2025 • Volume • • Electronic publication date:

Australian Group on Antimicrobial Resistance (AGAR) Australian Gram-negative Surveillance Outcome Program (GnSOP) Bloodstream Infection Annual Report 2023

Jan M Bell, Alicia Fajardo Lubian, Sally R Partridge, Thomas Gottlieb, Jennifer Robson, Jonathan R 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. From 1 January 2023 to 31 December 2023, a total of 57 hospitals across Australia participated in the Australian Gram-negative Surveillance Outcome Program (GnSOP).

The 2023 survey tested 10,453 isolates, comprising *Enterobacterales* (9,503; 90.9%), *P. aeruginosa* (806; 7.7%) and *Acinetobacter* species (144; 1.4%), using commercial automated methods. The results were analysed using European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints (January 2024). Key resistances reported are to the third-generation cephalosporin ceftriaxone in 12.9% of *Escherichia coli* and in 6.9% of *Klebsiella pneumoniae* complex isolates. Resistance rates to ciprofloxacin were 14.5% for *E. coli*; 7.8% for the *K. pneumoniae* complex; 3.2% for the *Enterobacter cloacae* complex; and 7.6% for *P. aeruginosa*. Resistance rates to piperacillin-tazobactam were 6.0%; 9.4%; 23.3%; and 13.7% for the same four species/complexes, respectively. Thirty *Enterobacterales* isolates from 30 patients were shown to harbour a carbapenemase gene: ten with a *bla*NDM gene (*bla*NDM-1 [4], *bla*NDM-5 [4], *bla*NDM-7 [2]); nine with a *bla*OXA-48-like gene (*bla*OXA-244 [4], *bla*OXA-48 [2], *bla*OXA-181 [1], *bla*OXA-232 [1], *bla*OXA-484 [1]); eight with *bla*IMP-4; two with *bla*NDM-5 + a *bla*OXA-181-like gene; and one with *bla*KPC-2 + *bla*NDM-5 + *bla*OXA-181. Transmissible carbapenemase genes were also detected in two *Acinetobacter baumannii* complex isolates (*bla*OXA-23; *bla*OXA-23 + *bla*OXA-58 + *bla*IMP-4) and one *P. aeruginosa* (*bla*IMP-4).

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 world-wide 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.[[1]](#footnote-2) In 2004 *Enterobacter*, another genus of gram-negative pathogens in which resistance can be of clinical importance, 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 resistance genes. *Enterobacter* species are less common in the community but are 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 *Enterobacterales* 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 β-lactams due to β-lactamases, especially extended-spectrum β-lactamases that inactivate the third-generation cephalosporins normally considered reserve antimicrobials, is of particular interest. Also of interest is resistance to agents important for treatment of serious infections, such as gentamicin and piperacillin-tazobactam; to highly bioavailable oral agents such as ciprofloxacin; and to reserve agents such as meropenem.

The objectives of the 2023 surveillance program were:

* to monitor resistance in *Enterobacterales*, *P. aeruginosa* and *Acinetobacter* species isolated from blood cultures taken from patients presenting to hospital or already inpatients 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 2023, thirty-three laboratories servicing 57 hospitals across Australia, including seven children’s hospitals and 13 regional or district hospitals from north-west Western Australia, collected either all or up to 200 isolates from different patient episodes of bacteraemia. An episode was defined as community-onset (CO) if the first positive blood culture was collected 48 hours or less after admission, and as hospital-onset (HO) if collected greater than 48 hours after admission.

## Species identification

Species were identified using the routine method at each institution; Vitek®, Phoenix™ 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® 2 (BioMérieux, France) or Phoenix™ (Becton Dickinson, USA), which are calibrated to the International Organization for Standardization (ISO) reference standard method of broth microdilution. Commercially available Vitek (AST-N246, AST-N435, AST-N410) or Phoenix NMIC-422 cards were utilised by all participants throughout the survey period. The EUCAST v14 breakpoints from January 2024 have been employed in the analysis.1

## Multidrug resistance

The definitions used by Magiorakos et al. were applied in this survey,2 where multidrug resistance (MDR) is defined as resistance to one or more agent in three or more antimicrobial categories. The antimicrobial categories (agents) included were aminoglycosides (gentamicin and/or tobramycin); antipseudomonal penicillins + β-lactamase inhibitor (piperacillin–tazobactam); carbapenems (meropenem); extended-spectrum cephalosporins (ceftriaxone and/or ceftazidime); cephamycins (cefoxitin); fluoroquinolones (ciprofloxacin); folate pathway inhibitors (trimethoprim–sulfamethoxazole); non-extended-spectrum cephalosporins (cefazolin or cefuroxime); and aminopenicillins (ampicillin). Antimicrobials were excluded from these counts for any species with a natural resistance mechanism. For *K. pneumoniae* complex, aminopenicillins were excluded, and for *E. cloacae* complex, cephamycins, non-extended spectrum cephalosporins and aminopenicillins were excluded.

## 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;

all *Enterobacterales* with meropenem MIC > 0.125 mg/L (> 0.25 mg/L if tested using Vitek®);

all *P. aeruginosa* and *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.

