84.4, 84.4
Ciprofloxacin	2,535	0.8, –†	8.9, 9.7	0.5, –†	14.1, 14.6
Clindamycin	2,535	0.0, 0.1	3.0, 3.1	0.0, 0.2	4.6, 5.0
Daptomycin	2,537	0.2#, –†	–†, 0.2	0.7#, –†	–†, 0.7
Erythromycin	2,536	3.1, 0.3	14.0, 15.2	2.8, 0.0	16.1, 17.4
Gentamicin	2,538	0.7, –†	2.2, 3.4	0.5, –†	3.8, 5.0
Linezolid	2,538	0.0, –†	0.0, 0.0	0.0, –†	0.0, 0.0
Oxacillin	2,537	–*, –*	18.5, 18.5	–*, –*	21.9, 21.9
Rifampicin	2,479	0.1, –##	0.5, 0.5	0.0, –##	1.0, 1.0
Trimethoprim–sulfamethoxazole	2,538	–†, 0.2	3.7, 3.6	–†, 0.3	5.5, 5.1
Teicoplanin	2,537	0.0, –†	0.0, 0.0	0.0, –†	0.0, 0.2
Tetracycline	2,231	0.0, 0.6	4.1, 4.1	0.0, 0.0	6.3, 6.3
Vancomycin	2,535	0.0, –†	0.0, 0.0	0.2, –†	0.0, 0.2

CLSI = Clinical and Laboratory Standards Institute; EUCAST = European Committee on Antimicrobial Susceptibility Testing; I = intermediate susceptibility; R = resistant

* Includes sensitive dose dependent category for CLSI

† No category defined

§ No guidelines for indicated species

\# Non-susceptible, resistance not defined

** For susceptibility testing purposes, EUCAST fixes the concentration of clavulanate at 2 mg/L, rather than the 2:1 ratio used in CLSI guidelines. All cards used in this study have a 2:1 ratio; therefore, no EUCAST categories can be determined.

‡ The ciprofloxacin concentration range available on the cards used restricts the ability to accurately determine susceptible (CLSI/EUCAST) and intermediate (CLSI) categories for *Salmonella* species.

§§ Not indicated on susceptibility testing cards

The rifampicin concentration range on cards restricts category interpretation to non-resistant or resistant.

3.8 Multidrug resistance

The most problematic pathogens are those with multiple acquired resistances. Although there is no agreed benchmark for the definition of multidrug resistance, acquired resistance to more than three antimicrobial classes has been chosen as the definition in this survey. For each species, antimicrobials were excluded from the count if they were affected by intrinsic resistance mechanisms, and/or neither CLSI nor EUCAST breakpoints were available. For this analysis, resistance included intermediate and resistant susceptibility results, if applicable.

Only isolates for which the full range of antimicrobial agents was tested were included for determination of multidrug resistance. EUCAST breakpoints were primarily used in the analysis. For cefazolin, the EUCAST-approved Australian National Antimicrobial Susceptibility Testing Committee guidelines were used. For amoxicillin–clavulanate, CLSI breakpoints were used, because the CLSI formulation for this agent was used in the Vitek and Phoenix susceptibility cards.

A. baumannii complex was not included because there are few breakpoints to permit analysis.

Multiple acquired resistances for key species are shown in Tables 14 to 20. The agents included for each species are listed in the notes after each table. For other common species, refer to Appendix D.

Table 14: Multiple acquired resistance in *Enterobacter cloacae* complex, by state and territory, 2016

State or territory	Total	Number of drug resistances (non-multidrug resistance)					Number of drug resistances (multidrug resistant)						
		0	1	2	3	%	4	5	6	7	8	9	%
NSW	90	58	9	2	7	84.4	9	0	1	3	1	0	15.6
Vic	75	52	3	2	4	81.3	11	0	0	1	2	0	18.7
Qld	86	46	10	1	13	81.4	3	6	2	2	3	0	18.6
SA	13	8	1	1	0	76.9	1	2	0	0	0	0	23.1
WA	42	32	1	1	2	85.7	5	0	1	0	0	0	14.3
Tas	12	6	3	0	1	83.3	1	0	0	0	0	1	16.7
NT	11	8	1	0	2	100.0	0	0	0	0	0	0	0.0
ACT	10	6	1	0	0	70.0	2	1	0	0	0	0	30.0
Total	339	216	29	7	29	82.9	32	9	4	6	6	1	17.1

Notes: Antimicrobials were piperacillin–tazobactam, ceftriaxone, ceftazidime, cefepime, gentamicin, amikacin, ciprofloxacin, trimethoprim and meropenem. *Enterobacter cloacae* complex includes *E. asburiae* (*n* = 8) and *E. ludwigii* (*n* = 2).

Table 15: Multiple acquired resistance in *Enterococcus faecalis*, by state and territory, 2016

State or territory	Total	Number of drug resistances (non-multidrug resistant)					Number of drug resistances (multidrug resistant)		
		0	1	2	3	%	4	5	%
NSW	151	129	11	11	0	100	0	0	0.0
Vic	130	115	14	1	0	100	0	0	0.0
Qld	84	77	6	1	0	100	0	0	0.0
SA	51	43	2	5	0	100	1	0	0.0
WA	87	80	7	0	0	100	0	0	0.0
Tas	14	11	3	0	0	98.0	0	0	2.0
NT	7	7	0	0	0	100	0	0	0.0
ACT	33	29	4	0	0	100	0	0	0.0
Total	557	491	47	18	0	99.8	1	0	0.2

Note: Antimicrobials were ampicillin, ciprofloxacin, linezolid, nitrofurantoin and vancomycin.

Table 16: Multiple acquired resistance in *Enterococcus faecium*, by state and territory, 2016

State or territory	Total	Number of drug resistances (non-multidrug resistant)					Number of drug resistances (multidrug resistant)	
		0	1	2	3	%	4	%
NSW	119	9	4	39	53	88.2	14	11.8
Vic	108	11	4	26	67	100	0	0.0
Qld	39	4	0	24	11	100	0	0.0
SA	43	1	0	6	20	62.8	16	37.2
WA	54	4	1	41	8	100	0	0.0
Tas	12	1	0	5	6	100	0	0.0
NT	4	0	0	1	3	100	0	0.0
ACT	19	2	0	5	12	100	0	0.0
Total	398	32	9	147	180	92.5	30	7.5

Note: Antimicrobials were ampicillin, ciprofloxacin, linezolid and vancomycin.

Table 17: Multiple acquired resistance in *Escherichia coli*, by state and territory, 2016

State or territory	Total	Number of drug resistances (non-multidrug resistant)					Number of drug resistances (multidrug resistant)										
		0	1	2	3	%	4	5	6	7	8	9	10	11	12	13	%
NSW	990	388	130	155	83	76.4	67	24	34	54	30	16	7	1	1	0	23.6
Vic	677	229	102	125	75	78.4	27	35	25	24	15	14	4	2	0	0	21.6
Qld	804	337	120	137	76	83.3	37	37	20	20	9	6	3	2	0	0	16.7
SA	428	199	44	57	39	79.2	24	17	13	11	7	10	7	0	0	0	20.8
WA	650	253	80	101	53	74.9	62	24	17	24	15	10	6	5	0	0	25.1
Tas	91	47	12	12	11	90.1	4	2	0	1	0	0	1	1	0	0	9.9
NT	152	42	27	31	18	77.6	10	12	3	8	0	0	1	0	0	0	22.4
ACT	152	57	25	30	12	81.6	8	6	5	6	0	2	1	0	0	0	18.4
Total	3,944	1,552	540	648	367	78.8	239	157	117	148	76	58	30	11	1	0	21.2

Note: Antimicrobials were ampicillin, amoxicillin–clavulanate (CLSI), piperacillin–tazobactam, cefazolin, ceftriaxone, ceftazidime, cefepime, gentamicin, amikacin, ciprofloxacin, nitrofurantoin, trimethoprim and meropenem.

Table 18: Multiple acquired resistance in *Klebsiella pneumoniae*, by state and territory, 2016

State or territory	Total	Number of drug resistances (non-multidrug resistant)					Number of drug resistances (multidrug resistant)								
		0	1	2	3	%	4	5	6	7	8	9	10	11	%
NSW	223	167	17	6	4	87.0	6	3	8	3	1	7	0	1	13.0
Vic	171	111	20	5	4	81.9	4	5	3	6	6	6	1	0	18.1
Qld	188	141	29	8	0	94.7	3	1	0	1	2	3	0	0	5.3
SA	79	53	14	4	3	93.7	1	1	1	1	1	0	0	0	6.3
WA	170	138	9	4	6	92.4	3	2	3	1	0	4	0	0	7.6
Tas	17	13	1	2	0	94.1	0	0	0	0	0	1	0	0	5.9
NT	38	26	8	2	1	97.4	0	0	0	0	1	0	0	0	2.6
ACT	33	27	1	4	0	97.0	0	0	0	0	1	0	0	0	3.0
Total	919	676	99	35	18	90.1	17	12	15	12	12	21	1	1	9.9

Note: Antimicrobials were amoxicillin–clavulanate (CLSI), piperacillin–tazobactam, cefazolin, ceftriaxone, ceftazidime, cefepime, gentamicin, amikacin, ciprofloxacin, trimethoprim and meropenem.

Table 19: Multiple acquired resistance in *Staphylococcus aureus* (methicillin resistant), by state and territory, 2016

State or territory	Total	Number of drug resistances (non-multidrug resistant)					Number of drug resistances (multidrug resistant)									
		0	1	2	3	%	4	5	6	7	8	9	10	11	12	%
NSW	148	37	30	33	11	75.0	21	11	5	0	0	0	0	0	0	25.0
Vic	65	25	21	13	3	95.4	0	3	0	0	0	0	0	0	0	4.6
Qld	65	36	20	3	4	96.9	0	2	0	0	0	0	0	0	0	3.1
SA	62	19	19	16	1	88.7	1	6	0	0	0	0	0	0	0	11.3
WA	81	34	36	8	2	98.8	0	1	0	0	0	0	0	0	0	1.2
Tas	10	1	2	5	1	90.0	1	0	0	0	0	0	0	0	0	10.0
NT	41	19	16	3	1	95.1	0	2	0	0	0	0	0	0	0	4.9
ACT	13	3	4	2	0	69.2	2	2	0	0	0	0	0	0	0	30.8
Total	485	174	148	83	23	88.2	25	27	5	0	0	0	0	0	0	11.8

Note: Antimicrobials were ciprofloxacin, daptomycin, erythromycin, fusidic acid, gentamicin, linezolid, mupirocin (high level), nitrofurantoin (CLSI), rifampicin, trimethoprim–sulfamethoxazole, tetracyclines (tetracycline, Vitex; doxycycline, Phoenix) and vancomycin.

Table 20: Multiple acquired resistance in *Staphylococcus aureus* (methicillin susceptible), by state and territory, 2016

State or territory	Total	Number of drug resistances (non-multidrug resistant)					Number of drug resistances (multidrug resistant)										
		0	1	2	3	%	4	5	6	7	8	9	10	11	12	13	%
NSW	438	79	309	41	8	99.8	1	0	0	0	0	0	0	0	0	0	0.2
Vic	351	73	227	41	6	98.9	3	1	0	0	0	0	0	0	0	0	1.1
Qld	425	81	271	48	23	99.5	2	0	0	0	0	0	0	0	0	0	0.5
SA	216	17	156	37	1	99.5	1	0	0	0	0	0	0	0	0	0	0.5
WA	331	66	215	42	5	99.1	2	1	0	0	0	0	0	0	0	0	0.9
Tas	41	10	23	5	2	97.6	1	0	0	0	0	0	0	0	0	0	2.4
NT	49	4	34	9	2	100	0	0	0	0	0	0	0	0	0	0	0.0
ACT	71	16	46	6	1	97.2	2	0	0	0	0	0	0	0	0	0	2.8
Total	1,922	346	1,281	229	52	99.3	12	2	0	0	0	0	0	0	0	0	0.7

Note: Antimicrobials were benzylpenicillin, ciprofloxacin, daptomycin, erythromycin, fusidic acid, gentamicin, linezolid, mupirocin (high level), nitrofurantoin (CLSI), rifampicin, trimethoprim–sulfamethoxazole, tetracyclines (tetracycline, Vitex; doxycycline, Phoenix) and vancomycin.

3.8.1 Multidrug resistance by onset setting and 30-day all-cause mortality

Multidrug resistances by onset setting (community or hospital) and 30-day all-cause mortality for the most common species are shown in Table 21.

Table 21: Multidrug resistance, by onset setting and 30-day all-cause mortality, 2015

		Total		Community onset		Hospital onset	
Species	**Category***	**Number**	**Deaths (%)**	**Number**	**Deaths (%)**	**Number**	**Deaths (%)**
Escherichia coli	Total	2,347	11.5 (269)	1,892	10.1 (192)	455	16.9 (77)
	Non-MDR (≤3)	1,834	10.5 (193)	1,505	9.4 (142)	329	15.5 (51)
	MDR (>3)	513	14.8 (76)	387	12.9 (50)	126	20.6 (26)
Enterobacter cloacae complex	Total	248	12.9 (32)	121	14.9 (18)	127	11.0 (14)
	Non-MDR (≤3)	209	12.4 (26)	103	13.6 (14)	106	11.3 (12)
	MDR (>3)	39	15.4 (6)	18	22.2 (4)	21	9.5 (2)
Enterococcus faecalis	Total	463	13.2 (61)	309	10.7 (33)	154	18.2 (28)
	Non-MDR (≤3)	462	13.2 (61)	309	10.7 (33)	153	18.3 (28)
	MDR (>3)	1	–† (0)	0	n/a	1	–† (0)
Enterococcus faecium	Total	365	27.4 (100)	92	21.7 (20)	273	29.3 (80)
	Non-MDR (≤3)	336	28.0 (94)	85	23.5 (20)	251	29.5 (74)
	MDR (>3)	29	20.7 (6)	7	0.0 (0)	22	27.3 (6)
Klebsiella pneumoniae	Total	584	12.5 (73)	398	11.8 (47)	186	14.0 (26)
	Non-MDR (≤3)	521	13.1 (68)	366	12.6 (46)	155	14.2 (22)
	MDR (>3)	63	7.9 (5)	32	3.1 (1)	31	12.9 (4)
Staphylococcus aureus	Total	1,895	16.6 (315)	1,414	16.3 (230)	481	17.7 (85)
	Non-MDR (≤3)	1,758	16.4 (288)	1,328	15.7 (208)	430	18.6 (80)
	MDR (>3)	137	19.7 (27)	86	25.6 (22)	51	9.8 (5)
Staphylococcus aureus, methicillin resistant	Total	372	22.6 (84)	266	24.4 (65)	106	17.9 (19)
	Non-MDR (≤3)	331	22.7 (75)	243	24.3 (59)	88	18.2 (16)
	MDR (>3)	41	22.0 (9)	23	26.1 (6)	18	16.7 (3)
Staphylococcus aureus, methicillin susceptible	Total	1,523	15.2 (231)	1,148	14.4 (165)	375	17.6 (66)
	Non-MDR (≤3)	1,510	15.3 (231)	1,137	14.5 (165)	373	17.7 (66)
	MDR (>3)	13	0.0 (0)	11	0.0 (0)	2	0.0 (0)
Pseudomonas aeruginosa	Total	458	20.5 (94)	238	23.1 (55)	220	17.7 (39)
	Non-MDR (≤3)	443	19.9 (88)	234	22.2 (52)	209	17.2 (36)
	MDR (>3)	15	40.0 (6)	4	3†	11	27.3 (3)
	Non-MDR (≤2)	431	19.5 (84)	230	21.7 (50)	201	16.9 (34)
	MDR (>2)	27	37.0 (10)	8	5†	19	26.3 (5)

MDR = multidrug resistant; n/a = not applicable

* For *Pseudomonas aeruginosa*, resistance to more than two agents was also included.

† Insufficient numbers (<10) to calculate percentage

3.9 Trend analysis (2013-2016)

This section describes the major trends seen in antimicrobial resistance and non-susceptibility in Australia for the four-year period 2013–2016.

3.9.1 Gram-negative species

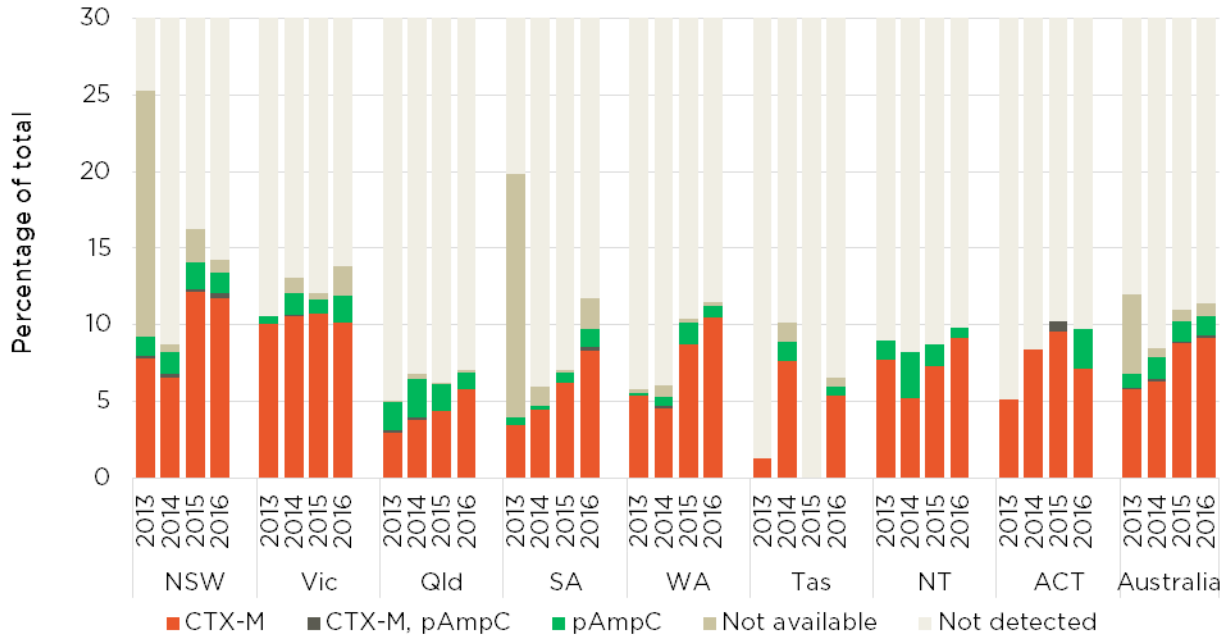
Trend data were available for Enterobacteriaceae for the period 2013 to 2016. *Acinetobacter* species and *P. aeruginosa* were introduced to the program in 2015. EUCAST interpretive criteria have been used throughout, with the notable exception of amoxicillin–clavulanate, as both the Vitek and Phoenix cards used the CLSI formulation for this agent.

Extended-spectrum β-lactamases

Nationally, there was no significant increase in the proportion of *E. coli* with CTX-M-type (see Section 3.10.1) and/or plasmid-borne AmpC β-lactamases from 2015 to 2016 (Figure 4). SHV and TEM types were not included in this analysis, because it was not possible to discriminate between genes that encode narrow-spectrum β-lactamases and those that encode ESBLs.

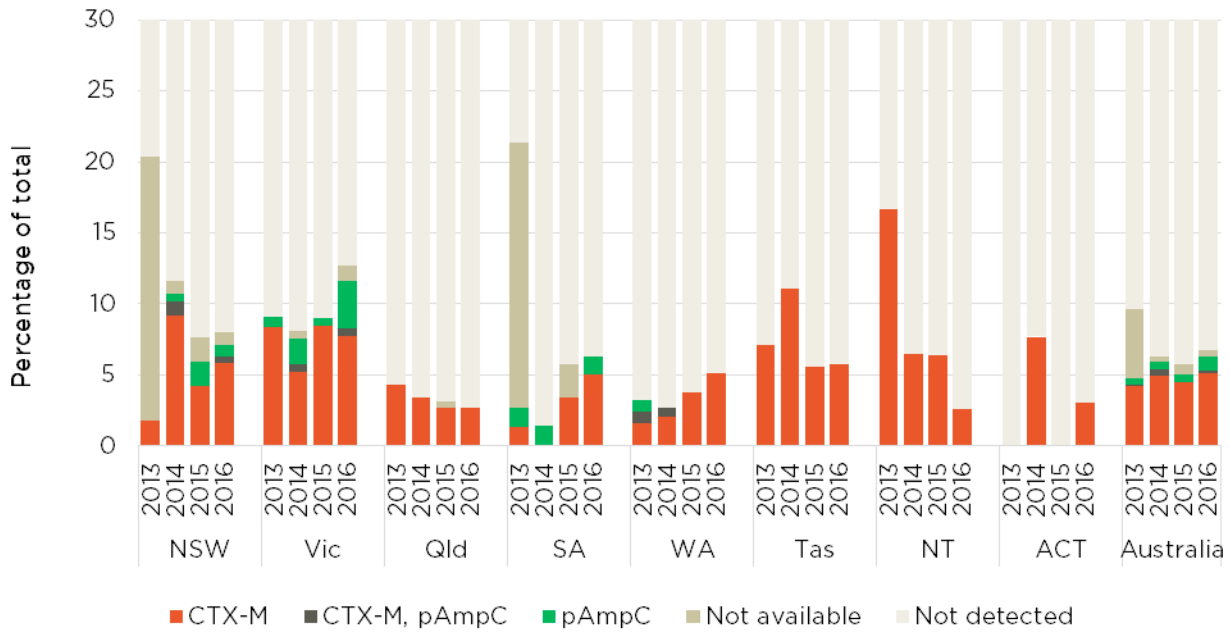
The proportion of *K. pneumoniae* with CTX-M-type or plasmid-borne AmpC β-lactamases remained steady during the period 2013–2016, although regional variations were seen (Figure 5).

Figure 4: Proportion of CTX-M-type and plasmid-borne AmpC β-lactamases in *Escherichia coli* by state and territory, and nationally, 2013–2016



Not available = ESBL phenotype, isolate not available for molecular confirmation

Figure 5: Proportion of CTX-M-type and plasmid-borne AmpC β-lactamases in *Klebsiella pneumoniae* by state and territory, and nationally, 2013–2016



Not available = ESBL phenotype, isolate not available for molecular confirmation

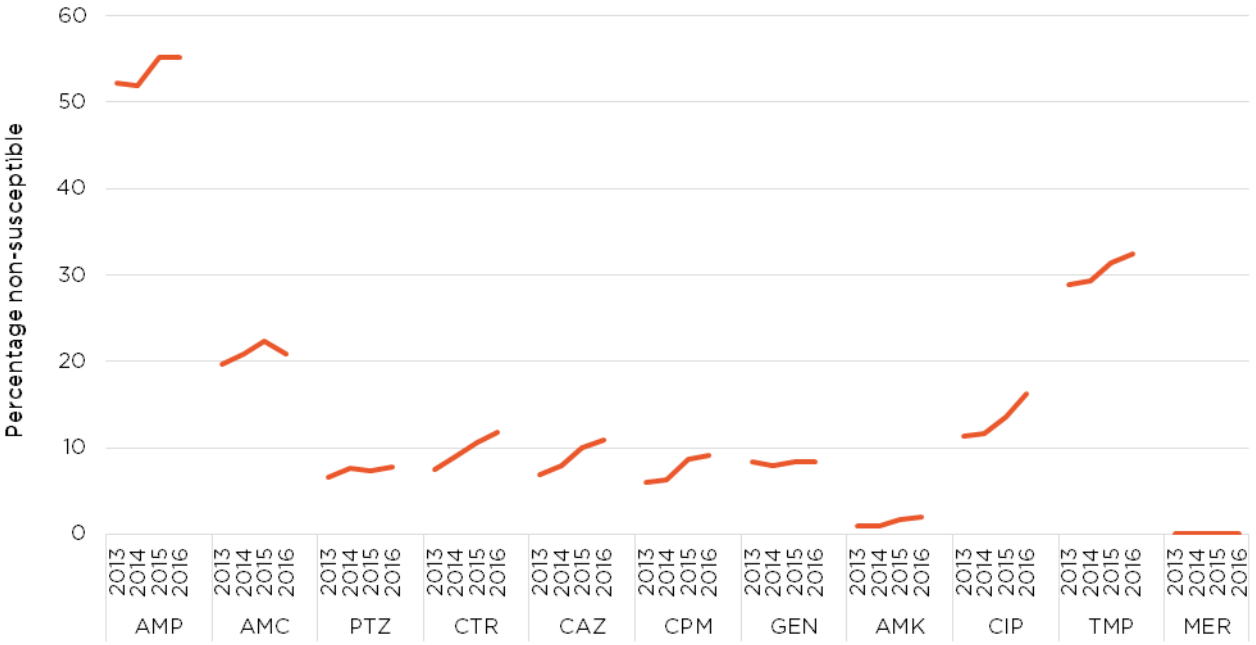
Escherichia coli

Non-susceptibility to key anti–gram negative antimicrobial agents showed a steady increase from 2013 to 2016 (Figure 6). There was a significant increase in non-susceptibility to amikacin (χ^2 for linear trend = 22.78, $P < 0.01$), ceftriaxone (χ^2 for linear trend = 32.82, $P < 0.01$), ceftazidime (χ^2 for linear trend = 33.28, $P < 0.01$), cefepime (χ^2 for linear trend = 30.29, $P < 0.01$), ciprofloxacin (χ^2 for linear trend = 34.78, $P < 0.01$), and trimethoprim (χ^2 for linear trend = 7.48, $P < 0.01$).

