Australian Group on Antimicrobial Resistance 2021 Surveillance Programs

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Background

The Australian Group on Antimicrobial Resistance (AGAR) commenced in 1985 and was established to collect national data on antimicrobial resistance (AMR) in bacteria causing important and life-threatening infections.

Historically, the focus of AGAR was AMR in *Staphylococcus aureus*. The scope broadened over time to include studies on *Escherichia coli, Enterobacter species, Klebsiella species, Haemophilus influenzae, Streptococcus pneumoniae* and *Enterococcus species*. It now concentrates on the three groups of pathogens within the programs; Australian *Staphylococcus aureus* Surveillance Outcome Program (ASSOP), Australian Enterococcal Surveillance Outcome Program (AESOP) and the Gram-negative Surveillance Outcome Program (GnSOP). The three programs are restricted to bloodstream infections.

AGAR's focus on bacteraemia allows examination of laboratory-confirmed, invasive infections and comparison of rates over time for hospitals, states and territories. AGAR compares Australian data with the European Antimicrobial Resistance Surveillance Network (EARS-Net), enabling benchmarking and trend projections. AGAR has collected ongoing data on the prevalence of AMR in Australia over a long period using standardised methods.

AGAR, under the auspices of the Australian Society for Antimicrobials (ASA), is part of the Antimicrobial Use and Resistance in Australia (AURA) surveillance system funded by the Australian Government Department of Health and Aged Care.

AGAR meets the data security requirements of the AURA surveillance system. These arrangements ensure that data conform to appropriate standards of data management and quality, and that data are used in accordance with appropriate approvals. The ASA, as data custodian for AGAR data, is responsible for:

- Approving access to, and use of, AGAR data
- Ensuring that AGAR data are protected from unauthorised access, alteration or loss
- Ensuring compliance with relevant legislation and policies regarding administration, quality assurance, and data access and release.

2021 Programs

In 2021 30 laboratories servicing 48 hospitals located across Australia contributed to the AGAR programs (Table 1). Three AGAR laboratories, two from Queensland and one from New South Wales were unable to participate due to staff shortages as a result of the COVID-19 pandemic; and one new laboratory from Victoria contributed data.

The AGAR laboratories collected all isolates from unique patient episodes of bacteraemia for ASSOP and AESOP, or either all or up to 200 isolates for GnSOP, from 1 January 2021 to 31 December 2021. Approval to conduct the prospective data collection, including de-identified demographic data, was given by the research ethics committees associated with each participating hospital.

In patients with more than one isolate, a new episode was defined as a new positive blood culture more than two weeks after the initial positive culture. An episode was defined as community onset if the first positive blood culture was collected 48 hours or less after admission, and as hospital onset if collected more than 48 hours after admission.

Isolates were identified to species level, if possible, using the routine method for each institution. This included the Vitek® and BD Phoenix™ automated microbiology systems, and if available, matrix assisted laser desorption ionization-time of flight (MALDI-TOF) mass spectrometry (Bruker MALDI biotyper® or Vitek® MS). Phenotypic susceptibility of the isolates was performed by either the Vitek® or BD Phoenix™ automated microbiology systems. The analysis used breakpoints from the Clinical and Laboratory Standards Institute (CLSI) M100–Ed32 and the European Committee on Antimicrobial Susceptibility Testing (EUCAST) v12.0.

All ASSOP and AESOP isolates were referred to the Antimicrobial Resistance Infectious Diseases (AMRID) Research Laboratory at Murdoch University. Whole genome sequencing using the Illumina NextSeq™ 500 platform was performed on the methicillin-resistant *S. aureus* (MRSA) and *E. faecium* isolates. Selected GnSOP isolates were referred to the Centre for Infectious Diseases and Microbiology at the Westmead Institute for Medical Research for whole genome sequencing using the Illumina NextSeq™ 500 platform.

ASSOP

The primary objective of ASSOP 2021 was to determine the proportion of SAB isolates demonstrating AMR with emphasis on:

- Assessing susceptibility to methicillin
- Molecular epidemiology of MRSA.

Key Findings

- A total of 2,928 *S. aureus* bacteraemia episodes were reported from 1 January to 31 December 2021, 78.4% of which were community-onset (CO). Of all episodes 16.9% were methicillin resistant.
- The 30-day all-cause mortality was 14.5%. There was no significant difference in mortality for MRSA (15.0%) and methicillin-susceptible S. aureus (MSSA) (14.4%) P = 0.76; or in hospital-onset (HO) (15.8%) and CO (14.1%) bacteraemia P =0.33.
- The 30-day all-cause mortality for *S. aureus* was significantly lower among paediatrics (<18 years) (0.8%, 2/236) compared to adults (16.0%, 342/2,139) (P < 0.01).
- Osteomyelitis/septic arthritis (22.6%) and skin and skin structure infections (19.0%) were the most common principal clinical manifestations.
- The hospital length of stay was more than 30 days in 23.6% of patients (25.2% in MRSA, 23.2% in MSSA).
- Resistance in MRSA has continued to decline overall, largely due to the substantial decline in the multi-resistant ST239-III clone.
- Community-associated MRSA (CA-MRSA) strains were the dominant cause of MRSA bacteraemia.
- Three healthcare-associated MRSA (HA-MRSA) clones were identified; the dominant HA-MRSA clone was ST22-IV (EMRSA-15). No HA-MRSA isolates harboured the Panton-Valentine leucocidin (PVL) associated genes.
- Most EMRSA-15 bacteraemia episodes were CO.