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 or the Australian Genome Research Facility (AGRF) using Illumina platforms. Data were analysed using a modification of the Nullarbor bioinformatic pipeline,3 incorporating searching contigs against the NCBI AMRFinder database[[2]](#footnote-3) using ABRicate4 and AMRFinder,5 followed by a custom AMR-specific pipeline which includes a read-based search using ARIBA6 against the CARD7 and NCBI databases. Ambiguities and potential multiple gene copies/variants were checked manually by mapping reads to reference genes[[3]](#footnote-4) using Geneious. Kleborate8 was used to screen *K. pneumoniae* complex species for virulence loci and K (capsule) serotype.

# Results

The species isolated, and the numbers of each, are listed in Table 1. *Enterobacterales* accounted for 90.9%, followed by *P. aeruginosa* (7.7%) and *Acinetobacter* species (1.4%). In the *Enterobacterales*, 86.3% of all isolates belonged to three genera—*Escherichia* (60.1%), *Klebsiella* (20.3%) and *Enterobacter* (5.9%). Major resistances for the top six ranked species are listed in Table 2. For gram-negative species, 77.0% of all episodes were CO, with differences seen between *Enterobacterales* (78.7%), *Acinetobacter* species (63.9%) and *P. aeruginosa* (59.4%).

The activity of antimicrobial agents tested against *E. coli* and *K. pneumoniae* complex by place of onset are shown in Table 3.

A more detailed breakdown of resistance by state and territory is provided in the online GnSOP 2023 report.[[4]](#footnote-5)

Table 1: Number and proportion of species isolated, blood cultures, AGAR, 2023

| Species | Percentage (n) | Onset setting, percentage (n) | |
| --- | --- | --- | --- |
| Community onset | Hospital onset |
| *Escherichia coli* | 54.6 (5,705) | 84.3 (4,808) | 15.7 (897) |
| *Klebsiella pneumoniae* complex | 13.8 (1,442) | 73.6 (1,061) | 26.4 (381) |
| *Pseudomonas aeruginosa* | 7.7 (806) | 59.4 (479) | 40.6 (327) |
| *Enterobacter cloacae* complex | 5.3 (557) | 54.0 (301) | 46.0 (256) |
| *Proteus mirabilis* | 3.4 (354) | 81.9 (290) | 18.1 (64) |
| *Klebsiella oxytoca* | 3.0 (315) | 70.5 (222) | 29.5 (93) |
| *Serratia marcescens* | 2.3 (242) | 59.5 (144) | 40.5 (98) |
| *Klebsiella aerogenes* | 1.6 (166) | 57.8 (96) | 42.2 (70) |
| *Salmonella* species (non-typhoidal) | 1.3 (140) | 91.4 (128) | 8.6 (12) |
| *Citrobacter freundii* complex | 1.1 (112) | 67.9 (76) | 32.1 (36) |
| *Morganella morganii* | 1.0 (106) | 67.9 (72) | 32.1 (34) |
| *Salmonella* species (typhoidal) | 0.9 (90) | 97.8 (88) | 2.2 (2) |
| *Acinetobacter baumannii* complex | 0.8 (87) | 58.6 (51) | 41.4 (36) |
| *Citrobacter koseri* | 0.7 (74) | 71.6 (53) | 28.4 (21) |
| *Raoultella ornithinolytica* | 0.3 (31) | 61.3 (19) | 38.7 (12) |
| *Pantoea agglomerans* | 0.2 (22) | 68.2 (15) | 31.8 (7) |
| *Acinetobacter* speciesa | 0.2 (21) | 57.1 (12) | 42.9 (9) |
| *Proteus vulgaris* | 0.2 (20) | 75.0 (15) | 25.0 (5) |
| *Providencia rettgeri* | 0.2 (18) | 83.3 (15) | 16.7 (3) |
| *Hafnia alvei* | 0.2 (16) | 50.0 (8) | 50.0 (8) |
| *Pantoea* speciesa | 0.1 (13) | 69.2 (9) | 30.8 (4) |
| *Acinetobacter ursingii* | 0.1 (12) | 83.3 (10) | 16.7 (2) |
| Other species (total *n* = 38) | 1.0 (94) | 74.0 (77) | 26.0 (27) |
| Total | 10,453 | 77.0 (8,049) | 23.0 (2,404) |

a Species not determined.

Table 2: Resistance rates for the top six ranked gram-negative species isolated from blood, AGAR, 2023

| Antimicrobial | Percentage resistant, EUCAST breakpoints (number)a | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| *E. coli* | *K. pneumoniae* complex | *P. aeruginosa* | *E. cloacae* complex | *P. mirabilis* | *K. oxytoca* |
| Ampicillin | 52.3 (5,648) | *b* | na | *b* | 18.7 (353) | *b* |
| Amoxicillin–clavulanic acid (2:1 ratio)c | 9.4 (4,295) | 3.9 (1,030) | na | *b* | 4.6 (262) | 2.6 (234) |
| Cefazolin | 22.7 (4,921) | 11.3 (1,246) | na | *b* | 25.3 (289) | 61.5 (244) |
| Cefepime | 3.4  (5,646) | 2.2 (1,428) | 5.8 (787) | 3.8 (555) | 1.1 (353) | 0.3 (312) |
| Ceftazidime | 6.5 (5,647) | 6.0 (1,428) | 8.9 (790) | 22.0 (555) | 1.7 (351) | 1.9 (312) |
| Ceftriaxone | 12.9 (5,649) | 6.9 (1,428) | na | 25.0 (555) | 2.0 (353) | 7.4 (312) |
| Ciprofloxacin | 14.5 (5,634) | 7.8 (1,421) | 7.6 (789) | 3.2 (554) | 3.3 (351) | 0.6 (311) |
| Gentamicin | 8.1 (5,645) | 3.3 (1,427) | na | 4.1 (555) | 7.7 (352) | 1.9 (312) |
| Meropenem | 0.2 (5,649) | 0.4 (1,427) | 2.0 (789) | 1.1 (554) | 0.0 (362) | 1.0 (312) |
| Nitrofurantoin | 0.5 (4,902) | na | na | na | *b* | na |
| Piperacillin-tazobactam | 6.0 (5,629) | 9.4 (1,425) | 13.7 (788) | 23.3 (553) | 0.0 (353) | 12.5 (311) |
| Tobramycin | 8.6 (5,616) | 3.7 (1,414) | 0.9 (786) | 4.1 (543) | 6.3 (352) | 1.9 (308) |
| Trimethoprimd | 32.6 (4,910) | 16.8 (1,203) | na | 14.2 (466) | 21.5 (307) | 5.6 (284) |
| Trimethoprim–sulfamethoxazole | 29.5 (5,646) | 13.7 (1,428) | na | 13.2 (555) | 17.3 (353) | 5.1 (312) |

