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## **Australian Group on Antimicrobial Resistance (AGAR) Australian Gram-negative Surveillance Outcome Program (GnSOP)**

Bloodstream Infection Annual Report 2021

Jan M Bell, Alicia Fajardo Lubian, Sally R Partridge, Thomas Gottlieb, Jenny Robson, Jonathan R Iredell,  
Denise A Daley, Geoffrey W Coombs

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# Australian Group on Antimicrobial Resistance (AGAR) Australian Gram-negative Surveillance Outcome Program (GnSOP)

## Bloodstream Infection Annual Report 2021

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### Abstract

The Australian Group on Antimicrobial Resistance (AGAR) performs regular period-prevalence studies to monitor changes in antimicrobial resistance in selected enteric gram-negative pathogens. The 2021 survey was the ninth year to focus on bloodstream infections caused by *Enterobacterales*, and the seventh year where *Pseudomonas aeruginosa* and *Acinetobacter* species were included.

The 2021 survey tested 8,947 isolates, comprising *Enterobacterales* (8,104; 90.6%), *P. aeruginosa* (745; 8.3%) and *Acinetobacter* species (98; 1.1%), using commercial automated methods. The results were analysed using Clinical and Laboratory Standards Institute (CLSI) and European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints (January 2022). Of the key resistances, resistance to the third-generation cephalosporin ceftriaxone was found in 12.5%/12.5% (CLSI/EUCAST criteria) of *Escherichia coli* and in 6.1%/6.1% of *Klebsiella pneumoniae*. Resistance rates to ciprofloxacin were 12.3%/12.3% for *E. coli*; 7.2%/7.2% for *K. pneumoniae*; 5.4%/5.4% for *Enterobacter cloacae* complex; and 3.7%/8.0% for *P. aeruginosa*. Resistance rates to piperacillin-tazobactam were 2.8%/6.5%; 2.9%/9.9%; 18.4%/28.1%; and 6.9%/12.8% for the same four species, respectively. Seventeen *Enterobacterales* isolates from 17 patients were shown to harbour a carbapenemase gene: 12 *bla*<sub>IMP-4</sub>; two *bla*<sub>NDM-7</sub>; one *bla*<sub>NDM-1</sub>; one *bla*<sub>OXA-181</sub>; and one *bla*<sub>KPC-2</sub>. No transmissible carbapenemase genes were detected among *P. aeruginosa* or *Acinetobacter* isolates in the 2021 survey.

Keywords: Australian Group on Antimicrobial Resistance (AGAR); antimicrobial resistance; bacteraemia; gram-negative; *Escherichia coli*; *Enterobacter*; *Klebsiella*

### Introduction

Emerging resistance in common pathogenic members of the *Enterobacterales* is a worldwide phenomenon and presents therapeutic problems, both in the community and in hospital practice. The Australian Group on Antimicrobial Resistance (AGAR) commenced surveillance of the key gram-negative pathogens, *Escherichia coli* and *Klebsiella* species, in 1992. Surveys were conducted biennially until 2008 when annual

surveys commenced, alternating between community- and hospital-onset infections.<sup>i</sup> In 2004 *Enterobacter*, another genus of gram-negative pathogens in which resistance can be of clinical importance, was added. *Escherichia coli* is the most common cause of community-onset urinary tract infection; *Klebsiella* species are less common but are known to harbour important resistances. *Enterobacter* species are

<sup>i</sup> <http://www.agargroup.org.au/agar-surveys>.

less common in the community, but of high importance due to intrinsic resistance to first-line antimicrobials used in that setting. Taken together, these three groups of species surveyed are valuable sentinels for multi-resistance and emerging resistance in enteric gram-negative bacilli. In 2013 AGAR commenced the *Enterobacteriales* Sepsis Outcome Program (EnSOP) which focused on the collection of resistance data and some demographic data on all isolates collected prospectively from patients with bacteraemia. In 2015, *Pseudomonas aeruginosa* and *Acinetobacter* species were added, with the program then referred to as the Gram-negative Sepsis Outcome Program (GnSOP), since renamed the Gram-negative Surveillance Outcome Program.

