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Original article

# Australian Group on Antimicrobial Research surveillance outcome programs – bloodstream infections and antimicrobial resistance patterns from patients less than 18 years of age, January 2020 – December 2021

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## Abstract

From 1 January 2020 to 31 December 2021, thirty-eight institutions across Australia submitted data to the Australian Group on Antimicrobial Resistance (AGAR) from patients aged < 18 years (AGAR-Kids). Over the two years, 1,679 isolates were reported from 1,611 patients. This AGAR-Kids report aims to describe the population of children and adolescents with bacteraemia reported to AGAR and the proportion of resistant isolates.

Overall, there were 902 gram-negative isolates reported: 800 Enterobacterales, 61 *Pseudomonas aeruginosa* and 41 *Acinetobacter* spp. Among the Enterobacterales, 12.9% were resistant to third generation cephalosporins; 11.6% to gentamicin/tobramycin; and 11.2% to piperacillin-tazobactam. In total, 14.5% of Enterobacterales were multi-drug resistant (MDR). Only 3.3% of *P. aeruginosa* were resistant to carbapenems and 4.9% were MDR. Resistance in *Acinetobacter* spp was uncommon.

Of 607 *Staphylococcus aureus* isolates, 12.9% were methicillin-resistant (MRSA). Almost half of *S. aureus* isolates from the Northern Territory were MRSA. In *S. aureus*, resistance to erythromycin was 13.2%; 12.4% to clindamycin; and 5.3% to ciprofloxacin. Resistance to all antibiotics tested was higher in MRSA. Overall, 6.5% of *S. aureus* were MDR, of which 65% were MRSA.

Almost three-quarters of the 170 *Enterococcus* spp. reported were *E. faecalis*, and half were from patients < 1 year old. Ampicillin resistance in enterococci was 19.6%. Eight isolates were vancomycin resistant and three isolates were teicoplanin resistant. Five *E. faecium* isolates were classified as MDR.

This AGAR-Kids report highlights clear differences in the geographic distribution of pathogens and resistance profiles across Australia.

Keywords: Australian Group on Antimicrobial Resistance (AGAR); antimicrobial resistance surveillance; paediatrics; bacteraemia; Enterobacterales; *Staphylococcus aureus*; *Enterococcus*

# Introduction

The Australian Group on Antimicrobial Resistance (AGAR) produces annual reports from the whole of the Australian population. However, previous analysis of the AGAR data, comparing adult (> 18 years) and paediatric (≤ 18 years) bacteraemia, suggests there are lower rates of antimicrobial-resistant organisms isolated in children, with different phenotypes and lower mortality rates.

In 2018, the World Society for Paediatric Infectious Diseases (WSPID) declared that antimicrobial resistance (AMR) surveillance programs should present neonatal- and paediatric-specific data to assist with strengthening knowledge.[1] Currently, age-specific data are not routinely reported in the majority of AMR surveillance programs, making paediatric-specific interventions difficult.[2] By monitoring paediatric bacteraemia, we are able to provide insight not only into the dynamic aetiology of bloodstream infections, but also into the impact of vaccine programs, and to inform strategies aimed at targeting invasive infections.[3]

The key influences on bacteraemia incidence are age, vaccination coverage and exposure to invasive procedures.[3] In previous studies, neonates were often over-represented, reflecting the immaturity of the immune system and the use of invasive devices (e.g., intravenous catheters). Various reports from Australia and Europe suggest there are differences in the AMR burden of various organisms, not only between adults and children, but within different age groups among children. For example, gram-negative multidrug resistant (MDR; resistant to three or more antimicrobial classes) organisms were previously found to disproportionately impact children, as demonstrated by a higher odds of death in children with bacteraemia secondary to an extended spectrum beta-lactamase (ESBL) containing organism vs non-ESBL bacteraemia when compared to the same ratio in adults.[4] In a European study, isolates from children < 1 year of age had less AMR than those isolated from children ≥ 1 year old.[2] In a Scottish study, instances of bacteraemia in children < 1 year old were more likely to be healthcare associated, whilst bacteraemia in children aged 1–15 years were more often community associated.[5] These findings impact the empiric treatment guidelines and stewardship initiatives, thereby highlighting the value of paediatric-specific reporting of bacteraemia.

# Methods

## Participants

Thirty-eight laboratories participating in AGAR who reported data from patients < 18 years old (0–17 years of age inclusive); 35 laboratories in each year respectively. AGAR collects data from 24 of the 29 principal referral centres and from all tertiary paediatric centres (8 hospitals) in Australia, as well as from seven public acute group A hospitals, three private group A hospitals, two private group B hospitals and all public group C hospitals in the north-west of Western Australia.[6]

## Collection period

From 1 January 2020 to 31 December 2021, participating laboratories submitted all isolates from unique patient episodes of bacteraemia for *S. aureus* and *Enterococcus* spp., and up to 200 isolates per year for Enterobacterales, *P. aeruginosa*, and *Acinetobacter* spp.

An episode was defined as a clinical event associated with a positive blood culture, irrespective of the number of bacterial species identified. A new episode of bacteraemia in the same patient was recorded if the blood culture was collected more than two weeks after the initial positive culture. An episode was defined as community-onset if the first positive blood culture of the episode was collected 48 hours or less after hospital admission, and as hospital-onset if collected more than 48 hours after admission.

## Laboratory methods

Isolates were identified to the species level by the participating laboratories using matrix-assisted laser desorption ionization (MALDI) [MALDI Biotyper (Bruker Daltonics, United States of America [USA]) or Vitek-MS (bioMérieux, France) or using Vitek2® (bioMérieux). Antimicrobial susceptibility testing was performed using the Vitek2® (bioMérieux) or BD Phoenix™ (Becton Dickinson, USA) automated microbiology systems according to the manufacturer's instructions.

