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Australian Group on Antimicrobial Resistance (AGAR) Australian Gram-negative Sepsis Outcome Programme (GnSOP) Annual Report 2020

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Annual Report

Australian Group on Antimicrobial Resistance (AGAR) Australian Gram-negative Sepsis Outcome Programme (GnSOP) Annual Report 2020

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

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 2020 survey was the eighth year to focus on bloodstream infections caused by *Enterobacteriales*, and the sixth year in which *Pseudomonas aeruginosa* and *Acinetobacter* species were included.

Eight thousand seven hundred and fifty-two isolates, comprising *Enterobacteriales* (7,871, 89.9%), *P. aeruginosa* (771, 8.8%) and *Acinetobacter* species (110, 1.3%), were tested 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 2021). Of the key resistances, resistance to the third-generation cephalosporin ceftriaxone was found in 13.5%/13.5% (CLSI/EUCAST criteria) of *Escherichia coli* and 8.7%/8.7% of *Klebsiella pneumoniae*. Resistance rates to ciprofloxacin were 16.1%/16.1% for *E. coli*; 9.9%/9.9% for *K. pneumoniae*; 5.8%/5.8% for *Enterobacter cloacae* complex; and 4.5%/8.1% for *P. aeruginosa*. Resistance rates to piperacillin-tazobactam were 2.5%/6.6%; 3.9%/12.5%; 16.9%/26.3%; and 5.5%/14.4% for the same four species respectively. Thirty-two isolates from 32 patients were shown to harbour at least one carbapenemase gene: 19 *bla*_{IMP-4}, three *bla*_{GES-5}, two *bla*_{NDM-1}, two *bla*_{NDM-5}, two *bla*_{OXA-48}, two *bla*_{OXA-181}, one *bla*_{IMI-1}, and one *bla*_{OXA-23+NDM-1}.

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 *Enterobacteriales* 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.ⁱ 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 less common in the community, but of high importance due to intrinsic resistance to first-line antimicrobials used in that setting. Taken together, the three groups of species surveyed are valuable

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

sentinels for multi-resistance and emerging resistance in enteric gram-negative bacilli. In 2013 AGAR commenced the Enterobacteriaceae Sepsis Outcome Programme (EnSOP) which focused on the collection of resistance and some demographic data on all isolates prospectively from patients with bacteraemia. In 2015, *Pseudomonas aeruginosa* and *Acinetobacter* species were added, with the program now referred to as the Gram-negative Sepsis Outcome Program (GnSOP).

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

The objectives of the 2020 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;
- examine the extent of co-resistance and multidrug resistance in the major species;
- detect emerging resistance to newer last-line agents such as carbapenems and colistin; and
- examine the molecular basis of resistance to third-generation cephalosporins, quinolones and carbapenems.

Methods

Study design

From 1 January to 31 December 2020, thirty laboratories servicing 49 institutions across Australia, including four private institutions

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[®] (BioMérieux, France) or Phoenix[™] (Becton Dickinson, United States of America) 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, Vitek2[®] (BioMérieux) or Phoenix[™] (Becton Dickinson), which are calibrated to the ISO reference standard method of broth microdilution. Commercially-available Vitek AST-N246 or Phoenix NMIC-422 cards were utilized by all participants throughout the survey period. The Clinical and Laboratory Standards Institute (CLSI) M100 and European Committee on Antimicrobial Susceptibility Testing (EUCAST) v11.0 breakpoints from January 2021 have been employed in the analysis.^{1,2}

Multidrug resistance

The definitions used by Magiorakos et al.³ were applied in this survey, where multidrug resistance was defined as resistance to one or more agents in three or more antimicrobial categories. For each species, antimicrobials were excluded from the count if affected by natural resistance mechanisms.