Resistance to  $\beta$ -lactams due to  $\beta$ -lactamases, especially extended-spectrum  $\beta$ -lactamases that inactivate the third-generation cephalosporins normally considered reserve antimicrobials, is of particular interest. Resistance to agents important for treatment of serious infections, such as gentamicin, and to reserve agents such as ciprofloxacin and meropenem, is also of interest.

The objectives of the 2021 surveillance program were:

- to monitor resistance in *Enterobacteriales*, *P. aeruginosa* and *Acinetobacter* species isolated from blood cultures taken from patients presenting to the hospital or already in hospital;
- to examine the extent of co-resistance and multidrug resistance in the major species;
- to detect emerging resistance to reserve agents such as carbapenems and colistin; and
- to examine the molecular basis of resistance to third-generation cephalosporins, quinolones and carbapenems.

## Methods

### Study design

From 1 January to 31 December 2021, thirty laboratories servicing 48 hospitals across Australia, including four private hospitals and 11 regional or district hospitals from north-west Western Australia, collected either all or up to 200 isolates from different patient episodes of bacteraemia.

### Species identification

Isolates were identified using the routine method at each institution: Vitek<sup>®</sup>, Phoenix<sup>™</sup> automated microbiology systems or, where available, matrix assisted laser desorption/ionisation – time of flight (MALDI-ToF) mass spectrometry.

### Susceptibility testing

Testing was performed by two commercial semi-automated methods, Vitek<sup>®</sup> 2 (BioMérieux, France) or Phoenix<sup>™</sup> (Becton Dickinson, USA), which are calibrated to the International Organization for Standardization (ISO) reference standard method of broth microdilution. Commercially available Vitek AST-N246, Vitek AST N-410 or Phoenix NMIC-422 cards were utilised by all participants throughout the survey period. The CLSI M100 and EUCAST v12.0 breakpoints from January 2022 have been employed in the analysis.<sup>1,2</sup>

### Multidrug resistance

The definitions used by Magiorakos et al. were applied in this survey,<sup>3</sup> where multidrug resistance (MDR) was defined as resistance to one or more agent in three or more antimicrobial categories. For each species, antimicrobials were excluded from the count if they are affected by natural resistance mechanisms.

## Whole genome sequencing

The following isolates were referred to a central laboratory (Centre for Infectious Diseases and Microbiology, The Westmead Institute for Medical Research):

- *E. coli*, *Klebsiella* spp., *Proteus* spp. and *Salmonella* spp. with ceftazidime or ceftriaxone minimum inhibitory concentration (MIC) > 1 mg/L, or cefoxitin MIC > 8 mg/L;
- any other *Enterobacterales* with cefepime MIC > 1 mg/L;
- *Salmonella* spp. with ciprofloxacin MIC > 0.25 mg/L;
- *Enterobacterales* with meropenem MIC > 0.125 mg/L (> 0.25 if tested using Vitek);
- *P. aeruginosa* or *Acinetobacter* spp. with meropenem MIC > 4 mg/L;
- any isolate with amikacin MIC > 32 mg/L;
- and any isolate with colistin MIC < 4 mg/L (except those with intrinsic resistance to colistin).

All referred isolates underwent whole genome sequencing (WGS).

Genomic DNA for WGS was extracted using the DNeasy® Blood & Tissue Kit (Qiagen) according to the manufacturer's instructions for gram-negative bacteria. WGS was performed by the Antimicrobial Resistance Laboratory, Microbial Genomics Reference Laboratory, Centre for Infectious Diseases and Microbiology Laboratory Services (CIDMLS), Institute of Clinical Pathology and Medical Research (ICPMR), Westmead Hospital using the Illumina NextSeq™ 500 platform. Data were analysed using a modification of the Nullarbor bioinformatic pipeline,<sup>4</sup> incorporating searching contigs against the NCBI AMRFinder database<sup>ii</sup>

ii <https://www.ncbi.nlm.nih.gov/bioproject/PRJNA313047>.

using ABRicate<sup>5</sup> and AMRFinder,<sup>6</sup> followed by a custom AMR-specific pipeline which includes a read-based search using ARIBA<sup>7</sup> against the CARD<sup>8</sup> and NCBI databases. Ambiguities and potential multiple gene copies/variants were checked manually by mapping reads to reference genes<sup>iii</sup> using Geneious.