## Data collection and analysis

Data were collected on age, sex, dates of admission and discharge , and mortality at seven and 30 days from date of blood culture collection. To avoid interpretive bias, no attempt was made to assign attributable mortality.

The AMR for R package (v2.0) was used to transform minimum inhibitory concentration data as per EUCAST 2022 (v12) breakpoints.[7,8] Multi-drug resistance (MDR) was defined as resistance to one or more agents in three or more antimicrobial categories.[9] Descriptive statistics for the population and isolates for the overall population and per year were stratified by age, sex, and state/territory where appropriate. Categorical data was assessed using the chi-square or Fisher's exact test. Continuous data was assessed using the Student t-test or Mann-Whitney U test. Proportions were not calculated where fewer than ten isolates in a category were tested.

## Ethics

Approval to conduct the prospective data collection was given by the research ethics committee associated with each participating healthcare facility.

# Results

## Patient characteristics

Overall, there were 1,679 isolates from 1,611 bacteraemic episodes in 1,611 patients: 826 episodes with 856 isolates in 2020, and 785 episodes with 823 isolates in 2021. The most frequently reported species were *S. aureus* (n: 607/1,679; 36.2%) and *Escherichia coli* (n: 378/1,679; 22.5%). In all states and mainland territories, *S. aureus* was the most frequently reported species, followed by *E. coli*, except in Queensland where non-typhoidal *Salmonella* was more frequent. For patients aged < 1 year, the most common species was *E. coli*, whereas in patients aged ≥ 1 year, the most common species was *S. aureus* (Table 1).

There was an over-representation of episodes in patients aged < 1 year (n: 623/1,611; 38.7%), and 15.1% of all episodes were in neonates (n: 244). More bacteraemia episodes affected males (n: 976/1,611; 60.6%). The median age of patients with *S. aureus* bacteraemia was older than for enterococcal or gram-negative bacteraemia.

Most bacteraemic episodes were community-onset (69.0%); however, enterococcal episodes were more often hospital-onset. The proportion of hospital-onset episodes was highest in the neonatal age group and decreased with age; the median age for community-onset bacteraemia was 3 years (interquartile range, IQR: 0–10 years), whereas the median age for hospital-onset bacteraemia was < 12 months (IQR: 0–5 years). Tasmania had the highest proportion of community-onset episodes (85% of all episodes) with Victoria having the lowest proportion (58% of episodes).

Overall, the mean length of stay following blood culture collection was 17.0 days (standard deviation, SD: 21.5) and the median was 10 days (IQR: 6–21 days). At 30 days, 21.7% of all children with bacteraemia (n = 350/1,611) were still admitted to hospital.

Over the two-year period, bone and joint infections were the most frequently reported clinical manifestations (n: 255/1,679; 15.2%), followed by device-related infections without metastatic focus (n: 210/1,679; 12.5%). Community-onset bacteraemic episodes were more frequently associated with an osteoarticular focus, whereas hospital-onset episodes were more frequently device-related or in patients with febrile neutropenia.

**Table 1: Characteristics of patients aged < 18 years with a bacteraemic event reported to AGAR, per survey, January 2020 – December 2021**

| | | *Enterococcus* spp. (N = 167) | | *S. aureus* (N = 606) | | Gram-negative bacteria (N = 867) | | Total patients (N = 1,611)[a] | |
|---|---|---|---|---|---|---|---|---|---|
| **Category** | **Characteristic** | **n** | **%** | **n** | **%** | **n** | **%** | **n** | **%** |
| Age (years) | Median | < 1 | — | 6 | — | 1 | — | 2 | — |
| | IQR[b] | 0–4 | — | 1–11.8 | — | 0–7 | — | 0–10 | — |
| Age group | ≤ 28 days | 38 | 22.8 | 51 | 8.4 | 160 | 18.5 | 244 | 15.1 |
| | 29–90 days | 26 | 15.6 | 51 | 8.4 | 104 | 12.0 | 173 | 10.7 |
| | 91–364 days | 24 | 14.4 | 45 | 7.4 | 139 | 16.0 | 206 | 12.8 |
| | 1–4 years | 38 | 22.8 | 133 | 21.9 | 198 | 22.8 | 359 | 22.3 |
| | 5–17 years | 41 | 24.6 | 326 | 53.8 | 266 | 30.7 | 629 | 39.0 |
| Sex | Female | 60 | 35.9 | 208 | 34.3 | 377 | 43.5 | 635 | 39.4 |
| | Male | 107 | 64.1 | 398 | 65.7 | 490 | 56.5 | 976 | 60.6 |
| Jurisdiction[c] | ACT | 3 | 1.8 | 20 | 3.3 | 22 | 2.5 | 45 | 2.8 |
| | NSW | 68 | 40.7 | 172 | 28.4 | 290 | 33.4 | 516 | 32.0 |
| | NT | 2 | 1.2 | 29 | 4.8 | 41 | 4.7 | 72 | 4.5 |
| | Qld | 10 | 6.0 | 88 | 14.5 | 116 | 13.4 | 213 | 13.2 |
| | SA | 13 | 7.8 | 57 | 9.4 | 63 | 7.3 | 130 | 8.1 |
| | Tas. | 4 | 2.4 | 15 | 2.5 | 20 | 2.3 | 39 | 2.4 |
| | Vic. | 56 | 33.5 | 152 | 25.1 | 239 | 27.6 | 438 | 27.2 |
| | WA | 11 | 6.6 | 73 | 12.0 | 76 | 8.8 | 158 | 9.8 |
| Length of stay (days) | Median | 12.5 | — | 11 | — | 10 | — | 10 | — |
| | IQR[b] | 7.8–34.3 | — | 7–18 | — | 5–21 | — | 6–21 | — |
| 30-day outcome | Died | 6 | 3.6 | 6 | 1.0 | 42 | 4.8 | 53 | 3.3 |
| | Survived | 150 | 89.8 | 515 | 85.0 | 702 | 81.0 | 1,340 | 83.2 |
| | Unknown | 11 | 6.6 | 85 | 14.0 | 123 | 14.2 | 218 | 13.5 |
| Onset | Community | 70 | 41.9 | 477 | 78.7 | 583 | 67.2 | 1,112 | 69.0 |
| | Hospital | 97 | 58.1 | 129 | 21.3 | 284 | 32.8 | 499 | 31.0 |
| Device-related infection | Yes | 72 | 43.1 | 108 | 17.8 | 212 | 24.5 | 379 | 23.5 |
| | No | 90 | 53.9 | 473 | 78.1 | 600 | 69.2 | 1,147 | 71.2 |
| | Unknown | 5 | 3.0 | 25 | 4.1 | 55 | 6.3 | 85 | 5.3 |
| Polymicrobial | | 60 | 35.9 | 43 | 7.1 | 100 | 11.5 | 174 | 10.8 |

