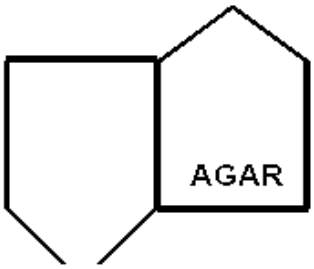

The Australian Group on Antimicrobial Resistance

Gram-negative Sepsis Outcome Programme (GNSOP)

2015 Antimicrobial Susceptibility Report

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1 BACKGROUND

OBJECTIVES OF THE PROGRAM

The Australian Group on Antimicrobial Resistance (AGAR) commenced surveillance of the key Gram-negative pathogens, *Escherichia coli* and *Klebsiella* species in 1992. Surveys have been conducted biennially until 2008 when annual surveys commenced alternating between community– and hospital-onset infections (http://www.agargroup.org/surveys). In 2004, another genus of Gram-negative pathogens in which resistance can be of clinical importance, *Enterobacter* species, was added. *E. coli* is the most common cause of community-onset urinary tract infection, while *Klebsiella* species are less common but are known to harbour important resistances. *Enterobacter* species are less common in the community, but of high importance due to intrinsic resistance to first-line antimicrobials in the community. Taken together, the three groups of species surveyed are considered to be valuable sentinels for multi-resistance and emerging resistance in enteric Gram-negative bacilli. In 2013 AGAR commenced the ongoing Enterobacteriaceae Sepsis Outcome Programme (EnSOP) which focuses 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, *Pseusomonas aeruginosa* and *Acinetobacter* species were added, and the program name changed to the Gram-negative Sepsis Outomce Programme (GNSOP).

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

The objectives of the 2015 surveillance program were to:

1. Monitor resistance in Enterobacteriaceae, *Pseudomonas aeruginosa* and *Acinetobacter* species isolated from blood cultures taken from patients presenting to the hospital or already in hospital
2. Examine the extent of co-resistance and multi-resistance in the major species, and
3. Detect emerging resistance to newer last-line agents such as carbapenems.

IMPORTANCE OF SPECIES SURVEYED

The family Enterobacteriaceae is a large collection of distantly related genuses and species sometimes referred to as the ‘enteric Gram-negative bacilli’. The family contains the most common and important Gram-negative pathogens, including the *Escherichia coli*, *Klebsiella pneumoniae* and *oxytoca, Enterobacter cloacae* and *aerogenes* and *Salmonella* species. All of these named species are causes community-onset and hospital-onset Gram-negative septicaemia, where they may cause life-threatening illness. The first three genuses are key reservoirs and therefore sentinel organisms for resistances and for multi-resistance, and for the mobile genetic elements that spread resistance genes amongst members of the Enterobacteriaceae family. Broad-spectrum and even ‘last-line antibiotics are now much more widely used for the treatment of Gram-negative septicaemia as a result on increasing resistance.

2 ISOLATES RECOVERED

All isolates were identified to species level wherever possible. For this report, *E. cloacae* complex includes *E. cloacae, E. asburiae, and E. kobei.*

A total of 7,330 isolates (60 species, 21 genera) were isolated from patients with bacteraemia. Enterobacteriaceae accounted for 89.6%, followed by *Pseudomonas aeruginosa* 9.0% and *Acinetobacter* species.Of the Enterobacteriaceae, three genera, *Escherichia* (61.0%), *Klebsiella* spp. (18.5%) and *Enterobacte*r spp. (7.4%) contributed 86.9% of all isolates. The top ten species according to rank were *E. coli* (54.7%), *K. pneumoniae* (13.3%), *P. aeruginosa* (9.0%), *E. cloacae* complex (4.4%), *K. oxytoca* (3.2%), *Proteus mirabilis* (3.0%), *Serratia marcescens* (2.6%), *E. aerogenes* (1.8%), *Salmonella* species (non-typhoidal (1.6%), and *Morganella morganii* (1.1%). These ten species comprised 94.7% of all isolates.

Table 1. Isolates recovered

Species	Total 7,330	(%)	ACT 280	NSW 1995	NT 265	QLD 1402	SA 777	TAS 142	VIC 1293	WA 1176
Escherichia coli	4,006	54.6	53.2	55.8	52.1	49.3	58.4	55.6	56.3	55.5
Klebsiella pneumoniae	977	13.3	12.5	11.9	17.7	13.5	11.2	12.7	13.7	15.9
Pseudomonas aeruginosa	658	9.0	12.9	8.4	7.2	11.8	10.9	2.8	5.7	9.1
Enterobacter cloacae complex	326	4.4	3.6	4.3	3.4	4.6	1.7	9.9	6.2	4.3
Klebsiella oxytoca	238	3.2	4.6	3.8	1.5	3.2	1.7	5.6	3.8	2.6
Proteus mirabilis	223	3.0	2.1	3.3	2.3	3.2	3.1	2.1	2.9	3.1
Serratia marcescens	189	2.6	2.9	3.4	1.1	3.7	1.2	2.1	2.2	1.6
Enterobacter aerogenes	131	1.8	1.4	1.7	1.1	1.9	1.4	0.7	2.1	2.1
Salmonella species (non-typhoidal)	115	1.6	0.4	1.0	9.1	2.0	1.3	1.4	1.6	0.9
Morganella morganii	79	1.1	1.4	1.3		1.8	0.9	0.7	0.7	0.6
Acinetobacter baumannii complex	59	0.8		0.5	1.9	1.4	0.1	1.4	0.8	0.9
Citrobacter koseri	55	0.8	0.4	1.1	0.4	0.4	1.3		0.4	0.9
Citrobacter freundii	45	0.6	1.4	1.0		0.4	0.5	0.7	0.7	0.2
Salmonella species (typhoidal)	26	0.4	0.4	0.3		0.4	0.6		0.5	0.2
Acinetobacter species	20	0.3		0.2	1.5	0.2	0.6		0.2	0.3
Pantoea agglomerans	14	0.2	0.4	0.1		0.3	0.1		0.3	0.3
Enterobacter species	12	0.2					1.5			
Raoultella ornithinolytica	12	0.2	0.7	0.3		0.1			0.1	0.2
Providencia rettgeri	11	0.2		0.2		0.2	0.3	0.7		0.2
Proteus vulgaris	11	0.2	0.4	0.2			0.4		0.1	0.3
Other species (total n=40)	123	1.7	1.4	1.7	0.8	1.6	2.7	3.5	1.8	1.1

3 ONSET OF BACTERAEMIA

Information on place of onset of bacteraemia was available for 6,719 (92%) episodes. An episode was designated healthcare-onset (HO) if the first positive blood culture was collected > 48 h after admission. Overall, 25.0% of episodes were HO, although differences were observed with different species. The proportion of HO episodes for the top 18 species is ahown in Table 2:

Table 2. Proportion of Healthcare-onset episodes (top 18 species)

Organism	Total	Community-onset (CO)	Healthcare -onset (HO)	%HO
Escherichia coli	3652	3051	601	16.5%
Klebsiella pneumoniae	908	643	265	29.2%
Pseudomonas aeruginosa	599	342	257	42.9%
Enterobacter cloacae complex	314	157	157	50.0%
Klebsiella oxytoca	221	154	67	30.3%
Proteus mirabilis	204	164	40	19.6%
Serratia marcescens	173	83	90	52.0%
Enterobacter aerogenes	117	64	53	45.3%
Salmonella species (non-typhoidal)	106	92	14	13.2%
Morganella morganii	78	51	27	34.6%
Acinetobacter baumannii complex	54	29	25	46.3%
Citrobacter koseri	51	35	16	31.4%
Citrobacter freundii	43	31	12	27.9%
Salmonella species (typhoidal)	22	22		0.0%
Acinetobacter species	18	13	5	27.8%
Pantoea agglomerans	14	10	4	28.6%
Raoultella ornithinolytica	11	7	4	36.4%
Providencia rettgeri	10	9	1	10.0%
Other species (n=41)	124	81	43	34.7%
All species	6719	5038	1681	25.0%

ONSET VERSUS 30-DAY ALL CAUSE MORTALITY

The 30-day all-cause mortality was available for 4,573 episodes of bacteraemia where onset was known.

Table 3. Onset versus 30-day all-cause Mortality (top 15 species)

	Total			Community-onset			Healthcare-onset			
Organism	N	Mortality (%)		N	Mortality (%)		N	Mortality (%)		P*
Escherichia coli	2,422	258	(10.7)	2,001	170	(8.5)	421	88	(20.9)	P <0.01
Klebsiella pneumoniae	645	87	(13.5)	454	57	(12.6)	191	30	(15.7)	ns
Pseudomonas aeruginosa	413	76	(18.4)	231	43	(18.6)	182	33	(18.1)	ns
Enterobacter cloacae complex	229	31	(13.5)	111	16	(14.4)	118	15	(12.7)	P <0.01
Klebsiella oxytoca	155	15	(9.7)	111	9	(8.1)	44	6	(13.6)	ns
Proteus mirabilis	137	31	(22.6)	111	21	(18.9)	26	10	(38.5)	ns
Serratia marcescens	130	21	(16.2)	59	7	(11.9)	71	14	(19.7)	ns
Enterobacter aerogenes	80	11	(13.8)	42	4	(9.5)	38	7	(18.4)	
Salmonella species (non-typhoidal)	72	4	(5.6)	60	1	(1.7)	12	3	(25.0)	ns
Morganella morganii	52	10	(19.2)	35	5	(14.3)	17	5	(29.4)	ns
Citrobacter koseri	42	5	(11.9)	28	2	(7.1)	14	3	(21.4)	
Acinetobacter baumannii complex	37	6	(16.2)	21	6	(28.6)	16	0	(0.0)	
Citrobacter freundii	31	9	(29.0)	24	6	(25.0)	7	3		
Salmonella species (typhoidal)	13	0	(0.0)	13	0	0.0	0	0		
Acinetobacter species	13	1	(7.7)	10	1	(10.0)	3	0		
All species	4,573	580	(12.7)	3,382	359	(10.6)	1,191	221	(18.6)	

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

4 PATIENT DEMOGRAPHICS

AGE AND GENDER

Age and gender were available for 7,016 patients. The sex ratio (number of males to 100 females) was 109

Table 4. Gender versus Decade of Life

Decade	Female	Male	Total	M/100F
1	95	126	221	133
2	48	39	87	81
3	164	115	279	70
4	209	128	337	61
5	247	229	476	93
6	455	497	951	109
7	557	765	1,322	137
8	633	843	1,476	133
9	675	733	1,408	109
10	267	181	448	68
11	4	6	10	150
Total	**3,354**	**3,662**	**7,016**	**109**

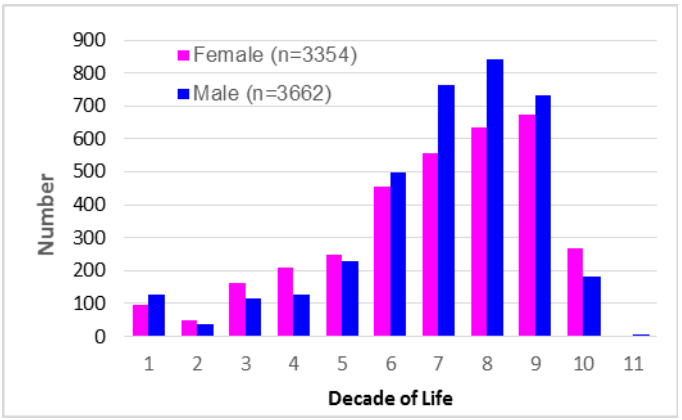


Figure 1. Gender versus Decade of Life

PRINCIPAL CLINICAL MANIFESTATION

Principal Clinical Manifestation was provided for 5,083 patient episodes.

Table 5. Principal Clinical Manifestation

Principal Clinical Manifestation	Total	Male	Female	P*
Urinary tract infection	2196	981	1215	p <0.01
Biliary tract infection (including cholangitis)	808	509	299	p <0.01
Intra-abdominal infection other than biliary tract	532	278	254	p <0.01
Other clinical syndrome	356	218	138	0.01 < p < 0.05
Febrile neutropenia	340	200	140	
No focus	333	176	157	p <0.01
Device-related infection without metastatic focus	200	122	78	ns
Skin and skin structure	145	100	45	p <0.01
No focus (e.g. in febrile neutropenia)	85	49	36	
Osteomyelitis/Septic Arthritis	53	37	16	ns
Device-related infection with metastatic focus	35	19	16	ns
All	**5083**	**2689**	**2394**	

* Fisher's exact test for difference between males and females

LENGTH OF STAY POST BACTERAEMIC EPISODE

Length of stay (post bacteraemia) was available for 5,279 episodes.

Table 6. Length of Stay Post Bacteraemic Episode

Length of Stay (days)	Total (%)		Median
< 7	2466	(46.7)	4
7 - 14	1611	(30.5)	9
15 - 30	781	(14.8)	20
31 - 60	319	(6.0)	39
> 60	102	(1.9)	77
	5279		**7 days**

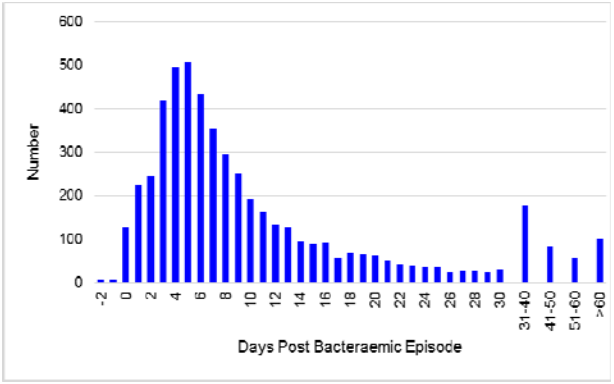


*Figure 2. Length of Stay Post Bacteraemic Episode **

* A negative value indicates that the blood culture was taken at least 24 hours prior to patient admission

PRINCIPAL ANTIMICROBIAL TREATMENT AND 30-DAY ALL-CAUSE MORTALITY

The top five principal antimicrobial treatments for the top 10 species vs 30-day all-cause mortality (where both treatment and outcome are known) is shown in Table 7. The principal antimicrobial treatment was included in the table if used for more than one bacteraemic episode for species recovered.

Table 7. Top Five Principal Antimicrobial Treatments versus Onset and 30-day all-cause Mortality

All episodes					Community-onset					Healthcare-onset				
Agent	Number (% of n)		Died (% mortality)		Agent	Number (% of n)		Died (% mortality)		Agent	Number (% of n)		Died (% mortality)	
Escherichia coli														
Ceftriaxone	784	(34.5)	39	(5.0)	Ceftriaxone	693	(37.1)	25	(3.6)	Piperacillin-tazobactam	149	(36.9)	30	(20.1)
Piperacillin-tazobactam	645	(28.4)	78	(12.1)	Piperacillin-tazobactam	496	(26.6)	48	(9.7)	Ceftriaxone	91	(22.5)	14	(15.4)
Meropenem	261	(11.5)	32	(12.3)	Meropenem	175	(9.4)	14	(8.0)	Meropenem	86	(21.3)	18	(20.9)
Cefazolin	101	(4.4)	7	(6.9)	Amoxycillin	89	(4.8)	0	(0.0)	Cefazolin	14	(3.5)	2	(14.3)
Amoxycillin	94	(4.1)	1	(1.1)	Cefazolin	87	(4.7)	5	(5.7)	Ciprofloxacin	13	(3.2)	1	(7.7)
Other	316	(13.9)	27	(8.5)	Other	270	(14.5)	17	(6.3)	Other	38	(9.4)	10	(26.3)
Not treated	70	(3.1)	57	(81.4)	Not treated	57	(3.1)	47	(82.5)	Not treated	13	(3.2)	10	(76.9)
Total	2271		241	(10.6)	Total	1867		156	(8.4)	Total	404		85	(21.0)
Klebsiella pneumoniae														
Piperacillin-tazobactam	254	(42.1)	31	(12.2)	Piperacillin-tazobactam	168	(39.7)	22	(13.1)	Piperacillin-tazobactam	86	(47.5)	9	(10.5)
Ceftriaxone	153	(25.3)	10	(6.5)	Ceftriaxone	128	(30.3)	7	(5.5)	Meropenem	39	(21.5)	10	(25.6)
Meropenem	89	(14.7)	17	(19.1)	Meropenem	50	(11.8)	7	(14.0)	Ceftriaxone	25	(13.8)	3	(12.0)
Ciprofloxacin	28	(4.6)	1	(3.6)	Cefazolin	22	(5.2)	1	(4.5)	Ciprofloxacin	11	(6.1)	1	(9.1)
Cefazolin	23	(3.8)	1	(4.3)	Ciprofloxacin	17	(4.0)		(0.0)	Cefepime	4			
Other	39	(6.5)	4	(10.3)	Other	24	(5.7)	2	(8.3)	Other	12	(6.6)	2	(16.7)
Not treated	18	(3.0)	16	(88.9)	Not treated	14	(3.3)	13	(92.9)	Not treated	4		3	
Total	604		80	(13.2)	Total	423		52	12.3)	Total	181		28	(15.5)
Pseudomonas aeruginosa														
Piperacillin-tazobactam	208	(52.7)	30	(14.4)	Piperacillin-tazobactam	123	(56.7)	18	(14.6)	Piperacillin-tazobactam	85	(47.8)	12	(14.1)
Meropenem	68	(17.2)	12	(17.6)	Meropenem	24	(11.1)	5	(20.8)	Meropenem	44	(24.7)	7	(15.9)
Ciprofloxacin	29	(7.3)	2	(6.9)	Ciprofloxacin	17	(7.8)	0	(0.0)	Ciprofloxacin	12	(6.7)	2	(16.7)
Ceftazidime	25	(6.3)	3	(12.0)	Ceftazidime	15	(6.9)	1	(6.7)	Ceftazidime	10	(5.6)	2	(20.0)
Cefepime	13	(3.3)	0	(0.0)	Cefepime	7		0		Cefepime	6			
Other	29	(7.3)	4	(13.8)	Other	16	(7.4)	2	(12.5)	Other	13	(7.3)	2	(15.4)
Not treated	23	(5.8)	20	(87.0)	Not treated	15	(6.9)	13	(86.7)	Not treated	8		7	
Total	395		71	(18.0)	Total	217		39	(18.0)	Total	178		32	(18.0)