Klebsiella pneumoniae

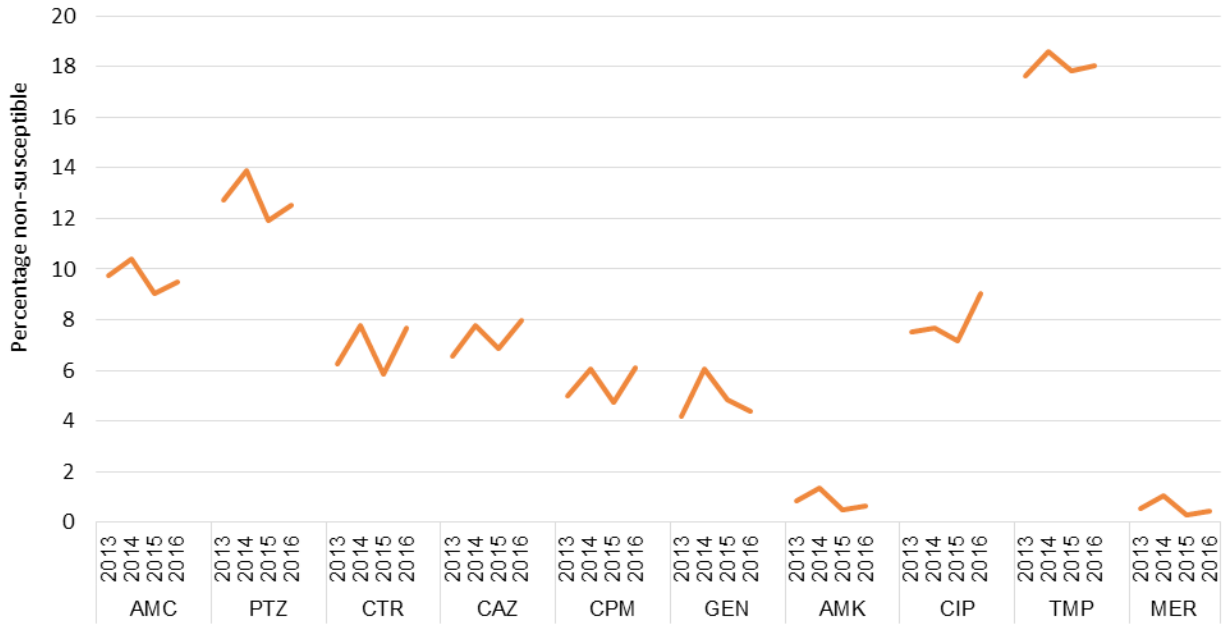
There were no significant changes in non-susceptibility to key antimicrobial agents for *K. pneumoniae* over the four-year period 2013–2016 (Figure 7).

Figure 6: Non-susceptibility of *Escherichia coli* to key antimicrobials (EUCAST), Australia, 2013–2016



AMC = amoxicillin–clavulanate (2:1 ratio); AMK = amikacin; AMP = ampicillin; CAZ = ceftazidime; CIP = ciprofloxacin; CPM = cefepime; CTR = ceftriaxone; EUCAST = European Committee on Antimicrobial Susceptibility Testing; GEN = gentamicin; MER = meropenem; PTZ = piperacillin–tazobactam; TMP = trimethoprim

Figure 7: Non-susceptibility of *Klebsiella pneumoniae* to key antimicrobials (EUCAST), Australia, 2013–2016

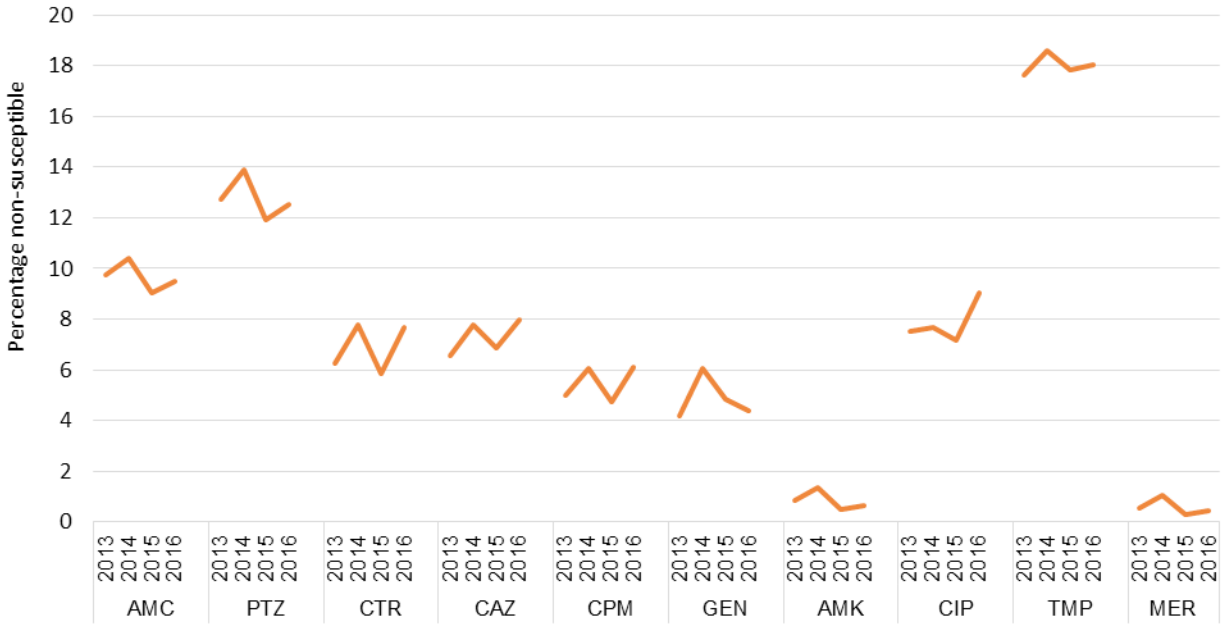


AMC = amoxicillin–clavulanate (2:1 ratio); AMK = amikacin; CAZ = ceftazidime; CIP = ciprofloxacin; CPM = cefepime; CTR = ceftriaxone; EUCAST = European Committee on Antimicrobial Susceptibility Testing; GEN = gentamicin; MER = meropenem; PTZ = piperacillin–tazobactam; TMP = trimethoprim

Enterobacter cloacae complex

There were no significant differences in non- susceptibility to key antimicrobials for *E. cloacae* over the three-year period 2013–2016 (Figure 8)

Figure 8: Non-susceptibility of *Enterobacter cloacae* to key antimicrobials (EUCAST), Australia, 2013–2016



AMK = amikacin; CAZ = ceftazidime; CIP = ciprofloxacin; CPM = cefepime; CTR = ceftriaxone; EUCAST = European Committee on Antimicrobial Susceptibility Testing; GEN = gentamicin; MER = meropenem; PTZ = piperacillin–tazobactam; TMP = trimethoprim

3.9.2 *Enterococcus* species

The 2016 program focused on the proportions of *E. faecium* and *E. faecalis* bacteraemia isolates demonstrating resistance to ampicillin, glycopeptides and other anti-enterococcal agents. Important trends for the period 2013–2016 are described below.

Vancomycin-resistant *Enterococcus faecium*

The proportion of vancomycin-resistant *enterococcus* (*E. faecium*) (VRE) by state and territory is shown in Table 22. Although VRE was detected in the Northern Territory and Tasmania, total numbers for each year were less than 10.

Table 22: Vancomycin-resistant *Enterococcus faecium*, by state and territory, 2013–2016

State or territory	2013		2014		2015		2016		*P**	Trend†
	Total	% R (*n*)	Total	% R (*n*)	Total	% R (*n*)	Total	% R (*n*)		
NSW	107	43.9 (47)	104	50.0 (52)	116	51.7 (60)	124	47.6 (59)	ns	
Vic	80	53.8 (43)	94	66.0 (62)	120	63.3 (76)	109	62.4 (68)	ns	
Qld	37	40.5 (15)	37	40.5 (15)	31	61.3 (19)	43	30.2 (13)	ns	
SA	32	59.4 (19)	46	56.5 (26)	44	52.3 (23)	43	46.5 (20)	ns	
WA	42	4.8 (2)	50	20.0 (10)	53	11.3 (6)	54	14.8 (8)	ns	
Tas	5	§ (0)	7	§ (1)	8	§ (1)	14	42.9 (6)	n/a	
NT	3	§ (3)	1	§ (0)	8	§ (6)	4	§ (3)	n/a	
ACT	18	33.3 (6)	41	24.4 (10)	22	50.0 (11)	22	68.2 (15)	0.0023	
Australia	324	41.7 (135)	380	46.3 (176)	402	50.2 (202)	413	46.5 (192)	ns	

n/a = not applicable; ns = not significant

* χ^2 for trend

† Sparkline, 2013–2016, with highest point shaded red

§ Insufficient numbers to calculate percentage

Enterococcus faecalis

Resistance (EUCAST) to key antimicrobial agents for *E. faecalis* by state and territory is shown in Table 23. There was no significant change in resistance for the states and territories in 2016 compared with 2015. The only significant trend over the years 2013–2016 was a decrease in ciprofloxacin resistance in New South Wales (χ^2 for linear trend = 6.68, P < 0.01) and South Australia (χ^2 for linear trend = 6.66, P < 0.01).

Table 23: *Enterococcus faecalis* (EUCAST), by state and territory, 2013–2016

Antimicrobial	Year	Number tested	Number non-susceptible (%)								
			NSW	Vic	Qld	SA	WA	Tas	NT	ACT	Australia
Ampicillin	2013	477	0.8 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
	2014	522	0.0 (0)	0.0 (0)	2.0 (2)	2.0 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.6 (3)
	2015	561	0.0 (0)	0.0 (0)	1.1 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
	2016	592	0.0 (0)	0.0 (0)	0.0 (0)	2.0 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
Vancomycin	2013	477	0.8 (1)	0.9 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.4 (2)
	2014	523	0.0 (0)	0.0 (0)	1.0 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
	2015	561	1.3 (2)	0.9 (1)	0.0 (0)	0.0 (0)	0.0 (0)	8.3 (1)	0.0 (0)	0.0 (0)	0.7 (4)
	2016	592	0.0 (0)	0.8 (1)	0.0 (0)	1.9 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.3 (2)
Teicoplanin	2013	476	0.8 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)
	2014	521	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	9.1 (1)	0.0 (0)	0.0 (0)	0.4 (2)
	2015	558	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)
	2016	592	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)
Ciprofloxacin	2013	439	24.6 (30)	11.3 (12)	14.9 (11)	37.8 (14)	9.9 (7)	n/a	24.6 (1)	17.4 (4)	18.0 (79)
	2014	477	23.1 (31)	20.0 (24)	15.7 (14)	37.5 (12)	11.1 (7)	n/a	23.1 (3)	42.4 (14)	22.0 (105)
	2015	521	14.8 (22)	15.5 (17)	9.6 (8)	25.6 (11)	8.8 (8)	n/a	14.8 (3)	14.3 (5)	14.2 (74)
	2016	559	14.5 (22)	11.5 (15)	8.2 (7)	15.7 (8)	8.0 (7)	21.4 (3)	0.7 (0)	12.1 (4)	11.8 (66)
Nitrofurantoin	2013	468	0.8 (1)	0.0 (0)	0.0 (0)	2.3 (1)	0.0 (0)	9.1 (1)	0.0 (0)	0.0 (0)	0.6 (3)
	2014	521	0.0 (0)	0.0 (0)	1.0 (1)	2.0 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.4 (2)
	2015	558	0.0 (0)	0.0 (0)	1 (1.1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	1 (0.2)
	2016	591	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)
Gentamicin (high-level)	2013	408	40.0 (34)	34.0 (36)	27.6 (24)	31.6 (6)	28.2 (20)	18.2 (2)	33.3 (2)	30.4 (7)	32.1 (131)
	2014	519	42.4 (56)	38.7 (46)	34.3 (35)	35.3 (18)	28.6 (18)	30.8 (4)	50.0 (3)	54.5 (18)	38.2 (198)
	2015	544	29.3 (41)	27.4 (29)	25.5 (24)	28.1 (16)	23.3 (21)	25.0 (3)	40.0 (4)	34.3 (12)	27.6 (150)
	2016	589	28.2 (42)	22.3 (29)	28.6 (28)	29.4 (15)	16.1 (14)	14.8 (4)	28.6 (2)	22.5 (9)	24.3 (143)

continued

Table 23: (continued)

Antimicrobial	Year	Number tested	Number non-susceptible (%)								
			NSW	Vic	Qld	SA	WA	Tas	NT	ACT	Australia
Linezolid	2013	477	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)
	2014	522	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)
	2015	561	0.0 (0)	0.0 (0)	1.1 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
	2016	591	0.0 (0)	0.0 (0)	2.0 (2)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.3 (2)

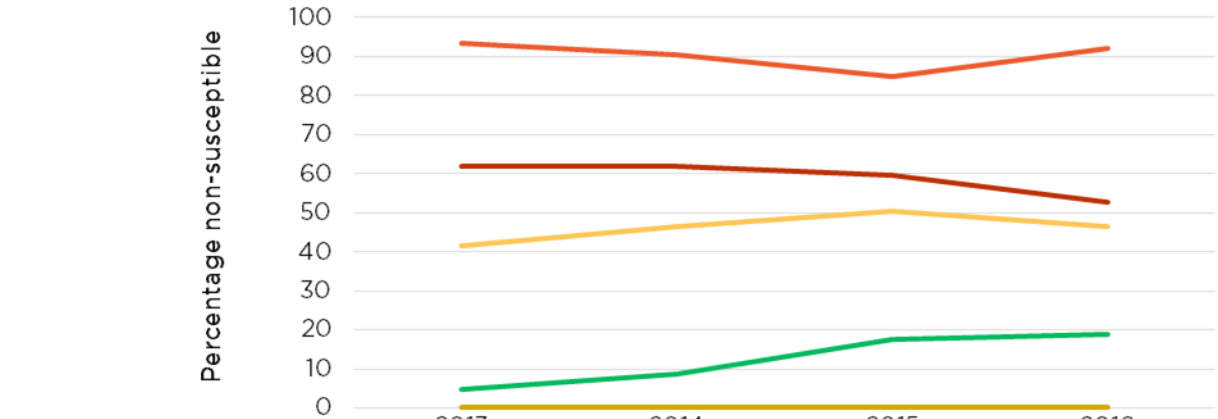
EUCAST = European Committee on Antimicrobial Susceptibility Testing; na = not applicable

Enterococcus faecium

For *E. faecium*, there was a significant decrease in gentamicin (high-level) resistance (χ^2 for linear trend = 6.93, P = 0.0085) from 2013 to 2016, and a significant increase in teicoplanin resistance (χ^2 for linear trend = 42.54, P < 0.0001) (Figure 9). No teicoplanin-resistant isolates were detected in either the Northern Territory or Tasmania; all other states and territories except South Australia and Western Australia had a significant increase. This increase was due to the increased prevalence of *E. faecium* carrying *vanA* genes in these regions. Linezolid resistance remained at less than 0.5%.

Non-susceptibility to the key antimicrobial agents for *E. faecium* is shown in Table 24.

Figure 9: Non-susceptibility of *Enterococcus faecium* to key antimicrobials (EUCAST), Australia, 2013–2015



EUCAST = European Committee on Antimicrobial Susceptibility Testing

Table 24 *Enterococcus faecium*, non-susceptible (EUCAST), by state and territory, 2013–2016

Antimicrobial	Year	Number tested	Number non-susceptible (%)								
			NSW	Vic	Qld	SA	WA	Tas	NT	ACT	Australia
Ampicillin	2013	321	90.7 (97)	93.8 (75)	88.9 (32)	96.9 (31)	97.6 (41)	100 (5)	100 (3)	100 (16)	93.5) (300)
	2014	379	89.3 (92)	93.6 (88)	86.5 (32)	89.1 (41)	94.0 (47)	71.4 (5)	0.0 (0)	92.7 (38)	90.5 (343)
	2015	400	86.1 (99)	90.0 (108)	83.3 (25)	93.2 (41)	79.2 (42)	50.0 (4)	87.5 (7)	95.5 (21)	86.8 (347)
	2016	412	92.7 (114)	89.9 (98)	90.7 (39)	97.7 (42)	92.6 (50)	92.9 (13)	100 (4)	90.9 (20)	92.2 (380)
Vancomycin	2013	324	43.9 (47)	53.8 (43)	40.5 (15)	59.4 (19)	4.8 (2)	0.0 (0)	100 (3)	33.3 (6)	41.7 (135)
	2014	380	50.0 (52)	66.0 (62)	40.5 (15)	56.5 (26)	20.0 (10)	14.3 (1)	0.0 (0)	24.4 (10)	46.3 (176)
	2015	402	51.7 (60)	63.3 (76)	61.3 (19)	52.3 (23)	11.3 (6)	12.5 (1)	75.0 (6)	50.0 (11)	50.2 (202)
	2016	413	47.6 (59)	62.4 (68)	30.2 (13)	46.5 (20)	14.8 (8)	42.9 (6)	75.0 (3)	68.2 (15)	46.5 (192)
Teicoplanin	2013	321	9.3 (10)	2.5 (2)	5.6 (2)	3.1 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	4.7 (15)
	2014	377	29.1 (30)	1.1 (1)	0.0 (0)	0.0 (0)	2.0 (1)	0.0 (0)	0.0 (0)	2.4 (1)	8.8 (33)
	2015	401	33.9 (39)	12.5 (15)	19.4 (6)	2.3 (1)	5.7 (3)	0.0 (0)	0.0 (0)	31.8 (7)	17.7 (71)
	2016	413	38.7 (48)	13.8 (15)	2.3 (1)	0.0 (0)	9.3 (5)	0.0 (0)	0.0 (0)	40.9 (9)	18.9 (78)
Gentamicin (high-level)	2013	271	77.1 (64)	51.3 (41)	77.8 (28)	33.3 (2)	31.0 (13)	60.0 (3)	100 (3)	87.5 (14)	62.0 (168)
	2014	377	70.6 (72)	57.4 (54)	69.4) (25)	67.4 (31)	40.0 (20)	14.3 (1)	0.0 (0)	73.2 (30)	61.8 (233)
	2015	387	65.7 (67)	59.2 (71)	63.3 (19)	81.8 (36)	26.4 (14)	25.0 (2)	75.0 (6)	86.4 (19)	60.5 (234)
	2016	403	70.1 (82)	39.8 (43)	38.1 (16)	71.4 (30)	24.1 (13)	57.1 (8)	100 (4)	72.7 (16)	52.6 (212)
Linezolid	2013	321	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)
	2014	378	1.0 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.3 (1)
	2015	400	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)
	2016	408	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)

EUCAST = European Committee on Antimicrobial Susceptibility Testing
Note: Tinted cells indicate a significant trend.

3.9.3 *Staphylococcus aureus*

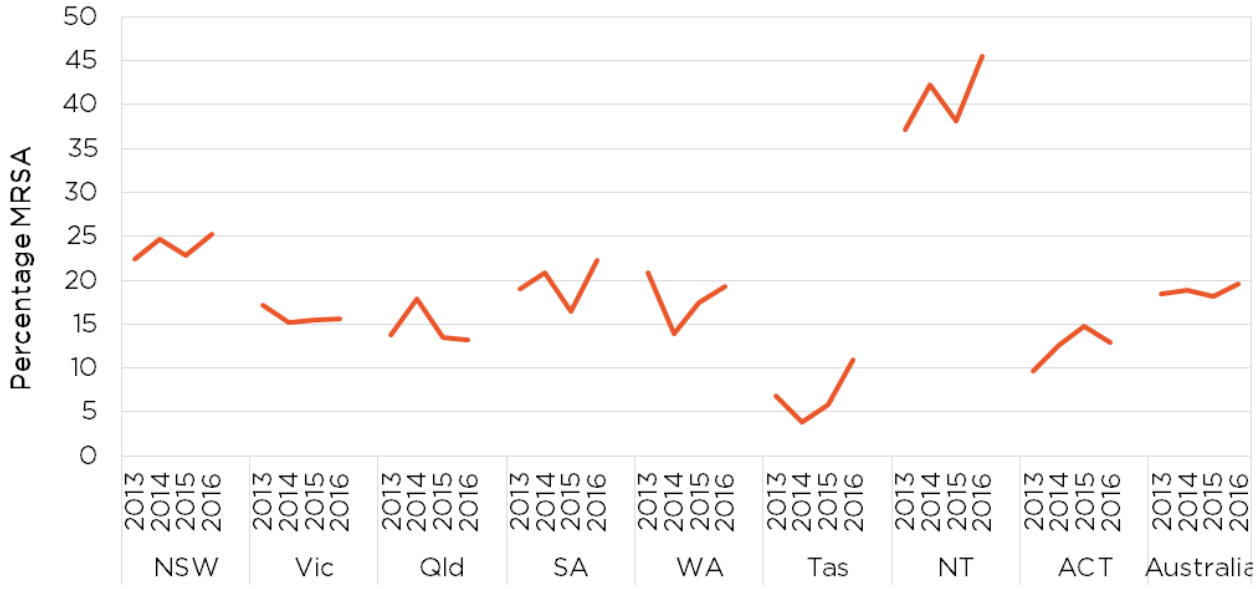
A primary aim of the 2016 program was to measure the proportion of SAB isolates demonstrating resistance to methicillin and other important anti-staphylococcal agents. The following sections describe the major trends observed for the period 2013–2016.

Methicillin-resistant *Staphylococcus aureus*

The proportion of *S. aureus* that was methicillin resistant throughout Australia remained constant over the years 2013–2016, although there were notable variations at state and territory level (Figure 10).

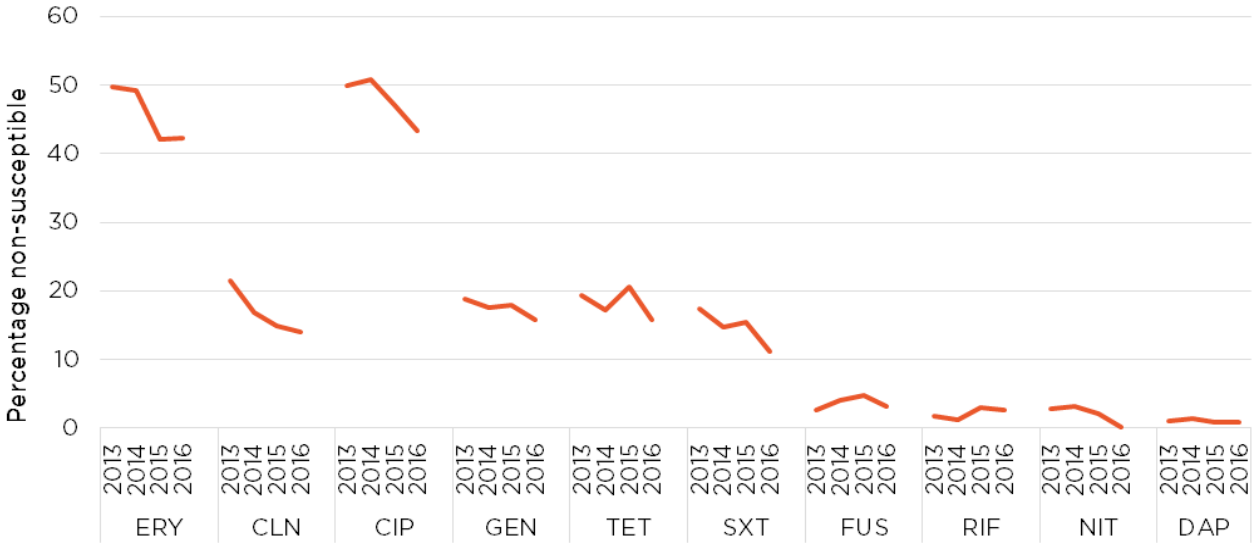
There was a significant decrease in erythromycin (χ^2 for linear trend = 5.006, P = 0.0253) and clindamycin (χ^2 for linear trend = 5.966, P = 0.0146) non-susceptible MRSA from 2013 to 2016 (Figure 11).