## Results

The species isolated, and the numbers of each, are listed in Table 1. *Enterobacterales* accounted for 90.6%, followed by *P. aeruginosa* (8.3%) and *Acinetobacter* species (1.1%). In the *Enterobacterales*, 87.6% of all isolates belonged to three genera: *Escherichia* (61.4%); *Klebsiella* (20.5%); and *Enterobacter* (5.7%). Major resistances and non-susceptibilities for the top six ranked species are listed in Table 2. We utilised non-susceptibility as an epidemiological tool to provide important information about emerging acquired resistance, recognising that even though some of these isolates remain within therapeutic range for specific antibiotics, these isolates tend to be divergent from the wild-type distribution. In addition to resistant isolates, isolates categorised as intermediate according to CLSI or 'sensitive, increased exposure' according to EUCAST were included as non-susceptible. Multiple acquired resistances by species are shown in Table 3. About one fifth of *E. coli* isolates (19.0%), 6.2% of *K. pneumoniae* complex isolates, and 7.1% of *E. cloacae* complex isolates would be considered multi-drug resistant. A more detailed breakdown of resistance and non-susceptibility by state and territory is provided in the online GnSOP 2021 report.<sup>iv</sup>

iii <https://www.ncbi.nlm.nih.gov/pathogens/isolates#/refgene/>.

iv <https://agargroup.org.au/agar-surveys/>.

**Table 1: Number and proportion of species isolated, blood cultures, AGAR, 2021**

Species	Percentage (n)	Onset setting, percentage (n)	
		Community onset	Hospital onset
<i>Escherichia coli</i>	55.5 (4,969)	85.0 (4,225)	15.0 (744)
<i>Klebsiella pneumoniae</i> complex	13.9 (1,247)	71.5 (891)	28.5 (356)
<i>Pseudomonas aeruginosa</i>	8.3 (745)	60.8 (453)	39.2 (292)
<i>Enterobacter cloacae</i> complex	5.0 (450)	56.4 (254)	43.6 (196)
<i>Proteus mirabilis</i>	3.5 (314)	87.3 (274)	12.7 (40)
<i>Klebsiella oxytoca</i>	3.0 (265)	69.1 (183)	30.9 (82)
<i>Serratia marcescens</i>	2.3 (202)	54.5 (110)	45.5 (92)
<i>Klebsiella aerogenes</i>	1.3 (119)	62.2 (74)	37.8 (45)
<i>Citrobacter koseri</i>	1.1 (94)	81.9 (77)	18.1 (17)
<i>Citrobacter freundii</i> complex	1.0 (88)	63.6 (56)	36.4 (32)
<i>Morganella morganii</i>	1.0 (88)	70.5 (62)	29.5 (26)
<i>Salmonella</i> species (non-typhoidal)	0.9 (81)	98.8 (80)	1.2 (1)
<i>Acinetobacter baumannii</i> complex	0.5 (48)	60.4 (29)	39.6 (19)
<i>Raoultella ornithinolytica</i>	0.3 (28)	67.9 (19)	32.1 (9)
<i>Klebsiella</i> species <sup>a</sup>	0.3 (26)	69.2 (18)	30.8 (8)
<i>Enterobacter</i> species <sup>a</sup>	0.2 (16)	56.3 (9)	43.8 (7)
<i>Providencia rettgeri</i>	0.1 (13)	69.2 (9)	30.8 (4)
<i>Serratia liquefaciens</i> complex	0.1 (12)	83.3 (10)	16.7 (2)
<i>Pantoea agglomerans</i>	0.1 (12)	75.0 (9)	25.0 (3)
<i>Acinetobacter lwoffii</i>	0.1 (11)	90.9 (10)	9.1 (1)
<i>Acinetobacter</i> species <sup>a</sup>	0.1 (11)	90.9 (10)	9.1 (1)
<i>Acinetobacter ursingii</i>	0.1 (10)	60.0 (6)	40.0 (4)
Other species (total n = 35)	1.1 (98)	72.4 (71)	27.6 (27)
<b>Total</b>	<b>8,947</b>	<b>77.6 (6,939)</b>	<b>22.4 (2,008)</b>

a Species not determined.