a The numbers in each organism group may not add up to the total column, as some patients have polymicrobial bacteraemic episodes and are reported in each respective column to their episode, but only counted once in the total number of patients.

b IQR: interquartile range.

c ACT: Australian Capital Territory; NSW: New South Wales; NT: Northern Territory; Qld: Queensland; SA: South Australia; Tas.: Tasmania; Vic.: Victoria; WA: Western Australia.

Overall, 23.5% of patients had a device-related bacteraemic episode (n: 379/1,611). The proportion was higher in 2021 (n: 213; 27.4%) than in 2020 (n: 166; 22.2%). The median length of stay was longer for patients with a device-related episode than for those patients without a device-related episode. More device-related episodes were reported with gram-negative isolates. Overall, 13% of episodes that were MDR were associated with a device-related infection.

Ten percent of patients had more than one isolate reported in a bacteraemia episode (174/1,611; 10.8%). The largest proportion of polymicrobial episodes were reported in children < 12 months (72/174; 41.4%).

At seven days after blood culture collection, 2.6% of patients had died (n: 42); the proportion of patients who died increased to 3.3% at 30 days (n: 53). The median age of patients who died was younger that for survivors ($X^2$: 12.5; *p*: < 0.001). More than half of the deaths occurred in patients ≤ 28 days of age (27/53; 51%), including ten neonates with community-onset bacteraemia.

## Gram-negative isolates

Overall, there were 902 gram-negative isolates reported from 867 bacteraemia episodes in patients aged < 18 years in 2020–2021; 800 Enterobacterales (88.7%), 61 *Pseudomonas aeruginosa* (6.8%) and 41 (4.5%) *Acinetobacter* spp. The most frequently reported Enterobacterales were *E. coli* and *Klebsiella pneumoniae* complex.

The largest proportion of Enterobacterales were from New South Wales, followed by Victoria. The highest proportion of isolates were from patients < 12 months old, and from males. Enterobacterales episodes were more frequently community-onset, and 14% of episodes were polymicrobial (Table 1). Overall, 18% of the Enterobacterales were MDR.

The proportion of Enterobacterales resistant to the aminoglycosides (gentamicin/tobramycin) was 11.6% (n: 92/793; 95% CI: 9.5–14.0%). Victoria reported the highest proportion of aminoglycoside-resistant isolates, followed by South Australia and New South Wales. No aminoglycoside-resistant isolates were reported in Tasmania. Resistant isolates were more frequently reported in children aged 1–4 years of age. Isolates from patients with a hospital-onset episode were more frequently reported as resistant than those with a community-onset episode (Table 2).

The proportion of Enterobacterales resistant to piperacillin-tazobactam was 11.2% (88/784; 95% CI: 9.1–13.6%). Victoria reported the highest proportion of resistant isolates, followed by New South Wales. No piperacillin-tazobactam resistant isolates were reported in Tasmania and the Australian Capital Territory (Table 2).

Overall, 13.2% of Enterobacterales (101/766; 95% CI: 10.9–15.8) were reported as ciprofloxacin resistant. Isolates from patients with a hospital-onset episode were more frequently reported as ciprofloxacin resistant than those with a community-onset bacteraemia. Isolates from children aged over 1 year were more frequently resistant. Victoria reported the highest proportion of resistant isolates (Table 2).

Of the 792 Enterobacterales that had meropenem susceptibility testing performed, only two *Enterobacter cloacae* complex isolates were resistant (0.3%; 95% CI: 0.0–0.9%). The isolates reported were from a community-onset bacteraemic episode in Queensland and a hospital-onset bacteraemic episode in Victoria, both in patients aged 5–17 years.

Fourteen percent of Enterobacterales isolates were identified as MDR. MDR Enterobacterales isolates were more likely to be hospital-onset (*p*: < 0.01) and associated with a device-related infection (*p*: < 0.01). MDR Enterobacterales isolates were more frequent in patients with febrile neutropenia. Of the 41 patients who died with an Enterobacterales episode, 19.5% of the isolates were MDR (n: 8). The highest proportion of MDR Enterobacterales isolates were from Victoria (n: 59, 39.6%) and New South Wales (n: 53, 35.6%). Victoria had the highest proportion of Enterobacterales isolates that were MDR (24.8%), followed by New South Wales (20.1%) [Table 3].

There were 61 *Pseudomonas aeruginosa* reported to AGAR: 31 isolates in 2020 and 30 isolates in 2021. No isolates were reported from the Australian Capital Territory, and only one isolate was reported from Tasmania. Overall, 4.9% of *P. aeruginosa* isolates were MDR, and two isolates were carbapenem resistant (3.3%), classified as a World Health Organization (WHO) priority pathogen.