Figure 10: Proportion of methicillin-resistant *Staphylococcus aureus,* by state and territory, and nationally, 2013–2016



MRSA = methicillin-resistant *Staphylococcus aureus*

Figure 11: Non-susceptibility of methicillin-resistant *Staphylococcus aureus* to key antimicrobials (EUCAST), Australia, 2013–2015

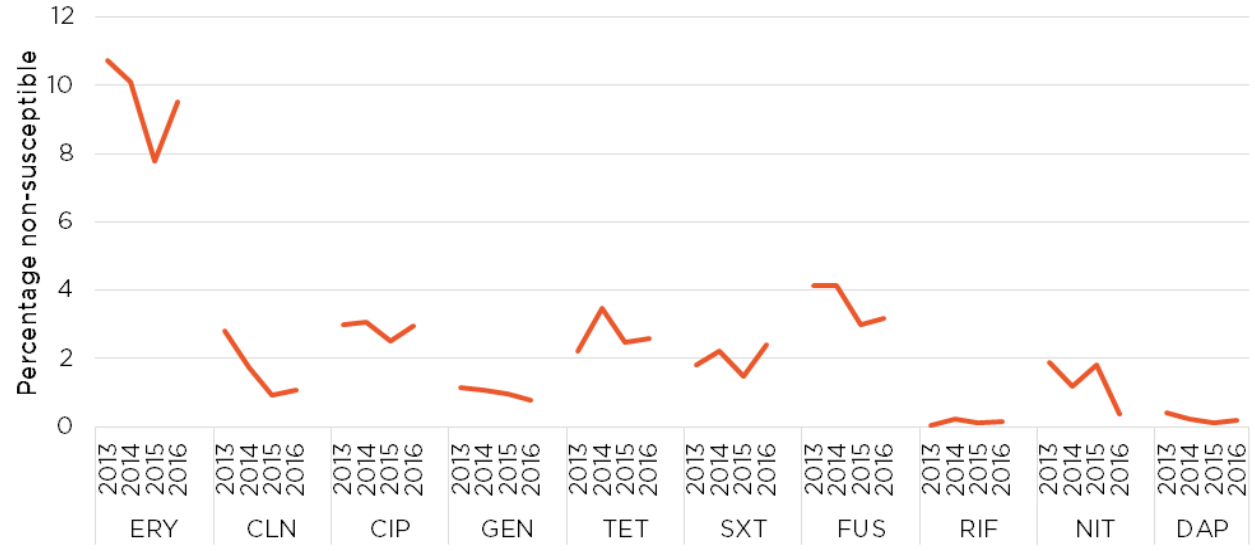


CIP = ciprofloxacin; CLN= clindamycin; DAP = daptomycin; ERY = erythromycin; EUCAST = European Committee on Antimicrobial Susceptibility Testing; FUS = fusidic acid; GEN = gentamicin; NIT = nitrofurantoin (CLSI); RIF = rifampicin; SXT = trimethoprim–sulfamethoxazole; TET = tetracycline

Methicillin-susceptible *Staphylococcus* aureus

There was a significant decrease in clindamycin (χ^{v2} for linear trend = 21.84, P < 0.0001) and nitrofurantoin (χ^2 for linear trend = 11.27, P = 0.0008) non-susceptible MSSA from 2013 to 2016 (Figure 12). There was also a decrease in fusidic acid non-susceptibility (χ^2 for linear trend = 4.063, P = 0.0438).

Figure 12: Non-susceptibility of methicillin-susceptible *Staphylococcus aureus* to key antimicrobials (EUCAST), Australia, 2013–2016



CIP = ciprofloxacin; CLN= clindamycin; DAP = daptomycin; ERY = erythromycin; EUCAST = European Committee on Antimicrobial Susceptibility Testing; FUS = fusidic acid; GEN = gentamicin; NIT = nitrofurantoin (CLSI); RIF = rifampicin; SXT = trimethoprim–sulfamethoxazole; TET = tetracycline

3.10 Molecular studies

This section describes the results of molecular studies of the resistance of gram-negative organisms, and the molecular epidemiology of *E. faecium* and MRSA.

3.10.1 Gram-negative organisms

Molecular studies were used to examine the resistance of gram-negative organisms to third-generation cephalosporins, quinolones and carbapenems, and to monitor the epidemiology of *E. coli* sequence type 131.

Extended-spectrum β-lactamases

Resistances conferred by ESBL-containing gram-negative organisms are important internationally, especially in hospital practice. Initially, ESBLs were more common in *Klebsiella* species than in *E. coli*. Recently, two new trends have appeared: the presence of ESBLs in *Enterobacter* species, and the emergence of specific types of ESBLs (CTX-M enzymes) in *E. coli* from the community. The latter is part of a global epidemic. It is unclear what is driving the community expansion of CTX-M ESBLs in Australia, as third-generation cephalosporins are not widely used in that setting; it is thought to be driven by cross-resistance and co-resistance to agents used in community practice. There is also increasing recognition that ESBLs are becoming established in long-term care facilities in Australia.

ESBLs are important because they compromise the efficacy of third-generation cephalosporins, which have been a useful therapeutic alternative for infections in patients presenting from the community. ESBL- producing isolates often have co-resistance to other non-β-lactam agents. This can result in delays in the use of effective empirical therapy. The lack of available oral options for treatment can result in unnecessary hospitalisation and, in the setting of sepsis, increased mortality risk.

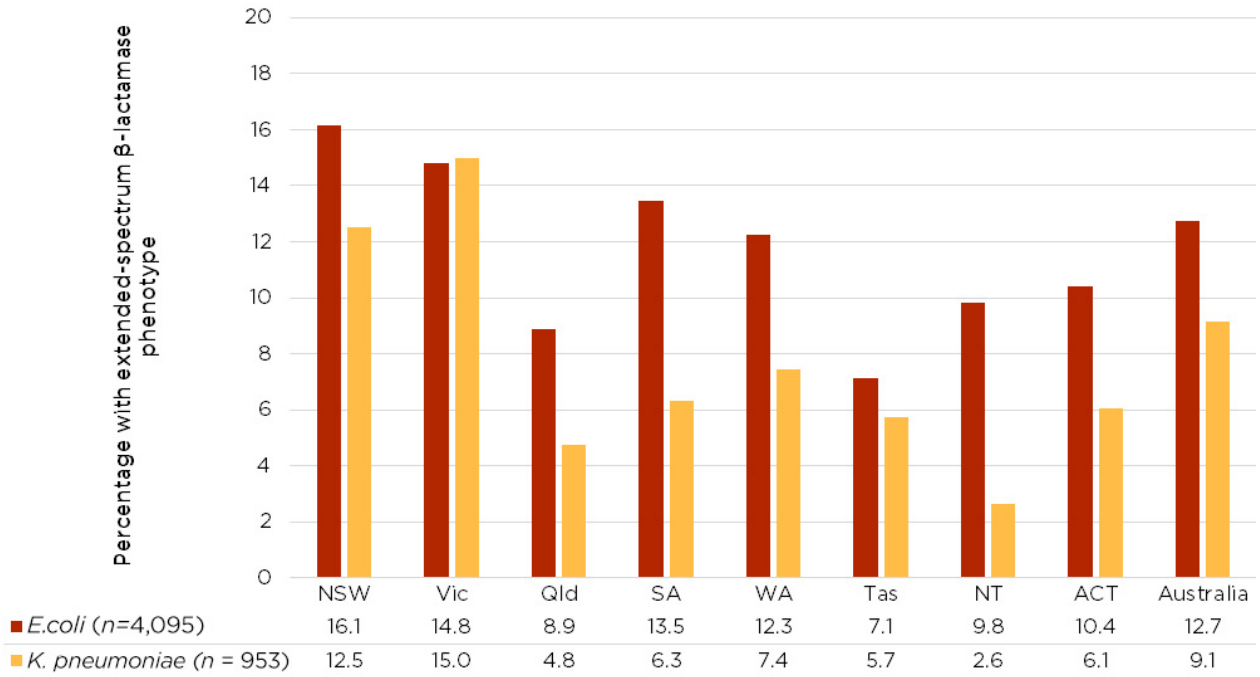
Most ESBL-producing isolates will be detected using the CLSI/EUCAST ceftriaxone 'susceptible' breakpoint of 1 mg/L. The CLSI 'susceptible' breakpoint of 4 mg/L for ceftazidime is less reliable for ESBL detection. Isolates with either ceftriaxone or ceftazidime minimum inhibitory concentrations (MICs) above 1 mg/L were selected for molecular testing.

Neither ceftriaxone nor ceftazidime testing will identify ESBL production in *Enterobacter* species because of their intrinsic chromosomal AmpC β-lactamase. In Enterobacter, cefepime MICs of greater than 0.25 mg/L suggest that an isolate of this genus harbours an ESBL.[22] However, because of the susceptibility card range, isolates with a cefepime MIC of greater than 1 mg/L were selected for molecular testing.

Testing included screening for TEM, SHV, CTX-M and plasmid-borne *ampC* genes using molecular methods outlined in Appendix B. TEM screening does not accurately discriminate between TEM-1/2 genes, which encode narrow-spectrum β-lactamases, and TEM genes with higher numbers, which encode ESBLs. Similarly, SHV screening does not discriminate between genes for narrow-spectrum β-lactamases and those that encode ESBLs. SHV-1 is the chromosomally encoded enzyme that gives *K. pneumoniae* its characteristic amoxicillin resistance. *E. coli* isolates containing only TEM genes and *Klebsiella* species containing only SHV genes have not been classified as carrying an ESBL in this analysis. All CTX-M genes encode ESBLs, as in effect do plasmid-borne *ampC* genes.

E. coli and *K. pneumoniae* resistant to ceftriaxone and/or ceftazidime (MIC >1 mg/L), and their variation across states and territories, are shown in Figure 13. The presumptive and confirmed ESBLs by state and territory are shown in Table 25.

Figure 13: Percentage of *Escherichia coli* and *Klebsiella pneumoniae* with extended-spectrum β-lactamase phenotype, by state and territory, and nationally, 2016



Based on the tests performed in this study, ESBLs were more common among *E. coli* (10.3% confirmed) and *K. pneumoniae* (6.9% confirmed) than among other species. For *Enterobacter* species with cefepime MIC greater than 1 mg/L, 17 of 44 *E. cloacae* (39%; 4.3% overall) and two of five *E. aerogenes* contained an ESBL. Of identified ESBLs, *E. cloacae* contained the following types: TEM and SHV (*n* = 6), CTX-M group 1 and TEM (*n* = 2), CTX-M group 9 only (*n* = 1), and TEM only (*n* = 8). Seven of 17 *E. cloacae* with ESBLs also contained $bla_{\text{IMP-4}}$ carbapenemases.

The majority (74%) of *K. oxytoca* isolates with a ceftriaxone-resistant phenotype were presumably hyperproducers of K1 β-lactamase, the natural chromosomal enzyme in this species, with characteristic resistance to piperacillin–tazobactam and borderline resistance to cefepime, but susceptibility to ceftazidime. This pattern is not typical of other types of gram-negative β-lactamases.

As expected, the CTX-M-type ESBL genes were prominent in *E. coli*. Of 423 confirmed ESBLs, 368 (87.0%; range 73.3–93.3%) had CTX-M types detected by consensus primers targeting CTX-M group 1 (*n* = 209), CTX-M group 9 (*n* = 155) or both (*n* = 4). Among *K. pneumoniae* with confirmed ESBLs, 48 of 66 (72.7%) contained CTX-M types: CTX-M group 1 (*n* = 36) and CTX-M group 9 (*n* = 12).

ESBL phenotypes were significantly more likely to be found among hospital-onset than community-onset episodes of *K. pneumoniae* bacteraemia (36/278 [12.9%] vs 51/603 [7.8%]; P = 0.02). However, for this survey, no significant difference was noted between hospital versus community onset for *E. coli* bacteraemia (97/678 [14.3%] vs 413/3,346 [12.3%]) and *E. cloacae* bacteraemia.

Table 25: Numbers of isolates with extended-spectrum β-lactamase phenotype, by state and territory, 2016

Species	NSW	Vic	Qld	SA	WA	Tas	NT	ACT	Australia
Escherichia coli	992	709	811	431	677	168	153	154	4,095
ESBL phenotype	160	105	72	58	83	12	15	16	521
Confirmed									
Any ESBL*/number received	131/152	84/91	51/71	42/49	75/82	10/11	15/15	15/16	423/487
CTX-M types	118	71	41	36	69	8	14	11	368
Plasmid-borne AmpC	17	12	9	6	5	1	1	4	55
SHV	0	2	1	1	2	1	0	0	7
Klebsiella pneumoniae	224	180	189	79	175	35	38	33	953
ESBL phenotype	28	27	9	5	13	2	1	2	87
Confirmed									
Any ESBL*/number received	17/26	24/25	6/9	4/4	11/13	2/2	1/1	1/2	66/82
CTX-M types	14	14	4	3	9	2	1	1	48
Plasmid-borne AmpC	3	7	0	1	0	0	0	0	11
TEM	10	21	5	1	2	2	1	1	43
Klebsiella oxytoca	64	52	37	24	37	14	2	13	243
ESBL phenotype	11	4	7	3	2	1	0	0	28
Confirmed									
Any ESBL*/number received	1/8	0/3	1/7	0/2	0/2	0/1	0/0	0/0	2/23†
CTX-M types	0	0	1	0	0	0	n/a	n/a	1
TEM	1	0	1	0	0	0	n/a	n/a	2
SHV	1	0	0	0	0	0	n/a	n/a	1
Proteus mirabilis	61	24	52	23	33	11	12	6	224
ESBL phenotype	1	0	0	0	1	0	0	0	2
Confirmed									
Any ESBL*/number received	1/1	0/0	0/0	0/0	1/1	0/0	0/0	0/0	2/2
CTX-M types	0	n/a	n/a	n/a	1	n/a	n/a	n/a	1
Plasmid-borne AmpC	1	n/a	n/a	n/a	0	n/a	n/a	n/a	1
TEM	0	n/a	n/a	n/a	1	n/a	n/a	n/a	1
Salmonella species (non-typhoidal)	16	18	29	12	12	2	24	1	114
ESBL phenotype	0	0	0	0	0	0	0	0	0

ESBL = extended-spectrum β-lactamase; n/a = not applicable

* Isolates may possess more than one type of ESBL gene.

† See text for an explanation of the low proportion of ESBL.

Plasmid-borne AmpC β-lactamases

Plasmid-borne AmpC β-lactamases have recently emerged internationally as a growing gram-negative resistance problem. They are the result of mobilisation of natural chromosomally located genes from common and uncommon species of Enterobacteriaceae onto transmissible plasmids, and transmission into more common pathogens. There are currently six separate classes of plasmid-borne AmpC β-lactamases. Like ESBLs, these enzymes confer resistance to the important third-generation cephalosporins, such as ceftriaxone and ceftazidime. Routine phenotypic detection methods have not yet been developed. Nevertheless, it is possible to exploit a special feature of these enzymes: their ability to inactivate the cephamycins, represented by cefoxitin. *Enterobacter* species already naturally possess chromosomally encoded AmpC enzymes.

The proportions of *E. coli* and *K. pneumoniae* with elevated cefoxitin MICs were low. Only 37% (53/144) of *E. coli* and 30% (11/37) of *K. pneumoniae* with cefoxitin MIC ≥32 mg/L that were available for molecular confirmation were confirmed to contain plasmid-borne *ampC* genes (Table 26).

The *bla*CMY gene was found in 81% (43/53) of *E. coli* with plasmid-borne *ampC* genes; *bla*DHA was found in 82% of *K. pneumoniae* with plasmid-borne *ampC* genes. Carbapenemase genes were detected in two of the cefoxitin-resistant *K. pneumoniae* (bla_{IMP-4}, n = 1; bla_{KPC-2}, n = 1) and one *E. coli* (bla_{IMP-4}) that did not have plasmid-borne *ampC* genes. Two *E. coli* with a cefoxitin MIC of 16 mg/L also contained either bla_{CMY} or bla_{DHA}.

Table 26: Numbers of isolates with presumptive plasmid-borne AmpC β-lactamase production, by state and territory, 2016

Species	NSW	Vic	Qld	SA	WA	Tas	NT	ACT	Australia
Escherichia coli	993	7029	806	431	677	168	153	154	4.091
Cefoxitin MIC ≥32 mg/L	38 (3.8%)	29 (4.1%)	36 (4.5%)	13 (3.0%)	21 (3.1%)	4 (2.4%)	7 (4.6%)	5 (3.2%)	153 (3.7%)
Confirmed/number received	17/37	12/24	8/36	6/12	5/19	1/4	1/7	3/5	53/144
bla_{CMY}	14	11	8	4	2	1	0	3	43
bla_{DHA}	3	1	0	2	3	0	1	0	10
Klebsiella pneumoniae	224	180	189	79	175	35	38	33	953
Cefoxitin MIC ≥32 mg/L	11 (4.9%)	13 (7.2%)	7 (3.7%)	3 (3.8%)	5 (2.9%)	0 (0.0%)	1 (2.6%)	2 (6.1%)	42 (4.4%)
Confirmed/number received	3/9	7/11	0/7	1/3	0/5	0/0	0/0	0/2	11/37
bla_{DHA}	1	7	0	1	0	n/a	0	0	9
bla_{CMY}	2	0	0	0	0	n/a	0	0	2
Klebsiella oxytoca	64	52	37	24	37	14	2	13	243
Cefoxitin MIC ≥32 mg/L	0 (0.0%)	0 (0.0%)	1 (2.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.4%)
Confirmed/ number received	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/1

MIC = minimum inhibitory concentration; n/a = not applicable

Carbapenemases

Twenty-eight (0.37%) isolates from 25 patients were found to harbour a carbapenemase gene (Table 27). The bla_{IMP-4} gene was detected in 13 isolates: *E. cloacae* (seven, from six patients), *E. coli* (one), *K. pneumoniae* (one), *M. morganii* (one), *S. marcescens* (one), *E. aerogenes* (one) and *K. pneumoniae* (one); bla_{IMP-14} was detected in one *P. aeruginosa*; $bla_{IMP-4 + OXA-23}$ was detected in three *A. baumannii* (from two patients); bla_{OXA-23} was detected in five *A. baumannii* (from four patients); bla_{NDM-1} was detected in one *K. pneumoniae*; bla_{NDM-4} was detected in one *K. pneumoniae*; bla_{OXA-48} was detected in one *K. pneumoniae*; bla_{KPC-2} was detected in one *K. pneumoniae*; $bla_{NDM + OXA-48}$ was detected in one *K. pneumoniae*; $bla_{OXA-181}$ was detected in one *K. pneumoniae*; and bla_{GES-5} was detected in one *P. aeruginosa*. Ten of 15 Enterobacteriaceae with confirmed metallo-β-lactamases also contained plasmid-mediated quinolone resistance genes (*aac[6']-Ib-cr* alone or with *qnrB* or *qnrS*).

Seven *E. cloacae* (from five patients) demonstrated carbapenemase activity by the carbapenem inactivation method, but were negative for IMP, VIM, KPC, NDM, OXA-48-like, SIM, GIM, SPM, BIC, DIM, AIM and GES carbapenemases. Phenotypic tests indicated a possible serine carbapenemase; however, they did not contain either SME, IMI or FRI. Interestingly, all isolates contained AmpC ACT-4, -7 or -9, along with plasmid-encoded efflux pump oqxAB.

Overall prevalence of carbapenemase genes among Enterobacteriaceae was 0.27% (18/6,750). It was 0.28% (2/723) for *P. aeruginosa* and 8.7% (8/92) for *Acinetobacter* species.

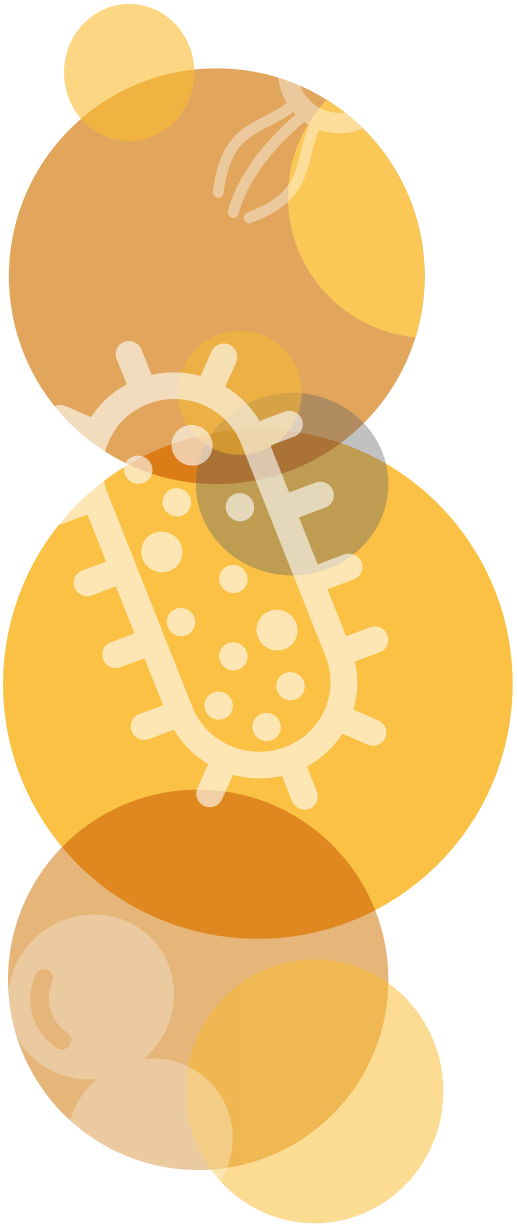


Table 27: Number of carbapenemases and associated resistance genes, by species and state and territory, 2015

Gene	State or territory	Species	Meropenem MIC (mg/L)	ESBL type*	PMQR gene†	16S rRNA methylases
bla$_{IMP-4}$ (*n* = 13)	NSW	*E. cloacae* (*n* = 1)	1	–§	*qnrB20*	–§
		E. cloacae (*n* = 1)	8	–§	–§	–§
		E. cloacae(*n*= 1)	≥16	–§	*aac(6')-Ib-cr, qnrB20*	–§
		E. coli (*n* = 1)	≥16	–§	*qnrB20*	–§
		M. morganii (*n* = 1)	4	–§	*aac(6')-Ib-cr*	–§
		S. marcescens (*n* = 1)	0.5	–§	*aac(6')-Ib-cr, qnrB13*	–§
		E. aerogenes (*n* = 1)	1	n/a	*n/a*	n/a
		K. pneumoniae (*n* = 1)	1	n/a	n/a	n/a
	Qld	*E. cloacae* (*n* = 2)#	≥16	–§	*aac(6')-Ib-cr, qnrB20*	–§
		E. cloacae(*n*= 1)	≥16	SHV-12	*aac(6')-Ib-cr, qnrB20*	–§
	WA	*K. pneumoniae* (*n* = 1)	4	–§	–§	–§
	ACT	*E. cloacae* (*n* = 1)	≥16	CTX-M-15	*aac(6')-Ib-cr, qnrB1*	–§
bla$_{IMP-14}$ (*n = 1)*	Vic	*P. aeruginosa* (*n* = 1)	≥16	–§	–§	–§
bla$_{IMP-4 + OXA-23}$ (*n* = 3)	Qld	*A. baumannii* (*n* = 3)**	≥16	–§	–§	–§
bla$_{OXA-23}$ (*n* = 5)	Qld	*A. baumannii* (*n* = 4)††	≥16	–§	–§	*armA*
	Vic	*A. baumannii* (*n* = 1)	≥16	–§	–§	– §
bla$_{NDM-1}$ (*n* = 1)	NSW	*K. pneumoniae* (*n* = 1)	8	SHV-28, CMY-6, CTX-M-15	–§	*rmtB,*
bla$_{NDM-4}$ (*n* = 1)	SA	*P. aeruginosa* (*n* = 1)	n/a	SHV-83, CTX-M-14	*qnrS*	*rmtC*
bla$_{KPC-2}$ (*n* = 1)	Vic	*K. pneumoniae* (*n* = 1)	≥16	–§	–§	–§
bla$_{OXA-181}$ (*n* = 1)	Vic	*P. aeruginosa* (*n* = 1)	1	DHA-1, CTX-M-15	*aac(6')-Ib-cr, qnrB*	–§
bla$_{OXA-48}$ (*n* = 1)	Vic	*K. pneumoniae* (*n* = 1)	1	SHV-99	–§	–§
bla$_{GES-5}$ (*n* = 1)	NSW	*P. aeruginosa* (*n* = 1)	≥16		–§	–§

ESBL = extended-spectrum β-lactamase; MIC = minimum inhibitory concentration; PMQR = plasmid-mediated quinolone resistance; RMT = 16S rRNA methyltransferase; n/a = not available for follow-up

* TEM types, SHV types, CTX-M types, pAmpC

† *aac(6')-Ib-cr*, *qnr*, efflux (qepA, oqxAB)

§ Not detected

\# *bla*I$_{MP-4}$ from the same patient

** *bla*IM$_{P-4+OXA-23,}$ two isolates from the same patient

†† *bla*$_{OXA-23}$, two isolates from the same patient

Plasmid-mediated quinolone resistance

Quinolone resistance is most commonly due to mutations in DNA gyrase and topoisomerase IV. More recently, transmissible plasmid-mediated quinolone resistance (PMQR) has emerged in Enterobacteriaceae. PMQR may be due to the presence of *qnr* genes (*qnrA, qnrB, qnrS, qnrC, qnrD);* *aac(6')-Ib-cr*, coding for a variant aminoglycoside acetyltransferase enzyme; or genes coding for efflux pumps (*qepA*, *oqxAB*).