All episodes					Community-onset				Healthcare-onset			
Agent	Number (% of n)		Died (% mortality)		Agent	Number (% of n)		Died (% mortality)	Agent	Number (% of n)		Died (% mortality)	
Enterobacter cloacae													
Meropenem	121	(56.8)	16	(13.2)	Meropenem	52	(51.0)	7 (13.5)	Meropenem	69	(62.2)	9	(13.0)
Piperacillin-tazobactam	38	(17.8)	4	(10.5)	Piperacillin-tazobactam	21	(20.6)	3 (14.3)	Piperacillin-tazobactam	17	(15.3)	1	(5.9)
Ciprofloxacin	26	(12.2)	4	(15.4)	Ciprofloxacin	13	(12.7)	1 (7.7)	Ciprofloxacin	13	(11.7)	3	(23.1)
Cefepime	7		1		Cefepime	5		1	Cefepime	2		0	
Ceftriaxone	5		0		Ceftriaxone	4			Amikacin	2		0	
Other	10		0		Other	5		0	Other	4		0	
Not treated	6		4		Not treated	2		2	Not treated	4		2	
Total	213		29	(13.6)	Total	102		14 (13.7)	Total	111		15	(13.5)
Klebsiella oxytoca													
Piperacillin-tazobactam	65	(44.2)	5	(7.7)	Piperacillin-tazobactam	45	(43.7)	2 (4.4)	Piperacillin-tazobactam	20	(45.5)	3	(15.0)
Ceftriaxone	37	(25.2)	0	(0.0)	Ceftriaxone	34	(33.0)	0 (0.0)	Meropenem	13	(29.5)	2	(15.4)
Meropenem	23	(15.6)	3	(13.0)	Meropenem	10	(9.7)	1 (10.0)	Ceftriaxone	3		0	
Ciprofloxacin	5		1		Ciprofloxacin	4		1	Gentamicin	2		0	
Gentamicin	5		0		Gentamicin	3			Cefotaxime	2		0	
Other	9		1		Other	4		0	Other	4		1	
Not treated	3		3		Not treated	3		3					
Total	147		13	(8.8)	Total	103		7 (6.8)	Total	44		6	(13.6)
Proteus mirabilis													
Ceftriaxone	39	(31.0)	8	(20.5)	Ceftriaxone	32	(31.4)	5 (15.6)	Piperacillin-tazobactam	12	(50.0)	4	(33.3)
Piperacillin-tazobactam	38	(30.2)	10	(26.3)	Piperacillin-tazobactam	26	(25.5)	6 (23.1)	Ceftriaxone	7	(29.2)	3	(42.9)
Meropenem	10	(7.9)	2	(20.0)	Meropenem	9		2	Amoxycillin-clavulanate	1		0	
Amoxycillin	6		0		Ampicillin	6		0	Meropenem	1		0	
Ampicillin	6		0	(0.0)	Amoxycillin	6		0	Gentamicin	1		1	
Other	20	(15.9)	4	(20.0)	Other	18	(17.6)	3 (16.7)	Other	0		0	
Not treated	7		5		Not treated	5		3	Not treated	2		2	
Total	126		29	(23.0)	Total	102		19 (18.6)	Total	24		10	(41.7)

All episodes					Community-onset				Healthcare-onset			
Agent	Number (% of n)		Died (% mortality)		Agent	Number (% of n)		Died (% mortality)	Agent	Number (% of n)		Died (% mortality)	
Serratia marcescens													
Meropenem	50	(43.9)	5	(10.0)	Meropenem	27	(52.9)	2	(7.4)	Meropenem	23	(36.5)	3	(13.0)
Piperacillin-tazobactam	24	(21.1)	2	(8.3)	Piperacillin-tazobactam	7		0		Piperacillin-tazobactam	17	(27.0)	2	(11.8)
Ciprofloxacin	13	(11.4)	2	(15.4)	Ciprofloxacin	7		1		Ciprofloxacin	6		1	
Cefepime	9		3		Cefepime	4		1		Cefepime	5		2	
Gentamicin	3		0		Gentamicin	2		0		Gentamicin	1			
Other	6		2		Other	2		1		Other	4		1	
Not treated	9		7		Not treated	2		2		Not treated	7		5	
Total	114		21	(18.4)	Total	51		7	(13.7)	Total	63		14	(22.2)
Enterobacter aerogenes													
Meropenem	47	(63.5)	4	(8.5)	Meropenem	23	(60.5)	1	(4.3)	Meropenem	24	(66.7)	3	(12.5)
Piperacillin-tazobactam	11	(14.9)	2	(18.2)	Piperacillin-tazobactam	6		0		Piperacillin-tazobactam	5		2	
Ciprofloxacin	10	(13.5)	3	(30.0)	Ciprofloxacin	5		1		Ciprofloxacin	5		2	
Gentamicin	2		0		Gentamicin	1		0		Gentamicin	1		0	
Cefepime	2		0		Cefepime	1		0		Cefepime	1		0	
Other	1		0		Other	1		0						
Not treated	1		1		Not treated	1		1						
Total	74		10	(13.5)	Total	38		3	(7.9)	Total	36		7	(19.4)
***Salmonella* species (non typhoidal)**													
Ceftriaxone	37	(56.9)	0	(0.0)	Ceftriaxone	33	(62.3)	0	(0.0)	Ceftriaxone	4		0	
Ciprofloxacin	8		0		Ciprofloxacin	7		0		Piperacillin-tazobactam	4		2	
Piperacillin-tazobactam	7		3		Piperacillin-tazobactam	3		1		Meropenem	2		1	
Amoxycillin	2		0		Amoxycillin	2		0		Ciprofloxacin	1		0	
Cefepime	2		0		Cefepime	1		0		Cefepime	1		0	
Other	8		1		Other	6		0						
Not treated	1		0		Not treated	1		0						
Total	65		4	(6.2)	Total	53		1	(1.9)	Total	12		3	(25.0)

5 SUSCEPTIBILITY TESTING RESULTS

Overall percentages of resistance or non-susceptibility for *E. coli*, *Klebsiella* spp. (*K. pneumoniae* and *K. oxytoca*), *Enterobacter* spp. (*E. cloacae* and *E. aerogenes*), Salmonella species and Pseudomonas aeruginosa are shown in Section 5.1 and the Appendix. Appendix 1 shows the details of percentages susceptible, intermediate and resistant for each antibiotic and all species. For some antibiotics, 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 strains.

PERCENTAGES RESISTANT/NON-SUSCEPTIBLE IN INDICATOR SPECIES (NATIONAL PRIORITY)

For Table 8 to Table 21, the percentage resistant/non-susceptible is presented for both CLSI and EUCAST criteria respectabilty.

Table 8. Ampicillin

Species		ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
E. coli	n	149	1,106	137	691	453	79	727	650	3,992
	%I	2.7 / -	2.2 / -	2.9 / -	1.6 / -	1.3 / -	2.5 / -	2.9 / -	1.7 / -	2.1 / -
	%R	48.3 / 51.0	55.4 / 57.6	56.9 / 59.9	51.5 / 53.1	44.2 / 45.5	43.0 / 45.6	56.9 / 59.8	54.0 / 55.7	53.1 / 55.1
P. mirabilis	n	6	66	6	44	24	3	37	36	222
	%I	-	0.0 / -	-	0.0 / -	0.0 / -	-	0.0 / -	0.0 / -	0.0 / -
	%R	-	22.7 / 22.7	-	4.5 / 4.5	12.5 / 12.5	-	18.9 / 18.9	30.6 / 30.6	17.1 / 17.1
***Salmonella* species (non Typhi/Paratyphi)**	n	1	19	24	28	9	2	21	10	114
	%I	-	0.0 / -	0.0 / -	0.0 / -	-	-	0.0 / -	0.0 / -	0.0 / -
	%R	-	5.3 / 5.3	0.0 / 0.0	10.7 / 10.7	-	-	23.8 /23.8	0.0 / 0.0	8.8 / 8.8
***S.* Typhi/Paratyphi**	n	1	5	0	6	4	0	7	2	25
	%I	-	-	-	-	-	-	-	-	4.0 / -
	%R	-	-	-	-	-	-	-	-	4.0 / 8.0

Comments: Resistance to ampicillin is intrinsic in *Klebsiella* and *Enterobacter* species, due to natural ß-lactamases, and hence resistance rates not reported here. Some strains may test as susceptible in vitro, but are generally reported as resistant

Table 9. Amoxycillin-clavulanate

Species		ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
E. coli	n	149	1,107	137	691	454	79	727	651	3,995
	%I	12.8 / -	14.1 / -	10.2 / -	15.2 / -	12.8 / -	10.1 / -	13.6 / -	13.4 / -	13.7 / -
	%R	3.4 / 16.1	9.1 / 23.2	13.1 / 23.4	7.8 / 23.0	6.2 / 18.9	12.7 / 22.8	10.6 / 24.2	8.6 / 22.0	8.7 / 22.4
K. pneumoniae	n	36	236	47	189	85	18	177	187	974
	%I	2.9 / -	3.8 / -	6.4 / -	5.3 / -	2.4 / -	5.6 / -	6.8 / -	5.3 / -	4.9 / -
	%R	8.6 / 11.4	5.1 / 8.9	4.3 / 10.6	3.7 / 9.0	2.4 / 4.7	5.6 / 11.1	5.6 / 12.4	2.1 / 7.5	4.2 / 9.1
K. oxytoca	n	13	76	4	45	13	8	49	30	238
	%I	0.0 / -	3.9 / -	-	2.2 / -	7.7 / -	-	6.1 / -	0.0 / -	4.2 / -
	%R	7.7 / 7.7	10.5 / 14.5	-	6.7 / 8.9	0.0 / 7.7	-	4.1 / 10.2	10.0 / 10.0	7.6 / 11.8
P. mirabilis	n	6	66	6	44	24	3	37	36	222
	%I	-	9.1 / -	-	6.8 / -	4.2 / -	-	5.4 / -	19.4 / -	8.6 / -
	%R	-	1.5 / 10.6	-	0.0 / 6.8	0.0 / 4.2	-	5.4 / 10.8	2.8 / 22.2	1.8 / 10.4
***Salmonella* species (non Typhi/Paratyphi)**	n	1	19	24	28	9	2	21	10	114
	%I	-	0.0 / -	0.0 / -	0.0 / -	-	-	9.5 / -	0.0 / -	1.8 / -
	%R	-	5.3 / 5.3	0.0 /0.0	0.0 / 0.0	-	-	9.5 /19.0	0.0 / 0.0	2.6 / 4.4
***S.* Typhi/Paratyphi**	n	1	5	0	6	4	0	7	2	25
	%I	-	-	-	-	-	-	-	-	8.0 / -
	%R	-	-	-	-	-	-	-	-	0.0 /8.0

* For EUCAST interpretation, the clavulanate is fixed at 2 mg/L, rather than a 2:1 ratio used in CLSI guidelines. As all cards used have a 2:1 ratio of clavulanate no EUCAST category has been applied.

Comments: Intermediate susceptibility or resistance to amoxycillin-clavulanate is intrinsic in *Enterobacter* spp., due to natural ß-lactamases, and hence resistance rates not reported here. Some strains may test as susceptible in vitro, but are generally reported as resistant. Intermediate susceptibility is common in *E. coli* due to hyperproduction of acquired narrow-spectrum ß-lactamases, and in *Klebsiella* spp. due to higher levels of natural ß-lactamases.

Table 10. Ticarcillin-clavulanate

Species		ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
E. coli	n	149	985	137	691	454	79	726	650	3,871
	%R	6.7 / 14.1	10.4 / 25.3	13.1 / 19.7	10.6 / 19.4	7.9 / 20.9	6.3 / 13.9	10.2 / 22.2	9.2 / 18.0	9.8 / 21.1
K. pneumoniae	n	35	213	47	189	85	18	177	187	951
	%R	8.6 / 11.4	7.0 / 10.8	4.3 / 8.5	6.3 / 7.9	4.7 / 10.6	5.6 / 11.1	10.7 / 13.0	3.2 / 8.0	6.5 / 10.0
K. oxytoca	n	13	66	4	45	13	8	49	30	228
	%R	7.7 / 7.7	12.1 / 15.2	-	8.9 / 8.9	7.7 / 7.7	-	6.1 / 10.2	10.0 / 10.0	9.2 / 11.4
***E. cloacae* complex**	n	10	74	9	65	13	14	80	50	315
	%R	0.0 / 0.0	16.2 / 23.0	-	21.5 / 26.2	0.0 / 0.0	14.3 / 21.4	31.3 / 31.3	22.0 / 22.0	21.0 / 23.8
E. aerogenes	n	6	25	0	26	11	2	18	13	101
	%R	-	32.0 / 40.0	.	23.1 / 34.6	27.3 / 63.6	-	33.3 / 44.4	23.1 / 46.2	26.7 / 40.6
P. mirabilis	n	6	51	6	44	24	3	37	36	207
	%R	-	0.0 / 0.0	-	0.0 / 0.0	0.0 / 0.0	-	2.7 / 2.7	0.0 / 0.0	0.5 / 0.5
***Salmonella* species (non Typhi/Paratyphi)**	n	1	17	24	28	9	2	21	10	112
	%R	-	5.9 / 5.9	0.0 / 0.0	0.0 / 0.0	-	-	9.5 / 14.3	0.0 / 0.0	2.7 / 3.6
***S.* Typhi/Paratyphi**	n	1	5	0	6	4	0	7	2	25
	%R	-	-	-	-	-	-	-	-	0.0 / 8.0

Comments: Resistance to ticarcillin-clavulanate in *E. coli* and *Klebsiella* spp. may indicate the presence of acquired plasmid-borne AmpC ß-lactamases.

Table 11. Piperacillin-tazobactam

Species		ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
E. coli	n	146	1,107	137	676	454	79	726	649	3,974
	%R	1.4 / 3.4	3.4 / 6.3	2.9 / 6.6	3.3 / 7.5	2.0 / 4.6	2.5 / 5.1	3.2 / 7.4	1.8 / 5.7	2.8 / 6.3
K. pneumoniae	n	35	235	47	184	85	18	176	186	966
	%R	5.7 / 5.7	4.3 / 6.4	2.1 / 12.8	3.8 / 7.1	2.4 / 4.7	0.0 / 5.6	4.0 / 7.4	2.7 / 4.3	3.5 / 6.4
K. oxytoca	n	13	76	4	43	13	8	49	30	236
	%R	7.7 / 7.7	13.2 / 14.5	-	7.0 / 7.0	7.7 / 15.4	-	6.1 / 6.1	10.0 / 10.0	8.9 / 10.2
***E. cloacae* complex**	n	5	57	9	64	13	11	77	41	277
	%R	-	5.3 / 14.0	-	14.1 / 18.8	0.0 / 7.7	9.1 / 18.2	26.0 / 27.3	24.4 / 26.8	15.9 / 20.6
E. aerogenes	n	4	34	3	25	11	1	27	25	130
	%R	-	17.6 / 38.2	-	16.0 / 24.0	18.2 / 27.3	-	44.4 / 55.6	28.0 / 40.0	27.7 / 40.0
P. mirabilis	n	6	65	6	42	24	3	37	36	219
	%R	-	0.0 / 1.5	-	0.0 / 0.0	0.0 / 0.0	-	2.7 / 2.7	0.0 / 0.0	0.5 / 0.9
***Salmonella* species (non Typhi/Paratyphi)**	n	1	19	24	28	9	2	21	10	114
	%R	-	0.0 / 5.3	0.0 / 0.0	0.0 / 0.0	-	-	0.0 / 0.0	0.0 / 0.0	0.0 / 0.9
***S.* Typhi/Paratyphi**	n	1	5	0	5	4	0	6	1	22
	%R	-	-	-	-	-	-	-	-	0.0 / 0.0
Pseudomonas aeruginosa	n	35	166	19	159	83	4	74	107	647
	%R	20.0 / 20.0	7.8 / 15.7	5.3 / 10.5	6.3 / 15.1	6.0 / 10.8	-	5.4 / 14.9	5.6 / 10.3	7.1 / 13.9

Comments: Resistance to piperacillin-tazobactam in *E. coli* and *Klebsiella* spp. may indicate the presence of acquired plasmid-borne AmpC ß-lactamases.