a EUCAST: European Committee on Antimicrobial Susceptibility Testing; na: not applicable (testing not recommended).

b Considered largely intrinsically resistant.

c For susceptibility testing purposes, the Clinical and Laboratory Standards Institute (CLSI) uses a 2:1 ratio. EUCAST fixes the concentration of clavulanic acid at 2 mg/L; this formulation is only available on specific cards. Data for the CLSI formulation is shown.

d Breakpoints apply only to isolates from patients with uncomplicated urinary tract infection.

Table 3: Number and resistance rates for *Escherichia coli* and *Klebsiella pneumoniae* complex isolated from blood, by place of onset, AGAR, 2023

| Species and antimicrobial | Community-onseta | | | Hospital-onseta | | |
| --- | --- | --- | --- | --- | --- | --- |
| No. | S-IE, % | R, % | No. | S-IE, % | R, % |
| ***Escherichia coli*** | | | | | | |
| Ampicillin | 4,758 | —b | 50.8 | 890 | —b | 60.6 |
| Amoxicillin-clavulanic acid (2:1 ratio)c | 3,642 | 9.7d | 7.2 | 653 | 8.1d | 13.8 |
| Piperacillin–tazobactam | 4,743 | —b | 4.8 | 886 | —b | 12.0 |
| Cefazolin | 4,167 | 78.8 | 21.2 | 754 | 69.0 | 31.0 |
| Cefuroxime | 437 | 85.4 | 14.6 | 111 | 71.2 | 28.8 |
| Ceftriaxone | 4,759 | 0.1 | 12.0 | 890 | 0.1 | 17.8 |
| Ceftazidime | 4,757 | 7.4 | 5.7 | 890 | 9.8 | 10.8 |
| Cefepime | 4,757 | 6.2 | 2.8 | 889 | 7.5 | 6.3 |
| Gentamicin | 4,757 | —b | 7.9 | 888 | —b | 9.1 |
| Tobramycin | 4,735 | —b | 8.3 | 881 | —b | 10.1 |
| Amikacin | 4,757 | —b | 1.1 | 889 | —b | 2.1 |
| Ciprofloxacin | 4,746 | 5.0 | 13.9 | 888 | 5.3 | 17.7 |
| Meropenem | 4,759 | 0.0 | 0.1 | 890 | 0.3 | 0.4 |
| ***Klebsiella pneumoniae* complex** | | | | | | |
| Amoxicillin–clavulanic acid (2:1 ratio)c | 767 | 2.7d | 2.1 | 263 | 5.3d | 9.1 |
| Piperacillin–tazobactam | 1,046 | —b | 7.0 | 379 | —b | 16.1 |
| Cefazolin | 927 | 90.6 | 9.4 | 319 | 83.1 | 16.9 |
| Cefuroxime | 92 | 91.3 | 8.7 | 47 | 85.1 | 14.9 |
| Ceftriaxone | 1,049 | 0.2 | 6.3 | 379 | 0.0 | 8.4 |
| Ceftazidime | 1,049 | 1.2 | 5.2 | 379 | 4.0 | 7.9 |
| Cefepime | 1,049 | 3.4 | 1.7 | 379 | 3.4 | 3.7 |
| Gentamicin | 1,048 | —b | 3.0 | 379 | —b | 4.2 |
| Tobramycin | 1,042 | —b | 3.1 | 372 | —b | 5.6 |
| Amikacin | 1,049 | —b | 0.2 | 379 | —b | 1.3 |
| Ciprofloxacin | 1,043 | 3.5 | 6.9 | 378 | 5.0 | 10.3 |
| Meropenem | 1,049 | 0.0 | 0.4 | 378 | 0.3 | 0.5 |

a No.: number of isolates; S-IE: susceptible, increased exposure; R: resistant.

b No category defined.

c For susceptibility testing purposes, the Clinical and Laboratory Standards Institute (CLSI) uses a 2:1 ratio. The European Committee on Antimicrobial Susceptibility Testing (EUCAST) fixes the concentration of clavulanic acid at 2 mg/L; this formulation is only available on specific cards. Data for the CLSI formulation is shown.

d Percentage sensitive dose dependent (CLSI breakpoints).