Of isolates with ciprofloxacin MIC greater than 0.25 mg/L, 23% of *E. coli,* 73% of *K. pneumoniae* and 75% of *E. cloacae* were confirmed to contain PMQRs (Table 28). The proportion and type of PMQR determinant found among isolates with ciprofloxacin MIC greater than 0.25 mg/L varied among the different species (Figure 14). The *aac(6')-Ib-cr* gene, with or without *qnr*, was dominant, and was present in five of the seven species.

Table 28: Number and percentage of isolates with plasmid-mediated quinolone resistance, by species, and state and territory, 2015

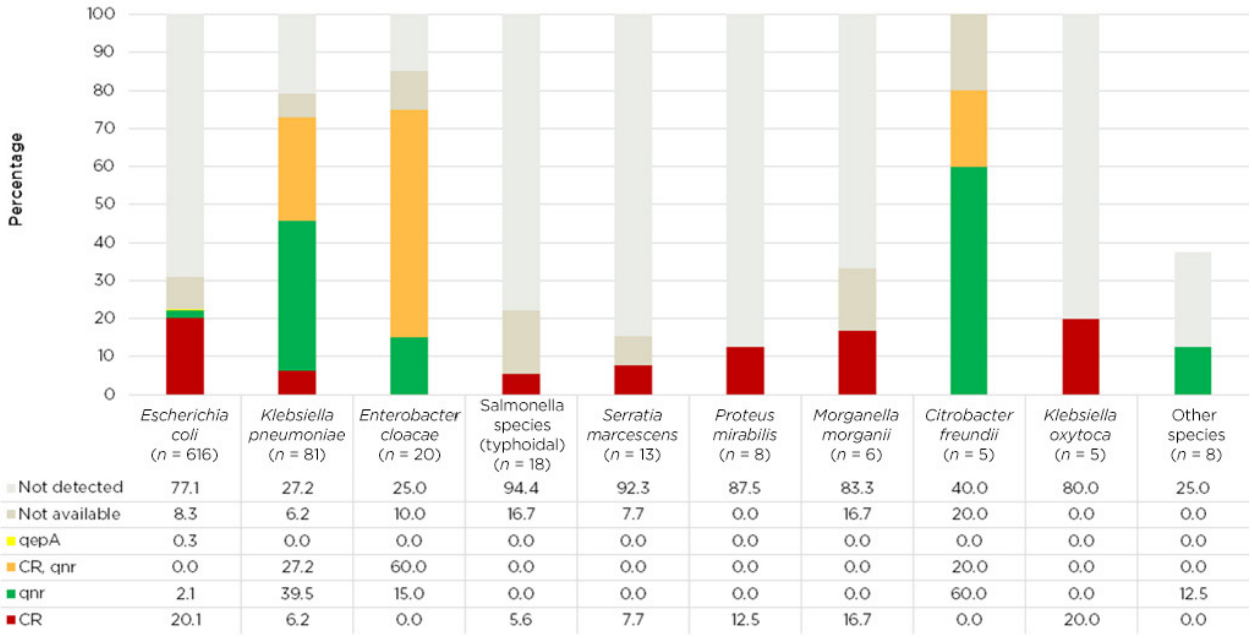
Species	NSW	Vic	Qld	SA	WA	Tas	NT	ACT	Australia
Escherichia coli									
Ciprofloxacin	194	127	96	68	117	20	17	26	665
MIC >0.25 mg/L* (%)	19.5	17.9	11.9	15.9	17.3	11.9	11.1	16.9	16.3
Confirmed/number received	26/181	26/105	14/94	15/59	42/114	5/18	6/17	5/26	139/614 (22.6%)
aac(6')-Ib-cr	22	24	12	14	39	5	4	4	124
qnrS	4	1	2	1	2	0	2	1	13
qepA	0	1	0	0	1	0	0	0	2
Klebsiella pneumoniae									
Ciprofloxacin	21	32	10	10	7	3	1	2	86
MIC >0.25 mg/L (%)	9.4	17.8	5.3	12.8	4.0	8.6	2.6	6.1	9.0
Confirmed/number received	16/20	21/28	4/10	8/10	4/7	3/3	1/1	2/2	59/81 (72.8%)
aac(6')-Ib-cr	2	0	1	1	1	0	0	0	5
aac(6')-Ib-cr + qnrB	6	11	0	1	0	1	1	0	20
aac(6')-Ib-cr + qnrS	0	0	2	0	0	0	0	0	2
qnrB	2	4	0	1	0	0	0	1	8
qnrS	6	6	1	5	3	2	0	1	24
Enterobacter cloacae									
Ciprofloxacin	8	4	4	3	0	1	0	2	22
MIC >0.25 mg/L (%)	7.3	4.8	4.6	12.5	0.0	7.7	0.0	14.3	5.6
Confirmed/number received	5/8	2/2	4/4	1/3	–†	1/1	–†	2/2	15/20 (75.0%)
qnrB	1	1	0	0	n/a	0	n/a	0	2
qnrS	0	0	0	1	n/a	0	n/a	0	1
aac(6')-Ib-cr + qnrA	4	1	1	0	n/a	1	n/a	0	7
aac(6')-Ib-cr + qnrB	0	0	3	0	n/a	0	n/a	2	5

MIC = minimum inhibitory concentration; na = not applicable

* Concentration used to select strains for molecular testing

† No isolates

Figure 14: Proportion of plasmid-mediated quinolone resistance genes among gram-negative species with ciprofloxacin MIC >0.25 mg/L, 2015



	Escherichia coli (*n* = 616)	*Klebsiella pneumoniae* (*n* = 81)	*Enterobacter cloacae* (*n* = 20)	Salmonella species (typhoidal) (*n* = 18)	*Serratia marcescens* (*n* = 13)	*Proteus mirabilis* (*n* = 8)	*Morganella morganii* (*n* = 6)	*Citrobacter freundii* (*n* = 5)	*Klebsiella oxytoca* (*n* = 5)	Other species (*n* = 8)
Not detected	77.1	27.2	25.0	94.4	92.3	87.5	83.3	40.0	80.0	25.0
Not available	8.3	6.2	10.0	16.7	7.7	0.0	16.7	20.0	0.0	0.0
qepA	0.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
CR, qnr	0.0	27.2	60.0	0.0	0.0	0.0	0.0	20.0	0.0	0.0
qnr	2.1	39.5	15.0	0.0	0.0	0.0	0.0	60.0	0.0	12.5
CR	20.1	6.2	0.0	5.6	7.7	12.5	16.7	0.0	20.0	0.0

CR = *aac(6')-Ib-cr*

Note: 'Other species' are *K. variicola* (*n* = 3), *Salmonella* species (non-typhoidal) (*n* = 2), *E. aerogenes* (*n* = 2), *S. sonnei* (*n* = 1)

Escherichia coli sequence type 131

Sequence type 131 (O25b-ST131) is the main *E. coli* lineage among extra-intestinal pathogenic *E. coli* worldwide. O25b-ST131 isolates are commonly reported to produce ESBLs, such as CTX-M-15, and almost all O25b-ST-131 isolates with CTX-M-15 are resistant to fluoroquinolones.

Most of the isolates with an ESBL phenotype harboured genes of the CTX-M type (368/487; 75.6%) (Table 29). Fifty-five per cent (117/213) of the *E. coli* with CTX-M group 1 types (CTX-M-15 like) were found to belong to the O25b-ST131 lineage. O25b-ST131 accounted for 62.9% (180/286) of *E. coli* ESBL phenotypes that were ciprofloxacin resistant (MIC >1 mg/L), but only 3.5% (7/201) of ciprofloxacin-susceptible ESBL phenotypes. O25b-ST131 often carried $bla_{\text{CTX-M-15}}$ and *aac(6')-Ib-cr*.

Table 29: Number of *Escherichia coli* clones with ESBL phenotype, by O25b-ST131 clone and ciprofloxacin resistance, 2016

Clone/subclone	Total	CTX-M types		Other ESBL types*	Ciprofloxacin MIC	
		CTX-M-15-like	Non-CTX-M-15		>1 mg/L	≤1 mg/L
O25b-ST131	185	116	60	3	178	7
Non-O25b-ST131	286	90	94	13	99	187
dna	16	7	1		9	7
Total	487	213	155	16	286	201

dna = did not amplify; ESBL = extended-spectrum β-lactamase; MIC = minimum inhibitory concentration

* TEM or SHV

mcr-1

Because colistin is currently only available on the Phoenix cards, only 873 (11.5%) isolates from two laboratories were tested for colistin susceptibility. Excluding intrinsically resistant species, 11/813 (1.4%) had colistin MIC >2 mg/L. Nine isolates (*E. coli, n* = 5; *E. cloacae*, *n* = 2; *P. aeruginosa*, *n* = 2) were available for confirmation. The *mcr-1* gene was detected in one (1/31, 3.2%) *E. cloacae* only.

All referred isolates were subsequently screened for the presence of *mcr-1*, regardless of the resistance profile. Of 1,204 (17.1%) isolates (which excluded intrinsically resistant species) available, *mcr-1* was detected in two (2/857, 0.23%) *E. coli,* and one (1/65, 1.5%) *E. cloacae* (the same isolate as above). These isolates were from three different states (Queensland, South Australia and Victoria). Neither *E. coli* exhibited ESBL activity, and all were meropenem susceptible. The *E. cloacae* and one *E. coli* also contained *qnrS*.

3.10.2 Molecular epidemiology of *Enterococcus faecium*

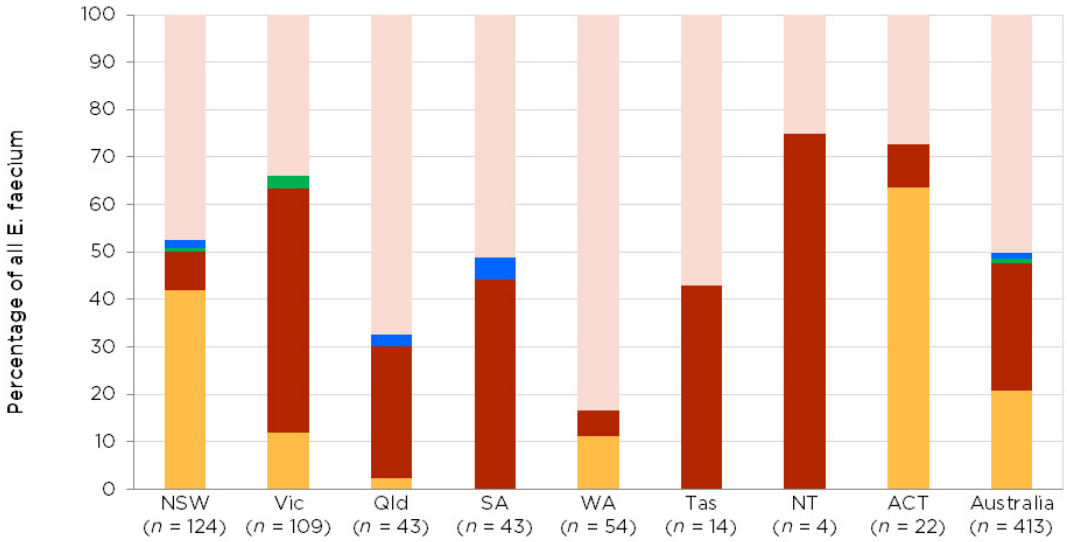
van genes

Results for *vanA* and *vanB* were available for 408 (98.8%) of the 413 *E. faecium* isolates. In *E. faecium* isolates, *van* genes were detected in 49.3% (201/408): *vanA* in 86 (21.1%), *vanB* in 111 (27.2%), and *vanA* and *vanB* in four (1.0%) isolates (Figure 15).

For vancomycin-resistant *E. faecium* (MIC >4 mg/L), *vanA* was detected in 79/190 (41.6%), *vanB* in 107 (56.3%), and *vanA* and *vanB* in four (2.1%).

In 25 of 197 (12.7%) vancomycin-susceptible *E. faecium*, *van* genes were detected: 8 with *vanA* and 17 with *vanB*. All isolates had vancomycin MIC ≤1 mg/L.

Figure 15: Vancomycin genotype of *Enterococcus faecium* isolates, by state and territory, and nationally, 2016



	NSW (*n* = 124)	Vic (*n* = 109)	Qld (*n* = 43)	SA (*n* = 43)	WA (*n* = 54)	Tas (*n* = 14)	NT (*n* = 4)	ACT (*n* = 22)	Australia (*n* = 413)
Not vanA or vanB (*n* = 207)	47.6	33.9	67.4	51.2	83.3	57.1	25.0	27.3	50.1
Not determined (*n* = 5)	1.6	0.0	2.3	4.7	0.0	0.0	0.0	0.0	1.2
vanA and vanB (*n*=4)	0.8	2.8	0.0	0.0	0.0	0.0	0.0	0.0	1.0
vanB (*n* = 111)	8.1	51.4	27.9	44.2	5.6	42.9	75.0	9.1	26.9
vanA (*n* = 86)	41.9	11.9	2.3	0.0	11.1	0.0	0.0	63.6	20.8

Multi-locus sequence type

Of the 413 *E. faecium* isolates reported, 400 (96.9%) were available for typing by whole genome sequencing (Table 30). Based on the multi-locus sequence type (MLST), 48 sequence types were identified. Overall, 84.0% of *E. faecium* could be characterised into nine STs: M-type 1 (*n* = 64), ST17 (*n* = 59), ST796 (*n* = 56), ST80 (*n* = 51), ST555 (*n* = 39), ST203 (*n* = 26), M-type 3 (*n* = 15), ST78 (*n* = 13) and ST262 (*n* = 12). The *pstS* housekeeping gene is absent in the M-type isolates.

M-type 1 was initially identified in 2015. In 2016, there were four M-type single-locus variants. There were 30 sequence types with a single isolate. ST796 was the main sequence type in Victoria. M-type 1 was detected in New South Wales, Victoria and the Australian Capital Territory; M-type 3 was only detected in Victoria. ST555 was the main sequence type in South Australia, and ST17 was the main sequence type in Western Australia.

There is considerable clonal diversity in *E. faecium* across Australia, including vancomycin-resistant strains, with distinct regional differences. This is consistent with the observation that much vancomycin resistance arises through the transmission of the vancomycin resistance gene complexes to susceptible clones, followed by subsequent amplification locally.

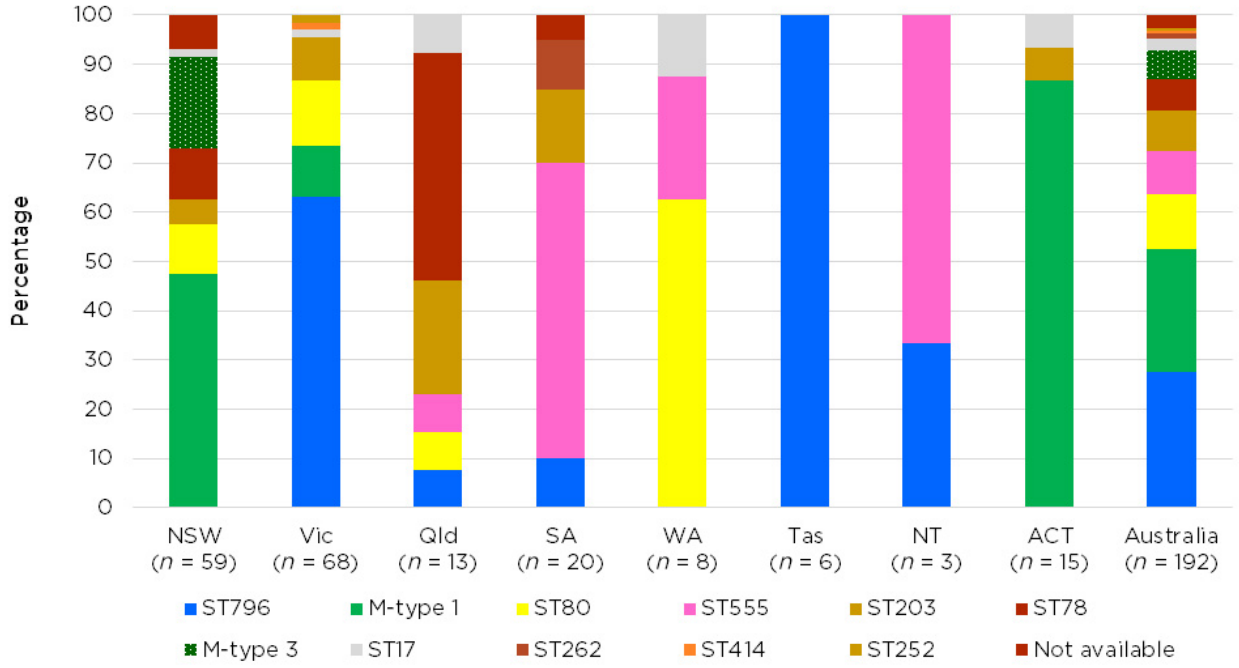
The distribution of vancomycin-resistant *E. faecium* sequence types throughout the states and territories is shown in Figure 16.

Table 30: *Enterococcus faecium* MLST, by state and territory, 2016

MLST	Percentage (*n*)								
	NSW	Vic	Qld	SA	WA	Tas	NT	ACT	Australia
M-type 1	34.8 (40)	8.3 (9)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	68.2 (15)	16.0 (64)
17	4.3 (5)	7.4 (8)	52.4 (22)	4.9 (2)	39.6 (21)	0.0 (0)	0.0 (0)	4.5 (1)	14.8 (59)
796	1.7 (2)	41.3 (45)	2.4 (1)	4.9 (2)	0.0 (0)	42.9 (6)	25.0 (1)	0.0 (0)	14.3 (57)
80	16.5 (19)	13.9 (15)	7.1 (3)	2.4 (1)	18.9 (10)	0.0 (0)	0.0 (0)	13.6 (3)	12.8 (51)
555	0.0 (0)	0.0 (0)	2.4 (1)	48.8 (20)	24.5 (13)	21.4 (3)	50.0 (2)	0.0 (0)	9.8 (39)
203	5.2 (6)	9.3 (10)	9.5 (4)	7.3 (3)	1.9 (1)	7.1 (1)	0.0 (0)	4.5 (1)	6.5 (26)
M-type 3	13.0 (15)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	3.8 (15)
78	6.1 (7)	0.0 (0)	14.3 (6)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	3.3 (13)
262	0.0 (0)	0.0 (0)	0.0 (0)	29.3 (12)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	3.0 (12)
Other types	18.3 (21)	20.4 (22)	11.9 (5)	2.4 (1)	15.1 (8)	28.6 (4)	25.0 (1)	9.1 (2)	16.0 (64)
Total	115	109	42	41	53	14	4	22	400

MLST = multilocus sequence type

Figure 16: Distribution of vancomycin-resistant *Enterococcus faecium* sequence types, by state and territory, 2015



MLST and *van* genes

The *vanA* gene was detected in seven sequence types: M-type 1 (*n* = 51); ST80 (*n* = 17); M-type 3 (*n* = 11); ST203 (*n* = 3); and ST17, ST555 and ST78 (*n* = 1 each). The *vanB* gene was detected in nine sequence types: ST796 (*n* = 55), ST555 (*n* = 17), ST203 (*n* = 14), ST78 (*n* = 11), ST80 (*n* = 5), ST17 (*n* = 4), ST262 (*n* = 2), M-type 1 (*n* = 1) and ST414 (*n* = 1) (Table 31).

Table 31: *Enterococcus faecium* MLST harbouring *vanA* and/or *vanB* genes, 2015

MLST	Percentage (*n*)				
	vanA	*vanB*	*vanA* and *vanB*	*vanA* or *vanB* not detected	Total
M-type 1	79.7 (51)	1.6 (1)	0.0 (0)	18.8 (12)	64
17	1.7 (1)	6.8 (4)	0.0 (0)	91.5 (54)	59
796	0.0 (0)	96.5 (55)	0.0 (0)	3.5 (2)	57
80	33.3 (17)	9.8 (5)	3.9 (2)	52.9 (27)	51
555	2.6 (1)	43.6 (17)	0.0 (0)	53.8 (21)	39
203	11.5 (3)	53.8 (14)	0.0 (0)	34.6 (9)	26
M-type 3	73.3 (11)	0.0 (0)	0.0 (0)	26.7 (4)	15
78	7.7 (1)	84.6 (11)	0.0 (0)	7.7 (1)	13
262	0.0 (0)	16.7 (2)	0.0 (0)	83.3 (10)	12
Other types	0.0 (0)	1.6 (1)	1.6 (1)	96.9 (62)	64
Total	21.3 (85)	27.5 (110)	0.8 (3)	50.4 (202)	400

MLST = multi-locus sequence type

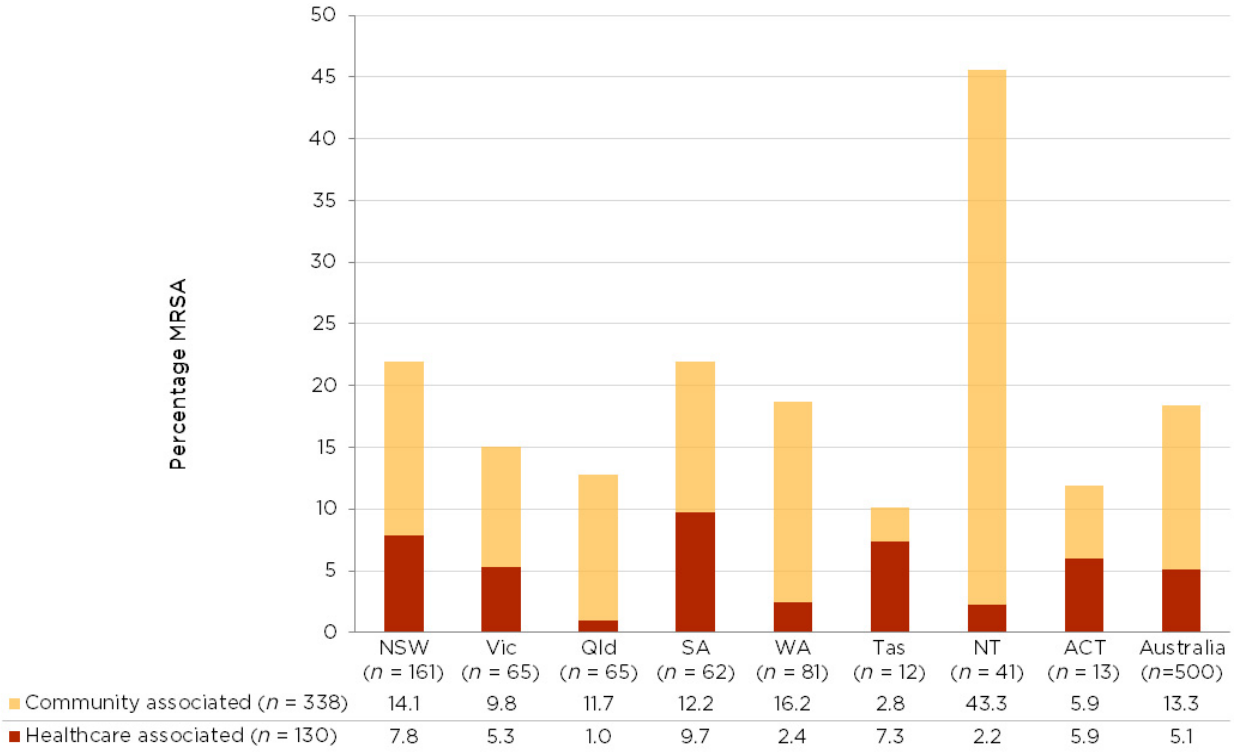
* Percentage of MLST with van genes

3.10.3 Molecular epidemiology of methicillin-resistant *Staphylococcus aureus*

Of the 500 MRSA reported, 468 were available for typing by whole genome sequencing.

There were significant differences among the states and territories in the percentage and types of MRSA clones. Prevalence of MRSA ranged from 11.0% in Tasmania to 45.6% in the Northern Territory (Figure 17).

Figure 17: Methicillin-resistant *Staphylococcus aureus* as a percentage of all *S. aureus* isolates, by state and territory, and nationally, 2016



	NSW (*n* = 161)	Vic (*n* = 65)	Qld (*n* = 65)	SA (*n* = 62)	WA (*n* = 81)	Tas (*n* = 12)	NT (*n* = 41)	ACT (*n* = 13)	Australia (*n*=500)
Community associated (*n* = 338)	14.1	9.8	11.7	12.2	16.2	2.8	43.3	5.9	13.3
Healthcare associated (*n* = 130)	7.8	5.3	1.0	9.7	2.4	7.3	2.2	5.9	5.1

MRSA = methicillin-resistant *Staphylococcus aureus*

Healthcare-associated MRSA

Based on the MLST and SCCmec type, five HA-MRSA clones were identified: ST22-IV (EMRSA-15), ST239-III (Aus 2/3 EMRSA), ST5-II (NY/Japan EMRSA or USA100), ST8-II (Irish-1) and ST8-III (EMRSA-7) (Table 32).

EMRSA-15 now outranks the long-established Aus2/3 clone in HA-MRSA bacteraemia. More EMRSA-15 bacteraemias arise in the community than in hospital, consistent with the prevalence of this clone in long-term care facilities in Australia.

The most frequently isolated HA-MRSA clone, ST22-IV, was identified in all states and territories except the Northern Territory. ST239-III was identified in all states and territories except Tasmania. Single isolates of ST8-II and ST8-III were identified in New South Wales, and a single isolate of ST5-II in Victoria (Table 33).