Table 12. Cefazolin

Species		ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
E. coli	n	149	1,107	137	691	453	49	604	574	3,764
	%R	18.8 / 18.8	25.1 / 25.1	21.9 / 21.9	20.1 / 20.1	18.1 / 18.1	10.2 / 10.2	24.7 / 24.7	19.0 / 19.0	21.8 / 21.8
K. pneumoniae	n	35	236	47	189	85	9	150	165	916
	%R	8.6 / 8.6	10.6 / 10.6	17.0 / 17.0	9.5 / 9.5	8.2 / 8.2	-	16.7 / 16.7	8.5 / 8.5	11.0 / 11.0
K. oxytoca	n	13	76	4	45	13	5	41	23	220
	%R	61.5 / 61.5	63.2 / 63.2	-	62.2 / 62.2	69.2 / 69.2	-	63.4 / 63.4	47.8 / 47.8	62.3 / 62.3
***E. cloacae* complex**	n	10	85	9	65	13	8	74	48	312
	%R	100 / 100	91.8 / 91.8	-	98.5 / 98.5	100 / 100	-	98.6 / 98.6	100 / 100	96.5 / 96.5
E. aerogenes	n	4	34	3	26	11	1	20	23	122
	%R	-	91.2 / 91.2	-	80.8 / 80.8	90.9 / 90.9	-	75.0 / 75.0	73.9 / 73.9	83.6 / 83.6
P. mirabilis	n	6	66	6	44	24	2	34	27	209
	%R	-	22.7 / 22.7	-	27.3 /27.3	12.5 / 12.5	-	32.4 / 32.4	44.4 / 44.4	25.4 / 25.4
***Salmonella* species (non Typhi/Paratyphi)**	n	1	19	24	28	9	0	16	9	106
	%R	-	5.3 / 5.3	0.0 / 0.0	0.0 / 0.0	-	-	12.5 / 12.5	-	2.8 / 2.8
***S.* Typhi/Paratyphi**	n	1	5	0	6	4	0	7	2	25
	%R	-	-	-	-	-	-	-	-	4.0 / 4.0

* Cefazolin MIC data was suppressed from reporting.

Comments: Interpretation based on MIC range available on Vitek/Phoenix cards, which currently do not match those of the CLSI breakpoints published in 2015. For this analysis, susceptible was defined as ≤ 4mg/L, Resistant as ≥8 mg/L (no intermediate range). Resistance to cefazolin, representative of first generation cephalosporins, is common in *E. coli* and *Klebsiella* spp. *Enterobacter* spp. are intrinsically resistant due to natural ß-lactamases.

Table 13. Cefoxitin

Species		ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
E. coli	n	149	1,107	137	691	454	79	727	650	3,994
	%R	1.3 / -	4.7 / -	2.9 / -	2.6 / -	2.6 / -	2.5 / -	3.6 / -	2.8 / -	3.4 / -
K. pneumoniae	n	35	236	47	188	85	18	177	187	973
	%R	5.7 / -	8.9 / -	2.1 / -	3.2 / -	2.4 / -	0.0 /	4.0 /	4.3 / -	4.8 / -
K. oxytoca	n	13	78	4	45	13	8	49	30	238
	%R	0.0 / -	5.3 / -	-	2.2 / -	7.7 / -	-	0.0 / -	0.0 / -	2.5 / -
P. mirabilis	n	6	66	6	44	24	3	37	36	222
	%R	-	0.0 / -	-	0.0 / -	0.0 / -	-	0.0 / -	2.8 / -	0.5 / -
***Salmonella* species (non Typhi/Paratyphi)**	n	1	19	24	28	9	2	21	10	114
	%R	-	0.0 / -	0.0 / -	0.0 / -	-	-	9.5 / -	0.0 / -	1.8 / -
***S.* Typhi/Paratyphi**	n	1	5	0	6	4	0	7	2	25
	%R	-	-	-	-	-	-	-	-	4.0 / -

Comments: Cefoxitin is tested solely for the purpose of screening for potential plasmid-borne AmpC β-lactamases in *E. coli* and *Klebsiella* spp. Because *Enterobacter* spp. Have an intrinsic AmpC β-lactamase, they will test as resistant or intermediate.

Table 14. Ceftriaxone

Species		ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
E. coli	n	149	1,107	137	691	454	79	727	650	3,994
	%NS	10.7 / 10.7	15.3 / 15.3	8.8 / 8.8	6.1 / 6.1	7.5 / 7.5	0.0 / 0.0	12.2 / 12.2	9.4 / 9.4	10.6 / 10.6
K. pneumoniae	n	35	236	47	189	85	18	177	187	974
	%NS	2.9 / 2.9	6.8 / 6.8	6.4 / 6.4	3.7 / 3.7	3.5 / 3.5	5.6 / 5.6	10.2 / 10.2	3.7 / 3.7	5.7 / 5.7
K. oxytoca	n	13	76	4	45	13	7	49	30	237
	%NS	7.7 / 7.7	10.5 / 10.5	-	6.7 / 6.7	23.1 / 23.1	-	6.1 / 6.1	6.7 / 6.7	7.6 / 7.6
***E. cloacae* complex**	n	10	85	9	65	13	14	80	50	326
	%NS	10.0 / 10.0	24.7 / 24.7	-	29.2 / 29.2	0.0 / 0.0	28.6 / 28.6	32.5 / 32.5	22.0 / 22.0	25.8 / 25.8
E. aerogenes	n	4	34	3	26	11	1	27	25	131
	%NS	-	50.0 / 50.0	-	19.2 / 19.2	36.4 / 36.4	-	55.6 / 55.6	36.0 / 36.0	42.0 / 42.0
P. mirabilis	n	6	66	6	44	24	3	37	36	222
	%NS	-	1.5 / 1.5	-	2.3 / 2.3	0.0 /	-	5.4 / 5.4	2.8 / 2.8	2.3 / 2.3
***Salmonella* species (non Typhi/Paratyphi)**	n	1	19	24	28	9	2	21	10	114
	%NS	-	0.0 / 0.0	0.0 / 0.0	0.0 / 0.0	-	-	14.3 / 14.3	0.0 / 0.0	2.6 / 2.6
***S.* Typhi/Paratyphi**	n	1	5	0	6	4	0	7	2	25
	%NS	-	-	-	-	-	-	-	-	4.0 / 4.0

* Ceftriaxone concentration range (Phoenix™ cards) unable to differentiate the intermediate from the susceptible category; for this report some ceftriaxone-intermediate isolates may be called sensitive.

Comments: In *E. coli* and *Klebsiella* spp. non-susceptibility to ceftriaxone is indicative of extended-spectrum ß-lactamase production. In *Enterobacter* spp. resistance is mostly indicative of stable de-repression of natural chromosomal cephalosporinase.

Table 15. Ceftazidime

Species		ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
E. coli	n	149	1,107	137	691	454	79	727	650	3,994
	%NS	5.4 / 9.4	9.9 / 14.5	3.6 / 8.0	3.2 / 5.6	4.4 / 7.0	0.0 / 1.3	6.3 / 11.4	4.8 / 8.6	6.1 / 9.9
K. pneumoniae	n	35	236	47	189	85	18	177	187	974
	%NS	2.9 / 5.7	6.8 / 8.9	2.1 / 2.1	3.2 / 3.7	2.4 / 4.7	5.6 / 5.6	9.6 / 12.4	2.1 / 4.8	4.9 / 6.9
K. oxytoca	n	13	76	4	45	13	8	49	30	238
	%NS	0.0 / 0.0	0.0 / 2.6	-	2.2 / 2.2	15.4 / 15.4	-	0.0 / 0.0	0.0 / 0.0	1.3 / 2.1
***E. cloacae* complex**	n	10	85	9	65	13	14	80	50	326
	%NS	0.0 / 0.0	23.5 / 23.5	-	23.1 / 24.6	0.0 / 0.0	28.6 / 35.7	27.5 / 31.2	20.0 / 22.0	22.4 / 24.2
E. aerogenes	n	4	34	3	26	11	1	27	25	131
	%NS	-	41.2 / 47.1	-	15.4 / 19.2	18.2 / 27.3	-	55.6 / 55.6	32.0 / 32.0	37.4 / 39.7
P. mirabilis	n	6	66	6	44	24	3	37	36	222
	%NS	-	0.0 / 0.0	-	2.3 / 2.3	0.0 / 0.0	-	2.7 / 5.4	2.8 / 2.8	1.4 / 1.8
***Salmonella* species (non Typhi/Paratyphi)**	n	1	19	24	28	9	2	21	10	114
	%NS	-	0.0 / 0.0	0.0 / 0.0	0.0 / 0.0	-	-	9.5 / 9.5	0.0 / 0.0	1.8 / 1.8
***S.* Typhi/Paratyphi**	n	1	4	0	6	4	0	7	2	24
	%NS	-	-	-	-	-	-	-	-	0.0 / 0.0

Comments: In *E. coli* and *Klebsiella* spp. non-susceptibility to ceftazidime is indicative of extended-spectrum ß-lactamase production. In *Enterobacter* spp. resistance is indicative of stable de-repression of natural chromosomal cephalosporinase

Table 16. Cefepime

Species		ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
E. coli	n	149	1,107	137	691	454	79	727	650	3,994
	%NS	4.0 / 9.4	6.2 / 13.6	1.5 / 8.0	0.9 / 3.9	4.0 / 6.2	0.0 / 0.0	4.1 / 9.8	2.6 / 7.2	3.7 / 8.7
K. pneumoniae	n	35	236	47	189	85	18	177	187	974
	%NS	0.0 / 2.9	3.4 / 5.5	0.0 / 4.3	1.1 / 2.6	2.4 / 3.5	0.0 / 5.6	2.3 / 9.0	0.0 / 2.7	1.6 / 4.7
K. oxytoca	n	13	76	4	45	13	8	49	30	238
	%NS	0.0 / 0.0	1.3 / 2.6	-	0.0 / 0.0	0.0 / 0.0	-	0.0 / 0.0	0.0 / 3.3	0.4 / 1.3
***E. cloacae* complex**	n	10	85	9	65	13	14	80	50	326
	%NS	0.0 / 0.0	2.4 / 12.9	-	3.1 / 13.8	0.0 / 0.0	0.0 / 7.1	3.8 / 18.7	0.0 / 12.0	2.1 / 12.9
E. aerogenes	n	4	34	3	26	11	1	27	25	131
	%NS	-	0.0 / 2.9		3.8 / 3.8	0.0 / 0.0	-	0.0 / 11.1	0.0 / 0.0	0.8 / 3.8
P. mirabilis	n	6	66	6	44	24	3	37	36	222
	%NS	-	0.0 / 0.0	-	2.3 / 2.3	0.0 / 0.0	-	2.7 / 2.7	0.0 / 2.8	0.9 / 1.4
***Salmonella* species (non Typhi/Paratyphi)**	n	1	19	24	28	9	2	21	10	114
	%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
***S.* Typhi/Paratyphi**	n	1	5	0	6	4	0	7	2	25
	%NS	-	-	-	-	-	-	-	-	0.0 / 0.0
Pseudomonas aeruginosa	n	36	165	19	165	83	4	74	107	653
	%NS	16.7 / 16.7	6.7 / 6.7	15.8 / 15.8	5.5 / 5.5	10.8 / 10.8		9.5 / 9.5	6.5 / 6.5	8.0 / 8.0

Comments: %NS includes SDD category for CLSI interpretation. In *E. coli* and *Klebsiella* spp. non-susceptibility to cefepime is suggestive of mixed or hyperproduction of extended-spectrum ß-lactamases. In *Enterobacter* spp. non-susceptibility is suggestive of the presence of acquired extended-spectrum ß-lactamases

Table 17. Meropenem

Species		ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
E. coli	n	149	1,107	137	691	453	79	727	650	3,993
	%NS	0.0 / 0.6	0.0 / 0.0	0.0 / 0.0	0.0 / 0.3	0.2 / 0.0	0.0 / 0.0	0.0 / 0.0	0.0 / 0.0	0.0 / 0.0
K. pneumoniae	n	35	236	47	189	85	18	177	187	974
	%NS	2.9 / 2.9	0.4 / 0.0	0.0 / 0.0	0.0 / 0.0	1.2 / 1.2	0.0 / 0.0	0.6 / 0.6	0.0 / 0.0	0.4 / 0.3
K. oxytoca	n	13	76	4	45	13	8	49	30	238
	%NS	0.0 / 0.0	0.0 / 0.0	-	2.2 / 2.2	7.7 / 0.0	-	0.0 / 0.0	0.0 / 0.0	0.8 / 0.4
***E. cloacae* complex**	n	10	85	9	65	13	14	80	50	326
	%NS	0.0 / 4.0	7.1 / 5.9	-	4.6 / 4.6	0.0 / 0.0	0.0 / 0.0	0.0 / 0.0	4.0 / 4.0	3.4 / 3.1
E. aerogenes	n	4	34	3	26	11	1	27	25	131
	%NS	-	2.9 / 2.9	-	0.0 / 0.0	0.0 / 0.0	-	3.7 / 3.7	0.0 / 0.0	1.5 / 1.5
P. mirabilis	n	6	66	6	44	24	3	37	35	221
	%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
***Salmonella* species (non Typhi/Paratyphi)**	n	1	19	24	28	9	2	21	10	114
	%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
***S.* Typhi/Paratyphi**	n	1	5	0	6	4	0	7	2	25
	%NS	-	-	-	-	-	-	-	-	0.0 / 0.0
Pseudomonas aeruginosa	n	36	166	19	165	82	4	74	107	653
	%NS	2.8 / 2.8	9.0 / 9.0	15.8 / 15.8	9.7 / 9.7	7.3 / 7.3	-	9.5 / 9.5	3.7 / 3.7	8.1 / 8.1

Comments: Non-susceptibility in Enterobacteriaceae suggests the possible presence of carbapenemases. However, isolates that contain ESBL or de-repressed AmpC enzymes and have decreased permeability may have meropenem MICs elevated above wild-type.

Table 18. Ciprofloxacin

Species		ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
E. coli	n	149	1,107	137	691	454	79	727	650	3,994
	%NS	10.1 / 13.4	16.9 / 19.3	8.8 / 10.9	8.1 / 10.4	8.6 / 11.2	3.8 / 8.9	13.3 / 16.4	14.5 / 20.3	12.6 / 15.8
K. pneumoniae	n	35	236	47	189	85	18	177	187	974
	%NS	5.7 / 5.7	5.1 / 10.2	2.1 / 6.4	2.6 / 7.4	2.4 / 5.9	5.6 / 5.6	5.6 / 13.6	2.7 / 8.6	3.9 / 9.2
K. oxytoca	n	13	76	4	45	13	8	49	30	238
	%NS	0.0 / 0.0	0.0 / 0.0	-	0.0 / 0.0	0.0 / 0.0	-	0.0/ 0.0	3.3 / 6.7	0.4 / 0.8
***E. cloacae* complex**	n	10	85	9	65	13	14	80	50	326
	%NS	0.0 / 10.0	5.9 / 11.8	-	3.1 / 6.2	0.0 / 0.0	0.0 / 0.0	5.0 / 8.7	0.0 / 4.0	3.4 / 7.4
E. aerogenes	n	4	34	3	26	11	1	27	25	131
	%NS	-	0.0 / 0.0	-	7.7 / 11.5	0.0 / 0.0	-	11.1 / 11.1	0.0 / 0.0	3.8 / 4.6
P. mirabilis	n	6	66	6	44	24	3	37	36	222
	%NS	-	3.0 / 3.0	-	2.3 / 4.5	8.3 / 8.3	-	2.7 / 2.7	5.6 / 5.6	4.1 / 4.5
***Salmonella* species (non Typhi/Paratyphi)**	n	1	19	24	28	9	2	21	10	114
	%R	-	10.5 / -	0.0 / -	0.0 / -	-	-	0.0 / -	0.0 / -	1.8 / -
***S.* Typhi/Paratyphi**	n	1	5	0	6	4	0	7	2	25
	%R	-	-	-	-	-	-	-	-	56.0 / -
Pseudomonas aeruginosa	n	36	166	19	165	82	4	74	107	653
	%NS	8.3 / 11.1	3.6 / 6.0	5.3 / 10.5	5.5 / 7.9	9.8 / 17.1	-	10.8 / 14.9	5.6 / 6.5	6.3 / 9.3

* Ciprofloxacin concentration range available on the cards used restricts ability to accurately determine susceptible CLSI/EUCAST) and intermediate (CLSI) categories for *Salmonella* species. The proposed revised EUCAST breakpoints have been applied for this report.