## *Escherichia coli*

The moderately high levels of resistance to ampicillin (and therefore amoxicillin) observed in *E. coli* were similar to those in the 2022 survey (2023: 52.3% versus 2022: 51.5%). Resistance to third generation cephalosporins was also maintained compared with 2022 (ceftriaxone 2023: 12.9% versus 2022: 12.7%; ceftazidime 2023: 6.5% versus 2022: 5.9%). An extended spectrum β-lactamase (ESBL) phenotype was significantly more prevalent among HO than CO episodes of *E. coli* (21.6% versus 14.1%; *p* < 0.01). Moderate levels of resistance to cefazolin (22.7%) and trimethoprim–sulfamethoxazole (29.5%) were detected. Ciprofloxacin resistance was found in 14.5% of *E. coli* isolates, 0.8 percentage points higher than in the 2022 survey. Resistance to gentamicin (8.1%), piperacillin-tazobactam (6.0%) and cefepime (3.4%) was low. Twenty-two isolates (0.4%) had an elevated meropenem MIC (≥ 0.5 mg/L), up from ten isolates (0.2%) in 2022. For the isolates with an ESBL phenotype, 51.7% and 30.2% were resistant to ciprofloxacin and gentamicin, respectively. Almost one-quarter of *E. coli* isolates (24.5%) would be considered multi-drug resistant.

Most of the referred *E. coli* with an ESBL phenotype (753/791; 95.2%) harboured an Ambler class A ESBL gene (579/791; 76.9%), a plasmid borne class C gene (pAmpC) (133; 17.7%), or a carbapenemase gene alone (3; 0.4%); or an ESBL plus a pAmpC gene (29; 3.9%); or a carbapenemase gene plus either an ESBL gene or a pAmpC gene (9; 1.1%). *bla*CTX-M types continue to be the dominant β-lactamase genes in *E. coli*. Of 753 isolates with a confirmed β lactamase gene, 609 (80.9%) had one or more *bla*CTX-M genes detected by WGS, predominantly *bla*CTX-M-27 (*n* = 271) or *bla*CTX-M-15 (*n* = 268). *E. coli* with pAmpC harboured *bla*DHA-1 (116/166; 69.9%) or a *bla*CMY-2-like gene (50/166; 30.1%).

## *Klebsiella pneumoniae* complex

*K. pneumoniae* complex isolates showed slightly higher levels of resistance to piperacillin-tazobactam compared with *E. coli*, but lower rates of resistance to cefazolin, ceftriaxone, ciprofloxacin, gentamicin, and trimethoprim-sulfamethoxazole. An ESBL phenotype was higher among HO than CO episodes (12.4% versus 7.1%, *p* < 0.01). Twelve *K. pneumoniae* complex isolates (0.8%) had an elevated meropenem MIC (see below). Most of the referred *K. pneumoniae* complex isolates with an ESBL phenotype (97/110; 88.2%) harboured an ESBL gene (74; 76.3%), a pAmpC gene (16; 16.5%), or a carbapenemase gene (1; 1.0%) alone; or an ESBL gene and a pAmpC gene (2; 2.1%); or a carbapenemase gene with either an ESBL gene or a pAmpC gene (4; 4.1%). Almost all the ESBL genes (78/79; 98.7%) were *bla*CTX-M types, mostly *bla*CTX-M-15 (64/78; 82.1%). *K. pneumoniae* complex isolates harboured either *bla*DHA-1 (19/20; 95.0%) or a *bla*CMY-2-like gene (1/20). In 2023, the proportion of *K. pneumoniae* complex isolates which would be considered multi-drug resistant was 8.9%.

In GnSOP 2023, twelve *K. pneumoniae* isolates (and one *K. oxytoca*) would be classified as hypervirulent (virulence score ≥ 3) by Kleborate.8 Nine isolates had a K1 or K2 capsule serotype, the most common types in hypervirulent *K. pneumoniae* (hvKp). Five isolates were ST23-K1, already identified globally as a high-risk clone of hvKp carrying carbapenemase genes. Four of these had a virulence score of 5, with each carrying *ybt*, *clb* and *iuc*, but no ESBL or carbapenemase genes. One ST23-K1 isolate with a virulence score of 3 (*iuc*only) had *bla*CTX-M-15.

## *Enterobacter cloacae* complex

Acquired resistance was common among *E. cloacae* complex isolates, to piperacillin-tazobactam (23.3%), ceftriaxone (25.0%) or ceftazidime (22.0%). There was a moderate level of resistance to trimethoprim–sulfamethoxazole (13.2%); cefepime, ciprofloxacin and gentamicin resistance all remain at less than 5%. Although *E. cloacae* complex isolates are generally more resistant than *E. coli* to β-lactam antimicrobials, resistance rates to non-β-lactams tend to be lower. Twenty-two (4.0%) *E. cloacae* complex isolates had an elevated meropenem MIC. In 2023, the proportion of *E. cloacae* complex isolates that would be considered multi-drug resistant was 8.5%.