### *Escherichia coli*

The moderately high levels of resistance to ampicillin (and therefore amoxicillin) observed were at similar levels to the 2020 survey (2021: 51.4%/53.2%; versus 2020: 51.4%/53.1%, CLSI/EUCAST criteria), with the same lower rates for amoxicillin-clavulanic acid (12.6%/intermediate, 7.7%/resistant). Non-susceptibility to third generation cephalosporins was also maintained (ceftriaxone 12.6%/12.6%,

ceftazidime 6.3%/13.2%) versus the degree of non-susceptibility found in 2020. Moderate levels of resistance to cefazolin (23.1%/23.1%) and trimethoprim-sulfamethoxazole (29.5%/29.5%) were detected. Ciprofloxacin non-susceptibility was found in 16.6%/16.6% of *E. coli* isolates, 2.8 percentage points lower than the 2020 survey. Resistance to gentamicin (7.9%/8.6%), piperacillin-tazobactam (2.8%/6.5%), and cefepime (2.6%/3.6%) was low. Four isolates (0.1%) had elevated meropenem MICs ( $\geq 0.5$  mg/L).

Table 2: Non-susceptibility and resistance rates for the top six ranked species tested, AGAR, 2021

Antimicrobial	Category <sup>a</sup>	E. coli (%) <sup>b</sup>		K. pneumoniae complex (%) <sup>b</sup>		P. aeruginosa (%) <sup>b</sup>		E. cloacae complex (%) <sup>b</sup>		P. mirabilis (%) <sup>b</sup>		K. oxytoca (%) <sup>b</sup>	
		CLSI	EUCAST	CLSI	EUCAST	CLSI	EUCAST	CLSI	EUCAST	CLSI	EUCAST	CLSI	EUCAST
Ampicillin	R	51.4	53.2	c	c	na	na	c	c	14.7	15.4	c	c
Amoxicillin-clavulanic acid (2:1)	R	7.7	d	3.8	d	na	na	c	c	1.8	d	7.4	d
Piperacillin-tazobactam	R	2.8	6.5	2.9	9.9	6.9	12.8	18.4	28.1	0.0	0.3	9.1	11.0
Cefazolin	R	23.1	23.1	10.0	10.0	na	na	c	c	19.2	19.2	52.4	52.4
Cefoxitin	R	3.2	/	4.4	/	na	na	c	c	0.3	/	1.1	/
Ceftriaxone	NS	12.6	12.6	6.1	6.1	na	na	27.0	27.0	2.2	2.2	7.6	7.6
Ceftazidime	NS	6.3	13.2	5.3	7.7	9.8	9.8 (e)	23.7	26.8	1.3	2.6	0.8	2.3
Cefepime	NS	4.6	9.3	2.7	5.2	6.3	6.3 (e)	6.5	13.4	2.2	2.2	0.0	0.8
Meropenem	NS	<0.1	<0.1	0.6	0.4	4.6 (e)	2.3 (e)	2.9	2.2	0.0	0.0	0.4	0.4
Ciprofloxacin	NS	16.6	16.6	9.4	9.4	8.0	8.0 (e)	7.6	7.6	5.8	5.8	1.1	1.1
Gentamicin	R	7.9	8.6	3.6	3.7	1.4	na	5.4	6.0	2.6	10.6	1.1	1.1
Trimethoprim-sulfamethoxazole	R	29.5	29.4	13.0	12.5	na	na	16.2	16.0	16.1	16.1	4.9	4.9
Nitrofurantoin	R	0.6	0.6	36.2	/	na	na	10.8	/	c	c	0.0	/

a R: resistant; NS: non-susceptible (intermediate (CLSI) or susceptible, increased exposure (EUCAST) + resistant), using criteria as published by the CLSI [2022] and EUCAST [2022].