Comments: Ciprofloxacin non-susceptibility indicates at least the presence of mutations in *gyrA*, the gene encoding a component of the target enzyme, DNA gyrase and, and more recently, the possibility of plasmid-mediated quinolone-resistance genes

Table 19. Gentamicin

Species		ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
E. coli	n	149	1,107	137	691	454	79	727	650	3,994
	%R	4.0 / 4.7	9.3 / 9.4	8.8 / 8.8	6.5 /6.7	7.3 / 7.3	2.5 / 2.5	6.9 / 6.9	9.2 / 9.2	7.8 / 7.9
K. pneumoniae	n	35	236	47	189	85	18	177	187	974
	%R	2.9 / 2.9	5.5 / 5.9	10.6 / 10.6	3.2 / 3.2	4.7 / 5.9	5.6 / 5.6	3.4 / 4.0	2.7 / 2.7	4.2 / 4.5
K. oxytoca	n	13	76	4	45	13	8	49	30	238
	%R	0.0 / 0.0	0.0 / 0.0	-	2.2 / 2.2	0.0 0.0	-	0.0 / 2.0	3.3 / 3.3	0.8 / 1.3
***E. cloacae* complex**	n	10	85	9	65	13	14	80	50	326
	%R	0.0 / 0.0	12.9 / 12.9	-	9.2 / 10.8	0.0 / 0.0	7.1 / 7.1	3.8 / 5.0	0.0 / 0.0	6.7 / 7.4
E. aerogenes	n	4	34	3	26	11	1	27	25	131
	%R	-	2.9 / 2.9	-	3.8 / 3.8	0.0 / 0.0	-	7.4 / 7.4	0.0 / 0.0	3.1 / 3.1
P. mirabilis	n	6	66	6	44	24	3	37	36	222
	%R	-	1.5 / 3.0	-	0.0 / 2.3	0.0 / 0.0	-	0.0 / 2.7	0.0 / 0.0	0.5 / 1.8
***Salmonella* species (non Typhi/Paratyphi)**	n	1	19	24	28	9	2	21	10	114
	%R	-	5.3 / 5.3	0.0 / 0.0	0.0 / 0.0	-	-	4.8 / 4.8	0.0 / 0.0	1.8 / 1.8
***S.* Typhi/Paratyphi**	n	1	5	0	5	4	0	7	2	25
	%R	-	-	-	-	-	-	-	-	0.0 / 0.0
Pseudomonas aeruginosa	n	36	166	19	165	83	4	74	107	654
	%R	0.0 / 0.0	4.8 / 5.4	0.0 / 5.3	0.6 / 1.8	2.4 / 2.4	-	4.1 / 6.8	1.9 / 1.9	2.4 / 3.4

Comments: Gentamicin resistance indicates the presence of at least one of a range of aminoglycoside modifying enzymes.

Table 20. Tobramycin

Species		ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
E. coli	n	149	1,107	137	679	454	79	727	650	3,982
	%R	1.3 / 4.0	4.7 / 10.2	5.1 / 11.7	2.1 /6.8	3.7 / 7.5	0.0 / 2.5	4.4 / 9.2	3.7 / 10.2	3.7 / 8.8
K. pneumoniae	n	35	236	47	184	85	18	177	187	969
	%R	0.0 / 2.9	3.0/ 6.8	2.1 / 10.6	2.2 / 3.8	1.2 / 5.9	5.6 / 5.6	3.4 / 6.8	1.6 / 3.2	2.4 / 5.5
K. oxytoca	n	13	76	4	43	13	8	49	30	236
	%R	0.0 / 0.0	0.0 / 0.0	-	0.0 / 2.3	0.0 0.0	-	0.0 / 2.0	0.0 / 3.3	0.0 / 1.3
***E. cloacae* complex**	n	10	85	9	64	13	14	80	50	325
	%R	0.0 / 0.0	7.1 / 14.1	-	4.7/ 12.5	0.0 / 0.0	0.0 / 7.1	2.5 / 10.0	0.0 / 0.0	3.4 / 9.2
E. aerogenes	n	4	34	3	25	11	1	27	25	130
	%R	-	0.0 / 2.9	-	4.0 / 4.0	0.0 / 0.0	-	7.4 / 11.1	0.0 / 0.0	2.3 / 3.8
P. mirabilis	n	6	66	6	43	24	3	37	36	221
	%R	-	0.0 / 3.0	-	2.3 / 2.3	0.0 / 0.0	-	2.7 / 2.7	0.0 / 0.0	0.9 / 1.8
***Salmonella* species (non Typhi/Paratyphi)**	n	1	19	24	28	9	2	21	10	114
	%R	-	5.3 / 5.3	0.0 / 0.0	0.0 / 0.0	-	-	0.0 / 0.0	0.0 / 0.0	0.9 / 0.9
***S.* Typhi/Paratyphi**	n	1	5	0	5	4	0	7	2	24
	%R	-	-	-	-	-	-	-	-	0.0 / 0.0
Pseudomonas aeruginosa	n	36	166	19	160	83	4	74	107	649
	%R	0.0 / 0.0	4.2 / 4.2	0.0 / 0.0	0.6 / 1.3	2.4 / 2.4	-	4.1 / 4.1	0.9 / 0.9	2.2 / 2.3

Comments: Gentamicin resistance indicates the presence of at least one of a range of aminoglycoside modifying enzymes.

Table 21. Trimethoprim

Species		ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
E. coli	n	149	1,107	137	679	454	79	727	650	3,982
	%R	30.2 / 30.9	34.7 / 34.8	35.0 / 35.0	30.2 / 30.2	24.0 / 24.4	15.2 / 15.2	32.2 / 33.0	30.3 / 30.6	31.0 / 31.3
K. pneumoniae	n	35	236	47	184	85	18	177	187	969
	%R	31.4 / 31.4	14.8 / 15.3	17.0 / 17.0	15.2 / 15.2	12.9 / 14.1	22.2 / 22.2	18.6 / 19.8	10.2 / 11.8	15.4 / 16.1
K. oxytoca	n	13	76	4	43	13	8	49	30	236
	%R	0.0 / 0.0	3.9 / 3.9	-	2.3 / 2.3	0.0 / 0.0	-	4.1/ 4.1	6.7 / 6.7	3.4 / 3.4
***E. cloacae* complex**	n	10	85	9	64	13	14	80	50	325
	%R	20.0 / 20.0	16.5 / 16.5	-	18.8 / 18.8	15.4 / 15.4	21.4 / 21.4	20.0 / 20.0	2.0 / 2.0	16.0 / 16.0
E. aerogenes	n	4	34	3	25	11	1	27	25	130
	%R	-	8.8 / 8.8	-	8.0 / 8.0	0.0 / 0.0	-	11.1 / 11.1	0.0 / 0.0	6.2 / 6.2
P. mirabilis	n	6	66	6	43	24	3	37	36	221
	%R	-	25.8 / 25.8	-	9.3 / 11.6	20.8 / 20.8	-	13.5 / 16.2	22.2 / 22.2	18.1 / 19.0
***Salmonella* species (non Typhi/Paratyphi)**	n	1	19	24	28	9	2	21	10	114
	%R	-	5.3 / 5.3	0.0 / 0.0	3.6 / 3.6	-	-	9.5 / 9.5	0.0 / 0.0	4.4 / 4.4
***S.* Typhi/Paratyphi**	n	1	5	0	5	4	0	7	2	24
	%R	-	-	-	-	-	-	-	-	4.2 / 4.2

Comments: Trimethoprim resistance is the result of mutations in the gene encoding dihydrofolate reductase (DHFR) or acquisition of a gene encoding a new low affinity DHFR.

Table 22. Nitrofurantoin

Species		ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
E. coli	n	149	1,107	137	691	454	79	727	650	3,994
	%R	1.3 / 1.3	1.0 / 1.0	0.0 / 0.0	0.7 / 0.7	1.3 / 1.3	0.0 / 0.0	2.2 / 2.2	1.5 / 1.5	1.3 / 1.3
K. pneumoniae	n	35	236	47	189	85	18	177	187	974
	%R	37.1 / -	30.9 / -	38.3 / -	20.6 / -	35.3 / -	22.2 / -	44.1 / -	32.6 / -	32.4 / -
K. oxytoca	n	13	76	4	45	13	8	49	30	238
	%R	0.0 / -	0.0 / -	-	2.2 / -	23.1 / -	-	0.0 / -	0.0 / -	2.1 / -
***E. cloacae* complex**	n	10	85	9	65	13	14	80	50	326
	%R	10.0 / -	16.5 / -	-	15.4 / -	46.2 / -	21.4 / -	25.0 / -	20.0 / -	20.6 / -
E. aerogenes	n	4	34	3	26	11	1	27	25	131
	%R	-	47.1 / -	-	46.2 / -	27.3 / -	-	51.9 / -	32.0 / -	43.5 / -
P. mirabilis	n	6	66	6	44	24	3	37	36	222
	%R	-	92.4 / -	-	100 / -	91.7 / -	-	94.6 / -	91.7 / -	94.6 / -
***Salmonella* species (non Typhi/Paratyphi)**	n	1	19	24	28	9	2	21	10	114
	%R	-	5.3 / -	0.0 / -	7.1 / -	-	-	9.5 / -	40.0 / -	8.8 / -
***S.* Typhi/Paratyphi**	n	1	5	0	6	4	0	7	2	25
	%R	-	-	-	-	-	-	-	-	4.0 / -

* For EUCAST interpretative breakpoints apply for *E. coli* only

Comments: Nitrofurantoin resistance in *K. pneumoniae* is mostly attributable to the resistance breakpoint falling within the wild-type distribution.

ANTIMICROBIAL RESISTANCE VERSUS ONSET

Table 23. Resistance versus onset (top nine species)

Organism	N	Community-onset (CO) %I	Community-onset (CO) %R	Healthcare –onset (HO) %I	Healthcare –onset (HO) %R	P*
Escherichia coli						
Community-onset, **83.5%;** healthcare-onset, **16.5%**						
Ampicilllin	3640	2.2 / -	51.2 / 53.4	1.5 / -	62.1 / 63.6	P < 0.01
Amoxycllin-calvulanate	3643	12.8 / -	7.9 / 20.7	18.2 / -	13.4 / 31.6	
Ticarcillin-clavulanate	3519	11.1 / 26.0	8.1 / 19.2	13.7 / 24.1	16.8 / 30.6	
Piperacillin-tazobactam	3622	3.1 / 1.0	2.1 / 5.2	5.2 / 1.4	6.8 / 12.0	
Ceftriaxone	3642	0.1 / 0.1	9.3 / 9.3	0.0 / 0.0	16.2 / 16.2	
Ceftazidime	3642	0.3 / 3.6	5.1 / 5.4	0.5 / 5.8	8.7 / 9.2	
Cefepime	3642	† 1.6 / 3.5	3.3 / 4.2	† 2.8 / 5.3	6.2 / 7.7	
Gentamicin	3642	0.1 / 0.5	7.4 / 7.5	0.0 / 0.7	8.7 / 8.7	
Tobramycin	3630	5.0 / 0.7	3.4 / 8.4	5.1 / 0.7	4.5 / 9.6	
Amikacin	3642	0.0 / 1.3	0.0 / 0.1	0.0 / 2.7	0.3 / 0.3	
Ciprofloxacin	3642	0.3 / 2.2	11.5 / 12.8	0.5 / 2.5	15.5 / 17.7	
Meropenem	3641	0.0 / 0.0	0.0 / 0.0	0.0 / 0.0	0.0 / 0.0	
Klebsiella pneumoniae						
Community-onset, **70.9%;** healthcare-onset, **29.1%**						
Ampicilllin	907	27.7 / -	67.5 / 95.2	24.2 / -	70.5 / 94.7	
Amoxycllin-calvulanate	907	4.2 / -	2.5 / 6.7	6.1 / -	8.7 / 14.8	
Ticarcillin-clavulanate	884	3.0 / 6.5	4.2 / 7.2	3.9 / 8.9	11.6 / 15.5	
Piperacillin-tazobactam	900	2.7 / 5.2	1.6 / 4.2	3.8 / 6.5	7.6 / 11.5	
Ceftriaxone	907	0.0 / 0.0	5.1 / 5.1	0.4 / 0.4	7.2 / 7.2	
Ceftazidime	907	0.2 / 1.2	3.7 / 3.9	0.4 / 3.4	6.8 / 7.2	
Cefepime	907	† 0.9 / 2.0	1.1 / 1.9	† 0.4 / 3.4	2.7 / 2.7	
Gentamicin	907	0.3 / 0.2	3.9 / 4.2	0.4 / 0.8	5.3 / 5.7	
Tobramycin	902	3.0 / 0.3	2.0 / 5.0	3.8 / 3.4	0.4 / 7.3	
Amikacin	907	0.0 / 0.3	0.2 / 0.2	0.0 / 0.0	0.8 / 0.0	
Ciprofloxacin	907	1.7 / 1.7	1.9 / 6.4	1.9 / 2.3	3.0 / 9.8	
Meropenem	907	0.0 / 0.0	0.3 / 0.3	0.4 / 0.0	0.4 / 0.4	
Pseudomonas aeruginosa						
Community-onset, **56.9%;** healthcare-onset, **43.1%**						
Ticarcillin-clavulanate	594	33.3 / 0.0	13.6 / 46.9	33.7 / 18.8	11.6 / 52.5	
Piperacillin-tazobactam	589	6.2 / 0.0	3.0 / 9.2	7.9 / 0.0	11.5 / 19.4	
Ceftazidime	596	4.7 / 0.0	2.1 / 6.8	5.8 / 0.0	8.6 / 14.4	
Cefepime	596	† 0.0 / 0.9	1.1 / 5.3	† 0.0 / 0.0	3.5 / 9.3	
Gentamicin	596	0.9 / 0.0	0.6 / 1.5	0.8 / 0.0	5.1 / 5.8	
Tobramycin	591	0.3 / 0.0	0.3 / 0.6	0.0 / 0.0	4.3 / 4.3	
Amikacin	596	0.0 / 1.5	0.0 / 0.0	0.8 / 1.9	1.2 / 1.9	
Ciprofloxacin	596	2.7 / 0.0	2.7 / 8.0	1.2 / 0.0	5.1 / 9.7	
Meropenem	596	2.7 / 3.5	2.1 / 1.2	5.1 / 6.6	6.2 / 4.7	

Organism	N	Community-onset (CO) %I	Community-onset (CO) %R	Healthcare –onset (HO) %I	Healthcare –onset (HO) %R	P*
Enterobacter cloacae						
Community-onset, **49.2%;** healthcare-onset, **50.8%**						
Ampicilllin	303	30.9 / -	57.0 / 87.9	25.3 / -	66.9 / 92.2	
Amoxycllin-calvulanate	314	3.8 / -	89.8 / 93.6	3.2 / -	89.8 / 93.0	
Ticarcillin-clavulanate	303	4.0 / 6.7	12.1 / 16.1	1.9 / 5.8	29.2 / 31.2	
Piperacillin-tazobactam	268	8.0 / 0.7	8.0 / 16.1	1.5 / 3.8	25.2 / 26.7	
Ceftriaxone	314	0.6 / 0.6	18.5 / 18.5	1.9 / 1.9	30.6 / 30.6	
Ceftazidime	314	0.6 / 2.5	15.9 / 16.6	0.0 / 1.3	28.0 / 28.0	
Cefepime	314	† 2.5 / 6.4	1.3 / 2.5	† 4.5 / 11.5	2.5 / 5.1	
Gentamicin	314	1.3 / 0.6	5.1 / 6.4	0.0 / 1.9	7.6 / 7.6	
Tobramycin	313	5.8 / 0.0	1.3 / 7.1	6.4 / 0.6	4.5 / 10.8	
Amikacin	314	0.0 / 1.3	0.0 / 0.0	0.0 / 1.3	0.0 / 0.0	
Ciprofloxacin	314	0.6 / 2.5	0.0 / 0.6	3.2 / 4.5	3.2 / 7.0	
Meropenem	314	0.6 / 1.3	2.5 / 1.3	0.0 / 0.6	3.2 / 2.5	
Klebsiella oxytoca						
Community-onset, **69.7%;** healthcare-onset, **30.3%**						
Ampicilllin	221	23.4 / -	73.4 / 96.8	14.9 / -	80.6 / 95.5	
Amoxycllin-calvulanate	221	1.9 / -	5.2 / 7.1	7.5 / -	13.4/ 20.9	
Ticarcillin-clavulanate	211	1.4 / 2.1	4.1 / 5.5	4.6 / 1.5	18.5 / 23.1	
Piperacillin-tazobactam	219	0.0 / 1.3	5.3 / 5.3	4.5 / 1.5	14.9 / 19.4	
Ceftriaxone	220	0.0 / 0.0	5.8 / 5.8	1.5 / 1.5	12.1 / 12.1	
Ceftazidime	221	0.6 / 0.6	0.0 / 0.6	0.0 / 1.5	3.0 / 3.0	
Cefepime	221	0.6 / 0.6	0.6 / 1.3	0.0 / 0.0	0.0 / 0.0	
Gentamicin	221	0.6 / 0.6	0.0 / 0.6	0.0 / 0.0	3.0 / 3.0	
Tobramycin	219	0.7 / 0.7	0.0 / 0.7	3.0 / 0.0	0.0 / 3.0	
Amikacin	221	0.0 / 0.0	0.0 / 0.0	0.0 / 0.0	0.0 / 0.0	
Ciprofloxacin	221	0.0 / 0.6	0.0 / 0.7	0.0 / 0.0	1.5 / 1.5	
Meropenem	221	0.0 / 0.0	0.0 / 0.0	0.0 / 1.5	0.0 / 1.5	
Proteus mirabilis						
Community-onset, **80.8%;** healthcare-onset: **19.2%**						
Ampicilllin	203	0.0 / -	20.1 / 20.1	0.0 / -	7.7 / 7.7	
Amoxycllin-calvulanate	203	9.8 / -	1.8 / 11.6	5.1 / -	0.0 / 5.1	
Ticarcillin-clavulanate	188	0.0 / 2.0	0.7 / 0.7	0.0 / 0.0	0.0 / 0.0	
Piperacillin-tazobactam	200	0.6 / 0.0	0.6 / 1.2	0.0 / 0.0	0.0 / 0.0	
Ceftriaxone	203	0.0 / 0.0	1.2 / 1.2	0.0 / 0.0	5.1 / 5.1	
Ceftazidime	203	0.0 / 0.0	1.2 / 1.2	0.0 / 0.0	2.6 / 2.6	
Cefepime	203	† 0.6 / 0.6	0.6 / 0.6	0.0 / 0.0	2.6 / 2.6	
Gentamicin	203	0.6 / 1.8	0.6 / 1.2	5.1 / 2.6	0.0 / 5.1	
Tobramycin	202	0.6 / 0.0	0.6 / 1.2	2.6 / 0.0	2.6 / 5.3	
Amikacin	203	0.0 / 0.6	0.0 / 0.0	0.0 / 5.1	0.0 / 0.0	
Ciprofloxacin	203	0.0 / 0.0	4.3 / 4.9	2.6 / 0.0	2.6 / 5.1	
Meropenem	202	0.0 / 0.0	0.0 / 0.0	0.0 / 0.0	0.0 / 0.0	