No *P. aeruginosa* isolates were reported tobramycin resistant. Overall, 19.7% of *P. aeruginosa* were piperacillin-tazobactam resistant (n: 12; 95% CI: 10.6–31.8%). All ciprofloxacin-resistant *P. aeruginosa* isolates were reported from patients aged 5-17 years. Only two *P. aeruginosa* were reported meropenem resistant (3.3%; 95%CI: 0.4–11.3%): one isolate from Queensland and one isolate from Victoria.

**Table 2: Number of Enterobacterales isolates tested and proportion of isolates resistant to gentamicin/tobramycin, ceftriaxone/ceftazidime, piperacillin-tazobactam, and ciprofloxacin from children aged < 18 years as reported to AGAR, January 2020 – December 2021**

| | | Gentamycin/tobramycin[a] | | | | Ceftriaxone/ceftazidime[a] | | | | Piperacillin–tazobactam[a] | | | | Ciprofloxacin[a] | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Category** | **Characteristic** | **N** | **n** | **R%** | **95% CI** | **N** | **n** | **R%** | **95% CI** | **N** | **n** | **R%** | **95% CI** | **N** | **n** | **R%** | **95% CI** |
| Overall | | 793 | 92 | 11.6 | 9.5–14.0 | 793 | 102 | 12.9 | 10.6–15.4 | 784 | 88 | 11.2 | 9.1–13.6 | 766 | 101 | 13.2 | 10.9–15.8 |
| Jurisdiction[b] | ACT | 23 | 1 | 4.3 | 0.1–21.9 | 23 | 1 | 4.3 | 0.1–21.9 | 23 | 0 | 0 | — | 23 | 1 | 4.3 | 1.1–28.0 |
| | NSW | 264 | 31 | 11.9 | 8.2–16.5 | 264 | 37 | 14.2 | 10.2–19.1 | 260 | 34 | 13.1 | 9.2–17.8 | 250 | 37 | 14.2 | 7.2–15.3 |
| | NT | 37 | 3 | 8.3 | 1.8–22.5 | 37 | 2 | 5.6 | 0.7–18.7 | 36 | 3 | 8.3 | 1.8–22.5 | 35 | 2 | 5.6 | — |
| | Qld | 99 | 6 | 6.1 | 2.3–12.7 | 99 | 6 | 6.1 | 2.3–12.7 | 97 | 8 | 8.2 | 3.6–15.6 | 85 | 6 | 6.1 | 5.8–20.6 |
| | SA | 56 | 8 | 14.5 | 6.5–26.7 | 56 | 4 | 7.3 | 2.0–17.6 | 55 | 1 | 1.8 | 0.0–9.7 | 55 | 4 | 7.3 | 6.5–26.7 |
| | Tas. | 17 | 0 | 0 | — | 17 | 1 | 5.9 | 0.1–28.7 | 17 | 0 | 0 | — | 17 | 1 | 5.9 | 1.5–36.4 |
| | Vic. | 238 | 40 | 16.8 | 12.3–22.2 | 238 | 46 | 19.3 | 14.5–24.9 | 235 | 36 | 15.3 | 11.0–20.6 | 236 | 46 | 19.3 | 15.4–26.0 |
| | WA | 66 | 3 | 4.6 | 1.0–12.9 | 66 | 5 | 7.7 | 2.5–17.0 | 61 | 6 | 9.8 | 3.7–20.2 | 65 | 5 | 7.7 | 1.7–15.0 |
| Age group | ≤ 28 days | 157 | 21 | 13.5 | 8.5–19.8 | 157 | 13 | 8.3 | 4.5–13.8 | 155 | 2 | 1.3 | 0.2–4.6 | 156 | 13 | 8.3 | 6.0–16.1 |
| | 29–90 days | 102 | 10 | 9.9 | 4.9–17.5 | 102 | 11 | 10.9 | 5.6–18.7 | 97 | 12 | 12 | 6.4–20.0 | 98 | 11 | 10.9 | 4.9–17.5 |
| | 91–364 days | 132 | 9 | 6.9 | 3.2–12.6 | 132 | 12 | 9.2 | 4.8–15.5 | 132 | 9 | 7 | 3.2–12.8 | 126 | 12 | 9.2 | 4.0–14.4 |
| | 1–4 years | 173 | 30 | 17.4 | 12.1–24.0 | 173 | 35 | 20.3 | 14.6–27.1 | 170 | 27 | 15.9 | 10.7–22.3 | 160 | 35 | 20.3 | 13.6–26.4 |
| | 5–17 years | 236 | 22 | 9.4 | 6.0–13.9 | 236 | 31 | 13.3 | 9.2–18.4 | 230 | 38 | 16.5 | 12.0–22.0 | 226 | 31 | 13.3 | 10.6–20.4 |
| Onset | Community | 540 | 39 | 7.2 | 5.2–9.7 | 540 | 44 | 8.1 | 6.0–10.8 | 534 | 38 | 7.1 | 5.1–9.6 | 513 | 44 | 8.1 | 7.7–13.1 |
| | Hospital | 253 | 53 | 20.9 | 16.1–26.5 | 253 | 58 | 22.9 | 17.9–28.6 | 250 | 50 | 20 | 15.2–25.5 | 253 | 58 | 22.9 | 14.7–24.8 |

a N: number of isolates tested; n: number of resistant isolates; R%: proportion of resistant isolates; 95% CI: 95% confidence interval.

b ACT: Australian Capital Territory; NSW: New South Wales; NT: Northern Territory; Qld: Queensland; SA: South Australia; Tas.: Tasmania; Vic.: Victoria; WA: Western Australia.