Polymerase chain reaction screening and whole genome sequencing

E. coli, *Klebsiella* spp., *Proteus* spp. and *Salmonella* spp. with ceftazidime or ceftriaxone minimum inhibitory concentration (MIC) > 1 mg/L, or ceftazidime MIC > 8 mg/L; any other *Enterobacteriales* with cefepime MIC > 1 mg/L;

Salmonella spp. with ciprofloxacin MIC > 0.25 mg/L; all *Enterobacterales* with meropenem MIC > 0.125 mg/L (> 0.25 mg/L if tested using Vitek); all *P. aeruginosa* or *Acinetobacter* spp. with meropenem MIC > 4 mg/L; all isolates with amikacin MIC > 32 mg/L; and all isolates with colistin MIC > 4 mg/L were referred to a central laboratory (Centre for Infectious Diseases and Microbiology, The Westmead Institute for Medical Research) and underwent polymerase chain reaction (PCR) screening to detect selected resistance genes (Centre for Infectious Diseases & Microbiology Laboratory Services (CIDMLS), Institute of Clinical Pathology and Medical Research (ICPMR), Westmead Hospital) or whole genome sequencing (WGS) (Antimicrobial Resistance Laboratory, Microbial Genomics Reference Laboratory, CIDMLS, ICPMR, Westmead Hospital).

All referred isolates of *P. aeruginosa*, *Acinetobacter* spp., *Salmonella* spp., and *Enterobacterales* with meropenem MIC > 0.125 mg/L (> 0.25 mg/L if tested using Vitek) underwent WGS. A subset of *E. coli* and *K. pneumoniae* complex isolates, chosen based on phenotypic data (ceftriaxone, ceftazidime and ciprofloxacin), were also analysed by WGS. The remaining isolates were screened using real-time multiplex PCR with published primers to detect extended spectrum β -lactamase (ESBL) genes (*bla*_{SHV-ESBL} with a G→A substitution at positions 700 and/or 703; *bla*_{CTX-M} groups 1 and 9; *bla*_{VEB}), and plasmid-borne AmpC (*bla*_{CMY-2-like}; *bla*_{DHA}).⁴

Other extended spectrum β -lactamases targets (*bla*_{ACT/MIR}) were detected using in-house, National Association of Testing Authorities (NATA) accredited primers and probes in routine use by CIDMLS ICPMR at Westmead Hospital.

Genomic DNA for WGS was extracted using the DNeasy[®] Blood & Tissue Kit (Qiagen, Germany) according to the manufacturer's instructions for gram-negative bacteria. Sequencing was performed by the Antimicrobial Resistance Laboratory, Microbial Genomics Reference Laboratory, CIDMLS, ICPMR, Westmead

Hospital using the Illumina NextSeq[™] 500 platform (Illumina, United States of America). Data were analysed using a modification of the Nullarbor bioinformatic pipeline,⁵ incorporating searching contigs against the National Center for Biotechnology Information (NCBI) AMRFinder databaseⁱⁱ using ABRicate⁶ and AMRFinder,⁷ followed by a custom AMR-specific pipeline which includes a read-based search using ARIBA⁸ against the CARD⁹ and NCBI databases. Ambiguities and potential multiple gene copies/variants were checked manually by mapping reads to reference genesⁱⁱⁱ using Geneious.

Results

The species isolated and the numbers of each are listed in Table 1. *Enterobacterales* accounted for 89.9%, followed by *P. aeruginosa* (8.8%) and *Acinetobacter* species (1.3%). In the *Enterobacterales*, 87.7% of all isolates belonged to three genera: *Escherichia* (62.1%), *Klebsiella* (19.8%) and *Enterobacter* (5.9%). Major resistances and non-susceptibilities for the top six ranked species are listed in Table 2. Non-susceptibility (which includes both intermediate (CLSI) or sensitive, increased exposure (EUCAST) and resistant categories) has been included for some agents because these figures provide information about important emerging acquired resistance. Multiple acquired resistances by species are shown in Table 3. A quarter of *E. coli* isolates (25.8%), 12.1% of *K. pneumoniae* complex isolates, and 11.9% of *E. cloacae* complex isolates would be considered multi-resistant. A more detailed breakdown of resistances and non-susceptibilities by state and territory is provided in the online GnSOP 2020 report.^{iv}