Organism	N	Community-onset (CO) %I	Community-onset (CO) %R	Healthcare –onset (HO) %I	Healthcare –onset (HO) %R	P*
Serratia marcescens						
Community-onset, **48.0%;** healthcare-onset: **52.0%**						
Ampicilllin	166	40.0 / -	33.8 / 73.8	39.5 / -	36.0 / 75.6	
Amoxycllin-calvulanate	173	22.9 / -	59.0 / 81.9	21.1 / -	65.6 / 86.7	
Ticarcillin-clavulanate	166	0.0 / 2.5	0.0 / 1.5	2.3 / 1.2	3.5 / 5.8	
Piperacillin-tazobactam **	129	-	-	-	-	
Ceftriaxone	173	0.0 / 0.0	0.0 / 0.0	1.1 / 1.1	5.6 / 5.6	
Ceftazidime	173	0.0 / 0.0	0.0 / 0.0	0.0 / 0.0	2.2 / 2.2	
Cefepime	173	0.0 / 0.0	0.0 / 0.0	1.1 / 1.1	0.0 / 1.1	
Gentamicin	173	0.0 / 0.0	0.0 / 0.0	0.0 / 0.0	4.4 / 4.4	
Tobramycin	172	6.1 / 12.2	0.0 / 6.1	13.3 / 7.8	3.3 / 16.7	
Amikacin	173	0.0 / 0.0	0.0 / 0.0	0.0 / 0.0	1.1 / 1.1	
Ciprofloxacin	173	1.2 / 0.0	0.0 / 2.4	0.0 / 1.1	1.1 / 3.3	
Meropenem	173	0.0 / 0.0	0.0 / 0.0	0.0 / 0.0	1.1 / 1.1	
Enterobacter aerogenes						
Community-onset, **54.7%;** healthcare-onset: **45.3%**						
Ampicilllin	116	18.6 / -	54.7 / 73.4	23.1 / -	61.5 / 84.6	
Amoxycllin-calvulanate	117	7.8 / -	82.8 / 90.6	9.4 / -	84.9 / 94.3	
Ticarcillin-clavulanate	116	6.3 / 3.1	28.1 / 34.4	15.4 / 3.8	32.7 / 48.1	
Piperacillin-tazobactam	116	4.7 / 3.1	29.7 / 34.4	19.2 / 3.8	28.8 / 48.1	
Ceftriaxone	117	0.0 / 0.0	37.5 / 37.5	3.8 / 3.8	45.3 / 45.3	
Ceftazidime	117	1.6 / 1.6	32.8 / 34.4	0.0 / 3.8	43.4 / 43.4	
Cefepime	117	† 3.1 / 0.0	1.6 / 4.7	3.8 / 0.0	0.0 / 3.8	
Gentamicin	117	0.0 / 1.6	3.1 / 3.1	0.0 / 0.0	1.9 / 1.9	
Tobramycin	116	0.0 / 0.0	3.1 / 3.1	1.9 / 0.0	1.9 / 3.8	
Amikacin	117	0.0 / 0.0	0.0 / 0.0	0.0 / 1.9	0.0 / 0.0	
Ciprofloxacin	117	1.6 / 0.0	3.1 / 6.3	0.0 / 0.0	3.8 / 3.8	
Meropenem	117	0.0 / 0.0	1.6 / 1.6	0.0 / 0.0	1.9 / 1.9	
***Salmonella* species (non Typhi)**						
Community-onset, **86.8%;** healthcare-onset: **13.2%**						
Ampicilllin	106	0.0 / 0.0	6.5 / 6.5	0.0 / -	21.4 / 21.4	
Amoxycllin-calvulanate	106	1.1 / 0.0	1.1 / 0.0	0.0 / 0.0	14.3 / 14.3	
Ticarcillin-clavulanate	104	0.0 / 5.6	1.1 / 1.1	7.1 / 7.1	7.1 / 14.3	
Piperacillin-tazobactam	106	0.0 / 0.0	0.0 / 0.0	7.1 / 0.0	0.0 / 7.1	
Ceftriaxone	106	0.0 / 0.0	1.1 / 1.1	0.0 / 0.0	7.1 / 7.1	
Ceftazidime	106	0.0 / 0.0	1.1 / 1.1	0.0 / 0.0	7.1 / 7.1	
Cefepime	106	0.0 / 0.0	0.0 / 0.0	0.0 / 0.0	0.0 / 0.0	
Gentamicin	106	0.0 / 0.0	1.1 / 1.1	0.0 / 0.0	7.1 / 7.1	
Tobramycin	106	0.0 / 1.1	0.0 / 0.0	0.0 / 0.0	7.1 / 7.1	
Amikacin	106	0.0 / 0.0	0.0 / 0.0	0.0 / 0.0	0.0 / 0.0	
Ciprofloxacin ‡	106	. / .	1.1 / 0.0	. / .	7.1 / 0.0	
Meropenem	106	0.0 / 0.0	0.0 / 0.0	0.0 / 0.0	0.0 / 0.0	

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

† SDD category for CLSI

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

5.1.1 EXTENDED-SPECTRUM B-LACTAMASES

Extended-spectrum ß-lactamases (ESBLs) are important problem resistances internationally. They have been predominantly a problem in hospital practice, and initially 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 (so-called CTX-M enzymes) in *E. coli* strains in the community. The latter is part of a global epidemic. It is unclear what is driving this community expansion of CTX-M ESBLs in Australia, as third-generation cephalosporins are not widely used in that setting. It is likely to be driven by cross-resistance and co-resistance to agents used in community practice. There is also increasing recognition of ESBLs becoming established in long-term care facilities in Australia. ESBLs are important because they compromise the efficacy of third-generation cephalosporins which have been such a useful therapeutic alternative for infections in patients presenting from the community, as evidenced by the freuqncy with which ceftriaxone was used for treatment in this survey. ESBL-harbouring strains frequently possess co-resistance to other non β-lactam agents. This can result in delays in the use of effective empiric therapy, with a lack of available oral options for treatment resulting in excess hospitalisation, and in the setting of sepsis, increased mortality.

Most ESBL-producing strains will be captured/recognised using the CLSI/EUCAST ceftriaxone "susceptible" breakpoint of 1 mg/L. The "susceptible"breakpoint of 4 mg/L for ceftazidime is less sensitive for ESBL detection, but an MIC > 1mg/L is more sensitive. **Isolates with either ceftriaxone or ceftazidime 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 that species, cefepime at 1 mg/L is suggestive that an isolate of this genus harbours an ESBL. However, due to card range limitations, **isolates with a cefepime MIC > 1mg/L were selected for molecular testing**.

Molecular testing involved screening for TEM, SHV, CTX-M and plasmid-borne AmpC genes. TEM screening does not accurately discriminiate between TEM-1/2 genes, which encode narrow-spectrum β-lactamases, from TEM genes with higher numbers that encode ESBLs. Similarly, SHV screening does not discriminate between SHV-1/11, which are narrow-spectrum β-lactamases, and SHV genes that encode ESBLs. SHV-1 is the dominant natural chromosomal enzyme of *K. pneumoniae* leading to natural ampicillin/amoxycillin resistance. *Therefore, E. coli isolates containing only TEM genes and Klebsiella species containing only SHV genes have not been classified as carrying an ESBL in this report*. All CTX-M genes encode ESBLs, as do plasmid-borne AmpC genes effectively.

Table 24. Presumptive and Confirmed Extended-spectrum ß-lactamase Production

Species	ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
Escherichia coli	149	1113	138	691	454	79	729	653	4006
ESBL phenotype	17	181	14	46	39	1	95	67	460
Ceftriaxone > 1 mg/L	10.7%	15.2%	8.7%	6.1%	7.5%	0.0%	12.2%	9.3%	10.6%
Ceftazidime > 1 mg/L	9.4%	14.5%	8.0%	5.6%	7.0%	1.3%	11.4%	8.6%	9.9%
Either of above	11.4%	16.3%	10.1%	6.7%	8.6%	1.3%	13.0%	10.3%	11.5%
Confirmed									
any ESBL* (No. received)	16/17	151/162	12/14	41/45	32/38	1/1	86/92	64/66	408/435
CTX-M types	15	135	10	28	28	0	78	55	349
plasmid-borne AmpC	1	18	2	12	3	0	7	9	52
SHV	1	1	0	2	1	0	2	1	14
Klebsiella pneumoniae	35	237	47	189	87	18	177	187	977
ESBL phenotype	2	22	3	8	5	1	23	11	75
Ceftriaxone > 1 mg/L	2.9%	6.8%	6.4%	3.7%	3.4%	5.6%	10.7%	3.7%	5.8%
Ceftazidime > 1 mg/L	5.7%	8.9%	2.1%	3.7%	4.6%	5.6%	12.4%	4.8%	6.9%
Either of above	5.7%	9.3%	6.4%	4.2%	5.7%	5.6%	13.0%	5.9%	7.7%
Confirmed									
any ESBL* (No. received)	1/2	15/19	3/3	6/7	3/5	1/1	17/23	7/11	53/71
CTX-M types	0	10	3	5	3	1	15	7	44
plasmid-borne AmpC	0	4	0	0	0	0	1	0	5
TEM	1	9	2	5	1	1	13	5	37

Species	ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
Klebsiella oxytoca	13	76	4	45	13	8	49	30	238
ESBL phenotype	1	10		3	3		3	2	22
Ceftriaxone > 1 mg/L	7.7%	10.5%	0.0%	6.7%	23.1%	0.0%	6.1%	6.7%	8.4%
Ceftazidime > 1 mg/L	0.0%	2.6%	0.0%	2.2%	15.4%	0.0%	0.0%	0.0%	2.1%
Either of above	7.7%	13.2%	0.0%	6.7%	23.1%	0.0%	6.1%	6.7%	9.2%
Confirmed									
any ESBL* (No. received)	0/1	0/9	0/0	1/3	0/3	0/0	2/3	0/2	3/21 †
CTX-M types	0	0	0	0	0	0	1	0	1
TEM	0	0	0	1	0	0	0	0	1
SHV	0	1	0	1	0	0	1	0	2
Proteus mirabilis	6	66	6	45	24	3	37	36	223
ESBL phenotype	0	1	0	1	0	0	2	1	5
Ceftriaxone > 1 mg/L	0.0%	1.5%	0.0%	2.2%	0.0%	0.0%	5.4%	2.8%	2.2%
Ceftazidime > 1 mg/L	0.0%	0.0%	0.0%	2.2%	0.0%	0.0%	5.4%	2.8%	1.8%
Either of above	0.0%	1.5%	0.0%	2.2%	0.0%	0.0%	5.4%	2.8%	2.2%
Confirmed									
any ESBL* (No. received)	-	1/1	-	1/1	-	-	1/2	1/1	4/5
CTX-M types	-	1	-	0	-	-	0	0	1
plasmid-borne AmpC	-	0	-	0	-	-	1	1	2
TEM	-	1	-	1	-	-	0	1	3
***Salmonella* (non-Typhi)**	1	19	24	28	10	2	21	10	115
ESBL phenotype	0	0	0	0	0	0	3	0	3
Ceftriaxone > 1 mg/L	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	14.3%	0.0%	2.6%
Ceftazidime > 1 mg/L	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	9.5%	0.0%	1.7%
Either of above	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	14.3%	0.0%	2.6%
Confirmed									
any ESBL* (No. received)	-	-	-	-	-	-	3/3	-	3/3
CTX-M types	-	-	-	-	-	-	1	-	1
plasmid-borne AmpC	-	-	-	-	-	-	2	-	2
TEM	-	-	-	-	-	-	2	-	2

* Strains may possess more than one type of ESBL gene

† See text for explanantion of low proportion of ESBL

Based on the tests performed in this study, ESBLs were more common among *E. coli* (10.2% confirmed) and *K. pneumoniae* (5.4% confirmed). For *Enterobacter* species with cefepime MIC > 1 mg/L, 22/42 *E. cloacae* (52%, 6.7% overall) and 2/4 *E. aerogenes* contained an ESBL. Of identified ESBLs, *E. cloacae* contained the following types: TEM and SHV-types (n=10), CTX-M group 1 and TEM (n=2), CTX-M group 9 only (n=2), and TEM only (n=8). Eight of 22 *E. cloacae* with ESBLs also contained bla_{IMP-4} carbapenemases.

The majority (67%) of *K. oxytoca* isolates with an ESBL phenotype were hyperproducers of K1 β-lactamase, the natural chromosomal enzyme in this species, rather than ESBL producers. Hyperproducers of K1 β-lactamase are consistently resistant to piperacillin-tazobactam, have borderline resistance to cefepime, but remain susceptible to ceftazidime. This pattern is not typical of other types of ESBL.

There was a notable presence of CTX-M enzymes in *E. coli.* Three hundred and forty-nine of 408 (85.5%; range 68.3%, -93.8%) confirmed ESBLs had CTX-M types; CTX-M group 1 (n=204), CTX-M group 9 (n=142), CTX-M group 1 and CTX-M group 9 (n=3). Among *K. pneumoniae* with confirmed ESBLs, 44/53 (83.0%) contained CTX-M types; CTX-M group 1 (n=37) and CTX-M group 9 (n=7).

ESBL phenotypes were significantly more likely to be found among healthcare- than community-onset episodes of *E. coli* (p=0.0017) and *E. cloacae* (p =0.0003) bacteraemia compared to all other species combined (Fisher's exact test). No significant difference was noted among *K. pneumoniae* (P=0.3475) for healthcare- versus community-onset.

5.1.2 PLASMID-BORNE AMPC B-LACTAMASES

Plasmid-borne AmpC ß-lactamases have recently emerged internationally as a growing Gram-negative resistance problem. They are the result of mobilization of natural chromosomally located genes from common and uncommon species of Enterobacteriaceae onto transmissible plasmids and into the common pathogens. There are currently six separate classes. 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 effectively 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.

Table 25. Presumptive plasmid-borne AmpC ß-lactamase Production

Species	ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
Escherichia coli	149	1113	138	691	454	79	729	653	4006
Cefoxitin ≥ 32 mg/L	2 (1.3%)	52 (4.7%)	4 (2.9%)	18 (2.6%)	12 (2.6%)	2 (2.5%)	26 (3.6%)	18 (2.8%)	134 (3.3%)
Confirmed (no. received)	0/2	18/49	2/4	10/17	3/12	0/2	6/26	8/17	47/129
bla_{CMY}	0	10	2	9	3	0	4	4	32
bla_{DHA}	0	8	0	1	0	0	2	4	15
Klebsiella pneumoniae	35	237	47	189	87	18	177	187	977
Cefoxitin ≥ 32 mg/L	2 (5.7%)	21 (8.9%)	1 (2.1%)	6 (3.2%)	2 (2.3%)	0	7 (4.0%)	8 (4.3%)	47 (4.8%)
Confirmed (no. received)	0/2	5/17	0/1	0/6	0/2	-	1/7	0/8	6/43
bla_{DHA}	0	4	0	0	0	-	1	0	5
bla_{CMY}	0	1	0	0	0	-	0	0	1
Klebsiella oxytoca	13	76	4	45	13	8	49	30	238
Cefoxitin ≥ 32 mg/L	0 (0.0%)	4 (5.3%)	0 (0.0%)	1 (2.2%)	1 (7.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	6 (2.5%)
Confirmed (no. received)	-	0/4	-	0/1	0/1	-	-	-	0/6

The proportions of *E. coli* and *K. pneumoniae* with elevated cefoxitin MICs were low. Only 36% (47/129) of cefoxitin-resistant *E. coli* and 14% (6/43) of *K. pneumoniae* that were available for molecular confirmation were confirmed to contain plasmid-borne AmpC. bla_{CMY} was found in 62% (33/53) of isolates with plasmid-borne AmpC genes. Carbapenamase genes were detected in three of the cefoxitin-resistant *K. pneumoniae* (bla_{IMP-4}, n=1; bla_{KPC-2}, n=1; $bla_{NDM+OXA-48}$, n=1) and one *K. oxytoca* (bla_{IMP-4}) that did not have plasmid-borne AmpC genes. Four *E. coli* with a cefoxitin MIC = 16 mg/L (intermediate) also contained bla_{CMY}.