Panton–Valentine leucocidin (PVL)–associated genes were not identified in HA-MRSA. Although two PVL-positive ST22-IV isolates were identified – one each in Western Australia and Victoria – PVL-positive ST22-IV, which is often isolated in the South Asian subcontinent, is not related to EMRSA-15 and is not considered to be an HA-MRSA clone.

Table 32: Healthcare-associated MRSA clones, by place of onset and PVL carriage, 2016

Clone	Percentage (*n*)				
	Clonal complex	Total (%)*	Community onset†	Hospital onset†	PVL positive (%)
ST22-IV (EMRSA-15)§	22	19.6 (98)	58.2 (57)	42.7 (41)	0.0 (0)
ST239-III (Aus2/3 EMRSA)	8	5.8 (29)	55.2 (16)	44.8 (13)	3.4 (1)
ST8-II (Irish-1)	8	0.2 (1)	100 (1)	0.0 (0)	0.0 (0)
ST8-III (EMRSA-7)	8	0.2 (1)	0.0 (0)	100 (1)	0.0 (0)
ST5-II	5	0.2 (1)	0.0 (0)	100 (1)	0.0 (0)
Total		26.1 (130)	56.9 (74)	43.1 (56)	0.8 (1)

MRSA = methicillin-resistant *Staphylococcus aureus*; PVL = Panton–Valentine leucocidin

* Percentage of all MRSA

† Percentage of the clone

§ Includes one isolate identified as ST22slv-IV and one identified as ST22-V (a variant of ST22-IV)

Table 33: Healthcare-associated MRSA clones, by state and territory, 2016

Clone	Percentage (*n*)								
	NSW	Vic	Qld	SA	WA	Tas	NT	ACT	Australia
ST22-IV (EMRSA-15)*	68.0 (34)	81.8 (18)	60.0 (3)	81.5 (22)	90.0 (9)	100 (8)	0.0 (0)	66.7 (4)	75.4 (98)
ST239-III (Aus2/3 EMRSA)	28.0 (14)	13.6 (3)	40.0 (2)	18.5 (5)	10.0 (1)	0.0 (0)	100 (2)	33.3 (2)	22.3 (29)
ST8-II	2.0 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.8 (1)
ST8-III	2.0 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.8 (1)
ST5-II	0.0 (0)	4.5 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.8 (1)
Total	50	22	(0)	27	10	8	2	6	130

MRSA = methicillin-resistant *Staphylococcus aureus*

* Includes one isolate identified as ST22slv-IV and one identified as ST22-V (a variant of ST22-IV)

Community-associated MRSA

Based on the MLST and SCCmec type, 40 CA-MRSA clones were identified. PVL was detected in 13 CA-MRSA clones. Overall, 40.9% of CA-MRSA were PVL positive (Table 34).

The most frequently isolated CA-MRSA clone, ST93-IV (Qld CA-MRSA), was isolated in all states and territories except the Australian Capital Territory (Table 35). It is now the most common CA-MRSA clone in Victoria, Queensland and Western Australia.

Of the hospital-onset SABs, 11.4% were caused by CA-MRSA

Table 34: Community-associated MRSA clones, by place of onset and PVL carriage, 2016

Clone	Clonal complex	Total (%)*	Community onset†	Hospital onset†	PVL positive (%)
ST93-IV (Qld CA-MRSA)	Singleton	21.8 (102)	88.2 (90)	11.8 (12)	95.1 (97)
ST5-IV	5	10.7 (50)	80.0 (40)	20.0 (10)	26.0 (13)
ST1-IV (WA1 MRSA)	1	9.6 (45)	73.3 (33)	26.7 (12)	6.7 (3)
ST45-Vt	45	8.8 (41)	75.6 (31)	24.4 (10)	0.0 (0)
ST30-IV (SWP MRSA)	30	3.8 (18)	72.2 (13)	27.8 (5)	66.7 (12)
ST78-IV (WA2 MRSA)	78	3.4 (16)	81.3 (13)	18.8 (3)	0.0 (0)
ST97-IV		1.3 (6)	–§ (5)	–§ (1)	0.0 (0)
ST188-IV		0.9 (4)	–§ (2)	–§ (2)	0.0 (0)
ST72-IV		0.9 (4)	–§ (3)	–§ (1)	0.0 (0)
ST5-Vt		0.6 (3)	–§ (2)	–§ (1)	0.0 (0)
ST59-Vt		0.6 (3)	–§ (3)	0.0 (0)	–§ (2)
ST872-IV		0.6 (3)	–§ (3)	0.0 (0)	0.0 (0)
ST1-I		0.6 (3)	–§ (3)	0.0 (0)	0.0 (0)
ST8-IV		0.6 (3)	–§ (2)	–§ (1)	–§ (3)
ST59-IV		0.6 (3)	–§ (3)	0.0 (0)	0.0 (0)
ST953-IV		0.6 (3)	0.0 (0)	–§ (3)	0.0 (0)
Other clones (*n* = 25)		6.6 (31)	74.2 (23)	25.8 (8)	22.6 (7)
Total		72.2 (338)	79.6 (269)	20.4 (69)	40.5 (137)

MRSA = methicillin-resistant *Staphylococcus aureus*; PVL = Panton–Valentine leucocidin

* Percentage of all MRSA

† Percentage of the clone

§ Insufficient numbers (<10) to calculate percentage

Table 35: Major community-associated MRSA clones (>10 isolates), by state and territory, and PVL carriage, 2015

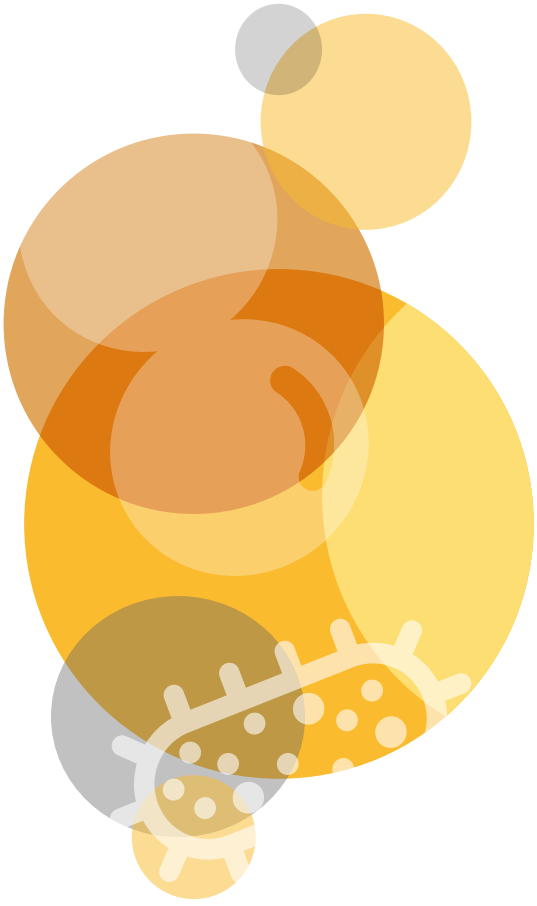
Clone	Percentage (*n*)								
	NSW	Vic	Qld	SA	WA	Tas	NT	ACT	Australia
ST93-IV (Qld CA-MRSA)	17.8 (16)	24.4 (10)	32.8 (19)	23.5 (8)	32.8 (22)	33.3 (1)	66.7 (26)	0.0 (0)	30.2 (102)
Number PVL positive	16	10	19	7	20	1	24	0	97
Number PVL negative	0	0	0	1	2	0	2	0	5
ST5-IV	12.2 (11)	14.6 (6)	24.1 (14)	11.8 (4)	10.4 (7)	0.0 (0)	20.5 (8)	0.0 (0)	14.8 (50)
Number PVL positive	0	2	0	1	4	0	6	0	13
Number PVL negative	11	4	14	3	3	0	2	0	37
ST1-IV (WA1 MRSA)	12.2 (11)	7.3 (3)	8.6 (5)	35.3 (12)	11.9 (8)	66.7 (2)	7.7 (3)	16.7 (1)	13.3 (45)
Number PVL positive	1	0	1	0	0	0	1	0	3
Number PVL negative	10	3	4	12	8	2	2	1	42
ST45-Vt (WA84 MRSA)	32.2 (29)	17.1 (7)	0.0 (0)	11.8 (4)	0.0 (0)	0.0 (0)	0.0 (0)	16.7 (1)	12.1 (41)
Number PVL positive	0	0	0	0	0	0	0	0	0
Number PVL negative	29	7	0	4	0	0	0	4	41
ST30-IV (SWP MRSA)	10.0 (9)	12.2 (5)	6.9 (4)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	5.3 (18)
Number PVL positive	6	3	3	0	0	0	0	0	12
Number PVL negative	3	2	1	0	0	0	0	0	6
ST78-IV (WA2 MRSA)	0.0 (0)	0.0 (0)	0.0 (0)	5.9 (2)	19.4 (13)	0.0 (0)	0.0 (0)	16.7 (1)	4.7 (16)
Number PVL positive	0	0	0	0	0	0	0	0	0
Number PVL negative	0	0	0	2	13	0	0	1	16
Other clones (n=35)	15.6 (14)	24.4 (10)	27.6 (16)	11.8 (4)	25.4 (17)	0.0 (0)	5.1 (2)	50.0 (3)	19.5 (66)
Number PVL positive	2	6	1	1	0	0	1	1	12
Number PVL negative	12	4	15	3	17	0	1	2	54
Total	90	41	58	34	67	3	39	6	338
PVL positive	25	21	24	9	24	1	32	1	137
PVL negative	65	20	34	25	43	2	7	5	201

CA-MRSA = community-associated methicillin-resistant *Staphylococcus aureus*; MRSA = methicillin-resistant *Staphylococcus aureus*; PVL = Panton–Valentine leucocidin

4 Limitations of the study

Although this study is comprehensive in its coverage of Australia, and the methods follow international standards, the data and their interpretation have a number of limitations:

- The data are not denominator controlled, and there is currently no consensus on an appropriate denominator for such surveys; institution size, patient throughput, patient complexity and local antibiotic use patterns all influence the types of resistance that are likely to be observed
- Although data have been collected from 32 large institutions across Australia, it is not yet clear how representative the sample is of Australia as a whole, because the proportion of the population that is served by these laboratories is not known; further, it is likely that the proportion of the population served differs across the state and territory groupings used in this report
- Because of the formulation of amoxicillin–clavulanate in both the Vitek and Phoenix cards used, interpretation using EUCAST guidelines for this agent was not possible
- Concentration ranges of some antimicrobial agents in both the Vitek and Phoenix cards limit the ability to accurately identify 'susceptible' for some combinations of antimicrobial agents and species.



5 Discussion, conclusions and areas of action

5.1 Discussion and conclusions

AGAR is a key component of the Antimicrobial Use and Resistance in Australia (AURA) program. As a targeted surveillance program, which focuses on selected bacterial pathogens and collects demographic, treatment and outcome data in addition to data on antimicrobial resistance rates, AGAR allows healthcare professionals to make informed clinical decisions and improve patient care. AGAR surveys have been conducted regularly since 1985. Since 2013, they have focused on bacteraemia and provide a comprehensive review of resistance rates in isolates causing bacteraemia in Australia. After four years, early longitudinal data have now been collected and standardised. These data will become increasingly valuable over time. The focus on bacteraemia allows a focus on true, invasive infections; it also allows comparison of rates in a meaningful way over time for institutions, states and territories. By focusing on bacteraemia, Australian data have become aligned with those of the European Antimicrobial Resistance Surveillance Network (EARS-Net*), which enables benchmarking and better predictions of future trends.

AGAR participants are clinical microbiology laboratories from all states and territories. In 2016, AGAR collected data on 7,565 episodes of gram-negative bacteraemia from 32 institutions Australia-wide. When the place of onset was known, three-quarters of episodes had their onset in the community. The most frequent clinical manifestations were urinary tract infection (41.9% of episodes), biliary tract infection (14.8%) and intra-abdominal infections (10.7%).

In Australia, fluoroquinolones are relied on as 'rear-guard' oral antibiotics, particularly for step-down treatment of invasive gram-negative infections, or when resistance exists to other oral gram-negative agents. Rates of non-susceptibility to amoxicillin–clavulanate in *E. coli* (20.9%) are no longer substantially different from rates of non-susceptibility to ciprofloxacin (16.3%), whereas, for *K. pneumoniae*, rates of non-susceptibility to amoxicillin–clavulanate and ciprofloxacin were similar in 2016, at 9.5% and 9.0%, respectively. Consequently, emerging fluoroquinolone resistance is of concern. Although there is a community perception that fluoroquinolone resistance in Australia is uncommon, this is not supported by the 2016 AGAR data. A decade ago, ciprofloxacin rates were consistently below 1%.[23] This was attributed to regulatory controls in human and veterinary prescribing, and national therapeutic guidelines, which sought to restrict unnecessary fluoroquinolone use. However, in 2016, ciprofloxacin resistance in *E. coli* bacteraemia was 14.0%. In community-onset *E. coli* bacteraemia, 13.1% of isolates were ciprofloxacin resistant. The percentage of fluoroquinolone-resistant *E. coli* in Australia is comparable to that in northern European countries. The steady rise in resistance to fluoroquinolones is more striking in hospital-onset bacteraemia, with a change from 13.7% to 20.2% between 2013 and 2016.

Because fluoroquinolone resistance is often linked to cephalosporin resistance caused by ESBLs of the CTX-M type, it is possible that the high use of oral cephalosporins in the community is driving this resistance.

* https://ecdc.europa.eu/en/about-us/partnerships-and-networks/disease-and-laboratory-networks/ears-net_)

Fluoroquinolone resistance in *E. coli* can also be linked to the emergence of O25b-ST131. O25b-ST131 is an international clone associated with third-generation cephalosporin and fluoroquinolone resistance, as well as increased virulence. In the 2016 survey, O25b-ST131 accounted for 62% of *E. coli* ESBL phenotypes that were ciprofloxacin resistant. This reflects the dynamics of clonal spread of resistance, leading to rapid international, and now Australian, emergence of clones such as O25b-ST131. It shows how quickly resistance 'successes' can be undermined, and also demonstrates the value of regular surveillance in identifying rapid changes in resistance.

E. coli is the most common organism causing bacteraemia in Australia. AGAR data show a longitudinal trend of increasing *E. coli* non-susceptibility to key anti–gram negative antimicrobial agents, such as ceftriaxone and ciprofloxacin (Figure 6). In 2016, ESBL phenotypes were found in 12.7% of *E. coli* and 9.1% of *K. pneumoniae*.

When ESBLs first arose, they were more common in hospital-onset infections in *K. pneumoniae* (TEM, SHV); as a result, there is a perception that ESBLs are primarily a hospital problem. However, this is no longer the case, with 83% of *E. coli* bacteraemias being community onset. This indicates that a substantial reservoir of resistance exists in the community, particularly in the elderly population and in long-term residential care settings. If the rate continues to rise, it will potentially affect the application of therapeutic guidelines such as guidelines for empirical treatment of severe infections. Current Australian guidelines recommend third-generation cephalosporins for empirical treatment, partly to avoid prescribing of broader-spectrum antibiotics. The AGAR data suggest that a greater focus on patient risk assessment may be required in empirical treatment decisions. Of interest, whereas rates of *E. coli* resistance to ceftriaxone continue to rise in the community (from 7.0% in 2013 to 11.4% in 2016), hospital-onset ceftriaxone resistance has not risen (15.7% in 2013 and 13.3% in 2016), suggesting that ceftriaxone resistance transmission has become a community phenomenon.

To date, carbapenemase-producing Enterobacteriaceae (CPE) remain uncommon (<0.1% in *E. coli*; 0.3% in *K. pneumoniae*). The low rates of CPE bacteraemia are encouraging. Examining previous and current AGAR surveys, most CPEs are endemic in origin.24 Sixteen of the 28 CPEs were due to the IMP-4 gene, which has previously been reported predominantly in eastern Australia. However, one $bla_{\text{IMP-4}}$ isolate was isolated in Western Australia. The 12 non-IMP-4 isolates are thought to be introductions of individual CPEs into hospitals by patients who acquired the isolates overseas; these isolates have the potential for secondary local transmission, as occurred recently in Victoria with KPC-producing *K. pneumoniae*.[25] The importance of infection control in limiting the transmission of CPE cannot be overestimated.[26]

The increasing prevalence of ESBLs and CPE worldwide emphasises the need for national collaboration to avoid establishment of CPE such as KPC and NDM in Australia. Practical consensus guidelines for CPE management in Australia were published in mid-2017 by the Australian Commission on Safety and Quality in Health Care (the Commission).[26] It is essential that healthcare facilities rigorously implement the guidelines, and the Commission will continue to actively promote their use.

Although colistin susceptibility testing cannot be performed on the current Vitek susceptibility cards, it is of concern that, of all the referred gram-negative isolates, two *E. coli* and one *E. cloacae* were found to harbour *mcr-1* genes. These isolates did not contain ESBLs or carbapenemases.

It should be noted that outbreaks of multidrug-resistant organisms occur in institutions, and substantial transmission occurs before invasive bloodstream infections develop. AGAR data may therefore underestimate local or regional spread of multidrug-resistant organisms and may be late in detecting sentinel resistances, such as certain CPEs. AGAR bacteraemia data need to be assessed with other sources of information to provide broader insights into antimicrobial resistance in Australia. In this context, AGAR is a key component of the AURA Surveillance System.

E. faecium bacteraemia has significant clinical consequences. Thirty-day all-cause mortality due to *E. faecium* in 2016 was high (27.1%); there were no significant differences in 30-day all-cause mortality between community- and hospital-onset cases, or between vancomycin-susceptible and -resistant isolates. The emergence of penicillin-resistant clonal complex 17 *E. faecium* bacteraemia is a worldwide phenomenon. In addition to penicillin resistance, the isolates are often multidrug resistant, with high-level gentamicin resistance and vancomycin resistance. The limited therapeutic options may be a factor in the differing 30-day all-cause mortality between *E. faecium* (27.1%) and *E. faecalis* (12.9%).

In the 2016 survey, 49.3% of *E. faecium* harboured *vanA* or *vanB* genes, or both. For almost two decades, and unlike in most other countries where vancomycin resistance is a problem, VRE in Australia has been dominated by the *vanB* genotype. However, in the 2016 survey, 22% of VRE bacteraemias were due to *vanA*. This type of vancomycin resistance has emerged rapidly in the past five years, particularly in New South Wales, where it is now the dominant genotype.

The percentage of *E. faecium* bacteraemia isolates that are resistant to vancomycin in Australia is significantly higher than that seen in almost all European countries. The European Union/European Economic Area (EU/EEA) population-weighted mean percentage is 8.3%; most other countries are below 29%, except for Ireland at 45.8%.[27]

Vancomycin, which until recently was the mainstay of therapy, can no longer be recommended; agents with less certain efficacy such as linezolid are the alternative.

The overall rates of MRSA increased from 18.6% in 2015 to 19.7% in the 2016 study. This compares with the EU/EEA population-weighted mean MRSA percentage of 16.8%, ranging from 0% in Iceland to 57.2% in Romania.[27]

The rate of community-onset SABs that are methicillin-resistant is increasing. Additionally, CA-MRSA clones are an increasing source of hospital-onset bacteraemia (particularly PVL-positive ST93 and ST5). Although HA-MRSA strains (for example, ST22) were more frequently found in community-onset bacteraemia, this may be due to previous hospital exposure or onset in a long-term care facility. The rapidly changing picture of MRSA in Australia, drawing from 15 years of AGAR surveillance, is further explored in *MRSA: A tale of three types*.[28] This technical paper will be updated as appropriate by AGAR and the Commission to provide further information on the issue.

From the findings noted above, it is clear that AGAR surveillance is a key component of Australia's response to the problem of increasing antimicrobial resistance. It defines where Australia stands with regard to antimicrobial resistance in human health. The way in which the data are communicated and used by healthcare networks across different speciality networks and in informing the national response to antimicrobial resistance is of continuing importance.

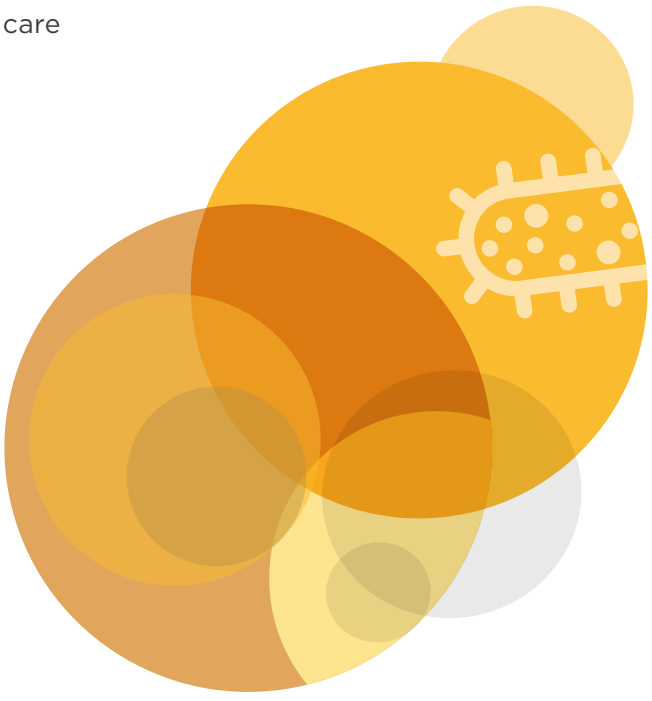
5.2 Areas for action

The Commission will continue to work with the Australian Society for Antimicrobials, a range of clinical experts, relevant colleges and professional organisations, state and territory health departments, private health service organisations, and the Australian Government Department of Health to ensure that the data and analyses are widely accessible, and are used to inform infection control and clinical practice.

The Commission will liaise with the Therapeutic Guidelines Antibiotic Expert Group to highlight findings and recommend consideration of them as part of review of guidance in relation to:

- Rising rate of ESBLs
- Implications of the rate of vancomycin resistance for therapy for *E. faecium* bacteraemia
- The link between fluoroquinolone resistance and high use of oral cephalosproins and penicillins in the community

The Commission will also work with the Australian Government Department of Health to ensure that antimicrobial stewardship and strict adherence to infection control guidelines are included in quality standards for aged care homes.



Abbreviations

Abbreviation	Term
AGAR	Australian Group on Antimicrobial Resistance
ANCU	*AURA National Coordinating Unit*
AURA	Antimicrobial Use and Resistance in Australia
CA-MRSA	community-acquired methicillin-resistant *Staphylococcus aureus*
CI	confidence interval
CLSI	Clinical and Laboratory Standards Institute
ESBL	extended-spectrum β-lactamase
EUCAST	European Committee on Antimicrobial Susceptibility Testing
HA-MRSA	healthcare-associated methicillin-resistant *Staphylococcus aureus*
MIC	minimum inhibitory concentration
MLST	multi-locus sequence type
MRSA	methicillin-resistant *Staphylococcus aureus*
MSSA	methicillin-sensitive *Staphylococcus aureus*
PVL	Panton–Valentine leucocidin
SAB	*Staphylococcus aureus* bacteraemia

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Participating members of AGAR:

Institution	AGAR members
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Alice Springs Hospital, NT	James McLeod
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Pathology Queensland, Central Laboratory, Qld	Graeme Nimmo and Narelle George
Pathology Queensland, Gold Coast Hospital, Qld	Petra Derrington and Cheryl Curtis
Pathology Queensland, Prince Charles Hospital, Qld	Robert Horvath and Laura Martin
Pathology Queensland, Princess Alexandra Hospital, Qld	Naomi Runnegar and Joel Douglas
PathWest Laboratory Medicine WA, Fiona Stanley Hospital	David McGechie and Denise Daley
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Reference laboratories:

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APPENDIX A

Study design

Thirty-two institutions participated in the 2016 survey. All states and territories were represented. The laboratories that participated in AGAR collected all isolates from different patient episodes of bacteraemia for either all isolates or up to 200 isolates for the Gram-negative Sepsis Outcome Program. In patients with more than one isolate, a new episode was defined as a new positive blood culture more than two weeks after the initial positive culture.

An episode was defined as community onset if the first positive blood culture was collected ≤48 hours after admission, and as hospital onset if collected >48 hours after admission.

All laboratories that participated in AGAR obtained basic laboratory information for each patient episode plus varying demographic information, depending on the level at which they are enrolled in the program. There are two levels of enrolment: Bronze and Silver (Tables A1–A3). At Bronze level, participating laboratories provided date of collection, date of birth, sex, postcode and admission date. At Silver level, participating laboratories provided discharge date, device-related infection, principal clinical manifestation, intensive care unit admission, outcome at 30 days and date of death.