**Table 3: Characteristics of patients aged < 18 years with a bacteraemic event reported to AGAR for which one or more isolate was multidrug resistant (MDR), per survey, January 2020 – December 2021**

| | | *Enterococcus* spp. (n = 4/163)[a] | | *S. aureus* (n = 34/572)[a] | | Gram-negative bacteria (n = 118/749)[a] | | Total patients (n = 156/1,484)[a,b] | |
|---|---|---|---|---|---|---|---|---|---|
| **Category** | **Characteristic** | **n** | **%** | **n** | **%** | **n** | **%** | **n** | **%** |
| Age (years) | Median | < 1 | — | < 1 | — | 2 | — | 1 | — |
| | IQR[c] | 0–0.3 | — | 0–3.8 | — | 0–8 | — | 0–8 | — |
| Age group | ≤ 28 days | 1 | 2.6 | 5 | 9.8 | 18 | 11.3 | 24 | 9.6 |
| | 29–90 days | 1 | 3.8 | 7 | 13.7 | 12 | 11.5 | 20 | 11.0 |
| | 91–364 days | 1 | 4.2 | 6 | 13.3 | 9 | 6.5 | 16 | 7.7 |
| | 1–4 years | 1 | 2.6 | 12 | 9.0 | 39 | 19.7 | 52 | 14.1 |
| | 5–17 years | 0 | 0 | 4 | 1.2 | 40 | 15.0 | 44 | 7.0 |
| Sex | Female | 0 | 0 | 15 | 7.2 | 48 | 12.7 | 63 | 9.8 |
| | Male | 4 | 3.7 | 19 | 4.8 | 70 | 14.3 | 93 | 9.3 |
| Jurisdiction[d] | ACT | 0 | 0 | 2 | 10.0 | 1 | 4.5 | 3 | 6.7 |
| | NSW | 0 | 0 | 15 | 8.7 | 40 | 13.8 | 55 | 10.4 |
| | NT | 0 | 0 | 4 | 13.8 | 2 | 4.9 | 6 | 8.3 |
| | Qld | 0 | 0 | 1 | 1.1 | 9 | 7.8 | 10 | 4.7 |
| | SA | 1 | 7.7 | 3 | 5.3 | 8 | 12.7 | 12 | 9.0 |
| | Tas. | 0 | 0 | 0 | 0 | 2 | 10.0 | 2 | 5.1 |
| | Vic. | 3 | 5.4 | 5 | 3.3 | 50 | 20.9 | 58 | 13.0 |
| | WA | 0 | 0 | 4 | 5.5 | 6 | 7.9 | 10 | 6.3 |
| Length of stay (days) | Median | 38.5 | — | 14.5 | — | 13 | — | 14 | — |
| | IQR[c] | 21.0–56.5 | — | 10.0–19.8 | — | 8.3–23.5 | — | 9.0–24.5 | — |
| 30-day outcome | Died | 0 | 0 | 1 | 16.7 | 8 | 19.0 | 9 | 16.7 |
| | Survived | 4 | 2.7 | 28 | 5.4 | 98 | 14.0 | 130 | 9.5 |
| | Unknown | 0 | 0 | 5 | 5.9 | 12 | 9.8 | 17 | 7.8 |
| Onset | Community | 0 | 0 | 18 | 3.8 | 58 | 9.9 | 76 | 6.7 |
| | Hospital | 4 | 4.1 | 16 | 12.4 | 60 | 21.1 | 80 | 15.7 |
| Device-related infection | Yes | 2 | 2.8 | 7 | 6.5 | 44 | 20.8 | 53 | 13.5 |
| | No | 2 | 2.2 | 23 | 4.9 | 65 | 10.8 | 90 | 7.7 |
| | Unknown | 0 | 0 | 4 | 16.0 | 9 | 16.4 | 13 | 15.3 |
| Polymicrobial | | 3 | 5.0 | 4 | 9.3 | 11 | 11.0 | 18 | 8.9 |

a n: number of MDR isolates; %: proportion of MDR isolates compared to all tested isolates of the indicated organism.

b The numbers in each organism group may not add up to the total column, as some patients have polymicrobial bacteraemic episodes and are reported in each respective column to their episode, but only counted once in the total number of patients.

c IQR: interquartile range.

d ACT: Australian Capital Territory; NSW: New South Wales; NT: Northern Territory; Qld: Queensland; SA: South Australia; Tas.: Tasmania; Vic.: Victoria; WA: Western Australia.

Only three *P. aeruginosa* were identified as MDR (3/61; 4.9%) – one from New South Wales and two from South Australia.

Forty-one *Acinetobacter* spp. isolates were reported to AGAR: most were *A. baumanii* complex (18/41; 43.9%). All *Acinetobacter* isolates were meropenem susceptible. One *Acinetobacter* isolate was reported as ciprofloxacin resistant and one isolate was resistant to amikacin. Three isolates were resistant to co-trimoxazole (8.6%; 95%CI: 1.8–23.1%), and all resistant isolates were reported from patients aged 1–4 years.

## *Staphylococcus aureus*

There were 607 *S. aureus* isolates reported to AGAR: 303 in 2020 and 304 in 2021. Overall, 12.9% of *S. aureus* were methicillin resistant (n: 78) and 5.6% of isolates were MDR (n: 34). The median age was 6 years, and the number of episodes reported across different age groups was similar. The majority of isolates were reported from New South Wales and Victoria. Most episodes were community-onset and were monomicrobial events (Table 1).

The Northern Territory reported the highest proportion of *S. aureus* isolates that were MRSA (45%). MRSA was not reported in the Australian Capital Territory or Tasmania. MRSA isolates were most frequently reported in patients aged 1–4 years and in hospital-onset infections (Table 4).