5.1.3 CARBAPENEMASES

Twenty-six (0.35%) isolates from 24 patients were found to harbour a carbapenemase gene. bla_{IMP-4} was detected in 14 strains (*E. cloacae* (8, from 6 patients), *C. freundii* (2), *K. pneumoniae* (1), *K. oxytoca* (1), *R. ornithinolytica* (1), *S. marcescens* (1); bla_{OXA-48} was detected in four *K. pneumoniae* isolates (from two patients); bla_{KPC-2} was detected in one *K. pneumoniae*; bla_{GES-5} was detected in one *P. aeruginosa*; $bla_{NDM+OXA-48}$ in one *K. pneumoniae* and $bla_{IMP-4+VIM-2}$ in one *P. aeruginosa*. Fourteen of 22 isolates with confirmed metallo-β-lactamases also contained plasmid-mediated quinolone resistance genes (*aac(6')Ib-cr* alone or with *qnrA* or *qnrB*).

Three *E. cloacae* demonstrated carbapenemase activity by the carapenem inactivation method (CIM), but were negative for IMP, VIM, KPC, NDM, OXA-48-like, SIM, GIM, SPM, BIC, DIM, AIM, and GES. Phenotypic tests indicated a possible serine carbapenemase, however they did not contain SME or IMI. These strains were confirmed by sequencing to contain the newly described bla_{FRI-1}.[12] An additional *E. cloacae* isolate with elevated meropenem MIC was also confirmed to contain bla_{FRI-1}. This strain was CIM negative.

Overall prevelance of carbapenemase genes among *Enterobacteriaceae* was 0.38% (25/6567); and for *P. aeruginosa,* 0.15% (1/660). No carbapenemase genes were detected among 105 *Acinetobacter* species.

Table 26. Carbapenemases and Associated Resistance genes

Gene	State	Species	Meropenem MIC (mg/L)	ESBL Types [a]	PMQR [b]	16S rRNA methylases
***bla*$_{IMP-4}$** (n=14)	ACT	*K. pneumoniae* (n=1)	≥16	TEM, SHV	- [c]	-
	NSW	*E. cloacae* (n=1) [d]	≥16	TEM, SHV	*aac(6')Ib-cr, qnrB*	-
		E. cloacae (n=1) [d]	≥16	TEM, CTX-M	*aac(6')Ib-cr, qnrB*	-
		E. cloacae (n=1)	≥16	TEM	*qnrB*	
		E. cloacae (n=1)	≥16	TEM, SHV	*aac(6')Ib-cr*	
		E. cloacae (n=1)	1	TEM	*qnrS*	-
		C. freundii (n=2)	≥16	TEM	*qnrB*	-
		R. ornithinolytica (n=1)	1	TEM, SHV	*aac(6')Ib-cr, qnrB*	-
		S. marcescens (n=1)	≥16	-	-	-
	QLD	*E. cloacae* (n=2)	≥16	TEM	*aac(6')Ib-cr, qnrB*	-
		E. cloacae (n=1)	≥16	TEM	*aac(6')Ib-cr, qnrA, qnrB*	-
		K. oxytoca (n=1)	≥16	TEM, SHV	*qnrB*	-
***bla*$_{IMP-4 + VIM-2}$**	NSW	*P. aeruginosa* (n=1)	≥16	-	-	-
***bla*$_{FRI-1}$** (n=4)	WA	*E. cloacae* (n=2)	4	-	-	-
	VIC	*E. cloacae* (n=2)	0.5	-	-	-
***bla*$_{OXA-48}$** (n=4)	QLD	*K. pneumoniae* (n=2) [e]	1	SHV	-	-
	VIC	*K. pneumoniae* (n=1)	1	SHV	*qnrB*	-
		K. pneumoniae (n=1)	0.5	SHV	-	
***bla*$_{KPC-2}$**	VIC	*K. pneumoniae* (n=1)	≥16	SHV	-	-
***bla*$_{NDM + OXA-48}$**	SA	*K. pneumoniae* (n=1)	16	TEM, SHV, CTX-M-15	*aac(6')Ib-cr, qnrB*	-
***bla*$_{GES-5}$**	NSW	*P. aeruginosa* (n=1)	≥16	-	-	-

[a] TEM types, SHV types, CTX-M types, pAmpC
[b] *aac(6')Ib-cr*, Qnr, efflux (*qepA*, *opxAB*)
[c] not detected
[d] *bla*$_{IMP-4}$ from same patient
[e] *bla*$_{KPC-2}$ from same patient

5.1.4 QUINOLONE RESISTANCE

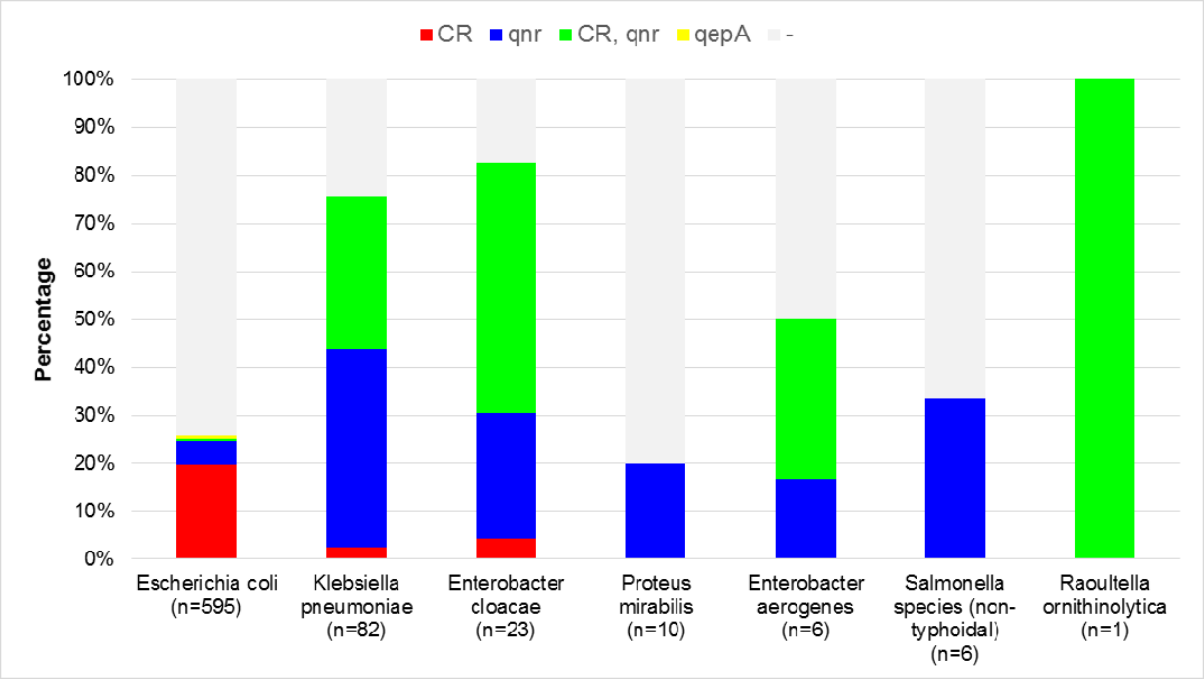
Quinolone resistance is most commonly due to mutations in DNA gyrase and topoisomerase IV. More recently plasmid-mediated quinolone resistance (PMQR) has emerged in Enterobacteriaceae. PMQR may be due to the presence of qnr genes (*qnrA*, *qnrB*, *qnrS*, q*nrC*, *qnrD*), *aac(6')-Ib-cr*, encoding for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

Table 27. Plasmid-mediated quinolone resistance

Species	ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
Escherichia coli	20	214	15	72	51	7	119	132	630
Ciprofloxacin > 0.25 mg/L	13.4%	19.3%	10.9%	10.4%	11.2%	8.9%	16.4%	20.2%	15.8%
Confirmed (no. received)	5/20	48/189	4/14	14/72	10/49	0/7	41/117	31/127	153/595 **[25.7%]**
aac(6')-Ib-cr	2	36	4	10	9	0	33	23	117
qnrS	2	8	0	2	1	0	5	6	24
qnrB	0	3	0	1	0	0	0	1	5
aac(6')-Ib-cr + *qnrB*	0	0	0	1	0	0	2	0	3
QepA	1	1	0	0	0	0	1	1	4
Klebsiella pneumoniae	2	24	3	14	5	1	24	16	89
Ciprofloxacin > 0.25 mg/L	5.7%	10.2%	6.4%	7.4%	5.9%	5.6%	13.6%	8.6%	9.1%
Confirmed (no. received)	0/2	18/21	2/3	11/13	2/4	1/1	20/23	8/15	62/82 **[75.6%]**
aac(6')-Ib-cr	0	0	0	0	1	0	1	0	2
qnrB	0	7	1	3	0	0	8	4	23
qnrS	0	3	0	2	0	0	0	2	7
qnrA	0	1	0	2	0	0	1	0	4
aac(6')-Ib-cr + *qnrB*	0	7	1	4	1	1	10	2	26
Enterobacter cloacae	1	10	0	4	0	0	7	2	24
Ciprofloxacin > 0.25 mg/L	10.0%	11.8%	0.0%	6.2%	0.0%	0.0%	8.8%	4.0%	7.4%
Confirmed (no. received)	1/1	7/9	-	4/4	-	-	7/7	0/2	19/23 **[82.6%]**
aac(6')-Ib-cr	0	0	-	0	-	-	1	0	1
qnrA	0	0	-	0	-	-	2	0	2
qnrB	0	0	-	1	-	-	1	0	2
qnrS	1	1	-	0	-	-	0	0	2
aac(6')-Ib-cr + *qnrA*	0	4	-	0	-	-	3	0	7
aac(6')-Ib-cr + *qnrB*	0	2	-	3	-	-	0	0	5

The proportion and type of PMQR determinant found among isolates with ciprofloxacin MIC > 0.25 mg/L varied among the different species (Figure 3). *Aac(6')-Ib-cr,* with or without Qnr, was dominant, and was present in five of the seven species.

Figure 3. Proportion of Plasmid-mediated quinolone resistance genes among species with ciprofloxacin MIC > 0.25 mg/L



CR = *aac(6')-Ib-cr*; qnr = qnrA, qnrB or qnrS

- = no PMQR detected; resistance likely due to mutations in DNA gyrase and topoisomerase IV

5.1.5 ESCHERICHIA COLI SEQUENCE TYPE 131

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

Most of the strains with an ESBL phenotype harboured genes of the CTX-M type (347/431, 81%). Sixty-four percent (132/206) 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 74% (200/269) of *E. coli* ESBL phenotypes that were ciprofloxacin resistant (MIC >1 mg/L), and only 6% (9/143) of ciprofloxacin susceptible ESBL phenotypes. Ninety-five percent (198/209) and 64% (133/209) of O25b-ST131 with an ESBL phenotype were associated with *H30* and *H30*-Rx subclones, respectively, which have a reported association with more antibiotic resistances and greater virulence potential.[13, 14] The *H30*-Rx subclone of ST131 often carried $bla_{CTX\text{-}M\text{-}15}$ and *aac(6')-Ib-cr.* As expected, > 98% of *E. coli* isolates received that were associated with the O25b-ST131 clone belonged to phylogenetic group B2.

Table 28. E. coli O25b-ST131 clone and ESBL phenotype

ESBL Type	N	*O25b-ST131*	*Non-O25b-ST131*
ESBL Phenotype	**431**	**209**	**222**
CTX-M types	347	200 (58%)	147 (42%)
CTX-M-15 like	201	132	69
H30 (*H30*-Rx) subclones	130 (125)	129 (125)	1 (0)
Non CTX-M-15 like	146	68	78
H30 (*H30*-Rx) subclones	66 (5)	65 (5)	1 (0)
Non CTX-M types	84	9 (11%)	75 (89%)
H30 (*H30*-Rx) subclones	5 (3)	4 (3)	1 (0)
ESBL with ciprofloxacin MIC > 1 mg/L	269	200 (74%)	69 (26%)
H30 (*H30*-Rx) subclones	199 (133)	198 (133)	1 (0)
ESBL with ciprofloxacin MIC ≤ 1 mg/L	143	9 (6%)	134 (94%)
H30 (*H30*-Rx) subclones	2 (0)	0 (0)	2 (0)

IMPORTANT CO-RESISTANCES

Strains harbouring extended-spectrum ß-lactamases are much more likely to harbour resistances to unrelated drug classes. The proportion of strains with ESBL phenoptype (MIC >1 mg/L to ceftriaxone or ceftazidime) which were resistant to other drug classes is shown in Table 29:

Table 29. Co-resistance percentages in strains with ESBL phenotype

EUCAST

Species	ESBL Phenotype Category	Ciprofloxacin	Gentamicin	Trimethoprim
Escherichia coli (n=460)	%I	4.1%	0.7%	0.2%
	%R	63.0%	32.4%	69.9%
Klebsiella pneumoniae (n=75)	%I	4.0%	1.3%	0.0%
	%R	49.3%	45.3%	76.0%

Further detail on co-resistances is contained in Appendix 2.

MULTI-RESISTANCE

The most problematic Gram-negative pathogens are those with multiple acquired resistances. Although there is no agreed benchmark for the definition of multi-resistance in Enterobacteriaceae, we have chosen acquired resistance to more than 3 agents to define multi-resistance in our survey. For each species, antibiotics were excluded from the count if they were affected by natural resistance mechanisms, so that only true acquired resistances were included. For the purposes of this analysis, resistance included intermediate susceptibility when the tested range did not go beyond the susceptible category.

Only isolates where the full range of antimicrobial agents were tested are included for multi-drug resistance determination. Note: Some institutions had either supressed reporting of cefazolin or used panels that did not include this agent. The agents included/excluded for each species are listed in the legend after Table 41. EUCAST breakpoints have been used with the proposed revised values for ciprofloxacin.

Table 30. Multiple acquired resistance in Escherichia coli [a]

	Non-multi-resistant						Multi-resistant										
Region	**Total**	**0**	**1**	**2**	**3**	**%**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**%**
ACT	146		67	22	29	80.8%	12	7	3	3	3	1	2					19.2%
NSW	1106	86	372	175	175	73.1%	95	74	34	41	21	25	8					26.9%
NT	137		47	26	32	76.6%	17	5	7	2		1						23.4%
QLD	676		286	105	143	79.0%	75	38	12	11		5	1					21.0%
SA	452	123	145	53	56	83.4%	29	19	12	7	2	5	1					16.6%
TAS	49		25	7	11	87.8%	3	1	2									12.2%
VIC	604		216	105	129	74.5%	54	52	20	9	14	3	2					25.5%
WA	573		218	109	103	75.0%	68	30	17	14	7	7						25.0%
Total	*3743*	*209*	*1376*	*602*	*678*	*76.5%*	*353*	*226*	*107*	*87*	*44*	*47*	*14*					*23.5%*

Table 31. Multiple acquired resistance in Klebsiella pneumoniae [b]

	Non-multi-resistant						Multi-resistant										
Region	**Total**	**0**	**1**	**2**	**3**	**%**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**%**
ACT	35		14	11	7	91.4%	2		1								8.6%
NSW	235	16	136	46	15	90.6%	6	1	3	5	5		2				9.4%
NT	47		18	19	5	89.4%	4					1					10.6%
QLD	184		121	41	10	93.5%	5	1		1	1	2	2				6.5%
SA	85	24	39	13	5	95.3%	1	1				1		1			4.7%
TAS	9		5	3	1	-											-
VIC	150		72	47	4	82.0%	5	8	4	5	3	1			1		17.3%
WA	164		92	48	9	90.9%	8	1	3	3							9.1%
Total	*909*	*40*	*497*	*228*	*56*	*90.3%*	*31*	*12*	*11*	*14*	*9*	*5*	*4*	*1*	*1*		*9.6%*

Table 32. Multiple acquired resistance in Enterobacter cloacae [c]

		Non-multi-resistant					Multi-resistant							
Region	**Total**	**0**	**1**	**2**	**3**	**%**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**%**
ACT	5	5				-								-
NSW	57	32	9	2	6	86.0%	3	3	2					14.0%
NT	9	4	3		1	-			1					-
QLD	64	38	8	1	7	84.4%	4	4		1	1			15.6%
SA	13	5	7	1		100.0%								0.0%
TAS	11	5	4		1	90.9%	1							9.1%
VIC	77	41	13	3	9	85.7%	5	1		4	1			14.3%
WA	41	24	6	1	6	90.2%	4							9.8%
Total	*277*	*154*	*50*	*8*	*30*	*87.4%*	*17*	*8*	*3*	*5*	*2*			*12.6%*

Table 33. Multiple acquired resistance in Proteus mirabilis [a]