Table A1: Level of participation of laboratories that contributed data on gram-negative* bacteraemia, by state and territory, 2016

State or territory	Number of institutions	Level of participation	
		Bronze	Silver
New South Wales	7	1	6
Victoria	5	0	5
Queensland	6	1	5
South Australia	3	2	1
Western Australia	6	3	3
Tasmania	2	0	2
Northern Territory	2	1	1
Australian Capital Territory	1	0	1
Total	32	8	24

* Enterobacteriaceae, *Acinetobacter* species and *Pseudomonas aeruginosa*

Table A2: Level of participation of laboratories that contributed data on *Staphylococcus aureus* bacteraemia, by state and territory, 2016

State or territory	Number of institutions	Level of participation	
		Bronze	Silver
New South Wales	7	1	6
Victoria	5	0	5
Queensland	6	1	5
South Australia	3	2	1
Western Australia	6	3	3
Tasmania	2	0	2
Northern Territory	2	1	1
Australian Capital Territory	1	0	1
Total	32	8	24

Table A3: Level of participation of laboratories that contributed data on enterococcal bacteraemia, by state and territory, 2016

State or territory	Number of institutions	Level of participation	
		Bronze	Silver
New South Wales	7	1	6
Victoria	5	0	5
Queensland	6	0	6
South Australia	3	0	3
Western Australia	6	3	3
Tasmania	2	0	2
Northern Territory	2	1	1
Australian Capital Territory	1	0	1
Total	32	5	27

APPENDIX B

Methods

Species identification

Isolates were identified using the routine methods for each institution. These included the Vitek® and Phoenix™ automated microbiology systems, and, if available, mass spectrometry (MALDI-TOF).

Susceptibility testing

Testing was performed using two commercial semi-automated methods: Vitek 2 (bioMérieux) (*n* = 28) and Phoenix (BD) (*n* = 2), which are calibrated to the ISO (International Organization for Standardization) reference standard method of broth microdilution. Commercially available Vitek 2 AST-N246 and AST-N247 cards or Phoenix NMIC-203 and NMIC-404 cards were used by all participants throughout the survey period.

The CLSI M100-A2720 and the EUCAST v7.0[21] breakpoints from January 2017 were used in the analysis. For analysis of cefazolin, breakpoints of ≤4 mg/L for susceptible and ≥8 mg/L for resistant were applied, because of the restricted MIC range available on the commercial cards (recognising that the January 2017 breakpoint is susceptible ≤2 mg/L).

Antimicrobials tested

Table B1 shows the antimicrobials tested.

Table B1: Antimicrobials available on susceptibility testing cards and interpretive guidelines for CLSI and EUCAST

Antimicrobial agent	Breakpoint (mg/L)						
	CLSI M100*				EUCAST v7.0†		
	S	SDD	I	R	S	I	R
Benzylpenicillin							
Enterococcus spp.	≤8		–§	≥16	–#	–#	–#
Staphylococcus aureus	≤0.12		–§	≥0.25	≤0.125	–#	≥0.25
Amikacin							
Acinetobacter spp.	≤16		32	≥64	≤8	16	≥32
Enterobacteriaceae	≤16		32	≥64	≤8	16	≥32
Pseudomonas spp.	≤16		32	≥64	≤8	16	≥32
Amoxicillin–clavulanate							
Enterobacteriaceae	≤8/4		16/8	≥32/16	≤8**	–§	≥16
Enterococcus spp.	–#		–#	–#	≤4	8	≥16
Ampicillin							
Enterobacteriaceae	≤8		16	≥32	≤8	–#	≥16
Enterococcus spp.	≤8		–§	≥16	≤4	8	≥16

continued

Table B1: (continued)

Antimicrobial agent	Breakpoint (mg/L)						
	CLSI M100*				EUCAST v7.0†		
	S	SDD	I	R	S	I	R
Aztreonam (Phoenix card)							
Enterobacteriaceae	≤4		8	≥16	≤1	2–4	≥8
Pseudomonas spp.	≤8		16	≥32	≤1	2–16	≥32
Cefazolin (Australian)‡	≤2		4	≥8	≤2	4	≥8
Cefepime							
Acinetobacter spp.	≤8		16	≥32	–#	–#	–#
Enterobacteriaceae	≤2	4–8	–#	≥16	≤1	2–4	≥8
Pseudomonas spp.	≤8		16	≥32	8	–§	≥16
Cefoxitin	≤8		16	≥32	–#	–#	–#
Cefalotin	≤8		16	≥32	–#	–#	–#
Cefalexin	–#		–#	–#	≤16	–§	≥32
Ceftazidime							
Acinetobacter spp.	≤8		16	≥32	–#	–#	–#
Enterobacteriaceae	≤4		8	≥16	≤1	2–4	≥8
Pseudomonas spp.	≤8		16	≥32	≤8	–§	≥16
Ceftriaxone							
Acinetobacter spp.	≤8		16–32	≥64	–#	–#	–#
Enterobacteriaceae	≤1		2	≥4	≤1	2	≥4
Chloramphenicol (Phoenix card)	≤8		16	≥32	≤8	–§	≥16
Ciprofloxacin							
Acinetobacter spp.	≤1		2	≥4	≤1	–§	≥2
Enterobacteriaceae	≤1		2	≥4	≤0.5	1	≥2
Salmonella spp.§§	≤0.06		0.12–0.5	≥1	≤0.06	–§	≥0.12
Enterococcus spp.##	≤1		2	≥4	≤4	–§	≥8
Staphylococcus aureus	≤1		2	≥4	≤1	–§	≥2
Pseudomonas spp.	≤1		2	≥4	≤0.5	1	≥2
Clindamycin							
Staphylococcus aureus	≤0.5		1–2	≥4	≤0.25	0.5	≥1
Colistin (Phoenix card)							
Acinetobacter spp.	≤2		4	≥8	≤2	–§	≥4
Enterobacteriaceae	–#		–#	–#	≤2	–§	≥4
Pseudomonas spp.	≤2		4	≥8	≤4	–§	≥8
Daptomycin							
Enterococcus spp.	≤4		–#	–#	–#	–#	–#
Staphylococcus aureus	≤1		–#	–#	≤1	–§	≥2
Doxycycline (Phoenix card)							
Enterococcus spp.	≤4		8	≥16	–#	–#	–#
Staphylococcus aureus	≤4		8	≥16	≤1	2	≥4
Ertapenem (Phoenix card)	≤0.5		1	≥2	≤0.5	1	≥2

continued

Table B1: (continued)

Antimicrobial agent	Breakpoint (mg/L)						
	CLSI M100*				EUCAST v7.0†		
	S	SDD	I	R	S	I	R
Erythromycin							
Enterococcus spp.	≤0.5		1–4	≥8	–#	–#	–#
Staphylococcus aureus	≤0.5		1–4	≥8	≤1	2	≥4
Fosfomycin (Phoenix card)	≤64		128	≥256	≤32	–§	≥64
Fusidic acid							
Staphylococcus aureus	–#		–#	–#	≤1	–§	≥2
Gentamicin							
Acinetobacter spp.	≤4		8	≥16	≤4	–§	≥8
Enterobacteriaceae	≤4		8	≥16	≤2	4	≥8
Pseudomonas spp.	≤4		8	≥16	≤4	–§	≥8
Staphylococcus aureus	≤4		8	≥16	≤1	–§	≥2
Imipenem (Phoenix card)							
Acinetobacter spp.	≤2		4	≥8	≤2	4–8	≥16
Enterobacteriaceae	≤1		2	≥4	≤2	4–8	≥16
Pseudomonas spp.	≤2		4	≥8	≤4	8	≥16
Linezolid							
Enterococcus spp.	≤2		4	≥8	≤4	–§	≥8
Staphylococcus aureus	≤4		8	≥16	≤4	–§	≥8
Meropenem							
Acinetobacter spp.	≤2		4	≥8	≤2	4–8	≥16
Enterobacteriaceae	≤1		2	≥4	≤2	4–8	≥16
Pseudomonas spp.	≤2		4	≥8	≤2	4–8	≥16
Nitrofurantoin							
Enterobacteriaceae	≤32		64	≥128	≤64††	–§	≥128
Enterococcus spp.	≤32		64	≥128	≤64††	–§	≥128
Staphylococcus aureus	≤32		64	≥128	–#	–#	–#
Norfloxacin							
Enterobacteriaceae	≤4		8	≥16	≤0.5	1	≥2
Pseudomonas spp.	≤4		8	≥16	–#	–#	–#
Oxacillin							
Staphylococcus aureus	≤2		–§	≥4	–#	–#	–#
Piperacillin–tazobactam							
Acinetobacter spp.	≤16/4		32/4–64/4	≥128/4	–#	–#	–#
Enterobacteriaceae	≤16/4		32/4–64/4	≥128/4	≤8	16	≥32
Pseudomonas spp.	≤16/4		32/4–64/4	≥128/4	≤16	–§	≥32
Rifampicin							
Enterococcus spp.	≤1		2	≥4	–#	–#	–#
Staphylococcus aureus	≤1		2	≥4	≤0.06***	0.12–0.5	≥1

continued

Table B1: (continued)

Antimicrobial agent	Breakpoint (mg/L)						
	CLSI M100*				EUCAST v7.0†		
	S	SDD	I	R	S	I	R
Teicoplanin							
Enterococcus spp.	≤8		16	≥32	≤2	–§	≥4
Staphylococcus aureus	≤8		16	≥32	≤2	–§	≥4
Tetracycline							
Acinetobacter spp.	≤4		8	≥16	–#	–#	–#
Enterobacteriaceae	≤4		8	≥16	–#	–#	–#
Enterococcus spp.	≤4		8	≥16	–#	–#	–#
Staphylococcus aureus	≤4		8	≥16	≤1	2	≥4
Ticarcillin–clavulanate							
Acinetobacter spp.	≤16/2		32/2–64/2	≥128/2	–#	–#	–#
Enterobacteriaceae	≤16/2		32/2–64/2	≥128/2	≤8	16	≥32
Pseudomonas spp.	≤16/2		32/2–64/2	≥128/2	≤16	–§	≥32
Tigecycline (Phoenix card)	–#		–#	–#	≤1	2	≥4
Tobramycin							
Acinetobacter spp.	≤4		8	≥16	≤4	–§	≥8
Enterobacteriaceae	≤4		8	≥16	≤2	4	≥8
Pseudomonas spp.	≤4		8	≥16	≤4	–§	≥8
Trimethoprim							
Enterobacteriaceae	≤8		–§	≥16	≤2	4	≥8
Enterococcus spp.	–#		–#	–#	≤0.03	0.06–1	≥2
Staphylococcus aureus	≤8		–§	≥16	≤2	4	≥8
Trimethoprim–sulfamethoxazole							
Acinetobacter spp.	≤2/38	–		≥4/76	≤2/38	4/76	≥8/152
Enterobacteriaceae	≤2/38	–		≥4/76	≤2/38	4/76	≥8/152
Enterococcus spp.	–#		–#	–#	≤0.03§§§	0.06–1	≥2
Staphylococcus aureus	≤2		–§	≥4	≤2	4	≥8
Vancomycin							
Enterococcus spp.	≤4		8–16	≥32	≤4	–§	≥8
Staphylococcus aureus	≤2		4–8	≥16	≤2	–§	≥4

CLSI = Clinical and Laboratory Standards Institute; EUCAST = European Committee on Antimicrobial Susceptibility Testing; I = intermediate; R = resistant; S = sensitive; SDD = sensitive dose dependent

* The breakpoints selected to identify resistance are described in Performance Standards for Antimicrobial Susceptibility Testing: Twenty-seventh informational supplement, CLSI document M100-S27, January 2017.

† EUCAST breakpoint tables for interpretation of MICs and zone diameters, version 7.0, 2017 (www.eucast.org)

§ No category defined

No guidelines for indicated species

** For susceptibility testing purposes, EUCAST fixes the concentration of clavulanate at 2 mg/L, rather than the 2:1 ratio used in CLSI guidelines. All cards used in this study have a 2:1 ratio; therefore, no EUCAST categories can be determined.

‡ The concentration range available on the current Vitek card restricts the ability to identify the susceptible category. For analysis, breakpoints of ≤4 mg/L for susceptible and ≥8 mg/L for resistant were applied.

continued

Table B1: (continued)

§§ The ciprofloxacin concentration range available on the cards used restricts the ability to accurately identify susceptible (CLSI/EUCAST) and intermediate (CLSI) categories for *Salmonella* species.

The ciprofloxacin concentration range on the Phoenix card restricts the ability to categorise *Enterococcus* spp.

†† Breakpoints apply to *E. coli* only.

‡‡ Breakpoints apply to *E. faecalis* only.

*** The rifampicin concentration on the cards restricts category interpretation to non-resistant or resistant.

§§§ The trimethoprim–sulfamethoxazole concentration on the cards restricts category interpretation to non-resistant or resistant.

Molecular confirmation of resistance

E. coli, *Klebsiella* spp., *Proteus* spp. and *Salmonella* spp. with ceftazidime or ceftriaxone MIC >1 mg/L, or cefoxitin MIC >8 mg/L; any other Enterobacteriaceae with cefepime MIC >1 mg/L; all isolates with ciprofloxacin MIC >0.25 mg/L; all isolates with meropenem MIC >0.25 mg/L; and all isolates with amikacin MIC >32 mg/L were referred to a central laboratory (the Australian Centre for Antimicrobial Resistance Ecology) for molecular confirmation of resistance.

All referred isolates were screened for the presence of the bla_{TEM} and bla_{SHV} genes using a real-time polymerase chain reaction (PCR) platform (LC-480) and published primers.[29,30] A multiplex real-time TaqMan PCR was used to detect CTX-M-type genes.[31] Isolates were probed for plasmid-borne AmpC enzymes using the method described by Pérez-Pérez and Hanson[32], and subjected to molecular tests for MBL (bla_{VIM}, bla_{IMP}, and bla_{NDM}), bla_{KPC} and $bla_{OXA\text{-}48\text{-}like}$ genes using real-time PCR.[33,34] Known plasmid-mediated quinolone resistance mechanisms (*qnr*, efflux [*qepA*, *oqxAB*] and *aac* (*6')-Ib-cr*) were examined by PCR on all referred isolates with ciprofloxacin MIC >0.25 mg/L using published methods.[35,36] All referred *E. coli* were examined for membership of the O25b-ST131 clone.[37,38]

All isolates with carbapenemase activity were subjected to whole genome sequencing using the Illumina MiSeq platform. Data were analysed using the Nullarbor bioinformatic pipeline.[39] The pipeline was used to identify the multi-locus sequence type and the resistome.

Quality control

Quality control strains used were those recommended by CLSI and EUCAST standards.

Data validation

Various checks were made to ensure that the data were valid. These included:

- Null values in the mandatory fields
- Missing MIC data
- Age ≥100 or <0 years
- Date of collection > discharge date
- Discharge date < date of admission
- Date of admission < date of birth
- Date of admission < date of collection + two days.

APPENDIX C

Susceptibility to antimicrobial agents

Overall percentages of resistance or non-susceptibility for the most common gram-negative species are shown in Table C1. For some antimicrobials, the concentration range tested did not distinguish between intermediate susceptibility (I) and resistant (R), and the term non-susceptible (NS) was used to describe these isolates. Similarly, non-resistant (NR) refers to both susceptible and intermediate.

Table C1: Susceptibility (CLSI and EUCAST) to antimicrobial agents in indicator species of national priority, by state and territory, 2016

Antimicrobial agent and species	Category*	CLSI and EUCAST percentage susceptibility at indicated category								
		NSW	Vic	Qld	SA	WA	Tas	NT	ACT	Australia
Ampicillin										
Escherichia coli	n	993	709	805	430	677	168	153	154	4,089
	%I	1.6, nd	1.0, nd	2.6, nd	0.7, nd	1.3, nd	3.6, nd	2.0, nd	1.3, nd	1.6, nd
	%R	53.1, 54.7	59.5, 60.5	50.4, 53.0	47.9, 48.6	54.8, 56.1	45.2, 48.8	63.4, 65.4	55.8, 57.1	53.6, 55.2
Proteus mirabilis	n	61	25	52	23	33	11	12	8	225
	%I	1.6, nd	0.0, nd	1.9, nd	0.0, nd	0.0, nd	0.0, nd	0.0, nd	n/a	1.3, nd
	%R	14.8, 16.4	16.0, 16.0	7.7, 9.6	30.4, 30.4	30.3, 30.3	18.2, 18.2	16.7, 16.7	n/a	16.9, 18.2
Salmonella species (non-typhoidal)	n	16	18	29	12	12	2	24	1	114
	%I	0.0, nd	0.0, nd	0.0, nd	n/a	0.0, nd	n/a	0.0, nd	n/a	0.0, nd
	%R	0.0, 0.0	11.1, 11.1	0.0, 0.0	8.3, 8.3	16.7, 16.7	n/a	0.0, 0.0	n/a	4.4, 4.4
Salmonella species (typhoidal)	n	4	8	4	0	11	2	1	2	32
	%I	n/a	n/a	n/a	n/a	0.0, 0.0	n/a	n/a	n/a	0.0, nd
	%R	n/a	n/a	n/a	n/a	0.0, 0.0	n/a	n/a	n/a	6.3, 6.3
Amikacin										
Acinetobacter baumannii	n	6	8	21	1	2	1	7	1	47
	%R	n/a	n/a	0.0, 0.0	n/a	na	n/a	n/a	n/a	0.0, 0.0
Escherichia coli	n	993	709	811	431	677	168	153	154	4,096
	%R	0.1, 0.5	0.1, 0.1	0.0, 0.0	0.2, 0.5	0.3, 0.3	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.1, 0.2
Klebsiella pneumoniae	n	224	180	189	79	175	35	38	33	953
	%R	0.4, 0.4	0.6, 0.6	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.2, 0.2

continued

Table C1: Continued

Antimicrobial agent and species	Category*	CLSI and EUCAST percentage susceptibility at indicated category								
		NSW	Vic	Qld	SA	WA	Tas	NT	ACT	Australia
Amikacin (continued)										
Klebsiella oxytoca	n	64	52	37	24	37	14	2	13	243
	%R	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0
Enterobacter cloacae complex	n	110	83	87	24	54	13	11	14	396
	%R	0.0, 0.9	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.3
Enterobacter aerogenes	n	32	21	27	10	24	6	2	5	127
	%R	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	n/a	n/a	n/a	0.0, 0.0
Proteus mirabilis	n	61	24	52	23	33	11	12	8	224
	%R	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0
Salmonella species (non-typhoidal)	n	16	18	29	12	12	2	24	1	114
	%R	0.0, 0.0	0.0, 0.0	0.0, 0.0	n/a	0.0, 0.0	n/a	0.0, 0.0	n/a	0.0, 0.0
Salmonella species (typhoidal)	n	4	8	4	0	11	2	1	2	32
	%R	n/a	n/a	n/a	n/a	0.0, 0.0	n/a	n/a	n/a	0.0, 0.0
Pseudomonas aeruginosa	n	182	99	192	79	92	16	23	31	714
	%R	1.1, 1.6	1.0, 1.0	0.0, 1.6	1.3, 1.3	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.6, 1.1
Amoxicillin–clavulanate										
Escherichia coli	n	993	680	805	430	677	168	153	154	4,060
	%I	12.6, –†	11.9, –†	11.4, –†	13.5, –†	13.9, –†	13.7, –†	15.0, –†	9.7, –†	12.6, –†
	%R	6.2, –†	10.7, –†	8.6, –†	7.7, –†	9.5, –†	5.4, –†	8.5, –†	9.1, –†	8.3, –†
Klebsiella pneumoniae	n	224	174	189	79	175	35	38	33	947
	%I	2.2, –†	9.8, –†	2.1, –†	3.8, –†	6.3, –†	2.9, –†	5.3, –†	3.0, –†	4.6, –†
	%R	6.7, –†	8.0, –†	3.7, –†	2.5, –†	3.4, –†	5.7, –†	0.0, –†	0.0, –†	4.9, –†
Klebsiella oxytoca	n	64	51	37	24	37	14	2	13	242
	%I	9.4, –†	2.0, –†	5.4, –†	8.3, –†	0.0, –†	0.0, –†	n/a	7.7, –†	5.0, –†
	%R	12.5, –†	5.9, –†	21.6, –†	8.3, –†	5.4, –†	7.1, –†	n/a	0.0, –†	9.9, –†
Proteus mirabilis	n	61	19	52	23	33	11	12	8	219
	%I	3.3, –†	10.5, –†	3.8, –†	4.3, –†	15.2, –†	18.2, –†	0.0, –†	n/a	6.4, –†
	%R	4.9, –†	5.3, –†	1.9, –†	0.0, –†	3.0, –†	0.0, –†	0.0, –†	n/a	2.7, –†
Salmonella species (non-typhoidal)	n	16	16	29	12	12	2	24	1	112
	%I	0.0, –†	0.0, –†	0.0, –†	8.3, –†	8.3, –†	n/a	0.0, –†	n/a	1.8, –†
	%R	0.0, –†	0.0, –†	0.0, –†	0.0, –†	0.0, –†	n/a	0.0, –†	n/a	0.0, –†
Salmonella species (typhoidal)	n	4	8	4	0	11	2	1	2	32
	%I	n/a	n/a	n/a	n/a	0.0, –†	n/a	n/a	n/a	0.0, –†
	%R	n/a	n/a	n/a	n/a	0.0, –†	n/a	n/a	n/a	0.0, –†

continued

Table C1: Continued

Antimicrobial agent and species	Category*	CLSI and EUCAST percentage susceptibility at indicated category								
		NSW	Vic	Qld	SA	WA	Tas	NT	ACT	Australia
Cefazolin										
Escherichia coli	n	993	709	807	431	653	91	153	154	3,991
	%R	25.2, 25.2	25.1, 25.1	22.4, 22.4	23.2, 23.2	26.8, 26.8	12.1, 12.1	25.5, 25.5	21.4, 21.4	24.2, 24.2
Klebsiella pneumoniae	n	224	180	189	79	170	17	38	33	930
	%R	13.4, 13.4	16.1, 16.1	7.4, 7.4	8.9, 8.9	10.6, 10.6	5.9, 5.9	10.5, 10.5	3.0, 3.0	11.2, 11.2
Klebsiella oxytoca	n	64	52	37	24	37	8	2	13	237
	%R	64.1, 64.1	65.4, 65.4	73.0, 73.0	75.0, 75.0	70.3, 70.3	n/a	n/a	46.2, 46.2	66.7, 66.7
Enterobacter cloacae complex	n	110	83	86	24	51	5	11	14	384
	%R	95.5, 95.5	96.4, 96.4	98.8, 98.8	95.8, 95.8	96.1, 96.1	n/a	100, 100	100, 100	96.6, 96.6
Enterobacter aerogenes	n	32	21	27	10	24	2	2	5	123
	%R	78.1, 78.1	90.5, 90.5	96.3, 96.3	100, 100	75.0, 75.0	n/a	n/a	n/a	85.4, 85.4
Proteus mirabilis	n	61	25	52	23	31	7	12	8	219
	%R	18.0, 18.0	8.0, 8.0	15.4, 15.4	21.7, 21.7	25.8, 25.8	n/a	8.3, 8.3	n/a	17.4, 17.4
Cefoxitin										
Escherichia coli	n	993	709	806	431	677	168	153	154	4,091
	%R	3.8, nd	4.1, nd	4.5, nd	3.0, nd	3.1, nd	2.4, nd	4.6, nd	3.2, nd	3.7, nd
Klebsiella pneumoniae	n	224	180	189	79	175	35	38	33	93
	%R	4.9, nd	7.2, nd	3.7, nd	3.8, nd	2.9, nd	0.0, nd	2.6, nd	6.1, nd	4.4, nd
Klebsiella oxytoca	n	64	52	37	24	37	14	2	13	243
	%R	0.0, nd	0.0, nd	2.7, nd	0.0, nd	0.0, nd	0.0, nd	n/a	0.0, nd	0.4, nd
Proteus mirabilis	n	61	25	52	23	33	11	12	8	225
	%R	0.0, nd	0.0, nd	0.0, nd	0.0, nd	0.0, nd	0.0, nd	0.0, nd	n/a	0.4, nd
Salmonella species (non-typhoidal)	n	16	18	29	12	12	2	24	1	114
	%R	0.0, nd	0.0, nd	0.0, nd	0.0, nd	0.0, nd	n/a	0.0, nd	n/a	0.0, nd
Salmonella species (typhoidal)	n	4	8	4	0	11	2	1	2	32
	%R	n/a	n/a	n/a	n/a	0.0, nd	n/a	n/a	n/a	0.0, nd
Cefepime										
Acinetobacter baumannii	n	6	8	21	1	2	0	7	1	46
	%R	n/a	n/a	33.3, nd	n/a	n/a	n/a	n/a	n/a	17.4, nd
Escherichia coli	n	993	709	810	430	677	168	153	154	4,094
	%NS§	9.4, 13.1	4.7, 9.9	3.1, 6.3	8.1, 9.5	4.0, 8.3	2.4, 4.2	2.6, 5.9	3.2, 6.5	5.5, 9.1