Overall, 12.4% of *S. aureus* were clindamycin resistant (n: 75; 95% CI: 9.8–15.2). The Northern Territory had the highest proportion of clindamycin-resistant isolates. No clindamycin-resistant isolates were reported in Tasmania. All age groups < 5 years of age reported approximately 15% of isolates resistant to clindamycin (Table 4).

Five percent of *S. aureus* were ciprofloxacin resistant (n: 32; 5.3%; 95% CI: 3.6–7.4%); 3.6% of *S. aureus* isolates were reported as resistant in 2020 (n: 11), and 6.9% in 2021 (n: 21). The highest proportion of isolates reported as ciprofloxacin resistance was in New South Wales (9.8%, n: 17). No isolates were ciprofloxacin resistant in Tasmania. Resistant isolates were most frequently reported in patients aged 91–364 days (Table 4).

Overall, 13.2% of *S. aureus* were erythromycin resistant (n: 80; 95% CI: 10.6–16.1%): The proportion of resistant isolates was 11.2% (n: 34) in 2020 and 15.1% (n: 46) in 2021. The highest proportion of erythromycin resistant isolates was reported in the Northern Territory, and from neonatal patients (Table 4). No *S. aureus* isolates were reported trimethoprim-sulfamethoxazole or vancomycin resistant.

Overall, 5.6% of all *S. aureus* were MDR (n: 34), 64.7% of which were MRSA (n: 22). A statistically significant difference in age was identified in patients with a MDR *S. aureus* episode compared to patients with a non-MDR *S. aureus* ($p < 0.001$). MDR *S. aureus* episodes are more likely to be hospital-onset ($p < 0.001$); however, MDR infections were not more device-related ($p = 0.06$). The largest number of all MDR *S. aureus* isolates were from New South Wales, whilst the Northern Territory and the Australian Capital Territory had the highest proportion of *S. aureus* that were MDR (Table 3).

## *Enterococcus* spp.

Overall, 170 enterococci were reported to AGAR, 95 isolates in 2020 and 75 isolates in 2021. Of the 170 isolates, 122 were *E. faecalis* and 41 were *E. faecium*. Five *E. faecium* isolates were MDR. Enterococci isolates were most frequently reported from patients < 1 year old. The largest proportions of episodes were from New South Wales and Victoria. The proportion of patients still in hospital at 30 days was higher in patients who had an enterococcal infection (Table 1).

Overall, 19.6% of isolates were ampicillin resistant (n: 33; 95% CI: 13.9–26.5%); one isolate was *E. faecalis*, whilst the rest were *E. faecium* (n: 32). Over 70% of ampicillin-resistant isolates were hospital-onset. Most isolates were reported in patients aged 5–17 years, and from patients living in New South Wales. Enterococci from hospital-onset episodes were more frequently ampicillin resistant compared to community-onset enterococcal episodes (Table 5).

Fewer than five percent of Enterococci isolates were vancomycin resistant (4.7%; 95% CI: 2.1–9.1%). Eight vancomycin-resistant *E. faecium* (VREfm) were identified (19.5%; 95% CI: 8.8–34.9%), all from hospital-onset episodes. VREfm isolates were identified in Queensland, Victoria, and New South Wales. Three *E. faecium* were identified as teicoplanin resistant (7.3%; 95% CI: 1.5–19.9%); all were from hospital-onset episodes. Teicoplanin resistant isolates were identified in New South Wales and Victoria (Table 5).

Five Enterococci were MDR (2.9%), all *E. faecium*. Four of the five MDR *Enterococcus* were identified in Victoria; the remaining isolate was identified in South Australia (Table 3).

**Table 4: Number of *Staphylococcus aureus* isolates tested and proportion of isolates resistant to clindamycin, ciprofloxacin, and erythromycin from children aged < 18 years as reported to AGAR, January 2020 – December 2021**

| | | | Clindamycin[b] | | | Ciprofloxacin[b] | | | Erythromycin[b] | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Category | Characteristic | N[a] | n | R% | 95% CI | n | R% | 95% CI | n | R% | 95% CI |
| Overall | | 607 | 75 | 12.4 | 9.8–15.2 | 32 | 5.3 | 3.6–7.4 | 80 | 13.2 | 10.6–16.1 |
| Jurisdiction[c] | ACT | 20 | 3 | 15 | 3.2–37.9 | 1 | 5.0 | 0.1–24.9 | 2 | 10 | 1.7–29.3 |
| | NSW | 173 | 29 | 16.8 | 11.5–23.2 | 17 | 9.8 | 5.8–15.3 | 28 | 16.2 | 11.3–22.2 |
| | NT | 29 | 6 | 20.7 | 8.0–39.7 | 1 | 3.4 | 0.1–17.8 | 6 | 20.7 | 8.8–38.2 |
| | Qld | 88 | 13 | 14.8 | 8.1–23.9 | 4 | 4.5 | 1.3–11.2 | 14 | 15.9 | 9.4–24.7 |
| | SA | 57 | 3 | 5.3 | 1.1–14.6 | 3 | 5.3 | 1.1–14.6 | 7 | 12.3 | 5.5–22.8 |
| | Tas. | 15 | 0 | 0.0 | — | 0 | 0.0 | — | 0 | 0.0 | — |
| | Vic. | 152 | 15 | 9.9 | 5.6–15.8 | 4 | 2.6 | 0.7–6.6 | 17 | 11.2 | 6.9–17.0 |
| | WA | 73 | 6 | 8.2 | 3.1–17.0 | 2 | 2.7 | 0.3–9.5 | 6 | 8.2 | 3.4–16.3 |
| Age group | ≤ 28 days | 51 | 9 | 17.6 | 8.4–30.9 | 4 | 7.8 | 2.2–18.9 | 10 | 19.6 | 9.8–33.1 |
| | 29–90 days | 51 | 8 | 15.7 | 7.0–28.6 | 2 | 3.9 | 0.5–13.5 | 9 | 17.6 | 8.4–30.9 |
| | 91–364 days | 46 | 7 | 15.2 | 6.3–28.9 | 6 | 13 | 4.9–26.3 | 5 | 10.9 | 3.6–23.6 |
| | 1–4 years | 133 | 21 | 15.8 | 1.0–23.1 | 8 | 6.0 | 2.6–11.5 | 24 | 18 | 11.9–25.6 |
| | 5–17 years | 326 | 30 | 9.2 | 6.3–12.9 | 12 | 3.7 | 1.9–6.3 | 32 | 9.8 | 6.8–13.6 |
| Onset | Community | 478 | 55 | 11.5 | 8.8–4.7 | 22 | 4.6 | 2.9–6.9 | 59 | 12.3 | 9.5–15.6 |
| | Hospital | 129 | 20 | 15.5 | 9.7–22.9 | 10 | 7.8 | 3.8–13.8 | 21 | 16.3 | 10.4–23.8 |
| Methicillin resistance[d] | MRSA | 78 | 15 | 19.2 | 11.2–29.7 | 13 | 16.7 | 9.2–26.8 | 18 | 23.1 | 14.3–34.0 |
| | MSSA | 529 | 60 | 11.3 | 8.8–14.4 | 19 | 3.6 | 2.2–5.6 | 62 | 11.7 | 9.1–14.8 |