Escherichia coli

Moderately high levels of resistance to ampicillin (and therefore amoxicillin) were at similar

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

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, 2020

Species	Percentage (n)	Onset setting, percentage (n)	
		Community onset	Hospital onset
<i>Escherichia coli</i>	55.8 (4,882)	85.0 (4,151)	15.0 (731)
<i>Klebsiella pneumoniae</i> complex	13.1 (1,147)	74.1 (850)	25.9 (297)
<i>Pseudomonas aeruginosa</i>	8.8 (771)	61.1 (471)	38.9 (300)
<i>Enterobacter cloacae</i> complex	5.2 (453)	53.9 (244)	46.1 (209)
<i>Proteus mirabilis</i>	3.2 (283)	85.2 (241)	14.8 (42)
<i>Klebsiella oxytoca</i>	2.9 (258)	73.3 (189)	26.7 (69)
<i>Serratia marcescens</i>	2.2 (195)	56.9 (111)	43.1 (84)
<i>Klebsiella aerogenes</i>	1.4 (124)	56.5 (70)	43.5 (54)
Salmonella species (non-typhoidal)	1.1 (93)	90.3 (84)	9.7 (9)
<i>Citrobacter freundii</i> complex	0.9 (82)	52.4 (43)	47.6 (39)
<i>Morganella morganii</i>	0.9 (80)	66.3 (53)	33.8 (27)
<i>Citrobacter koseri</i>	0.8 (73)	83.6 (61)	16.4 (12)
<i>Acinetobacter baumannii</i> complex	0.7 (60)	56.7 (34)	43.3 (26)
Salmonella species (typhoidal)	0.5 (40)	100.0 (40)	0.0 (0)
<i>Acinetobacter</i> species	0.4 (37)	67.6 (25)	32.4 (12)
<i>Klebsiella</i> species	0.3 (26)	73.1 (19)	26.9 (7)
<i>Raoultella ornithinolytica</i>	0.2 (19)	84.2 (16)	15.8 (3)
<i>Enterobacter</i> species	0.2 (14)	64.3 (9)	35.7 (5)
<i>Acinetobacter lwoffii</i>	0.2 (13)	69.2 (9)	30.8 (4)
<i>Proteus vulgaris</i>	0.1 (11)	81.8 (9)	18.2 (2)
<i>Providencia rettgeri</i>	0.1 (10)	70.0 (7)	30.0 (3)
<i>Pantoea agglomerans</i>	0.1 (10)	60.0 (6)	40.0 (4)
Other species (total n = 22)	0.8 (71)	78.9 (56)	21.1 (15)
Total	8,752	77.7 (6,798)	22.3 (1,954)

levels to the 2019 survey (51.4%/53.1%, CLSI/EUCAST criteria), with lower rates for amoxicillin-clavulanic acid (11.8%/– intermediate, 7.7%/– resistant). Non-susceptibility to third generation cephalosporins was also maintained (ceftriaxone 13.5%/13.5%, ceftazidime 6.5%/13.3%). Moderate levels of resistance to cefazolin (23.1%/23.1%) and trimethoprim–sulfamethoxazole (30.3%/30.1%) were detected.

Ciprofloxacin non-susceptibility was found in 19.4%/19.4% of *E. coli* isolates. Resistance to gentamicin (8.2%/8.8%), piperacillin-tazobactam (2.5%/6.6%) and cefepime (2.6%/3.6%) was low. Eighteen isolates (0.4%) had elevated meropenem MICs (≥ 0.5 mg/L). For the strains with an ESBL phenotype, ciprofloxacin and gentamicin resistance was found in 60.2%/60.2% and 28.2%/29.3% of isolates respectively.