continued

Table C1: Continued

Antimicrobial agent and species	Category*	CLSI and EUCAST percentage susceptibility at indicated category								
		NSW	Vic	Qld	SA	WA	Tas	NT	ACT	Australia
Cefepime (continued)										
Klebsiella pneumoniae	n	224	180	189	79	175	35	38	33	953
	%NS	5.8, 8.9	3.3, 10.0	1.6, 2.6	2.5, 2.5	2.9, 5.1	2.9, 5.7	2.6, 2.6	0.0, 3.0	3.3, 6.1
Klebsiella oxytoca	n	64	52	37	24	37	14	2	13	243
	%NS	3.1, 3.1	0.0, 0.0	2.7, 2.7	0.0, 0.0	0.0, 0.0	0.0, 0.0	n/a	0.0, 0.0	1.2, 1.2
Enterobacter cloacae complex	n	108	83	87	24	54	13	11	14	388
	%NS	5.6, 11.1	7.2, 16.9	8.0, 18.4	0.0, 4.2	5.6, 9.3	7.7, 7.7	0.0, 0.0	7.1, 14.3	6.1, 12.9
Enterobacter aerogenes	n	32	21	27	10	24	6	2	5	127
	%NS	6.3, 6.3	0.0, 0.0	3.7, 3.7	0.0, 0.0	0.0, 0.0	n/a	n/a	n/a	2.4, 2.4
Proteus mirabilis	n	61	25	52	23	33	11	12	8	225
	%NS	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	3.0, 3.0	n/a	n/a	n/a	0.4, 0.4
Pseudomonas aeruginosa	n	182	99	192	79	92	16	23	31	714
	%R	3.8, 5.5	3.0, 6.1	1.6, 5.7	3.8, 7.6	3.3, 6.5	6.3, 18.8	0.0, 4.3	3.2, 3.2	2.9, 6.2
Salmonella species (non-typhoidal)	n	16	18	29	12	12	2	24	1	114
	%NS	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	n/a	0.0, 0.0	n/a	0.0, 0.0
Salmonella species (typhoidal)	n	4	8	4	0	11	2	1	2	32
	%NS	n/a	n/a	n/a	n/a	0.0, 0.0	n/a	n/a	n/a	0.0, 0.0
Ceftazidime										
Acinetobacter baumannii	n	6	8	21	1	2	0	7	1	46
	%NS	n/a	n/a	42.9, nd	n/a	n/a	n/a	n/a	n/a	32.6, nd
Escherichia coli	n	992	709	811	431	677	168	153	154	4,095
	%NS	9.7, 13.9	8.0, 12.8	4.6, 7.8	7.2, 13.0	5.2, 9.6	1.8, 5.4	2.0, 2.6	7.1, 9.7	6.7, 10.8
Klebsiella pneumoniae	n	224	180	189	79	175	35	38	33	953
	%NS	6.7, 10.7	11.1, 14.4	2.6, 3.7	3.8, 3.8	2.9, 6.3	2.9, 5.7	2.6, 2.6	3.0, 6.1	5.4, 8.0
Klebsiella oxytoca	n	64	52	37	24	37	14	2	13	243
	%NS	3.1, 3.1	1.9, 1.9	2.7, 5.4	0.0, 0.0	0.0, 0.0	0.0, 0.0	n/a	0.0, 0.0	1.6, 2.1
Enterobacter cloacae complex	n	110	83	87	24	54	13	11	14	396
	%NS	24.5, 25.5	25.3, 26.5	28.7, 34.5	12.5, 20.8	18.5, 18.5	23.1, 23.1	18.2, 18.2	35.7, 35.7	24.2, 26.5
Enterobacter aerogenes	n	32	21	27	10	24	6	2	5	127
	%NS	31.3, 40.6	28.6, 28.6	14.8, 14.8	60.0, 60.0	20.8, 20.8	n/a	n/a	n/a	29.1, 31.5

continued

Table C1: Continued

Antimicrobial agent and species	Category*	CLSI and EUCAST percentage susceptibility at indicated category								
		NSW	Vic	Qld	SA	WA	Tas	NT	ACT	Australia
Ceftazidime (continued)										
Proteus mirabilis	n	61	24	52	23	33	11	12	8	224
	%NS	0.0, 1.6	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	n/a	0.0, 0.4
Pseudomonas aeruginosa	n	182	99	192	78	92	16	23	31	713
	%NS/R	7.1, 7.1	10.1, 10.1	7.3, 7.3	7.7, 7.7	8.7, 8.7	6.2, 6.2	8.7, 8.7	6.5, 6.5	7.9, 7.9
Salmonella species (non-typhoidal)	n	16	18	29	12	12	2	24	1	114
	%NS	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	n/a	0.0, 0.0	n/a	0.0, 0.0
Salmonella species (typhoidal)	n	4	7	4	0	11	2	1	2	31
	%NS	n/a	n/a	n/a	n/a	0.0, 0.0	n/a	n/a	n/a	0.0, 0.0
Ceftriaxone										
Acinetobacter baumannii	n	6	8	21	0	2	0	7	1	45
	%NS	n/a	n/a	85.7, nd	n/a	n/a	n/a	n/a	n/a	84.4, nd
Escherichia coli	n	993	709	811	431	677	168	153	154	4,096
	%NS	15.3, 15.3	13.5, 13.5	8.3, 8.3	11.6, 11.6	11.7, 11.7	6.0, 6.0	9.2, 9.2	9.7, 9.7	11.8, 11.8
Klebsiella pneumoniae	n	224	180	189	79	175	35	38	33	953
	%NS	10.7, 10.7	12.8, 12.8	3.7, 3.7	6.3, 6.3	5.7, 5.7	5.7, 5.7	2.6, 2.6	3.0, 3.0	7.7, 7.7
Klebsiella oxytoca	n	64	52	37	24	37	14	2	13	243
	%NS	17.2, 17.2	7.7, 7.7	16.2, 16.2	12.5, 12.5	5.4, 5.4	7.1, 7.1	n/a	0.0, 0.0	11.1, 11.1
Enterobacter cloacae complex	n	110	83	87	24	54	13	11	14	396
	%NS	24.5, 24.5	28.9, 28.9	35.6, 35.6	16.7, 16.7	18.5, 18.5	23.1, 23.1	27.3, 27.3	35.7, 35.7	27.0, 27.0
Enterobacter aerogenes	n	32	21	27	10	24	6	2	5	127
	%NS	43.8, 43.8	28.6, 28.6	14.8, 14.8	60.0, 60.0	25.0, 25.0	n/a	n/a	n/a	33.1, 33.1
Proteus mirabilis	n	61	25	52	23	33	11	12	8	225
	%NS	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	3.0, 3.0	0.0, 0.0	0.0, 0.0	n/a	0.4, 0.4
Salmonella species (non-typhoidal)	n	16	18	29	12	12	2	24	1	114
	%NS	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	n/a	0.0, 0.0	n/a	0.0, 0.0
Salmonella species (typhoidal)	n	4	8	4	0	11	2	1	2	32
	%NS	n/a	n/a	n/a	n/a	0.0, 0.0	n/a	n/a	n/a	0.0, 0.0

continued

Table C1: Continued

Antimicrobial agent and species	Category*	CLSI and EUCAST percentage susceptibility at indicated category								
		NSW	Vic	Qld	SA	WA	Tas	NT	ACT	Australia
Ciprofloxacin										
Acinetobacter baumannii	n	6	8	21	1	2	1	7	1	47
	%NS/R	n/a	n/a	19.0, 19.0	n/a	n/a	n/a	n/a	n/a	12.8, 12.8
Escherichia coli	n	993	709	811	429	677	168	153	154	4,094
	%NS	16.6, 19.5	14.1, 18.1	8.6, 12.0	11.4, 15.9	13.7, 17.3	9.5, 11.9	8.5, 11.1	13.0, 16.9	12.8, 16.3
Klebsiella pneumoniae	n	224	180	189	79	175	35	38	33	953
	%NS	3.1, 9.4	8.3, 17.8	3.7, 5.3	2.5, 12.7	1.1, 4.0	2.9, 8.6	2.6, 2.6	3.0, 6.1	3.8, 10.0
Klebsiella oxytoca	n	64	52	37	24	37	14	2	13	243
	%NS	1.6, 1.6	0.0, 3.8	0.0, 2.7	0.0, 0.0	2.7, 2.7	0.0, 0.0	n/a	0.0, 0.0	0.8, 2.1
Enterobacter cloacae complex	n	110	83	87	24	54	13	11	14	396
	%NS	0.9, 7.3	2.4, 4.8	2.3, 4.6	4.2, 12.5	0.0, 0.0	0.0, 7.7	0.0, 0.0	7.1, 14.3	1.8, 5.6
Enterobacter aerogenes	n	32	21	27	10	24	6	2	5	127
	%NS	0.0, 3.1	0.0, 0.0	0.0, 3.7	0.0, 0.0	0.0, 0.0	n/a	n/a	n/a	0.0, 1.6
Proteus mirabilis	n	61	25	52	23	33	11	12	8	225
	%NS	1.6, 1.6	0.0, 4.0	0.0, 1.9	0.0, 0.0	3.0, 9.1	18.2, 18.2	0.0, 0.0	n/a	1.8, 3.6
Salmonella species (non-typhoidal)	n	16	16	29	12	12	2	24	1	112
	%R#	0.0, –#	12.5, –#	0.0, –#	0.0, –#	0.0, –#	n/a	0.0, –#	n/a	1.8, –#
Salmonella species (typhoidal)	n	4	7	4	0	11	2	1	2	31
	%NR#	n/a	n/a	n/a	n/a	63.6, 63.6	n/a	n/a	n/a	67.7, –#
Pseudomonas aeruginosa	n	183	99	192	79	92	16	23	31	715
	%NS	6.0, 9.3	6.1, 8.1	1.6, 7.3	11.4, 15.2	6.5, 8.7	6.2, 12.5	0.0, 0.0	9.7, 19.4	5.5, 9.4
Gentamicin										
Acinetobacter baumannii	n	6	8	21	1	2	1	7	1	47
	%R	n/a	n/a	19.0, 19.0	n/a	n/a	n/a	n/a	n/a	8.5, 8.5
Escherichia coli	n	993	709	811	430	677	168	153	154	4,095
	%R	6.8, 7.3	6.8, 6.8	7.0, 7.3	6.5, 6.7	10.5, 10.8	3.6, 3.6	10.5, 10.5	5.8, 5.8	7.4, 7.6
Klebsiella pneumoniae	n	224	180	189	79	175	35	38	33	953
	%R	5.8, 5.8	5.0, 5.0	3.7, 3.7	2.5, 2.5	4.6, 4.6	2.9, 2.9	0.0, 0.0	3.0, 3.0	4.3, 4.3
Klebsiella oxytoca	n	64	52	37	24	37	14	2	13	243
	%R	1.6, 1.6	0.0, 0.0	2.7, 2.7	0.0, 0.0	0.0, 0.0	0.0, 0.0	n/a	7.7, 7.7	1.2, 1.2

continued

Table C1: Continued

Antimicrobial agent and species	Category*	CLSI and EUCAST percentage susceptibility at indicated category								
		NSW	Vic	Qld	SA	WA	Tas	NT	ACT	Australia
Gentamicin (continued)										
Enterobacter cloacae complex	n	110	83	87	24	54	13	11	14	396
	%R	6.4, 6.4	4.8, 4.8	9.2, 9.2	0.0, 0.0	0.0, 0.0	15.4, 15.4	0.0,	7.1, 7.1	5.6, 5.6
Enterobacter aerogenes	n	32	21	27	10	24	6	2	5	127
	%R	3.1, 3.1	0.0, 0.0	3.7, 3.7	0.0, 0.0	0.0, 0.0	n/a	n/a	n/a	1.6, 1.6
Proteus mirabilis	n	61	25	52	23	33	11	12	8	225
	%R	1.6, 3.3	0.0, 0.0	0.0, 0.0	0.0, 8.7	0.0, 3.0	0.0, 0.0	0.0, 0.0	n/a	0.4, 2.2
Pseudomonas aeruginosa	n	183	99	191	79	92	16	23	31	714
	%R	5.5, 7.1	1.0, 2.0	0.0, 5.2	1.3, 3.8	0.0, 0.0	0.0, 6.3	0.0, 0.0	0.0, 3.2	1.7, 4.2
Meropenem										
Acinetobacter baumannii	n	6	8	21	1	2	1	7	1	47
	%NS	n/a	n/a	33.3, 33.3	n/a	n/a	n/a	n/a	n/a	17.0, 17.0
Escherichia coli	n	992	709	811	431	677	168	153	154	4,095
	%NS	0.2, 0.2	0.6, 0.2	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.1, 0.1
Klebsiella pneumoniae	n	224	180	189	79	175	35	38	33	953
	%NS	0.9, 0.9	1.1, 0.6	0.0, 0.0	0.0, 0.0	0.6, 0.6	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.5, 0.4
Klebsiella oxytoca	n	64	52	37	24	37	14	2	13	243
	%NS	0.0, 0.0	0.0, 0.0	2.7, 2.7	0.0, 0.0	0.0, 0.0	0.0, 0.0	n/a	0.0, 0.0	0.4, 0.4
Enterobacter cloacae complex	n	110	83	87	24	54	13	11	14	396
	%NS	1.8, 1.8	0.0, 0.0	4.6, 4.5	0.0, 0.0	0.0, 0.0	7.7, 7.7	0.0, 0.0	14.3, 14.3	2.5, 2.3
Enterobacter aerogenes	n	32	21	27	10	24	6	2	5	127
	%NS	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	n/a	n/a	n/a	0.0, 0.0
Proteus mirabilis	n	61	25	52	23	33	11	12	8	225
	%NS	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	n/a	0.0, 0.0
Salmonella species (non-typhoidal)	n	16	18	29	12	12	2	24	1	114
	%NS	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	n/a	0.0, 0.0	n/a	0.0, 0.0
Salmonella species (typhoidal)	n	4	8	4	0	11	2	1	2	32
	%NS	n/a	n/a	n/a	n/a	0.0, 0.0	n/a	n/a	n/a	0.0, 0.0
Pseudomonas aeruginosa	n	180	99	191	79	91	16	23	31	710
	%NS	10.0, 10.0	10.1, 10.1	4.7, 4.7	5.1, 5.1	8.8, 8.8	18.7, 18.7	8.7, 8.7	9.7, 9.7	8.0, 8.0

continued

Table C1: Continued

Antimicrobial agent and species	Category*	CLSI and EUCAST percentage susceptibility at indicated category								
		NSW	Vic	Qld	SA	WA	Tas	NT	ACT	Australia
Nitrofurantoin										
Escherichia coli	n	993	709	806	430	677	168	153	154	4,090
	%R	0.8, 0.8	1.1, 1.1	0.5, 0.5	1.6, 1.6	0.3, 0.3	0.6, 0.6	0.0, 0.0	2.6, 2.6	0.8, 0.8
Klebsiella pneumoniae	n	224	180	189	79	175	35	38	32	952
	%R	21.4, nd	24.4, nd	15.3, nd	46.8, nd	26.3, nd	14.3, nd	15.8, nd	18.8, nd	23.2, nd
Klebsiella oxytoca	n	64	52	37	24	37	14	2	13	243
	%R	1.6, nd	3.8, nd	8.1, nd	4.2, nd	0.0, nd	0.0, nd	n/a	0.0, nd	2.9, nd
Enterobacter cloacae complex	n	110	83	85	24	54	13	11	14	394
	%R	6.4, nd	12.0, nd	14.1, nd	20.8, nd	22.2, nd	0.0, nd	45.5, nd	14.3, nd	13.5, nd
Enterobacter aerogenes	n	32	21	27	10	24	6	2	5	127
	%R	25.0, nd	23.8, nd	22.2, nd	30.0, nd	41.7, nd	n/a	n/a	n/a	29.1, nd
Proteus mirabilis	n	60	25	52	23	33	11	12	7	223
	%R	88.3, nd	100, nd	90.4, nd	91.3, nd	97.0, nd	90.9, nd	100, nd	n/a	92.4, nd
Salmonella species (non-typhoidal)	n	16	18	29	12	12	2	24	1	114
	%R	0.0, nd	0.0, nd	0.0, nd	0.0, nd	25.0, nd	n/a	4.2, nd	n/a	3.5, nd
Salmonella species (typhoidal)	n	4	8	4	0	11	2	1	1	31
	%R	n/a	n/a	n/a	n/a	0.0, nd	n/a	n/a	n/a	3.2, nd
Piperacillin–tazobactam										
Acinetobacter baumannii	n	6	6	17	1	2	0	1	1	34
	%R	n/a	n/a	41.2, nd	n/a	n/a	n/a	n/a	n/a	20.6, nd
Escherichia coli	n	991	706	810	431	674	167	152	152	4,083
	%R	2.0, 5.0	4.4, 7.8	3.7, 6.8	1.6, 4.4	4.3, 9.2	2.4, 4.8	3.3, 7.2	0.7, 3.3	3.1, 6.5
Klebsiella pneumoniae	n	223	177	188	79	175	35	38	33	948
	%R	5.8, 8.1	4.5, 10.7	2.1, 5.3	2.5, 3.8	3.4, 6.9	0.0, 0.0	2.6, 10.5	0.0, 3.0	3.6, 7.1
Klebsiella oxytoca	n	64	52	36	24	36	14	2	13	241
	%R	18.8, 21.9	9.6, 9.6	25.0, 25.0	16.7, 16.7	5.6, 5.6	7.1, 7.1	n/a	7.7, 7.7	14.1, 14.9
Enterobacter cloacae complex	n	87	75	86	13	39	12	11	9	332
	%R	14.9, 17.2	22.7, 24.0	25.6, 29.1	15.4, 15.4	17.9, 20.5	16.7, 16.7	18.2, 18.2	n/a	19.9, 22.3
Enterobacter aerogenes	n	30	21	27	10	23	6	2	5	124
	%R	16.7, 30.0	23.8, 23.8	14.8, 14.8	50.0, 50.0	26.1, 30.4	n/a	n/a	n/a	25.0, 29.0

continued

Table C1: Continued

Antimicrobial agent and species	Category*	CLSI and EUCAST percentage susceptibility at indicated category								
		NSW	Vic	Qld	SA	WA	Tas	NT	ACT	Australia
Piperacillin–tazobactam (continued)										
Proteus mirabilis	n	61	25	52	23	33	11	12	8	225
	%R	0.0, 1.6	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 3.0	0.0, 0.0	0.0, 0.0	n/a	0.0, 0.9
Pseudomonas aeruginosa	n	181	99	190	78	92	16	23	31	710
	%R	4.4, 11.0	8.1, 14.1	3.7, 10.5	6.4, 12.8	6.5, 10.9	6.3, 25.0	8.7, 8.7	0.0, 12.9	5.2, 11.8
Salmonella species (non-typhoidal)	n	16	18	29	12	12	2	24	1	114
	%R	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	n/a	0.0, 0.0	n/a	0.0, 0.0
Salmonella species (typhoidal)	n	4	8	4	0	11	2	1	2	32
	%R	n/a	n/a	n/a	n/a	0.0, 0.0	n/a	n/a	n/a	0.0, 0.0
Ticarcillin–clavulanate										
Acinetobacter baumannii	n	6	8	21	1	2	0	7	1	46
	%R	n/a	n/a	33.3, nd	n/a	n/a	n/a	n/a	n/a	17.4, nd
Escherichia coli	n	799	709	811	357	677	168	153	153	3,827
	%R	10.5, 25.8	9.9, 20.2	9.2, 18.2	10.4, 24.4	13.3, 22.9	8.3, 18.5	10.5, 21.6	11.1, 18.3	10.5, 21.7
Klebsiella pneumoniae	n	192	180	189	67	175	35	38	33	909
	%R	9.4, 15.6	10.0, 17.2	3.7, 9.0	7.5, 7.5	6.3, 10.3	5.7, 8.6	2.6, 7.9	0.0, 6.1	6.8, 12.0
Klebsiella oxytoca	n	53	52	37	20	37	14	2	13	228
	%R	20.8, 22.6	7.7, 9.6	24.3, 24.3	20.0, 20.0	5.4, 5.4	7.1, 7.1	n/a	15.4, 15.4	14.5, 15.4
Enterobacter cloacae complex	n	95	83	87	23	54	13	11	14	380
	%R	21.1, 28.4	24.1, 27.7	28.7, 34.5	13.0, 26.1	18.5, 20.4	15.4, 30.8	27.3, 27.3	28.6, 35.7	22.9, 28.7
Enterobacter aerogenes	n	30	21	27	8	24	6	2	5	123
	%R	33.3, 36.7	23.8, 23.8	14.8, 14.8	n/a	25.0, 29.2	n/a	n/a	n/a	27.6, 30.1
Proteus mirabilis	n	51	25	52	21	33	11	12	8	213
	%R	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	n/a	0.0, 0.0
Pseudomonas aeruginosa	n	181	99	191	63	91	16	23	31	695
	%R	17.1, 61.9	19.2, 57.6	12.6, 58.1	7.9, 54.0	9.9, 51.6	25.0, 68.8	8.7, 56.5	16.1, 35.5	14.2, 57.0
Salmonella species (non-typhoidal)	n	13	18	29	11	12	2	24	1	110
	%R	0.0, 0.0	0.0, 0.0	0.0, 0.0	9.1, 9.1	8.3, 8.3	n/a	0.0, 0.0	n/a	1.8, 1.8
Salmonella species (typhoidal)	n	3	8	4	0	11	2	1	2	31
	%R	n/a	n/a	n/a	n/a	0.0, 0.0	n/a	n/a	n/a	0.0, 0.0

continued

Table C1: Continued

Antimicrobial agent and species	Category*	CLSI and EUCAST percentage susceptibility at indicated category								
		NSW	Vic	Qld	SA	WA	Tas	NT	ACT	Australia
Tobramycin										
Acinetobacter baumannii	n	6	8	21	1	2	1	7	1	47
	%R	n/a	n/a	19.0, 19.0	n/a	n/a	n/a	n/a	n/a	8.5, 8.5
Escherichia coli	n	992	709	811	431	677	168	153	154	4,095
	%R	2.9, 7.8	4.1, 7.9	2.3, 7.3	4.4, 9.5	5.9, 12.9	2.4, 5.4	3.9, 11.1	2.6, 7.1	3.7, 8.7
Klebsiella pneumoniae	n	224	180	189	79	175	35	38	33	953
	%R	3.6, 5.8	6.1, 10.0	3.2, 3.7	0.0, 3.8	4.0, 5.1	2.9, 2.9	2.6, 2.6	3.0, 3.0	3.7, 5.6
Klebsiella oxytoca	n	64	52	37	24	37	14	2	13	243
	%R	0.0, 3.1	0.0, 0.0	0.0, 2.7	0.0, 0.0	0.0, 0.0	0.0, 0.0	n/a	0.0, 7.7	0.0, 1.6
Enterobacter cloacae complex	n	110	83	87	24	54	13	11	14	396
	%R	4.5, 7.3	3.6, 6.0	6.9, 9.2	0.0, 0.0	0.0, 0.0	7.7, 15.4	0.0, 0.0	7.1, 14.3	4.0, 6.3
Enterobacter aerogenes	n	32	21	27	10	24	6	2	5	127
	%R	6.3, 6.3	0.0, 0.0	3.7, 3.7	0.0, 0.0	0.0, 0.0	n/a	n/a	n/a	2.4, 2.4
Proteus mirabilis	n	61	25	52	23	33	11	12	8	225
	%R	0.0, 1.6	0.0, 0.0	0.0, 1.9	4.3, 8.7	0.0, 3.0	0.0, 0.0	0.0, 0.0	n/a	0.4, 2.2
Pseudomonas aeruginosa	n	182	99	192	79	92	16	23	31	714
	%R	4.9, 4.9	1.0, 1.0	0.0, 0.0	1.3, 1.3	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	1.5, 1.5
Trimethoprim										
Escherichia coli	n	993	709	807	430	677	168	153	154	4,091
	%R	35.2, 35.5	32.9, 33.0	28.5, 28.5	27.9, 28.1	31.5, 31.9	24.4, 24.4	50.3, 50.3	31.2, 31.2	32.1, 32.3
Klebsiella pneumoniae	n	224	180	189	79	175	35	38	33	953
	%R	17.9, 18.3	25.6, 26.1	14.3, 14.3	15.2, 20.3	8.0, 8.6	11.4, 11.4	10.5, 10.5	12.1, 12.1	15.8, 16.6
Klebsiella oxytoca	n	64	52	37	24	37	14	2	13	243
	%R	4.7, 4.7	0.0, 0.0	5.4, 5.4	0.0, 0.0	0.0, 0.0	0.0, 0.0	n/a	15.4, 15.4	2.9, 2.9
Enterobacter cloacae complex	n	110	83	86	24	54	13	11	14	395
	%R	15.5, 15.5	6.0, 6.0	23.3, 23.3	33.3, 33.3	3.7, 3.7	38.5, 38.5	0.0, 0.0	21.4, 28.6	15.2, 15.4
Enterobacter aerogenes	n	32	21	27	10	24	6	2	5	127
	%R	6.3, 6.3	0.0, 0.0	0.0, 0.0	30.0, 30.0	0.0, 0.0	n/a	n/a	n/a	3.9, 3.9
Proteus mirabilis	n	61	25	52	23	33	11	12	8	225
	%R	18.0, 18.0	20.0, 20.0	13.5, 13.5	26.1, 26.1	33.3, 33.3	36.4, 36.4	16.7, 16.7	n/a	20.9, 20.9

continued

Table C1: Continued

Antimicrobial agent and species	Category*	CLSI and EUCAST percentage susceptibility at indicated category								
		NSW	Vic	Qld	SA	WA	Tas	NT	ACT	Australia
Trimethoprim										
Salmonella species (non-typhoidal)	n	16	18	29	12	12	2	24	1	114
	%R	0.0, 0.0	11.1, 11.1	0.0, 0.0	0.0, 0.0	0.0, 0.0	n/a	0.0, 0.0	n/a	2.6, 2.6
Salmonella species (typhoidal)	n	4	8	4	0	11	2	1	2	32
	%R	n/a	n/a	n/a	n/a	0.0, 0.0	n/a	n/a	n/a	3.1, 3.1
Trimethoprim–sulfamethoxazole										
Acinetobacter baumannii	n	6	8	21	1	2	1	7	1	47
	%R	n/a	n/a	33.3, 33.3	n/a	n/a	n/a	n/a	n/a	19.1, 19.1
Escherichia coli	n	992	709	811	430	677	168	153	154	4,094
	%R	34.4, 34.4	31.9, 31.7	27.0, 26.6	27.0, 27.0	30.3, 30.3	23.8, 23.8	45.8, 45.8	28.6, 28.6	30.8, 30.7
Klebsiella pneumoniae	n	224	180	189	79	175	35	38	33	953
	%R	15.2, 14.3	23.3, 22.8	13.8, 13.8	15.2, 15.2	7.4, 6.9	11.4, 11.4	10.5, 10.5	15.2, 15.2	14.7, 14.3
Klebsiella oxytoca	n	64	52	37	24	37	14	2	13	243
	%R	4.7, 4.7	0.0, 0.0	8.1, 5.4	0.0, 0.0	0.0, 0.0	0.0, 0.0	n/a	30.8, 30.8	4.1, 3.7
Enterobacter cloacae complex	n	110	83	87	24	54	13	11	14	396
	%R	16.4, 16.4	6.0, 6.0	24.1, 24.1	29.2, 25.0	3.7, 3.7	38.5, 38.5	0.0, 0.0	42.9, 42.9	16.2, 15.9
Enterobacter aerogenes	n	32	21	27	10	24	6	2	5	127
	%R	3.1, 3.1	0.0, 0.0	0.0, 0.0	30.0, 30.0	0.0, 0.0	n/a	n/a	n/a	3.1, 3.1
Proteus mirabilis	n	61	25	52	23	33	11	12	8	225
	%R	13.1, 13.1	8.0, 8.0	9.6, 9.6	17.4, 17.4	18.2, 18.2	27.3, 27.3	16.7, 16.7	n/a	13.8, 13.8
Salmonella species (non-typhoidal)	n	16	18	29	12	12	2	24	1	114
	%R	0.0, 0.0	16.7, 16.7	0.0, 0.0	0.0, 0.0	0.0, 0.0	n/a	0.0, 0.0	n/a	3.5, 3.5
Salmonella species (typhoidal)	n	4	8	4	0	11	2	1	2	32
	%R	n/a	n/a	n/a	0.0, 0.0	n/a	n/a	n/a	n/a	3.1, 3.1

CLSI = Clinical and Laboratory Standards Institute; EUCAST = European Committee on Antimicrobial Susceptibility Testing; I = intermediate; n/a = insufficient numbers (<10) to calculate; nd = no breakpoints defined; NR = susceptible plus intermediate (concentration range limitation); NS = sensitive dose dependent or intermediate plus resistant; R = resistant

* Category analysed for each organism. If different for CLSI and EUCAST, they are separated by a comma.