## Carbapenemase genes

Overall, 33 isolates (33 patients) from 18 hospitals from six states/territories were found to harbour a carbapenemase gene. A *bla*NDM gene was detected in ten isolates: five *E. coli* (*bla*NDM-5 [4]; *bla*NDM-7 [1]), two *K. pneumoniae* complex (*bla*NDM-1), two *E. cloacae* complex (*bla*NDM-1) and one *K. oxytoca* (*bla*NDM-7). A *bla*OXA-48-like gene was detected in nine isolates: seven *E. coli* (*bla*OXA-244 [4]; *bla*OXA-48 [2]; *bla*OXA-484 [1]), one *K. oxytoca* (*bla*OXA-232) and one *K. aerogenes* (*bla*OXA-232). *bla*IMP-4 was detected in nine isolates: *E. cloacae* complex (three), *E. coli* (two), *K. oxytoca* (one), *Citrobacter freundii* complex (one), *Serratia marcescens* (one), and *P. aeruginosa* (one). Other *Enterobacterales* had multiple carbapenemase genes: *bla*NDM-5 + a *bla*OXA 181-like gene (*n* = 2), or *bla*KPC-2 + *bla*NDM-5 + *bla*OXA-181 (*n* = 1). *bla*OXA-23 was detected in two *Acinetobacter baumannii* complex isolates, one of which also had *bla*OXA-58 and *bla*IMP-4.

## Plasmid-borne colistin determinants

Two isolates with *bla*NDM carbapenemase genes also harboured *mcr-9.1* (*E. cloacae* complex *bla*NDM-1, *K. oxytoca* *bla*NDM-7). Seven additional isolates (*E. cloacae* complex, *n* = 5; *E. coli*, *n* = 1; *K. oxytoca*, *n* = 1) that did not carry a carbapenemase gene had either *mcr-9* (*n* = 5) or *mcr-10* (*n* = 2). *mcr-9* has recently been found among several species of *Enterobacterales*. It is not associated with a resistant phenotype,9 but is typically carried on HI2 plasmids.10,11

# Discussion

AGAR has been tracking resistance in sentinel enteric gram-negative bacteria since 1992. From 2008, surveillance was separated into HO versus CO infections. The last year of HO-only surveillance was 2011.12 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.13 The 2023 survey was the eleventh of antimicrobial resistance among *Enterobacterales*, and the ninth for *P. aeruginosa* and *Acinetobacter* spp. from bacteraemic patients through Australia.

The percentages of resistant *E. coli* in 2023 were similar to those seen in 2022 for all antimicrobial agents tested, except for trimethoprim-sulfamethoxazole, which increased slightly from 27.9% in 2022 to 29.5% in 2023. For the *K. pneumoniae* complex, the percentage of resistant isolates in 2023 was similar to that seen in 2022 for all antimicrobials, with slight increases (0.7 percentage point each) in resistance to both piperacillin-tazobactam and trimethoprim-sulfamethoxazole.

AGAR data show a longitudinal trend of increasing *E. coli* resistance to key anti-gram-negative antimicrobial agents, including ceftriaxone and ciprofloxacin. Resistance to both agents stabilised in 2018–2020 (ceftriaxone 13.3–13.4%, ciprofloxacin 15.2–16.1%); the levels of resistance declined to 12.5% and 12.3% respectively in 2021. In 2023, the level of resistance increased (12.9% and 14.5%). The steady rise in resistance to fluoroquinolones in *E. coli* is more striking in HO bacteraemia, with a change from 13.7% to 19.8% between 2013 and 2018, to 21.3% in 2019, and to 21.8% in 2020. In 2021 the level of resistance fell to 16.7%; it increased slightly to 17.8% in 2022, and was 17.7% in 2023. In *K. pneumoniae* complex isolates, rates of resistance to ciprofloxacin were lower than for *E. coli*. Resistance in *K. pneumoniae* complex isolates peaked in 2018–2019 at 11.0% and 10.2% respectively, falling to 7.3% in 2021, and was at 7.8% in both 2022 and 2023.

Carbapenem resistance attributable to acquired carbapenemase genes is still uncommon in patients with bacteraemia in Australia. Seven different gene profiles (*bla*NDM [10]; *bla*OXA-48-like [9]; *bla*IMP-4 [9]; *bla*NDM-5 + *bla*OXA 181-like [2]; *bla*KPC-2 + *bla*NDM-5 + *bla*OXA-181 [1]; *bla*OXA-23 [1]; and *bla*OXA-23 + *bla*OXA-58 + *bla*IMP-4 [1]) were detected in 33 isolates from 18 of the participating hospitals. Compared with many other countries in our region, antimicrobial resistance rates in Australian gram-negative bacteria are still relatively low,14,15 but similar to those observed in 2022 in many Northern European countries.16,17 Resistance to third generation cephalosporins in *E. coli* from bacteraemic patients in Australia is similar to the European Union and European Economic Area average.17 Rates of resistance in *K. pneumoniae* complex are low in Australia (< 10%) , compared to rates > 25% in parts of Europe. Some of this is explained by the relatively greater predisposition for *Klebsiella* species to carry carbapenemase types found in Europe (such as *bla*KPC) and to the unregulated fluoroquinolone use compared to Australia where this antimicrobial class has been under greater usage scrutiny and regulation in both the human and animal husbandry sectors. Nonetheless this illustrates the potential for greater increases in resistance rates over time and the need for ongoing surveillance.

Just under one-fifth of *E. coli* would be classed as MDR, little changed from the 2022 survey. The proportion of *K. pneumoniae* complex isolates classed as MDR fell from 9.9% in 2019 and 2020 to 8.8% in 2021 and 8.0% in 2022. In 2023, the MDR proportion increased to 8.8%.