a N: number of isolates tested.

b n: number of resistant isolates; R%: proportion of resistant isolates; 95% CI: 95% confidence interval.

c ACT: Australian Capital Territory; NSW: New South Wales; NT: Northern Territory; Qld: Queensland; SA: South Australia; Tas.: Tasmania; Vic.: Victoria; WA: Western Australia.

d MRSA: methicillin-resistant *S. aureus*; MSSA: methicillin-susceptible *S. aureus*.

**Table 5: Number of *Enterococcus* spp. isolates tested and proportion of isolates resistant to ampicillin, vancomycin, and teicoplanin from children aged < 18 years as reported to AGAR, January 2020 – December 2021**

| | | Ampicillin[a] | | | | Vancomycin[a] | | | | Teicoplanin[a] | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Category | Characteristic | N | n | R% | 95% CI | N | n | R% | 95% CI | N | n | R% | 95% CI |
| Overall | | 168 | 33 | 19.6 | 13.9–26.5 | 170 | 8 | 4.7 | 2.1–9.1 | 170 | 3 | 1.8 | 0.4–5.1 |
| Jurisdiction[b] | ACT | 3 | 1 | 33.3 | — | 3 | 0 | 0 | — | 3 | 0 | 0 | — |
| | NSW | 68 | 15 | 22.7 | 13.3–34.7 | 68 | 2 | 2.9 | 0.4–10.2 | 68 | 2 | 2.9 | 0.4–10.2 |
| | NT | 2 | 1 | 50 | — | 2 | 0 | 0 | — | 2 | 0 | 0 | — |
| | Qld | 10 | 0 | 0 | — | 10 | 0 | 0 | — | 10 | 0 | 0 | — |
| | SA | 14 | 7 | 50 | 23.0–77.0 | 14 | 2 | 14.3 | 1.8–42.8 | 14 | 0 | 0 | — |
| | Tas. | 4 | 1 | 25 | — | 4 | 0 | 0 | — | 4 | 0 | 0 | — |
| | Vic. | 58 | 8 | 13.8 | 6.1–25.4 | 58 | 4 | 6.9 | 1.9–16.7 | 58 | 1 | 1.7 | 0.0–9.2 |
| | WA | 11 | 0 | 0 | — | 11 | 0 | 0 | — | 11 | 0 | 0 | — |
| Age group | ≤ 28 days | 37 | 2 | 5.4 | 0.7–18.2 | 38 | 1 | 2.6 | 0.1–13.8 | 38 | 0 | 0 | — |
| | 29–90 days | 26 | 2 | 7.7 | 0.9–25.1 | 26 | 1 | 3.8 | 0.1–19.6 | 26 | 0 | 0 | — |
| | 91–364 days | 23 | 3 | 13 | 2.8–33.6 | 24 | 1 | 4.2 | 0.1–21.1 | 24 | 0 | 0 | — |
| | 1–4 years | 41 | 7 | 17.1 | 7.2–32.1 | 41 | 3 | 7.3 | 1.5–19.9 | 41 | 2 | 4.9 | 0.6–16.5 |
| | 5–17 years | 41 | 19 | 46.3 | 30.7–62.6 | 41 | 2 | 4.9 | 0.6–16.5 | 41 | 1 | 2.4 | 0.1–12.9 |
| Onset | Community | 71 | 9 | 12.7 | 6.0–22.7 | 71 | 0 | 0 | — | 72 | 0 | 0 | — |
| | Hospital | 97 | 24 | 24.7 | 16.5–34.5 | 98 | 8 | 8.2 | 3.6–15.5 | 98 | 3 | 3.1 | 0.6–8.7 |

a N: number of isolates tested; n: number of resistant isolates; R%: proportion of resistant isolates; 95% CI: 95% confidence interval.

b ACT: Australian Capital Territory; NSW: New South Wales; NT: Northern Territory; Qld: Queensland; SA: South Australia; Tas.: Tasmania; Vic.: Victoria; WA: Western Australia.

# Discussion

This AGAR Kids report is the first comprehensive AGAR report describing the epidemiology of AMR in the Australian paediatric population. The AGAR surveillance programs provide the opportunity to specifically analyse and report on bacteraemia from Australian children. The programs also provide an opportunity to compare paediatric data with the Australian adult population. Although there are some similarities, numerous differences warrant ongoing paediatric specific reporting.