Table 2: Non-susceptibility and resistance rates for the top six ranked species tested, 2020^a

Antimicrobial	Category ^b	<i>E. coli</i> (%)		<i>K. pneumoniae</i> complex (%)		<i>P. aeruginosa</i> (%)		<i>E. cloacae</i> complex (%)		<i>P. mirabilis</i> (%)		<i>K. oxytoca</i> (%)	
		CLSI	EUCAST	CLSI	EUCAST	CLSI	EUCAST	CLSI	EUCAST	CLSI	EUCAST	CLSI	EUCAST
Ampicillin	R	51.4	53.1	— ^c	— ^c	na	na	— ^c	— ^c	19.9	20.3	— ^c	— ^c
Amoxicillin-clavulanic acid (2:1) ^d	R	7.7	— ^d	5.0	— ^d	na	na	— ^c	— ^c	3.6	— ^d	7.3	— ^d
Piperacillin-tazobactam	R	2.5	6.6	3.9	12.5	5.5	14.4	16.9	26.3	0.0	0.4	8.7	10.6
Cefazolin	R	23.1	23.1	11.5	11.5	na	na	— ^c	— ^c	17.5	17.5	54.3	54.3
Cefoxitin	R	3.3	/	4.8	/	na	na	— ^c	— ^c	0.4	/	2.0	/
Ceftriaxone	NS	13.5	13.5	8.7	8.7	na	na	28.7	28.7	3.6	3.6	7.9	7.9
Ceftazidime	NS	6.5	13.3	7.4	9.2	7.7	7.7 ^e	23.8	27.4	0.7	2.1	1.2	2.0
Cefepime	NS	5.0	10.6	3.5	7.0	5.9	5.9 ^e	6.2	11.6	1.8	1.8	0.8	0.8
Meropenem	NS	0.1	0.1	0.6	0.4	4.3 ^e	3.6 ^e	4.2	4.0	0.0	0.0	0.0	0.0
Ciprofloxacin	NS	19.4	19.4	12.3	12.3	8.1	8.1 ^e	7.6	7.6	4.3	4.3	1.2	1.2
Gentamicin	R	8.2	8.8	4.9	5.4	1.1	na	7.6	8.4	3.2	7.1	0.8	0.8
Trimethoprim-sulfamethoxazole	R	30.3	30.1	15.6	15.4	na	na	20.3	20.3	15.4	15.0	4.7	4.7
Nitrofurantoin	R	0.9	0.9	33.8	/	na	na	17.5	/	— ^c	— ^c	2.6	/

a /: no breakpoints defined; na: not applicable (testing not recommended).

b R = resistant, I = intermediate (CLSI) or susceptible, increased exposure (EUCAST), NS = non-susceptible (intermediate + resistant), using criteria as published by the CLSI [2021] and EUCAST [2021].

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% (27/30) of pathology services 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, 2020

Species	Number of acquired resistances (EUCAST breakpoints) ^a													
	Total	Non-multi-resistant			Cumulative %	Multi-resistant							Cumulative %	
		0	1	2		3	4	5	6	7	8	9		10
<i>E. coli</i>	4,198	1785	667	661		302	263	281	134	60	36	9	0	
%		42.5	15.9	15.7	74.2	7.2	6.3	6.7	3.2	1.4	0.9	0.2	0.0	25.8
<i>K. pneumoniae</i> complex ^b	995	750	76	49		27	30	23	26	10	4	0	na	
%		75.4	7.6	4.9	87.9	2.7	3.0	2.3	2.6	1.0	0.4	0.0		12.1
<i>E. cloacae</i> complex ^c	446	269	54	70		20	10	16	7	na	na	na	na	
%		60.3	12.1	15.7	88.1	4.5	2.2	3.6	1.6					11.9
<i>P. mirabilis</i>	249	179	19	26		10	9	2	4	0	0	0	0	
%		71.9	7.6	10.4	90.0	4.0	3.6	0.8	1.6	0.0	0.0	0.0	0.0	10.0
<i>K. oxytoca</i> ^b	219	96	98	7		4	9	4	0	1	0	0	na	
%		43.8	44.7	3.2	91.8	1.8	4.1	1.8	0.0	0.5	0.0	0.0		8.2
<i>Salmonella</i> species (non-typhoidal) ^d	87	81	4	2		0	0	0	0	0	0	0	na	
%		93.1	4.6	2.3	100.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0		0.0
<i>S. marcescens</i> ^e	163	57	76	24		3	2	1	0	0	na	na	na	
%		35.0	46.6	14.7	96.3	1.8	1.2	0.6	0.0	0.0				3.7
<i>K. aerogenes</i> ^c	122	74	5	40		2	1	0	0	na	na	na	na	
%		60.7	4.1	32.8	97.5	1.6	0.8	0.0	0.0					2.5