b -: no category defined; /: no breakpoints defined; na: not applicable (testing not recommended).

c Considered largely intrinsically resistant.

d For EUCAST interpretation, clavulanic acid is fixed at 2 mg/L, rather than the 2:1 ratio of amoxicillin to clavulanic acid used in CLSI guidelines. As 90% of pathology services (27/30) used susceptibility test cards with a 2:1 ratio of clavulanate, no EUCAST category has been applied.

e Percent resistant.

**Table 3: Multiple acquired resistances by species, AGAR, 2021**

Species	Number of acquired resistances (EUCAST breakpoints) <sup>a,b</sup>												
	Non multi-drug resistant						Multi-drug resistant						
	0	1	2	Cumulative %	3	4	5	6	7	8	Cumulative %		
<i>E. coli</i>	Total	4,878	2,052	1,010	887		443	287	153	41	5	0	
	%	42.1	20.7	18.2	81.0	9.1	5.9	3.1	0.8	0.1	0.0	0.0	19.0
<i>K. pneumoniae</i> complex <sup>c</sup>	Total	1,236	969	113	77		28	17	29	2	1	na	
	%	78.4	9.1	6.2	93.8	2.3	1.4	2.3	0.2	0.1			6.2
<i>E. cloacae</i> complex <sup>d</sup>	Total	440	266	55	85		13	5	9	7	na	na	
	%	60.5	12.5	19.3	92.3	3.0	1.1	2.0	1.6				7.7
<i>P. mirabilis</i>	Total	307	218	45	26		10	4	3	1	0	0	
	%	71.0	14.7	8.5	94.1	3.3	1.3	1.0	0.3	0.0	0.0	0.0	5.9
<i>K. oxytoca</i> <sup>e</sup>	Total	264	223	17	21		2	0	1	0	0	na	
	%	84.5	6.4	8.0	98.9	0.8	0.0	0.4	0.0	0.0			1.1
<i>Salmonella</i> species (non-typhoidal) <sup>e</sup>	Total	80	77	0	2		1	0	0	0	0	na	
	%	96.3	0.0	2.5	98.8	1.3	0.0	0.0	0.0	0.0			1.3
<i>S. marcescens</i> <sup>e</sup>	Total	160	48	82	27		1	2	0	0	0	na	
	%	30.0	51.3	16.9	98.1	0.6	1.3	0.0	0.0	0.0			1.9
<i>K. aerogenes</i> <sup>d</sup>	Total	119	66	6	41		4	1	1	0	na	na	
	%	55.5	5.0	34.5	95.0	3.4	0.8	0.8	0.0				5.0

a Antimicrobial categories (agents) included: aminoglycosides (gentamicin or tobramycin); antipseudomonal penicillins +  $\beta$ -lactamase inhibitor (piperacillin-tazobactam); carbapenems (meropenem); extended-spectrum cephalosporins (ceftriaxone or ceftazidime); cephamycins (cefoxitin); fluoroquinolones (ciprofloxacin); folate pathway inhibitors (trimethoprim-sulfamethoxazole); and penicillins (ampicillin).

b na: not applicable.

c Antimicrobial categories excluded: penicillins.

d Antimicrobial categories excluded: penicillins, cephamycins.

e Antimicrobial categories excluded: aminoglycosides.



For the strains with an extended spectrum  $\beta$ -lactamase (ESBL) phenotype, ciprofloxacin and gentamicin resistance was found in 50.1%/50.1% and 30.1%/31.1% respectively.