The impact of the SARS-CoV-2 pandemic on antimicrobial resistance may be due to a number of contributing factors. A combination of coronavirus disease 2019 (COVID-19)-related travel restrictions on incoming travellers throughout much of 2020 and 2021,18 and an increasing awareness of and utilization of antimicrobial stewardship as part of the Australia-wide implementation and accreditation of National Safety and Quality Health Service Standards,19 may have reduced some resistance rates particularly for ESBLs.

Compared to previous AGAR surveys, there was an increase in the number of *bla*NDM genes reported in isolates from patients with bacteraemia in 2023.20 This may be due to the return of international travel. In 2023, one-third (10/30, 33.3%) of all CPE carried a *bla*NDM gene, 30.0% carried a *bla*OXA-48-like gene (*n* = 9), 10.0% carried both *bla*NDM and *bla*OXA-48-like genes (*n* = 3), and 26.7% carried *bla*IMP 4 (*n* = 8); the latter compared with 62.1% (18/29) CPE in 2022. More than three-quarters (23/30; 76.7%) of all CPE in 2023 were from New South Wales (*n* = 17; 56.7%) or Victoria (*n* = 6; 20.0%).

The 2023 survey suggests that there was a slight increase in resistance rates versus 2022 to pre-COVID-19 levels. Future AGAR surveys will help determine if this observed increase in resistance rates is sustained.

# Acknowledgments

This study was funded by the Australian Government Department of Health and Aged Care.

AGAR gratefully acknowledges Jenny Draper for processing WGS data and the Antimicrobial Resistance Laboratory, Microbial Genomics Reference Laboratory, CIDMLS, ICPMR, Westmead Hospital (Elena Martinez), the Genomics Facility at WIMR (Joey Lai) and the Australian Genome Research Facility for performing whole genome sequencing.

Members of AGAR in 2023 were:

Australian Capital Territory

Peter Collignon and Susan Bradbury, Canberra Hospital

New South Wales

Alison Kesson and Andrew Jarrett, Children’s Hospital Westmead

Thomas Gottlieb and John Huynh, Concord Hospital

Gabrielle O’Kane and Nola Hitchick, Gosford Hospital

Hemalatha Varadhan and Bree Harris, John Hunter Hospital

Michael Maley and Helen Ziochos, Liverpool Hospital

James Branley and Linda Douglass, Nepean Hospital

Angela Wong, Royal North Shore Hospital

Sebastiaan van Hal and Thomas Le, Royal Prince Alfred Hospital

David Lorenz, St Vincent’s Hospital Sydney

Monica Lahra and Peter Huntington, Sydney Children’s Hospital and Prince of Wales Hospital

Jonathan Iredell and Elena Martinez, Westmead Hospital

Peter Newton and Melissa Hoddle, Wollongong Hospital

Northern Territory

James McLeod, Alice Springs Hospital

Rob Baird and Jann Hennessy, Royal Darwin Hospital

Queensland

Claire Heney and Narelle George, Pathology Queensland Central Laboratory, Royal Brisbane and Women’s Hospital, Queensland Children’s Hospital

Petra Derrington and Cheryl Curtis, Pathology Queensland Gold Coast University Hospital

Robert Horvath, Pathology Queensland Prince Charles Hospital

Naomi Runnegar and Anna Jones, Pathology Queensland Princess Alexandra Hospital

Jennifer Robson and Marianne Allen, Sullivan Nicolaides Pathology, Greenslopes Private Hospital and Mater Private Hospital Townsville

South Australia

Kelly Papanaoum and Xiao Ming Chen, SA Pathology, Flinders Medical Centre

Morgyn Warner and Kija Smith, SA Pathology, Royal Adelaide Hospital and Women’s and Children’s Hospital

Tasmania

Pankaja Kalukottege and Kathy Wilcox, Launceston General Hospital

Louise Cooley and David Jones, Royal Hobart Hospital

Victoria

Adam Jenney and Jacqueline Williams, Alfred Hospital

Marcel Leroi and Elizabeth Grabsch, Austin Health

Tony Korman, Despina Kotsanas and Kathryn Cisera, Dandenong Hospital, Monash Children’s Hospital, Monash Medical Centre

Katherine Bond and Rose Cotronei, Royal Melbourne Hospital

Andrew Daley and Gena Gonis, Royal Women’s and Children’s Hospital

Amy Crowe and Lisa Brenton, St Vincent’s Hospital

Western Australia

Shalinie Perera and Ian Meyer, Western Diagnostic Pathology, Joondalup Hospital

Shakeel Mowlaboccus and Denise Daley, PathWest Laboratory Medicine WA, Fiona Stanley Hospital

Christopher Blyth, PathWest Laboratory Medicine WA, Perth Children’s Hospital

Ronan Murray and Jacinta Bowman, PathWest Laboratory Medicine WA, Sir Charles Gairdner Hospital

Michael Leung, PathWest Laboratory Medicine WA, north-west regional WA

Owen Robinson and Geoffrey Coombs, PathWest Laboratory Medicine WA, Royal Perth Hospital

Sudha Pottumarthy-Boddu and Jacqueline Foster, Australian Clinical Laboratories, St John of God Hospital Murdoch