† For susceptibility testing purposes, EUCAST fixes the concentration of clavulanate at 2 mg/L, rather than the 2:1 ratio used in CLSI guidelines. All cards used in this study have a 2:1 ratio; therefore, no EUCAST categories can be determined.

§ NS category for cefepime includes CLSI sensitive dose dependent for Enterobacteriaceae.

The ciprofloxacin concentration range available on the cards used restricts the ability to accurately identify susceptible (CLSI/EUCAST) and intermediate (CLSI) categories for *Salmonella* species.

** The concentration range on the Phoenix card prohibits interpretation for *Enterococcus* species. Figures reflect the number of isolates that can be interpreted using CLSI and EUCAST, respectively.

APPENDIX D

Multiple acquired resistance by species and state or territory

The most problematic pathogens are those with multiple acquired resistances. Although there is no agreed benchmark for the definition of multidrug resistance, acquired resistance to more than three agents has been chosen to define multidrug resistance in this survey. For each species, antimicrobials were excluded from the count if they were affected by natural resistance mechanisms, and/or neither CLSI nor EUCAST breakpoints were available. For this analysis, resistance included intermediate susceptibility, if applicable.

Tables D1–D13 show multiple acquired resistances for a number of species. Only isolates for which the full range of antimicrobial agents was tested were included for determination of multidrug resistance. The agents included for each species are listed in the notes after each table. EUCAST breakpoints were used throughout the analysis. For cefazolin, the EUCAST-approved Australian National Advisory Committee guidelines were used. For amoxicillin–clavulanate, CLSI breakpoints were used, because both the Vitek and Phoenix cards used the CLSI formulation for this agent.

Acinetobacter baumannii complex is not included because there are few breakpoints to permit analysis.

Table D1: Multiple acquired resistance in *Citrobacter koseri*, by state and territory, 2016

State or territory	Total	Number of drug resistances (non- multidrug resistant)					Number of drug resistances (multidrug resistant)							
		0	1	2	3	%	4	5	6	7	8	9	10	%
NSW	12	11	0	0	0	–*	1	0	0	0	0	0	0	–*
Vic	8	6	1	0	0	–*	0	1	0	0	0	0	0	–*
Qld	11	9	1	0	0	–*	1	0	0	0	0	0	0	–*
SA	2	2	0	0	0	–*	0	0	0	0	0	0	0	–*
WA	12	11	1	0	0	–*	0	0	0	0	0	0	0	–*
Tas	0	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
NT	1	1	0	0	0	–*	0	0	0	0	0	0	0	–*
ACT	2	2	0	0	0	–*	0	0	0	0	0	0	0	–*
Total	48	42	3	0	0	93.8	2	1	0	0	0	0	0	6.2

n/a = not applicable (no isolates)

* Not applicable (insufficient numbers)

Note: Antimicrobials were amoxicillin–clavulanate (CLSI), piperacillin–tazobactam, ceftriaxone, ceftazidime, cefepime, gentamicin, amikacin, ciprofloxacin, trimethoprim and meropenem.

Table D2: Multiple acquired resistance in *Citrobacter freundii*, by state and territory, 2016

State or territory	Total	Number of drug resistances (non-multidrug resistant)					Number of drug resistances (multidrug resistant)						
		0	1	2	3	%	4	5	6	7	8	9	%
NSW	30	15	2	4	5	–*	2	1	1	0	0	0	–*
Vic	21	14	2	1	4	–*	0	0	0	0	0	0	–*
Qld	11	5	2	1	1	–*	0	0	0	1	1	0	–*
SA	5	2	0	1	2	–*	0	0	0	0	0	0	–*
WA	7	1	0	0	0	–*	0	0	0	0	0	0	–*
Tas	2	1	1	0	0	–*	0	0	0	0	0	0	–*
NT	0	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	–*
ACT	7	2	2	0	3	–*	0	0	0	0	0	0	–*
Total	83	46	9	7	15	92.8	2	1	1	1	1	0	7.2

n/a = not applicable (no isolates)

* Not applicable (insufficient numbers)

Notes: Antimicrobials were piperacillin–tazobactam, ceftriaxone, ceftazidime, cefepime, gentamicin, amikacin, ciprofloxacin, trimethoprim and meropenem. *Citrobacter freundii* complex includes *Citrobacter braakii* (*n* = 5), *Citrobacter werkmanii* (*n* = 2) and *Citrobacter sedlakii* (*n* = 1).

Table D3: Multiple acquired resistance in *Enterobacter aerogenes*, by state and territory, 2016

State or territory	Total	Number of drug resistances (non-multidrug resistant)					Number of drug resistances (multidrug resistant)						
		0	1	2	3	%	4	5	6	7	8	9	%
NSW	30	17	1	2	8	–*	1	0	1	0	0	0	–*
Vic	21	13	2	0	6	–*	0	0	0	0	0	0	–*
Qld	27	22	1	0	2	–*	1	0	1	0	0	0	–*
SA	10	4	0	1	1	–*	4	0	0	0	0	0	–*
WA	23	16	1	1	5	–*	0	0	0	0	0	0	–*
Tas	6	2	0	0	3	–*	1	0	0	0	0	0	–*
NT	2	0	0	0	2	–*	0	0	0	0	0	0	–*
ACT	5	4	1	0	0	–*	0	0	0	0	0	0	–*
Total	124	78	6	4	27	92.7	7	0	2	0	0	0	7.3

* Not applicable (insufficient numbers)

Note: Antimicrobials were piperacillin–tazobactam, ceftriaxone, ceftazidime, cefepime, gentamicin, amikacin, ciprofloxacin, trimethoprim and meropenem.

Table D4: Multiple acquired resistance in *Enterococcus faecium* (vancomycin resistant), by state and territory, 2016

State or territory	Total	Number of drug resistances (non-multidrug resistant)				
		0	1	2	3	%
NSW	58	0	0	44	14	100
Vic	67	0	0	67	0	100
Qld	11	0	0	11	0	–*
SA	20	0	0	4	16	–*
WA	8	0	0	8	0	–*
Tas	6	0	0	6	0	–*
NT	3	0	0	3	0	–*
ACT	12	0	0	12	0	–*
Total	185	0	0	155	30	100

* Not applicable (insufficient numbers)

Note: Antimicrobials were ampicillin, ciprofloxacin and linezolid.

Table D5: Multiple acquired resistance in *Enterococcus faecium* (vancomycin susceptible), by state and territory, 2016

State or territory	Number of drug resistances (non-multidrug resistant)			Number of drug resistances (multidrug resistant)		
	Total	0	1	2	3	%
NSW	61	9	4	39	9	100
Vic	41	11	4	26	6	100
Qld	28	4	0	24	6	–*
SA	23	1	0	6	16	–*
WA	46	4	1	41	0	100
Tas	6	1	0	5	0	–*
NT		0	0	1	0	–*
ACT	7	2	0	5	0	–*
Total	213	32	9	147	25	100

* Not applicable (insufficient numbers)

Note: Antimicrobials were ampicillin, ciprofloxacin and linezolid.

Table D6: Multiple acquired resistance in *Klebsiella oxytoca*, by state and territory, 2016

State or territory	Total	Number of drug resistances (non-multidrug resistant)					Number of drug resistances (multidrug resistant)								
		0	1	2	3	%	4	5	6	7	8	9	10	11	%
NSW	64	17	31	0	6	84.4	7	1	0	0	2	0	0	0	15.6
Vic	51	15	30	0	2	92.2	3	1	0	0	0	0	0	0	7.8
Qld	36	8	17	1	3	80.6	5	0	1	1	0	0	0	0	19.4
SA	24	3	17	0	1	–*	3	0	0	0	0	0	0	0	–*
WA	36	9	24	1	0	94.4	1	0	1	0	0	0	0	0	5.6
Tas	8	2	5	0	0	–*	3	0	0	0	0	0	0	0	–*
NT	2	2	0	0	0	–*	0	0	0	0	0	0	0	0	–*
ACT	13	5	6	0	2	–*	0	0	0	0	0	0	0	0	–*
Total	234	61	130	2	14	88.5	20	2	2	1	2	0	0	0	11.5

* Not applicable (insufficient numbers)

Note: Antimicrobials were amoxicillin–clavulanate (CLSI), piperacillin–tazobactam, cefazolin, ceftriaxone, ceftazidime, cefepime, gentamicin, amikacin, ciprofloxacin, trimethoprim and meropenem.

Table D7: Multiple acquired resistance in *Morganella morganii*, by state and territory, 2016

State or territory	Total	Number of drug resistances (non-multidrug resistant)					Number of drug resistances (multidrug resistant)						
		0	1	2	3	%	4	5	6	7	8	9	%
NSW	20	14	2	2	0	–*	0	0	1	0	0	1	–*
Vic	6	5	1	0	0	–*	0	0	0	0	0	0	–*
Qld	18	12	2	2	1	–*	0	1	0	0	0	0	–*
SA	7	4	3	0	0	–*	0	0	0	0	0	0	–*
WA	11	9	1	1	0	–*	0	0	0	0	0	0	–*
Tas	3	2	0	1	0	–*	0	0	0	0	0	0	–*
NT	1	1	0	0	0	–*	0	0	0	0	0	0	–*
ACT	2	1	0	0	0	–*	1	0	0	0	0	0	–*
Total	68	48	8	6	2	94.1	1	1	1	0	0	1	5.9

* Not applicable (insufficient numbers)

Note: Antimicrobials were piperacillin–tazobactam, ceftriaxone, ceftazidime, cefepime, gentamicin, amikacin, ciprofloxacin, trimethoprim and meropenem.

Table D8: Multiple acquired resistance in *Proteus mirabilis*, by state and territory, 2016

State or territory	Total	Number of drug resistances (non-multidrug resistant)					Number of drug resistances (multidrug resistant)									
		0	1	2	3	%	4	5	6	7	8	9	10	11	12	%
NSW	61	32	16	7	1	91.8	3	1	0	1	0	0	0	0	0	8.2
Vic	18	10	3	3	2	–*	0	0	0	0	0	0	0	0	0	–*
Qld	52	36	12	1	2	98.1	1	0	0	0	0	0	0	0	0	1.9
SA	23	6	9	3	2	–*	3	0	0	0	0	0	0	0	0	–*
WA	31	13	8	4	4	93.5	2	0	0	0	0	0	0	0	0	6.5
Tas	7	4	1	1	1	–*	0	0	0	0	0	0	0	0	0	–*
NT	12	10	0	1	1	–*	0	0	0	0	0	0	0	0	0	–*
ACT	8	6	1	1	0	–*	0	0	0	0	0	0	0	0	0	–*
Total	212	117	50	21	13	94.8	9	1	0	1	0	0	0	0	0	5.2

* Not applicable (insufficient numbers)

Note: Antimicrobials were ampicillin, amoxicillin–clavulanate (CLSI), piperacillin–tazobactam, cefazolin, ceftriaxone, ceftazidime, cefepime, gentamicin, amikacin, ciprofloxacin, trimethoprim and meropenem.

Table D9: Multiple acquired resistance in *Pseudomonas aeruginosa*, by state and territory, 2016

State or territory	Total	Number of drug resistances (non-multidrug resistant)					Number of drug resistances (multidrug resistant)		
		0	1	2	3	%	4	5	%
NSW	179	140	20	11	3	97.2	2	3	2.8
Vic	99	78	8	7	4	98.0	1	1	2.0
Qld	190	163	9	11	3	97.9	4	0	2.1
SA	77	57	13	6	0	98.7	0	1	1.3
WA	91	75	7	5	0	95.6	4	0	4.4
Tas	16	10	3	2	1	–*	0	0	–*
NT	23	20	1	1	1	–*	0	0	–*
ACT	31	20	8	2	1	100	0	0	0.0
Total	706	563	69	45	13	97.7	11	5	2.3

* Not applicable (insufficient numbers)

Note: Antimicrobials were ceftazidime, ciprofloxacin, piperacillin–tazobactam, tobramycin and meropenem.

Table D10: Multiple acquired resistance in *Salmonella* species (non-typhoidal), by state and territory, 2016

State or territory	Total	Number of drug resistances (non-multidrug resistant)					Number of drug resistances (multidrug resistant)						
		0	1	2	3	%	4	5	6	7	8	9	%
NSW	16	16	0	0	0	–*	0	0	0	0	0	0	–*
Vic	14	10	2	1	1	–*	0	0	0	0	0	0	–*
Qld	29	29	0	0	0	–*	0	0	0	0	0	0	–*
SA	12	10	1	0	1	–*	0	0	0	0	0	0	–*
WA	12	10	1	0	1	–*	0	0	0	0	0	0	–*
Tas	1	1	0	0	0	–*	0	0	0	0	0	0	–*
NT	24	24	0	0	0	–*	0	0	0	0	0	0	–*
ACT	1	0	1	0	0	–*	0	0	0	0	0	0	–*
Total	109	101	4	1	3	100	0	0	0	0	0	0	0.0

* Not applicable (insufficient numbers)

Notes: Antimicrobials were ampicillin, amoxicillin–clavulanate (CLSI), piperacillin–tazobactam, ceftriaxone, ceftazidime, cefepime, ciprofloxacin, trimethoprim and meropenem.

Table D11: Multiple acquired resistance in *Salmonella* species (typhoidal), by state and territory, 2016

State or territory	Total	Number of drug resistances (non-multidrug resistant)					Number of drug resistances (multidrug resistant)						
		0	1	2	3	%	4	5	6	7	8	9	%
NSW	4	1	3	0	0	–*	0	0	0	0	0	0	–*
Vic	6	2	3	0	1	–*	0	0	0	0	0	0	–*
Qld	4	0	3	0	0	–*	1	0	0	0	0	0	–*
SA	0	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
WA	11	4	7	0	0	–*	0	0	0	0	0	0	–*
Tas	2	2	0	0	0	–*	0	0	0	0	0	0	–*
NT	1	0	1	0	0	–*	0	0	0	0	0	0	–*
ACT	2	0	2	0	0	–*	0	0	0	0	0	0	–*
Total	30	9	19	0	1	96.7	1	0	0	0	0	0	3.3

n/a = not applicable (no isolates)

* Not applicable (insufficient numbers)

Note: Antimicrobials were ampicillin, amoxicillin–clavulanate (CLSI), piperacillin–tazobactam, ceftriaxone, ceftazidime, cefepime, ciprofloxacin, trimethoprim and meropenem.

Table D12: Multiple acquired resistance in *Serratia marcescens*, by state and territory, 2016

State or territory	Total	Number of drug resistances (non-multidrug resistant)					Number of drug resistances (multidrug resistant)						
		0	1	2	3	%	4	5	6	7	8	9	%
NSW	42	39	1	0	0	95.2	0	0	1	0	1	0	4.8
Vic	21	16	2	2	0	–*	0	1	0	0	0	0	–*
Qld	50	48	0	0	0	96.0	0	0	2	0	0	0	4.0
SA	11	9	1	1	0	–*	0	0	0	0	0	0	–*
WA	3	3	0	0	0	–*	0	0	0	0	0	0	–*
Tas	4	3	0	1	0	–*	0	0	0	0	0	0	–*
NT	1	1	0	0	0	–*	0	0	0	0	0	0	–*
ACT	6	5	0	0	0	–*	1	0	0	0	0	0	–*
Total	138	124	4	4	0	95.7	1	1	3	0	1	0	4.3

na = not applicable (no isolates)

* Piperacillin–tazobactam minimum inhibitory concentrations not provided

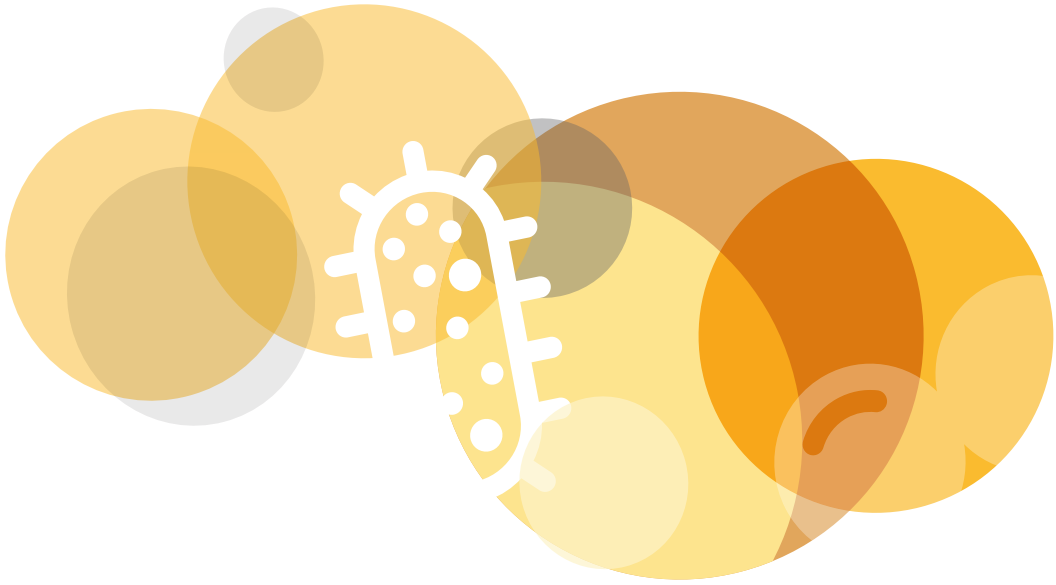
Note: Antimicrobials were piperacillin–tazobactam, ceftriaxone, ceftazidime, cefepime, gentamicin, amikacin, ciprofloxacin, trimethoprim, meropenem.

Table D13: Multiple acquired resistance in *Staphylococcus aureus*, by state and territory, 2016

State or territory	Total	Number of drug resistances (non-multidrug resistant)					Number of drug resistances (multidrug resistant)										
		0	1	2	3	%	4	5	6	7	8	9	10	11	12	13	14	%
NSW	586	79	310	77	40	86.3	32	12	20	11	5	0	0	0	0	0	0	13.7
Vic	416	73	227	67	27	94.7	16	3	0	3	0	0	0	0	0	0	0	5.3
Qld	490	81	271	85	43	98.0	4	4	0	2	0	0	0	0	0	0	0	2.0
SA	278	17	157	55	24	91.0	17	1	1	6	0	0	0	0	0	0	0	9.0
WA	412	66	214	79	39	96.6	10	3	0	1	0	0	0	0	0	0	0	3.4
Tas	51	10	23	6	4	84.3	6	2	0	0	0	0	0	0	0	0	0	15.7
NT	90	4	34	31	15	93.3	3	1	0	2	0	0	0	0	0	0	0	6.7
ACT	84	16	46	10	4	90.5	4	0	2	2	0	0	0	0	0	0	0	9.5
Total	2,407	346	1,282	410	196	92.8	92	26	23	27	5	0	0	0	0	0	0	7.2

* Not applicable (insufficient numbers)

Note: Antimicrobials were benzylpenicillin, ciprofloxacin, daptomycin, erythromycin, fusidic acid, gentamicin, linezolid, mupirocin (high level), nitrofurantoin (CLSI), oxacillin, rifampicin, trimethoprim–sulfamethoxazole, tetracyclines (tetracycline, Vitex; doxycycline, Phoenix) and vancomycin.



APPENDIX E

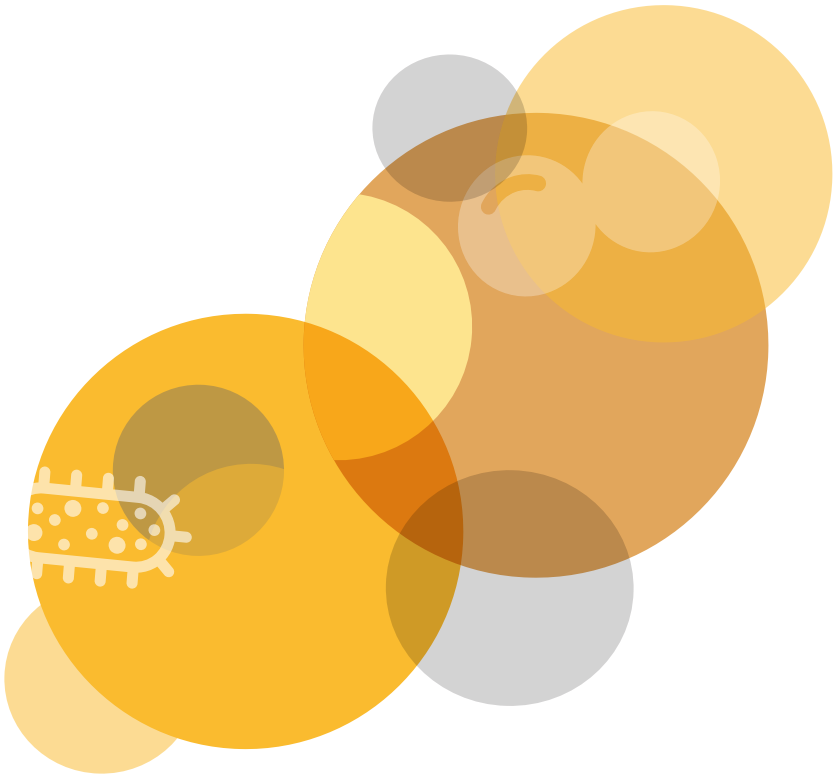
Summary reports

Susceptibility results

National reports provide summary susceptibility data (number, and percentage if more than 10 isolates) using both CLSI and EUCAST interpretive guidelines for all species isolated. They can be accessed through the AGAR website (www.agargroup.org.au/agar-surveys).

Antimicrobial resistance profiles by frequency

Only isolates for which the full range of antimicrobial agents was tested are included in the profiles. The regional antibiotic profiles for the top 12 species are available on the AGAR website (www.agargroup.org.au). Profiles are generated using EUCAST guidelines.



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