a Antimicrobial categories (agents) included: aminoglycosides (gentamicin or tobramycin or amikacin), antipseudomonal penicillins + β-lactamase inhibitor (piperacillin-tazobactam), carbapenems (meropenem), non-extended cephalosporins (cefazolin), extended-spectrum cephalosporins (ceftriaxone or ceftazidime or ceftipime), cephamycins (cefoxitin), fluoroquinolones (ciprofloxacin), folate pathway inhibitors (trimethoprim-sulfamethoxazole), penicillins (ampicillin), and penicillins + β-lactamase inhibitor (amoxicillin-clavulanic acid, CLSI); na: not applicable.

b Antimicrobial categories excluded: penicillins.

c Antimicrobial categories excluded: penicillins, non-extended cephalosporins, cephamycins, penicillins + β-lactamase inhibitor.

d Antimicrobial categories excluded: aminoglycosides.

e Antimicrobial categories excluded: penicillins, non-extended cephalosporins, penicillins + β-lactamase inhibitor.

Most of the referred *E. coli* with an ESBL phenotype (652/685; 95.2%) harboured Ambler class A ESBL (552/652, 84.7%), plasmid borne class C (pAmpC) (73; 11.2%) or both ESBL and pAmpC (27; 4.1%) genes. Almost all with an ESBL gene (574/579; 99.1%) had *bla*_{CTX-M} types: *bla*_{CTX-M} group 9 (*n* = 304); *bla*_{CTX-M} group 1 (*n* = 259); or both *bla*_{CTX-M} group 1 and *bla*_{CTX-M} group 9 (*n* = 11). *E. coli* with pAmpC harboured *bla*_{DHA} (50/100; 50.0%); *bla*_{CMY-2-like} (47/100; 47.0%); or both *bla*_{DHA} and *bla*_{CMY-2-like} genes (3/100; 3.0%).

***Klebsiella pneumoniae* complex**

K. pneumoniae complex isolates showed slightly higher levels of resistance to piperacillin-tazobactam than did *E. coli*, but lower rates of resistance to amoxicillin-clavulanic acid, cefazolin, ceftriaxone, ciprofloxacin, gentamicin, and trimethoprim-sulfamethoxazole. Seventeen *K. pneumoniae* complex isolates (1.5%) had elevated meropenem MICs (see below). Most of the referred *K. pneumoniae* complex isolates with an ESBL phenotype (99/108; 91.7%) harboured ESBL (86; 86.9%); pAmpC (11; 11.1%); or both ESBL and pAmpC (2; 2.0%) genes. The vast majority of ESBLs (76/88; 86.4%) were *bla*_{CTX-M} types, mostly *bla*_{CTX-M} group 1 (67/76; 88.2%). *K. pneumoniae* complex with pAmpC mostly harboured *bla*_{DHA} (11/13; 84.6%).