Most of the referred *E. coli* with an ESBL phenotype (628/659; 95.3%) harboured an Ambler class A ESBL gene (507/628, 80.7%); a plasmid borne class C gene (pAmpC) (103/628; 16.4%); both an ESBL and pAmpC gene (17/628; 2.7%); or both an ESBL and a carbapenemase gene (1/628; 0.2%). The dominant  $\beta$ -lactamase genes in *E. coli* were *bla*<sub>CTX-M</sub> types, as found previously. Of 628 *E. coli* isolates with a confirmed  $\beta$ -lactamase gene, 524 (83.4%) had one or more *bla*<sub>CTX-M</sub> genes detected by WGS, either *bla*<sub>CTX-M</sub> group 9 ( $n = 265$ ); *bla*<sub>CTX-M</sub> group 1 ( $n = 253$ ); both *bla*<sub>CTX-M</sub> group 1 and group 9 ( $n = 4$ ); or a *bla*<sub>CTX-M</sub> group 1/9/1 hybrid ( $n = 2$ ). Of 120 *E. coli* isolates with pAmpC, 66 (55.0%) harboured *bla*<sub>DHA-1</sub>; 52 (43.3%) harboured a *bla*<sub>CMY-2</sub>-like gene; and two (1.7%) harboured both *bla*<sub>DHA-1</sub> and a *bla*<sub>CMY-2</sub>-like gene.

### *Klebsiella pneumoniae* complex

*K. pneumoniae* complex isolates showed slightly higher levels of resistance to piperacillin-tazobactam than *E. coli*, but showed lower rates of resistance to amoxicillin-clavulanic acid, ceftazolin, ceftriaxone, ciprofloxacin, gentamicin, and trimethoprim-sulfamethoxazole. Eleven *K. pneumoniae* complex isolates (0.9%) had elevated meropenem MICs (see below). Most of the referred *K. pneumoniae* complex isolates with an ESBL phenotype (81/94; 86.2%) harboured an ESBL gene (57/81; 70.4%), a pAmpC gene (17/81; 21.0%), or a carbapenemase gene (4/81; 4.9%) alone; or both an ESBL and a pAmpC gene (2/81; 2.5%); or both an ESBL and a carbapenemase gene (1/81, 1.2%). The majority of ESBL genes (57/60; 95.0%) were *bla*<sub>CTX-M</sub> types, mostly *bla*<sub>CTX-M</sub> group 1 (46/54; 86.0%) or both *bla*<sub>CTX-M</sub> group 1 and *bla*<sub>SHV-27</sub> (3; 5.0%). The only pAmpC gene detected in *K. pneumoniae* complex isolates was *bla*<sub>DHA-1</sub> (19/19).

### *Enterobacter cloacae* complex

Acquired resistance was common among *E. cloacae* complex isolates, to piperacillin-tazobactam (18.4%/28.1%); ceftriaxone (27.0%/27.0%); and ceftazidime (23.7%/26.8%). There was a moderate level of resistance to gentamicin (12.6%/13.6%) and trimethoprim-sulfamethoxazole (16.2%/16.0%); cefepime and ciprofloxacin resistance remained at less than 10%. Although *E. cloacae* complex isolates are generally more resistant than *E. coli* to  $\beta$ -lactam antimicrobials, resistance rates to non- $\beta$ -lactams tend to be lower. Eighteen *E. cloacae* complex isolates (4.0%) had elevated meropenem MICs.

### Carbapenemase genes

Overall, 17 isolates (17 patients) from 13 hospitals from five states/territories were found to harbour a carbapenemase gene. Twelve isolates harboured *bla*<sub>IMP-4</sub>: *E. cloacae* complex (six), *K. pneumoniae* (two), *K. michiganensis* (one), *K. oxytoca* (one), *K. variicola* (one) and *E. coli* (one). The *bla*<sub>NDM-7</sub> gene was detected in one *E. cloacae* complex isolate and one *K. pneumoniae* complex isolate; *bla*<sub>NDM-1</sub> was detected in one *E. cloacae* complex isolate. The *bla*<sub>OXA-181</sub> gene was detected in one *K. variicola* isolate. The *bla*<sub>KPC-2</sub> gene was detected in one *K. pneumoniae* isolate. No carbapenemase genes were detected among *Acinetobacter* or *P. aeruginosa* in the 2021 survey.