# Author details

Ms Jan M Bell1

Dr Alicia Fajardo Lubian2,3

A/Prof. Sally R Partridge2,3,4

A/Prof. Thomas Gottlieb3,5

Dr Jennifer Robson6

Prof. Jonathan R Iredell2,3,4

Ms Denise A Daley7

Prof. Geoffrey W Coombs8,9

1. Australian Group on Antimicrobial Resistance, Canberra, the Australian Capital Territory, Australia
2. Westmead Institute for Medical Research, Westmead, New South Wales, Australia
3. The University of Sydney, New South Wales, Australia
4. Westmead Hospital, Westmead, New South Wales, Australia
5. Department of Microbiology and Infectious Diseases, Concord Hospital, Concord, New South Wales, Australia
6. Department of Microbiology, Sullivan Nicolaides Pathology, Bowen Hills, Queensland
7. Australian Group on Antimicrobial Resistance, Fiona Stanley Hospital, Murdoch, Western Australia, Australia
8. Antimicrobial Resistance and Infectious Diseases (AMRID) Research Laboratory, Murdoch University, Murdoch, Western Australia, Australia
9. Department of Microbiology, PathWest Laboratory Medicine-WA, Fiona Stanley Hospital, Murdoch, Western Australia, Australia

Corresponding author

A/Prof. Thomas Gottlieb

Department of Microbiology and Infectious Diseases, Concord Hospital, Concord, New South Wales, Australia

Telephone: +61 2 9767 7533

Email: thomas.gottlieb@health.nsw.gov.au

# References

1. The European Committee on Antimicrobial Susceptibility Testing (EUCAST). *Breakpoint tables for interpretation of MICs and zone diameters*. Version 14.0. Basel: EUCAST; 1 January 2024. Available from: https://www.eucast.org/fileadmin/src/media/PDFs/EUCAST\_files/Breakpoint\_tables/v\_14.0\_Breakpoint\_Tables.pdf.
2. Magiorakos AP, Srinivasan A, Carey RB, Carmeli Y, Falagas ME, Giske CG et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. *Clin Microbiol Infect*. 2012;18(3):268–81. doi: https://doi.org/10.1111/j.1469-0691.2011.03570.x.
3. Seemann T, Goncalves da Silva A, Bulach DM, Schultz MB, Kwong JC, Howden BP. *Nullarbor*. San Francisco: Github; 2020. Available from: https://github.com/tseemann/nullarbor.
4. Seemann T. *Abricate*. San Francisco: Github; 2020. Available from: https://github.com/tseemann/abricate.
5. National Center for Biotechnology Information (NCBI). *AMRFinderPlus*. [Website.] Bethesda; United States National Library of Medicine, NCBI: 2020. Available from: https://ncbi.nlm.nih.gov/pathogens/antimicrobial-resistance/AMRFinder/.
6. Hunt M, Mather AE, Sánchez-Busó L, Page AJ, Parkhill J, Keane JA et al. ARIBA: rapid antimicrobial resistance genotyping directly from sequencing reads. *Microb Genom*. 2017;3(10):e000131. doi: https://doi.org/10.1099/mgen.0.000131.
7. Alcock BP, Raphenya AR, Lau TTY, Tsang KK, Bouchard M, Edalatmand A et al. CARD 2020: antibiotic resistome surveillance with the comprehensive antibiotic resistance database. *Nucleic Acids Res*. 2020;48(D1):D517–25. doi: https://doi.org/10.1093/nar/gkz935.
8. Lam MMC, Wick RR, Watts SC, Cerdeira LT, Wyres KL, Holt KE. A genomic surveillance framework and genotyping tool for *Klebsiella pneumoniae* and its related species complex. *Nat Commun*. 2021;12(1):4188. doi: https://doi.org/10.1038/s41467-021-24448-3.
9. Tyson GH, Li C, Hsu CH, Ayers S, Borenstein S, Mukherjee S et al. The *mcr-9* gene of *Salmonella* and *Escherichia coli* is not associated with colistin resistance in the United States. *Antimicrob Agents Chemother*. 2020;64(8):e00573-20. doi: https://doi.org/10.1128/AAC.00573-20.
10. Kieffer N, Royer G, Decousser JW, Bourrel AS, Palmieri M, Ortiz De La Rosa JM et al. *mcr-9*, an inducible gene encoding an acquired phosphoethanolamine transferase in *Escherichia coli*, and its origin. *Antimicrob Agents Chemother*. 2019;63(9):e00965-19. doi: https://doi.org/10.1128/AAC.00965-19.
11. Li Y, Dai X, Zeng J, Gao Y, Zhang Z, Zhang L. Characterization of the global distribution and diversified plasmid reservoirs of the colistin resistance gene *mcr-9*. *Sci Rep*. 2020;10(1):8113. doi: https://doi.org/10.1038/s41598-020-65106-w.
12. Turnidge JD, Gottlieb T, Mitchell D, Pearson J, Bell JM, on behalf of the Australian Group for Antimicrobial Resistance (AGAR). *Gram-negative Survey: 2011 Antimicrobial Susceptibility Report*. AGAR; 2012. Available from:   
    http://agargroup.org.au/wp-content/uploads/2017/08/AGAR-GNB11-Report-FINAL.pdf.
13. European Centre for Disease Prevention and Control (ECDC). European Antimicrobial Resistance Surveillance Network (EARS-Net). [Webpage.] Solna: ECDC; 17 November 2023. [Accessed on 2 April 2024.] Available from: https://www.ecdc.europa.eu/en/about-us/networks/disease-networks-and-laboratory-networks/ears-net-data.
14. Diekema DJ, Hsueh PR, Mendes RE, Pfaller MA, Rolston KV, Sader HS et al. The microbiology of bloodstream infection: 20-year trends from the SENTRY Antimicrobial Surveillance Program. *Antimicrob Agents Chemother*. 2019;63(7):63:e00355-19. doi: https://doi.org/10.1128/AAC.00355-19.
15. Sheng WH, Badal RE, Hsueh PR, on behalf of the SMART Program. Distribution of extended-spectrum ß-lactamases, AmpC ß-lactamases, and carbapenemases among Enterobacteriaceae isolates causing intra-abdominal infections in the Asia-Pacific region: results of the study for Monitoring Antimicrobial Resistance Trends (SMART). *Antimicrob Agents Chemother*. 2013;57(7):2981–8. doi: https://doi.org/10.1128/AAC.00971-12.
16. ECDC. *Antimicrobial resistance in the EU/EEA (EARS-Net) – Annual epidemiological report for 2022*. Solna: ECDC; 17 November 2023. Available from: https://www.ecdc.europa.eu/en/publications-data/surveillance-antimicrobial-resistance-europe-2022.
17. ECDC/World Health Organization (WHO) Regional Office for Europe. *Antimicrobial resistance surveillance in Europe 2023 – 2021 data*. Solna: ECDC; 14 April 2023. Available from: https://www.ecdc.europa.eu/en/publications-data/antimicrobial-resistance-surveillance-europe-2023-2021-data.
18. Collignon P, Beggs J, Robson J. COVID-19 restrictions limited interactions of people and resulted in lowered *E. coli* antimicrobial resistance rates. *JAC Antimicrob Resist*. 2024;6(4):dlae125. doi: https://doi.org/10.1093/jacamr/dlae125.
19. Australian Commission on Safety and Quality in Health Care (ASCQHC). *National Safety and Quality Health Service Standards*. 2nd ed; updated May 2021. Sydney: ACSQHC; May 2021. Available from: https://www.safetyandquality.gov.au/publications-and-resources/resource-library/national-safety-and-quality-health-service-standards-second-edition.
20. Bell JM, Fajardo Lubian A, Partridge SR, Gottlieb T, Robson J, Iredell JR et al. Australian Group on Antimicrobial Resistance (AGAR) Australian Gram-negative Surveillance Outcome Program (GnSOP) Bloodstream Infection Annual Report 2022. *Commun Dis Intell (2018)*. 2023;47. doi: https://doi.org/10.33321/cdi.2023.47.69.