***Enterobacter cloacae* complex**

Acquired resistance was common among *E. cloacae* complex isolates, to piperacillin-tazobactam (16.9%/26.3%), ceftriaxone (27.8%/27.8%), ceftazidime (22.9%/23.8%) and trimethoprim-sulfamethoxazole (20.3%/20.3%). There was a moderate level of resistance to gentamicin (12.6%/13.6%); cefepime and ciprofloxacin resistance remain at less than 10%. Nineteen *E. cloacae* complex isolates (4.2%) had elevated meropenem MICs.

Carbapenemases

Overall, 32 isolates (32 patients) from 17 institutions from five states/territories were found to harbour a carbapenemase gene. *bla*_{IMP-4} was

detected in 19 isolates: *E. cloacae* complex (15), *K. pneumoniae* (1), *C. freundii* complex (1), *K. aerogenes* (1), and *S. marcescens* (1). *bla*_{NDM-5} was detected in two *E. coli* and *bla*_{NDM-1} in one *E. cloacae* complex and one *K. pneumoniae*. *bla*_{OXA-181} was detected in two *E. coli* and *bla*_{OXA48} in one *E. coli* and one *K. pneumoniae*. *bla*_{IMI-1} was detected in one *E. cloacae* complex. *bla*_{OXA-23} was detected in one *A. baumannii*, which also harboured *bla*_{NDM-1}. Among *P. aeruginosa*, three *bla*_{GES-5} were detected from one institution. Over 40.6% (13/32) of carbapenemase producing organisms were from two institutions (one in Victoria [8]; one in New South Wales [5]).

Plasmid mediated colistin determinants

Of 1,230 referred isolates (excluding species intrinsically resistant to colistin), 568 were sequenced. *mcr-1.1* was detected in 1/259 *E. coli*.

Discussion

AGAR has been tracking resistance in sentinel enteric gram-negative bacteria since 1992. From 2008, surveillance was segregated into hospital-versus community-onset infections. The last year of hospital-onset only surveillance was 2011.¹⁰ In 2013, the first survey of antimicrobial resistance among *Enterobacterales* isolates from bacteraemic patients throughout Australia was conducted using an approach similar to that conducted by the European EARS-Net program. 2020 was the eighth survey of antimicrobial resistance among *Enterobacterales*, and the sixth for *P. aeruginosa* and *Acinetobacter* spp. from bacteraemic patients through Australia.

The percentage of resistance in *E. coli* in 2020 was similar to that seen in 2019 for all antimicrobial agents tested, except for ampicillin, where a 5.7% decrease in resistance was seen relative to 2019. For *K. pneumoniae* complex, the percentage resistance in 2020, relative to 2019, declined by more than 10% for four of the 10 antimicrobial agents tested.

AGAR data show a longitudinal trend of increasing *E. coli* resistance to key anti-gram-negative

antimicrobial agents, such as ceftriaxone and ciprofloxacin (notably in Victoria and the Northern Territory), although both these resistance levels have stabilised since 2019. The steady rise in resistance to fluoroquinolones is more striking in hospital-onset bacteraemia, with a change from 13.7% to 21.8% between 2013 and 2020.

Carbapenem resistance attributable to acquired carbapenemase genes is still uncommon in patients with bacteraemia in Australia, although six different types (*bla*_{IMP}, *bla*_{NDM}, *bla*_{OXA-48}-like, *bla*_{OXA-23}, *bla*_{GES-5}, and *bla*_{IMI-1}) were detected in isolates from 17 of the 49 participating institutions. Compared with many other countries in our region, antimicrobial resistance rates in Australian gram-negative bacteria are still relatively low,¹¹ but similar to those observed in 2019 in many Northern European countries.^{12,13} Resistance to third generation cephalosporins in *E. coli* from bacteraemic patients in Australia is similar to the European Union and European Economic Area average.¹³

One-quarter of *E. coli* and 12% of *K. pneumoniae* complex would be classed as multi-resistant, little changed from the 2019 survey. This is likely to drive more broad-spectrum antibiotic use and increase the resistance selection pressure for important reserve classes, especially the carbapenems and colistin.

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