		Non-multi-resistant					Multi-resistant											
Region	**Total**	**0**	**1**	**2**	**3**	**%**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**%**
ACT	6			6		-												-
NSW	65	1	8	40	6	84.6%	5	2	2	1								15.4%
NT	6			4	2	-												-
QLD	42			33	7	95.2%	1					1						4.8%
SA	24	1	11	7	2	87.5%	3											12.5%
TAS	2			2		-												-
VIC	34			25	4	85.3%	2	2				1						14.7%
WA	26		1	18		73.1%	5	1	1									26.9%
Total	*205*	*2*	*20*	*135*	*21*	*86.8%*	*16*	*5*	*3*	*1*		*2*						*13.2%*

Table 34. Multiple acquired resistance in Klebsiella oxytoca [b]

		Non-multi-resistant					Multi-resistant										
Region	**Total**	**0**	**1**	**2**	**3**	**%**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**%**
ACT	13		12			92.3%	1										7.7%
NSW	76	8	51	6	7	94.7%	4										5.3%
NT	4		4			-											-
QLD	43		38	1	1	93.0%	2			1							7.0%
SA	13	2	8			76.9%	2	1									23.1%
TAS	4		3	1		-											-
VIC	41		37		2	95.1%	1	1									4.9%
WA	23		18	1	1	87.0%	3										13.0%
Total	*217*	*10*	*171*	*9*	*11*	*92.6%*	*13*	*2*		*1*							*7.4%*

Table 35. Multiple acquired resistance in Serratia marcescens [c]

Region	Total	Non-multi-resistant					Multi-resistant							
		0	1	2	3	%	4	5	6	7	8	9	10	%
ACT	0					-								-
NSW	59		52	3	2	96.6%	1		1					3.4%
NT	3		2	1		-								-
QLD	42		40		1	97.6%	1							2.4%
SA	9		8		1	-								-
TAS	3		3			-								-
VIC	19		18	1		100.0%								0.0%
WA	7		7			-								-
Total	142		*130*	*5*	*4*	*97.9%*	*2*		*1*					2.1%

Table 36. Multiple acquired resistance in Enterobacter aerogenes [c]

Region	Total	Non-multi-resistant					Multi-resistant							
		0	1	2	3	%	4	5	6	7	8	9	10	%
ACT	4		1		2	-	1							-
NSW	34	8	9	4	7	82.4%	4	1	1					17.6%
NT	3	2				-	1							-
QLD	25	9	8	2	3	92.0%		1	1					8.0%
SA	11	5	3		2	90.9%	1							9.1%
TAS	1					-	1							-
VIC	27	6	6		5	63.0%	6		2	2				37.0%
WA	25	10	6		7	92.0%	2							8.0%
Total	*130*	*40*	*34*	*6*	*26*	*81.5%*	*16*	*2*	*4*	*2*				*18.5%*

Table 37. Multiple acquired resistance in Salmonella species (non-typhoidal) [a]

Region	Total	Non-multi-resistant					Multi-resistant										
		0	1	2	3	%	4	5	6	7	8	9	10	11	12	13	14	%
ACT	1		1			-												-
NSW	19	1	16	1		94.7%			1									5.3%
NT	24		24			100.0%												0.0%
QLD	28		24	3		96.4%	1											3.6%
SA	9	7	2			-												-
TAS	0					-												-
VIC	16		12	1	2	87.5%	1		1									12.5%
WA	9		6	3		-												-
Total	106	*8*	*85*	*8*	*1*	*96.2%*	*2*		*2*									3.8%

Table 38. Multiple acquired resistance in Morganella morganii [c]

Region	Total	Non-multi-resistant					Multi-resistant							
		0	1	2	3	%	4	5	6	7	8	9	10	%
ACT	4	1	3			-								-
NSW	26	3	18	4	1	100.0%								0.0%
NT	0					-								-
QLD	25	5	17	2		96.0%		1						4.0%
SA	7	1	3	2		-			1					-
TAS	1			1		-								-
VIC	9	2	4	3		-								-
WA	7	1	5			-	1							-
Total	79	*13*	*50*	*12*	*1*	*96.2%*	*1*	*1*	*1*					3.8%

Table 39. Multiple acquired resistance in Citrobacter koseri [c]

Region	Total	Non-multi-resistant					Multi-resistant							
		0	1	2	3	%	4	5	6	7	8	9	10	%
ACT	1		1			-								-
NSW	20	18	1		1	100.0%								0.0%
NT	1					-		1						-
QLD	6	6				-								-
SA	10	10				100.0%								0.0%
TAS	0					-								-
VIC	5	5				-								-
WA	11	11				100.0%								0.0%
Total	*54*	*50*	*2*		*1*	*98.1%*		*1*						*1.9%*

Table 40. Multiple acquired resistance in Citrobacter freundii [c]

Region	Total	Non-multi-resistant					Multi-resistant							
		0	1	2	3	%	4	5	6	7	8	9	10	%
ACT	4	3		1		-								-
NSW	19	8		2	5	78.9%	3	1						21.1%
NT	0					-								-
QLD	4	3		1		-								-
SA	4	3			1	-								-
TAS	1	1				-								-
VIC	9	8		1		-								-
WA	2	1	1			-								-
Total	*43*	*27*	*1*	*5*	*6*	*90.7%*	*3*	*1*						*9.3%*

Table 41. Multiple acquired resistance in Salmonella species (typhoidal) [a]

		Non-multi-resistant					Multi-resistant										
Region	**Total**	**0**	**1**	**2**	**3**	**%**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**%**
ACT	1		1			-												-
NSW	4		4			-												-
NT	0																	-
QLD	5		3	1	1	-												-
SA	4	3		1		-												-
TAS	0					-												-
VIC	6		6			-												-
WA	1		1			-												-
Total	21	3	15	2	1	100.0%												0.0%

Legend: (Tables 29 to 40)

[a] **Antibiotics included**: ampicillin, amoxycillin-clavulanate, piperacillin-tazobactam, cefazolin, cefoxitin, ceftriaxone, ceftazidime, cefepime, gentamicin, amikacin, ciprofloxacin, nitrofurantoin, trimethoprim, meropenem
Antibiotics excluded: ticarcillin-clavulanate, tobramycin, norfloxacin, nalidixic acid, sulfamethoxazole-trimethoprim.

[b] **Antibiotics included**: amoxycillin-clavulanate, piperacillin-tazobactam, cefazolin, cefoxitin, ceftriaxone, ceftazidime, cefepime, gentamicin, amikacin, ciprofloxacin, nitrofurantoin, trimethoprim, meropenem
Antibiotics excluded: ampicillin, ticarcillin-clavulanate, tobramycin, norfloxacin, nalidixic acid, sulfamethoxazole-trimethoprim

[c] **Antibiotics included**: piperacillin-tazobactam, ceftriaxone, ceftazidime, cefepime, gentamicin, amikacin, ciprofloxacin, nitrofurantoin, trimethoprim, meropenem
Antibiotics excluded: ampicillin, amoxycillin-clavulanate, cefazolin, cefoxitin, ticarcillin-clavulanate, tobramycin, norfloxacin, nalidixic acid, sulfamethoxazole-trimethoprim

5.1.6 ONSET SETTING AND 30-DAY ALL-CAUSE MORTALITY BY MULTIDRUG RESISTANCE

Onset setting (community or hospital) and 30-day all-cause mortality by multi-drug resistance for the most common species is shown in Table 42.

Table 42. Onset Setting and 30-day all-cause Mortaiity by multidrug resistance

		Community onset		Hospital-onset		Total	
Species	**Category** [a]	**n**	**mortality, % (n)**	**n**	**mortality, % (n)**	**n**	**mortality, % (n)**
Escherichia coli	Total	1880	8.6% (162)	392	20.9% (82)	2272	10.7% (244)
	non-MDR (<=3)	1475	8.4% (124)	259	20.8% (54)	1734	10.3% (178)
	MDR (>3)	405	9.4% (38)	133	21.1% (28)	538	12.3% (66)
Klebsiella pneumoniae	Total	431	12.8% (55)	179	16.2% (29)	610	13.8% (84)
	non-MDR (<=3)	395	12.7% (50)	153	15.7% (24)	548	13.5% (74)
	MDR (>3)	36	13.9% (5)	26	19.2% (5)	62	16.1% (10)
Pseudomonas aeruginosa	Total	228	18.4% (42)	178	18.5% (33)	406	18.5% (75)
	non-MDR (<=3)	228	18.4% (42)	169	16.6% (28)	397	17.6% (70)
	MDR (>3)	0		9	55.6% (5)	9	55.6% (5)
Pseudomonas aeruginosa	Total	228	18.4% (42)	178	18.5% (33)	406	18.5% (75)
	non-MDR (<=2)	225	18.7% (42)	163	16.0% (26)	388	17.5% (68)
	MDR (>2)	3	0.0% (0)	15	46.7% (7)	18	38.9% (7)
Enterobacter cloacae complex	Total	99	12.1% (12)	101	10.9% (11)	200	11.5% (23)
	non-MDR (<=3)	89	9.0% (8)	78	10.3% (8)	167	9.6% (16)
	MDR (>3)	10	40.0% (4)	23	13.0% (3)	33	21.2% (7)

[a] Multidrug resistance was as defined in 5.2. For *P. aeruginosa*, MDR (>2 agents) was also included.

LIMITATIONS OF THE STUDY

Although this study is comprehensive in its coverage of Australia, and the methodology follows international standards, there are a small number of limitations to the data and its interpretation.

1. The data are not denominator controlled. There is currently no consensus on an appropriate denominator for such surveys. Institution size, patient throughput, patient complexity and local antibiotic use patterns very much determine the types of resistance likely to be observed.
2. Although data have been collected from 31 large laboratories across Australia, it is unclear how representative the sample is of Australia as a whole, i.e. what proportion of the population are served by these laboratories. Further it is likely that the proportion of the population served differs across the jurisdictional groupings used in this report.

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Royal Prince Alfred Hospital, NSW	Sebastian van Hal and Bradley Watson
SA Pathology, Flinders Medical Centre, SA	Kelly Papanaoum and Nicholas Wells
SA Pathology, Royal Adelaide Hospital, SA	Morgyn Warner and Kija Smith
SA Pathology, Women's and Children's Hospital, SA	Morgyn Warner and Kija Smith
St John of God Pathology, WA	Sudha Pottumarthy-Boddu and Fay Kappler
St Vincent's Hospital, VIC	Mary Jo Waters and Lisa Brenton
Sullivan Nicolaides Pathology, QLD	Jenny Robson and Georgia Peachey
The Canberra Hospital, ACT	Peter Collignon and Susan Bradbury
Westmead Hospital, NSW	Jon Iredell and Andrew Ginn
Wollongong Hospital, NSW	Peter Newton and Melissa Hoddle

8 SUMMARY REPORTS

SUSCEPTIBILITY RESULTS BY STATE

Summary reports for all species can be accessed by following pdf hyperlink. National reports provide summary susceptbility data (number and percent (if more than 10 isolates) using both CLSI and EUCAST interpretative guidelines for all species isolated. Where more than ten isolates this data is seperated into state summaries.

NOTE: These links to be redirected to the 2015 data

National Reports		State Reports	
Amikacin.pdf	Gentamicin.pdf	Amikacin.pdf	Gentamicin.pdf
Amoxicillin-clavulanate.pdf	Meropenem.pdf	Amoxicillin-clavulanate.pdf	Meropenem.pdf
Ampicillin.pdf	Nitrofurantoin.pdf	Ampicillin.pdf	Nitrofurantoin.pdf
Cefazolin.pdf	Norfloxacin.pdf	Cefazolin.pdf	Norfloxacin.pdf
Cefepime.pdf	Piperacillin-tazobactam.pdf	Cefepime.pdf	Piperacillin-tazobactam.pdf
Cefoxitin.pdf	Ticarcillin-clavulanate.pdf	Cefoxitin.pdf	Ticarcillin-clavulanate.pdf
Ceftazidime.pdf	Tobramycin.pdf	Ceftazidime.pdf	Tobramycin.pdf
Ceftriaxone.pdf	Trimethoprim.pdf	Ceftriaxone.pdf	Trimethoprim.pdf
Ciprofloxacin.pdf		Ciprofloxacin.pdf	

ANTIBIOTIC PROFILES BY FREQUENCY

Only isolates where the full range of antimicrobial agents were tested are included in the profiles. The regional antibiotic profiles for the top 12 species can be accessed by following the hyperlinks. Profiles are generated using EUCAST guidelines.

Citrobacter freundii.pdf
Citrobacter koseri.pdf
Enterobacter aerogenes.pdf
Enterobacter cloacae.pdf
Escherichia coli.pdf
Klebsiella oxytoca.pdf
Klebsiella pneumoniae.pdf
Morganella morganii.pdf
Proteus mirabilis.pdf
Salmonella spp. (nonTyphi/Paratyphi).pdf
Salmonella Typhi/Paratyphi.pdf
Serratia marcescens.pdf

APPENDIX A. STUDY DESIGN

Thirty-one institutions from each State and mainland Territories of Australia participated in the EnSOP 2015 survey. Each institution collected either all or up to 200 isolates from different patient episodes of bacteraemia. In patients with more than one isolate, a new episode was defined as a new positive blood culture more that 2 weeks after the initial positive culture.

All laboratories obtained basic laboratory information, plus the following demographic information for each patient episode. At *Bronze* level; date of collection, date of birth, gender, postcode, admission date. Enrollment at *Silver* level participating laboratories provided discharge date, device related infection, principal clinical manifestation, ICU admission, outcome at 30 days, and date of death. Additional provision of principal antimicrobial treatment was obtained with *Gold* level enrollment.

Table A1. Level of Participation

State	Number of Institutions	Level of Participation		
		Bronze	*Silver*	*Gold*
Australian Capital Territory (ACT)	1	1		
New South Wales (NSW)	7	1		6
Northern Territory (NT)	2	1		1
Queensland (QLD)	6	1	1	4
South Australia (SA)	3	2		1
Tasmania (TAS)	1			1
Victoria (VIC)	5	1		4
Western Australia (WA)	6	3		3
Total	31	10	1	20

APPENDIX B. METHODS

SPECIES IDENTIFICATION

Isolates sampled were all members of the Enterobacteriaceae family. Isolates were identified using the routine method for each institution; Vitek®, Phoenix™ Automated Microbiology System, or where available mass spectrometry (MALDI-TOF).

SUSCEPTIBILITY TESTING

Testing was performed by two commercial semi-automated methods, Vitek® 2 (BioMérieux) (n=24) or Phoenix™ (BD) (n=2), which are calibrated to the ISO reference standard method of broth microdilution. Commercially available Vitek® 2 AST-N246 or Phoenix™ NMIC-203 cards were utilized by all participants throughout the survey period.
The CLSI M100-A26[1] and EUCAST v6.0[2] breakpoints from January 2016 have been employed in the analysis. For analysis of cefazolin, breakpoints of ≤4 for susceptible, ≥8 for resistant were applied due to the restricted minimum inhibitory concentration (MIC) range available on the commercial cards, recognising that the January 2016 breakpoint is actually susceptible ≤2 mg/L.