### Plasmid-borne colistin determinants

The only *mcr* genes detected among referred isolates were *mcr-9* ( $n = 14$ ), which is not associated with a colistin resistant phenotype but is typically found on HI2 plasmids that may carry *bla*<sub>IMP-4</sub>, and *mcr-10* ( $n = 1$ ).

### Discussion

AGAR has been tracking resistance in sentinel enteric gram-negative bacteria since 1992. From 2008, surveillance was segregated into hospital-onset versus community-onset infections. The last year of hospital-onset only surveillance was

2011.<sup>9</sup> In 2013, the first survey of antimicrobial resistance among *Enterobacterales* isolates from bacteraemic patients throughout Australia was conducted using an approach similar to the European EARS-Net program. The 2021 survey was the ninth of antimicrobial resistance among *Enterobacterales*, and the seventh for *P. aeruginosa* and *Acinetobacter* spp. from bacteraemic patients throughout Australia.

The percentage of resistance in *E. coli* in 2021 was similar to that seen in 2020 for all antimicrobial agents tested, except for ciprofloxacin, where a 23.3% decrease in resistance was seen. For *K. pneumoniae* complex, the percentage of resistance in 2021, relative to 2020, decreased by more than 25% for ceftriaxone, ceftazidime, gentamicin and ciprofloxacin.

AGAR data show a longitudinal trend of increasing *E. coli* resistance to key anti-gram-negative antimicrobial agents, such as ceftriaxone and ciprofloxacin, although both have stabilised since 2019. The steady rise in resistance to fluoroquinolones in *E. coli* is more striking in hospital-onset bacteraemia, with a change from 13.7% to 21.8% between 2013 and 2020; in 2021 resistance fell to 16.7%.

Carbapenem resistance attributable to acquired carbapenemase genes is still uncommon in patients with bacteraemia in Australia. Four different types ( $bla_{IMP}$  [12],  $bla_{NDM}$  [3],  $bla_{OXA-48}$ -like [1], and  $bla_{KPC-2}$  [1]) were detected in 17 isolates from 13 of the participating hospitals. Compared with many other countries in our region, antimicrobial resistance rates in Australian gram-negative bacteria are still relatively low,<sup>10</sup> but similar to those observed in 2020 in many Northern European countries.<sup>11,12</sup> Resistance to third-generation cephalosporins in *E. coli* from bacteraemic patients in Australia is similar to the European Union and European Economic Area average.<sup>12</sup>

Just under one-fifth of *E. coli* would be classed as MDR, a proportion little changed from the 2020 survey. The proportion of *K. pneumoniae*

complex isolates classed as MDR fell to 6.2% in 2021, the lowest level recorded since the GnSOP surveys commenced.

The impact of COVID-19 on antimicrobial resistance remains unclear and may be influenced by a number of contributing factors. A combination of COVID-19-related travel restrictions on incoming travellers throughout much of 2020 and 2021, and an increasing awareness of and utilization of antimicrobial stewardship as part of the National Safety and Quality Health Service Standards 3 implementation and accreditation Australia-wide,<sup>13</sup> may have reduced some resistance, particularly for ESBLs.

Pharmaceutical Benefits Scheme (PBS) data indicate that the COVID-19 pandemic had a profound impact on antimicrobial use in 2020, with a 40% drop in antimicrobials dispensed between March and April in 2020, with use remaining at this lower level for the rest of the year.<sup>14</sup> It is also possible that PBS policy changes (effective from 1 April 2020) contributed to this drop, as repeat prescriptions and maximum quantities were restricted for the five most commonly dispensed antimicrobials: amoxicillin, amoxicillin-clavulanic acid, cefalexin, doxycycline and roxithromycin. In 2020, there was also a change in policy to stop repeats on key antibiotics.<sup>15</sup>

It is also possible that a reduction in elective surgery and, related to this, in post-surgical bloodstream infections, may have occurred during 2020 and 2021.

Future AGAR surveys will help determine if the observed reduction in resistance rates is sustained.

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