© Commonwealth of Australia as represented by the Department of Health and Aged Care

ISSN: 2209-6051 Online

This journal is indexed by Index Medicus and Medline.

Creative Commons Licence

This publication is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International Licence (CC BY-NC-ND) available from https://creativecommons.org/licenses/by-nc-nd/4.0/legalcode (Licence). You must read and understand the Licence before using any material from this publication.

Restrictions

The Licence does not cover, and there is no permission given for, use of any of the following material found in this publication (if any):

* the Commonwealth Coat of Arms (by way of information, the terms under which the Coat of Arms may be used can be found on the Department of Prime Minister and Cabinet website;
* any logos (including the Department of Health and Aged Care’s logo) and trademarks;
* any photographs and images;
* any signatures; and
* any material belonging to third parties.

Disclaimer

Opinions expressed in *Communicable Diseases Intelligence* are those of the authors and not necessarily those of the Department of Health and Aged Care or the Communicable Diseases Network Australia. Data may be subject to revision.

Enquiries

Enquiries regarding any other use of this publication should be addressed to the CDI Editor at: cdi.editor@health.gov.au.

Communicable Diseases Network Australia

Communicable Diseases Intelligence contributes to the work of the [Communicable Diseases Network Australia](http://www.health.gov.au/cdna).

About Communicable Diseases Intelligence

*Communicable Diseases Intelligence* (CDI) is a peer-reviewed scientific journal published by the Health Security & Emergency Management Division, Department of Health and Aged Care. The journal aims to disseminate information on the epidemiology, surveillance, prevention and control of communicable diseases of relevance to Australia.

**Editor**: Christina Bareja • **Deputy Editor**: Simon Petrie • **Design and Production**: Lisa Thompson

**Editorial Advisory Board**: David Durrheim, Mark Ferson, Clare Huppatz, John Kaldor, Martyn Kirk and Meru Sheel

Submit an Article

Submit your next communicable disease related article to CDI for consideration. [Information for authors](https://www1.health.gov.au/internet/main/publishing.nsf/Content/cda-pubs-cdi-auth_inst.htm) and details on how to [submit your publication](https://www1.health.gov.au/internet/main/publishing.nsf/Content/cda-pubs-cdi-auth_inst.htm#submission_package) is available on our website, or by email at [cdi.editor@health.gov.au](mailto:cdi.editor@health.gov.au).

Contact us

Communicable Diseases Intelligence (CDI)

Health Security & Emergency Management Division

Department of Health and Aged Care

GPO Box 9848, CANBERRA ACT 2601

Website: [www.health.gov.au/cdi](http://www.health.gov.au/cdi)

Email: [cdi.editor@health.gov.au](mailto:cdi.editor@health.gov.au)

1. http://www.agargroup.org.au/agar-reports. [↑](#footnote-ref-2)
2. www.ncbi.nlm.nih.gov/bioproject/PRJNA313047. [↑](#footnote-ref-3)
3. www.ncbi.nlm.nih.gov/pathogens/isolates#/refgene/. [↑](#footnote-ref-4)
4. www.agargroup.org.au/agar-reports. [↑](#footnote-ref-5)