ANTIBIOTICS TESTED

Table A2. Antimicrobials Tested

	Breakpoints (mg/L)						
	CLSI M100 [a]				EUCAST v6.0 [b]		
Antimicrobial Agent	**S**	**SDD**	**I**	**R**	**S**	**I**	**R**
Ampicillin	≤ 8		16	≥ 32	≤ 8	.	≥ 16
Amoxicillin-Clavulanic Acid	≤ 8/4		16/8	≥ 32/16	≤ 8	.	≥ 16
Amikacin	≤ 16		32	≥ 64	≤ 8	16	≥ 32
Aztreonam							
***Acinetobacter* spp.**	-		-	-	-	-	-
Enterobacteriaceae	≤ 4		8	≥ 16	≤ 1	2 - 4	≥ 8
***Pseudomonas* spp.**	≤ 8		16	≥ 32	≤ 1	2 - 16	≥ 32
Ceftazidime							
***Acinetobacter* spp.**	≤ 8		16	≥ 32	-	-	-
Enterobacteriaceae	≤ 4		8	≥ 16	≤ 1	2 - 4	≥ 8
***Pseudomonas* spp.**	≤ 8		16	≥ 32	≤ 8	.	≥ 16
Ciprofloxacin							
***Acinetobacter* spp.**	≤ 1		2	≥ 4	≤ 1	.	≥ 2
Enterobacteriaceae	≤ 1		2	≥ 4	≤ 0.5	1	≥ 2
***Salmonella* spp.** [c]	≤ 0.06		0.12 - 0.5	≥ 1	≤ 0.06	.	≥ 0.12
***Pseudomonas* spp.**	≤ 1		2	≥ 4	≤ 0.5	1	≥ 2
Ceftriaxone							
***Acinetobacter* spp.**	≤ 8		16 - 32	≥ 64	-	-	-
Enterobacteriaceae	≤ 1		2	≥ 4	≤ 1	2	≥ 4
***Pseudomonas* spp.**	-		-	-	-	-	-
Cephalothin	≤ 8		16	≥ 32	-	-	-
Cefazolin (Australian) [d]	≤ 2		4	≥ 8	≤ 2	4	≥ 8
Cephalexin	-		-	-	≤ 16	.	≥ 32
Cefepime							
***Acinetobacter* spp.**	≤ 8		16	≥ 32	-	-	-
Enterobacteriaceae	≤ 2	4 - 8	-	≥ 16	≤ 1	2 - 4	≥ 8
***Pseudomonas* spp.**					≤ 8	.	≥ 16

Antimicrobial Agent	Breakpoints (mg/L)						
	CLSI M100 [a]				EUCAST v6.0 [b]		
	S	SDD	I	R	S	I	R
Cefoxitin	≤ 8		16	≥ 32	-	-	-
Chloramphenicol	≤ 8		16	≥ 32	≤ 8	.	≥ 16
Colistin	-		-	-	≤ 2	.	≥ 4
***Acinetobacter* spp.**	≤ 2		4	≥ 8	≤ 2	.	≥ 4
Enterobacteriaceae	-		-	-	≤ 2	.	≥ 4
***Pseudomonas* spp.**	≤ 2		4	≥ 8	≤ 4		≥ 8
Ertapenem	≤ 0.5		1	≥ 2	≤ 0.5	1	≥ 2
Fosfomycin	≤ 64		128	≥ 256	≤ 32	.	≥ 64
Gentamicin							
***Acinetobacter* spp.**	≤ 4		8	≥ 16	≤ 4	.	≥ 8
Enterobacteriaceae	≤ 4		8	≥ 16	≤ 2	4	≥ 8
***Pseudomonas* spp.**	≤ 4		8	≥ 16	≤ 4	.	≥ 8
Imipenem							
***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
Meropenem	≤ 1		2	≥ 4	≤ 2	4 - 8	≥ 16
***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	≤ 32		64	≥ 128	≤ 64	.	≥ 128
Norfloxacin							
***Acinetobacter* spp.**	-		-	-	-	-	-
Enterobacteriaceae	≤ 4		8	≥ 16	≤ 0.5	1	≥ 2
***Pseudomonas* spp.**	≤ 4		8	≥ 16	-	-	-
Tetracycline							
***Acinetobacter* spp.**	≤ 4		8	≥ 16	-	-	-
Enterobacteriaceae	≤ 4		8	≥ 16	-	-	-
***Pseudomonas* spp.**	-		-	-	-	-	-
Ticarcillin-Clavulanic Acid							
***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	-		-	-	≤ 1	2	≥ 4
Trimethoprim	≤ 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
***Pseudomonas* spp.**	-		-	-	-	-	-
Tobramycin							
***Acinetobacter* spp.**	≤ 4		8	≥ 16	≤ 4	.	≥ 8
Enterobacteriaceae	≤ 4		8	≥ 16	≤ 2	4	≥ 8
***Pseudomonas* spp.**	≤ 4		8	≥ 16	≤ 4	.	≥ 8
Piperacillin-Tazobactam							
***Acinetobacter* spp.**					-	-	-
Enterobacteriaceae	≤ 16/4		32/4 - 64/4	≥ 128/4	≤ 8	16	≥ 32
***Pseudomonas* spp.**					≤ 16	.	≥ 32

[a] The breakpoints selected to determine resistance are described in Performance Standards for Antimicrobial Susceptibility Testing: Twenty-fifth Information Supplement, CLSI document M100-S26, January 2016

[b] The European Committee on Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs and zone diameters. Version 6.0, 2016. http://www.eucast.org.

[c] Concentration range available on the cards restricts ability to determine susceptible category.

[d] For analysis, breakpoints of ≤4 mg/L for susceptible and ≥8 mg/L for resistant were appied due to the MIC range available on the Vitek card, recognising that the January 2013 breakpoint is actually susceptible ≤ 2 mg/L

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 (SA Pathology) 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.[3,4] A multiplex real-time TaqMan PCR was used to detect CTX-M-type genes.[5] Strains were probed for plasmid-borne AmpC enzymes using the method described by Pérez-Pérez and Hanson,[6]. and subjected to molecular tests for MBL (bla_{VIM}, bla_{IMP}, and bla_{NDM}), bla_{KPC}, and $bla_{OXA-48-like}$ genes using real-time PCR.[7,8]
Known plasmid mediated quinolone resistance (PMQR) 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.[9,10] All referred *E. coli* were examined for phylogenetic group and membership of the O25b-ST131 clone and its *H30*- and *H30*-Rx subclones.[11-13]

QUALITY CONTROL

Quality control strains utilised were those recommended by CLSI/EUCAST standards.

DEMOGRAPHICS

DATA REQUIREMENT	RATIONALE
BASIC DATA	
Blood culture isolate data for ONE patient episode	It is not uncommon to have multiple positive blood culture sets from a single patient episode of bacteraemia. For epidemiological purposes, only episodes count, so we need only record laboratory data from the first positive culture from that episode.
Vitek or Phoenix raw data (MIC required)	Data are best analysed on the basis of MIC, rather than categorical interpretation. This is because: • It permits re-analysis if and when breakpoints change • It captures additional information about acquired resistance with strains that have MICs elevated above wild-type, but still susceptible when the clinical breakpoint is applied
Date of blood culture collection	This allows calculation of the onset category (community versus hospital)
Laboratory number (for isolate being reported)	Laboratory number allows the database managers to contact the participating laboratory should there be questions about particular database entries (errors or omissions)
Patient Date of Birth	This field permits analysis of outcome by age, known to have a strong association with outcome
Patient Sex	Bacteraemia is more likely in males than females, and linked with age, can help explain variation in outcomes
Patient Date of Admission	This information is essential to assist us in categorising the bacteraemia as • Community-onset: first positive BC collected ≤ 2days after admission • Hospital-onset: first positive BC collected > 2days after admission We realise that many laboratories are unable to get time of admission easily, and hence some episodes which are greater than 48 hours after admission will be categorised as ≤ 2 days after admission
Storage and shipping of isolates (one per episode)	We require all isolates to be stored and sent to the two reference laboratories for more detailed testing
DEMOGRAPHIC DATA	
Patient Postcode	Postcode is linked to Socio-Economic Indexes for Areas (SEIFA) scores (http://www.abs.gov.au/websitedbs/censushome.nsf /home/seifa), another potential influence on outcome
Date of Discharge	Length of stay can be estimated using this field and Date of Admission

DATA MANAGEMENT

From January 1, 2014 AGAR national resistance surveillance comprises three major programs (*Staphylococcus aureus*, *Enterococcus* spp., and Enterobacteriaceae; *Pseudomonas aeruginosa* and *Acinetobacter* species added in 2015) and will monitor resistance in isolates from blood cultures only. Participating laboratories selected three levels of participation, based on availability of appropriate technology and personnel:

- **Gold Participant**: able to collect all required laboratory, demographic and clinical data
- **Silver Participant**: able to collect all required laboratory data and a limited set of additional demographic data
- **Bronze Participant**: able to collect all required laboratory data only plus Date of Admission

Participating laboratories that service more than one hospital collect data from only one of the hospitals (usually the largest) that they serve.

DATA REQUIREMENT	GOLD	SILVER	BRONZE	NOTE
BASIC DATA				1
Blood culture isolate data for each patient episode				2
S. aureus and *Enterococcus* spp.	●	●	●	3
Enterobacteriaceae	●	●	●	4
Vitek or Phoenix raw data (MIC required)	●	●	●	5
Date of blood culture collection	●	●	●	
Laboratory number (for isolate being reported)	●	●	●	
Species isolated	●	●	●	6
Patient Date of Birth	●	●	●	
Patient Sex	●	●	●	
Patient Postcode	●	●	●	
Patient Date of Admission	●	●	●	7
Storage and shipping of isolates (one per episode)	●	●	●	8
DEMOGRAPHIC DATA				
Patient is an Aboriginal or TS Islander Y/N	●	●		
Date of Discharge	●	●		9
CLINICAL AND OUTCOME DATA				
Device-related Infection Y/N (*S. aureus* only)	●	●		
Principal Clinical Manifestation	●	●		10
ICU admission required Y/N/Already in ICU	●	●		
Outcome at 30 days (Died/Survived/Unknown)	●	●		
Date of Death ≤ 30 days if died	●	●		
Principal Antimicrobial Treatment	●			10,11

Notes

1. Episode is defined as a single bacteraemic event, with compatible clinical symptoms, no matter how many sets of blood cultures were taken or how many were positive during that event. Isolation of the same species from the same patient more than 14 days after the initial positive blood culture is considered a new episode, regardless of any treatment, unless that species was also isolated at least one more time within that 14 days.
2. Data should be collected on all isolates for *S. aureus* and *Enterococcus* spp.
3. All members of the Enterobacteriaceae family are to be included. Please note that while *Salmonella* Typhi remains on the SSBA Tier 2 list, this serotype should be handled according to legislative requirements and referred to an SSBA-registered laboratory where necessary. This does NOT apply to *Salmonella* Paratyphi serotypes, which can be included in the data collection.
4. All blood culture isolates that are presumed associated with disease (as the targeted species are) should be tested on a semi-automated instrument (Vitek 2 or Phoenix). Raw MIC data is extracted from the instrument used.
5. Blood cultures that have more than one AGAR surveillance program organism in them can be entered. For instance, finding *E. coli* and *K. pneumoniae* in the one episode can still be entered twice into EnSOP, or *E. coli* plus *S. aureus* in the one episode can be entered into EnSOP and ASSOP respectively. Organisms found in polymicrobial bacteraemia that are not part of any of the surveillance programs are ignored for reporting purposes.
6. Date of Admission (assuming the patient has been admitted) is required for all levels of participation.
7. All isolates of *S. aureus* and *Enterococcus* spp. were shipped on a quarterly basis to the *ACCESS* Typing and Research Laboratory at Fiona Stanley Hospital, Perth. Selected isolates of Enterobacteriaceae were shipped to the ACARE laboratory, The University of Adelaide
8. Date of Discharge, or Date of Death if ≤ 30 days, or not discharged > 60 days after date of blood culture collection
9. Drop down menus specific to each of the 3 programs have been created for the data entry screens. See Appendix 4
10. Principal antimicrobial treatment is the definitive initial therapy, usually intravenous, used to treat the infection, not the empirical regimen initially used (they could be the same of course), nor the oral-switch therapy, even though that could be given for longer than the IV in a total treatment course.

DATA VALIDATION

Various checks are made to ensure data is valid. These include:

Null values in the mandatory fields
Missing MIC data
Age ≥ 100 or < 0 years of age
Date of collection > discharge date
Discharge date < date of admission
Date of admission < date of birth
Date of admission < date of collection + 2 d

APPENDIX C. RELEVANCE OF ANTIMICROBIALS TESTED

B-LACTAMS

This group of agents are the **mainstay of treatment** for Gram-negative infections in all settings, being the drugs of choice for both minor outpatient infections (e.g. lower UTI), and serious community-acquired infections (e.g. septicaemia)

Ampicillin: an aminopenicillin, used to predict resistance to ampicillin and amoxycillin. Considered the drugs of choice for susceptible *E. coli.* [Parenteral, oral; widespread community, mainly as amoxycillin, and hospital use]

Amoxycillin-clavulanate: a ß-lactamase inhibitor combination. Multiple uses including infections caused by ampicillin-resistant strains of *E. coli* and *Klebsiella* species. [Oral, widespread hospital and community use]

Piperacillin-tazobactam: a ß-lactamase inhibitor combination. Broad spectrum agent with multiple uses including against Gram-negative bacteria resistant to other agents. Similar activity to ticarcillin-clavulanate, another widely used ß-lactamase inhibitor combination. [Parenteral, limited hospital use]

Cefazolin: first-generation cephalosporin used for treating common Gram-negative and Gram-positive pathogens. Cefazolin is an important agent for surgical prophylaxis and penicillin-allergic patients. [Parenteral, cephalexin is the nearest oral equivalent, widespread community and hospital use]

Cefoxitin: second-generation cephalosporin, although better described as a cephamycin due to its unique spectrum. Very limited clinical use in surgical prophylaxis. Used in this study to screen for potential AmpC ß-lactamases. [Parenteral, very limited hospital use]

Ceftriaxone: a third-generation cephalosporin. For Enterobacteriaceae, testing results predict cefotaxime. Susceptible to extended-spectrum β-lactamases and to derepressed AmpC β-lactamases. Multiple specialised clinical uses. [Parenteral, extensive hospital use, strictly avoided in some hospitals]

Ceftazidime: a third-generation cephalosporin but with additional antipseudomonal activity. Susceptible to extended-spectrum ß-lactamases and to derepressed AmpC β-lactamases and included in this study for that reason. Main role in Australia as an antipseudomonal agent. [Parenteral, modest hospital use in specialized units]

Cefepime: a fourth generation cephalosporin, but with activity against organisms producing AmpC ß-lactamases, both natural (chromosomal cephalosporinases) and acquired. [Parenteral, modest hospital use in specialized units]

Meropenem: a carbapenem. Predicts activity of most of the other carbapenems, imipenem and doripenem, against Enterobacteriaceae. Last-line agent used for multi-resistant Gram-negative infections, presumptive and proven. [Parenteral, modest restricted hospital use]

OTHER ANTIMICROBIAL CLASSES

Ciprofloxacin: a fluoroquinolone. Predicts resistance in Gram-negatives to other fluoroquinolones, ofloxacin, moxifloxacin. Resistance to ciprofloxacin confirms resistance to norfloxacin. Valuable oral agent reserved for infections caused by Gram-negatives resistant to other antibacterials, and as an antipseudomonal. [Oral, IV, restricted community and hospital use]

Gentamicin: an aminoglycoside. Generally predicts resistance in Gram-negatives to tobramycin (but not Amikacin). Valuable first line agent for presumptive Gram-negative sepsis. [IV, high first line hospital use].

Amikacin: an aminoglycoside. It is unaffected by the common aminoglycoside-modifying enzymes that cause Gram-negative bacteria to become resistant to gentamicin and tobramycin.

Trimethoprim: a folate synthesis (dihydrofolate reductase) inhibitor. Standard treatment for uncomplicated urinary tract infection. [Oral, moderate community use, limited hospital use, both mainly as trimethoprim or in combination with suplhamethoxazole as cotrimoxazole]

Nitrofurantoin: a nitrofuran. A unique mechanism of action but its role, based on its pharmacology and reduced systemic levels, is restricted to the treatment and prevention of urinary tract infection.

APPENDIX D. RESISTANCES OF CONCERN

B-LACTAMASES

ß-lactamases are the principal resistance mechanism to ß-lactams in Gram-negative bacteria. There is an enormous range of these enzymes now described. Like antibiotics themselves, each ß-lactamase has a "spectrum" of ß-lactams that it can hydrolyze and inactivate. The ß-lactamases of worldwide importance are listed in Table 1.

Table D1 Important ß-lactamases in Enterobacteriaceae

ß-lactamase	Mainly found in	ß-lactams affected or usual co-resistances	Comments
TEM-1,2	*E. coli*	Ampicillin, amoxycillin, piperacillin, (cephalothin)	Very common
TEM-1 hyperproduction	*E. coli*	Amoxycillin-clavulanate (piperacillin-tazobactam)	Increased prevalence in recent years
TEM, SHV and CTX-M extended spectrum ß-lactamases (ESBLs)	*E. coli*, *K. pneumoniae*, *Enterobacter* spp.	Ampicillin, amoxycillin, piperacillin, first-, second- (excluding cephamycins (cefoxitin) and third generation cephalosporins, monobactam	Mainly hospital-associated until recent emergence of CTX-M types in community practice overseas
K1 hyperproduction	*K. oxytoca*	Ampicillin, amoxicillin, piperacillin, first- and second-generation cephalosporins, aztreonam, ceftriaxone > cefotaxime	Natural enzyme selected to hyperproduction
Chromosomal cephalosporinases	ESCaPPM*	Ampicillin, amoxicillin, first-, second-generation cephalosporins, third generation cephalosporins in de-repressed mutants.	Natural enzymes. Selection for stably de-repressed mutants can occur during treatment and strains with this are common
Plasmid-borne AmpC ß-lactamases	*E. coli, K. pneumoniae*	Ampicillin, amoxycillin, first, second and third-generation cephalosporins, including cephamycins	Emerging overseas as a significant problem
Carbapenemases	Rare, but increasing	Ampicillin, amoxycillin, extended-spectrum penicillins; first-, second and third-generation cephalosporins +/-aztreonam	Have been rare in Enterobacteriaceae but now being seen for the first time locally acquired in Australia and imported from overseas

* ***E****nterobacter* species, ***S****erratia* species, ***C****itrob****a****cter freundii*, [***P****roteus vulgaris* and *penneri*, ***P****rovidencia* species and ***M****organella morganii*]

FLUOROQUINOLONES

In Enterobacteriaceae, resistance to fluoroquinolones such as ciprofloxacin is generally the result of mutations in the *gyrA* gene, leading to amino acid changes in the target protein DNA gyrase. Two or three mutation and amino acid changes are required to develop full resistance to ciprofloxacin. Occasionally resistance can be brought about through efflux, usually in combination with DNA gyrase mutations. Plasmid-mediated quinolone resistance is emerging, but is not addressed in this report.

AMINOGLYCOSIDES

Resistance to gentamicin and other aminoglycosides is most commonly the result of aminoglycoside modifying enzymes. The types prevalent in Enterobacteriaceae can vary widely by hospital, region and country.
Trimethoprim resistance is most commonly the result of mutations in the gene encoding the dihydrofolate reductase.