AMR surveillance of paediatric bacteraemia is a powerful public health tool, providing an understanding of the aetiology of disease, susceptibility patterns, and the impact of infection prevention and control strategies.[3,10] AMR surveillance can also point to potential targets for therapeutics specifically for paediatrics: the development of medicines for children lags unacceptably behind that for adults, and industry and funders remain unguided by robust health costing data to prioritise paediatric AMR strategies.[11] It is estimated that every year, globally, AMR infection result in 700,000 deaths, including 200,000 newborns.[12]

There are few reports on paediatric populations from similar AMR national surveillance systems. Whilst the European system (EARS-Net) requests age to the nearest year, the data point is not mandatory and thus EARS-Net data are not routinely stratified by age.[2] In the UK, the English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR) does stratify patient age, but paediatric-specific reports are not available.[13] The Canadian AMR surveillance program presents key highlights of age-stratified data.[14] One-off epidemiological reports have been produced from different regions and countries, yet interpretation and comparison to AGAR Kids is difficult because of differences in the organisms selected for surveillance.[2,4,10,15–23]

This report is one of the most detailed paediatric-specific reports to date and facilitates the national public health benchmarking of AMR in children and neonates to ensure the effectiveness of AMR programs. In Australian children (excluding neonates), the most frequently reported organism was *S. aureus* (36% of isolates) and *E. coli* (23%); in neonates and the adult population this is reversed, with *E. coli* being the most frequently reported organism (43.1% and 39% respectively) followed by *S. aureus* (20.2% and 20.9% respectively). A similar observation has been identified in Japan by Kusama et al.,[22] and likely reflects the commonality of urinary tract infections as the predominant source of bacteraemia in the neonatal and adult population and bone and joint infection the predominant source in children.[24] Several papers globally have demonstrated that *E. coli* bacteraemia is more frequent in children < 1 year of age and *S. aureus* is more frequent in children with increasing age.[10,16,19,25–28]

In enterococcal bacteraemia, differences in the predominant species in adults and children were identified. In paediatrics, whilst approximately 25% of enterococci were identified as *E. faecium*, in adults almost 40% of episodes were due to *E. faecium*. Similarly, in several studies assessing paediatric bacteraemia, *E. faecalis* was more frequently identified than *E. faecium*.[15,29] Interestingly, on a population level, the UK has reported a shift in enterococcal bacteraemia, with more *E. faecium* and less *E. faecalis* reported during the coronavirus disease 2019 (COVID-19) pandemic; future AGAR Kids reports will be needed to investigate if a similar trend occurs in the Australian paediatric population.[13] Additionally, whilst when compared to the EARS-Net data, Australia ranks in the top third of countries for vancomycin-resistant *E. faecium* (VREfm), the proportion of resistance in children is significantly lower: in 2021, AGAR reported 37.9% VREfm, whilst in children there were only eight VREfm isolates (19.5%). This vast difference is important in the way infection prevention and stewardship programs need to be targeted for specific populations.

Regional differences were noted in the pathogens causing paediatric bacteraemia. The increased proportion of *Salmonella* bacteraemia in Queensland is consistent with previous Australian reports,[17,26] and is consistent with the literature of bacteraemia in tropical environments.[30–32] Significant differences in the antimicrobial susceptibility patterns were also observed between jurisdictions. The proportions of Enterobacterales in Victoria resistant to gentamicin/tobramycin and to third-generation cephalosporins were both significantly higher than the national average: 16.8% compared to 11.6% for gentamicin/tobramycin (*p*: 0.04) and 19.3% compared to 12.9% for third-generation cephalosporins (*p*: 0.01). Similar to gram-negative bacteraemia, regional differences in *S. aureus* were noted; there was a clear disproportion in the geographic distribution of MRSA episodes reported across Australia, and the over representation from the NT is found in both adults and children. The higher proportions of resistance in MRSA compared to MSSA and an older age group is aligned with the literature.[13] A more detailed investigation in the geographic distribution of pathogens in paediatrics is proposed and it is hypothesised that there will be a higher proportion of MRSA across the north of Australia which has been reported in the literature.[33–36] These geographical differences have important implications for jurisdictional infection prevention and stewardship programs.

As per the WHO-defined priority list of pathogens,[37] only four critical priority isolates were identified: two *P. aeruginosa* and two *E. cloacae* complex carbapenem-resistant (CRE). However, 21 WHO-defined high priority pathogens were identified other than MRSA: eight vancomycin-resistant *E. faecium* and 13 fluroquinolone-resistant *Salmonella*. These findings suggest that despite the increasing levels of AMR in the general Australian population, WHO priority pathogens are rarely detected in the Australian paediatric population. This also demonstrates the benefit of using local paediatric data to strengthen antimicrobial stewardship programs and inform antibiotic guidelines.

The AGAR surveillance system only captures *S. aureus*, *Enterococcus* spp., Enterobacterales, *P. aeruginosa* and *Acinetobacter* spp. This limits the understanding of the true burden of bacteraemia, as key pathogens such as *Streptococcus* spp. are not recorded. Additionally, vaccine-preventable bacteraemic pathogens are not reported, and thus any changes in incidence or proportion of aetiology of bacteraemia is not captured.

Additional data analysis will be undertaken on a regular basis to track the emergence of AMR in Australian children, to investigate the differences in AMR between adults and paediatric bacteraemia isolates, and to assess the trends in paediatric AMR across Australia.

Overall, this report highlights key differences in antimicrobial resistance and geographic distributions of bacteraemic pathogens in Australian children. These differences emphasise the importance of paediatric-specific infection prevention and stewardship programs, and the need to continue AMR surveillance in the paediatric population.

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