- Sixty-seven CA-MRSA clones were identified; the dominant CA-MRSA clone was ST93-IV (Queensland clone).
- Overall, 37.9% of CA-MRSA isolates harboured the PVL associated genes.
- The Queensland clone (ST93-IV), which harbours the PVL associated genes, was seen in all states and territories except Tasmania; it is now the most frequently isolated CA-MRSA in Queensland, South Australia, Western Australia and the Northern Territory.
- The multi-resistant ST45-V CA-MRSA clone remains prominent in New South Wales, Victoria and the Australian Capital Territory and is associated with both CO and HO infections.

AESOP

The primary objective of AESOP 2021 was to determine the proportion of *E. faecalis* and *E. faecium* bacteraemia isolates demonstrating AMR with emphasis on:

- Assessing susceptibility to ampicillin
- Assessing susceptibility to glycopeptides, and the associated resistance genes
- Monitoring the molecular epidemiology of *E. faecium.*

Key Findings

- Between 1 January to 31 December 2021 a total of 1,297 episodes of enterococcal bacteraemia were reported; the majority (94.4%) of enterococcal bacteraemia episodes were caused by *Enterococcus faecalis* or *Enterococcus faecium.*
- The majority of *E. faecalis* bacteraemia episodes were CO (68.7%), while in *E. faecium* bacteraemia episodes only 32.1% were CO.
- The most frequent source of bacteraemia or clinical manifestation for *E. faecalis* was urinary tract infection (21.8%); for *E. faecium*, it was intra-abdominal infection other than biliary tract (19.3%).
- The combined 30-day all-cause mortality for *E. faecalis* and *E. faecium* was 19.1%.
- There was significant difference in 30-day all-cause mortality between *E. faecalis* (14.5%) and *E. faecium* (25.2%) (P <0.01) and between vancomycin-resistant and vancomycin-susceptible *E. faecium* episodes (31.0% and 21.3% respectively) (P =0.03).
- The length of stay in hospital following enterococcal bacteraemia was more than 30 days for 22.7% of patients.
- Of the bloodstream infections caused by *E. faecium*, 37.9% were phenotypically vancomycin resistant. There has been a significant decreasing trend in vancomycin resistance in Australia since 2017.
- In 2021, 39.6% of *E. faecium* harboured *vanA* and/or *vanB* genes (*vanA* 14.2%, *vanB* 25.4%). In 2020 35.2% of *E. faecium* harboured *vanA* and/or *vanB* genes.
- Of the vancomycin-resistant *E. faecium* (VRE) bacteraemia episodes, 36.4% were due to *vanA*-harbouring isolates. *vanA* is the dominant genotype in New South Wales, Queensland and Western Australia.
- There were 73 *E. faecium* multi-locus sequence types (STs), of which ST17, ST1424, ST796, ST78, ST80, ST1421 and ST555 were the most frequently identified.
- *vanA* genes were detected in five STs, and *vanB* genes were detected in 13 STs. The clonal diversity of *E. faecium* harbouring *van* genes varied across Australia.
- In 2021, for rates of resistance to vancomycin in *E. faecium,* compared to the EARS-Net countries, Australia ranked eighth highest. From 2017 to 2020, Australia has ranked first, second, fourth and tenth respectively.

GNSOP

The objectives of the 2021 surveillance program were to:

- Monitor AMR in *Enterobacterales*, *P. aeruginosa* and *Acinetobacter* species isolated from blood cultures taken from patients presenting to the hospital or already in hospital
- Study the extent of co-resistance and multidrug resistance in the major species
- Detect emerging AMR to reserve agents such as carbapenems and colistin
- Examine the molecular basis of AMR to third generation cephalosporins, quinolones and carbapenems.

Key Findings

- From 1 January 2021 to 31 December 2021, a total of 8,947 episodes of gram-negative bacteraemia were reported, including *Enterobacterales* (90.6%), *Pseudomonas aeruginosa* (8.3%) and *Acinetobacter* (1.1%). Of the *Enterobacterales*, three genera – *Escherichia* (61.4%), *Klebsiella* (20.5%) and *Enterobacter* (5.8%) – contributed 87.6% of all *Enterobacterales* bacteraemias.
- The all-cause 30-day mortality rate for gram-negative bacteraemia was 12.4% (10.4% for *E. coli*, 19.0% for *P. aeruginosa*).
- Urinary tract infection was the most frequent source of sepsis or clinical manifestation (*Enterobacterales* 45.0%; *P. aeruginosa* 23.4%). For *Enterobacterales*, device related urinary tract infections were more common with HO than CO episodes (23.0% versus 9.7%, P < 0.01).
- Of *E. coli* isolates causing CO bacteraemia, which accounted for 85% of all *E. coli* bacteraemia cases, 11.5% were ceftriaxone resistant.
- There was a significant difference in 30-day all-cause mortality between CO and HO (9.8% versus 13.3%, P < 0.01) *E. coli* bacteraemia episodes.
- In 2021, 14.2% of *E. coli* (CO 13.1%, HO 20.7%) and 7.9% of *Klebsiella pneumoniae* complex (CO 7.0%, HO 10.2%) had an extended-spectrum β-lactamase (ESBL) phenotype.
- *K. pneumoniae* complex with an ESBL phenotype was significantly more common among paediatrics (17.9%, 10/56) compared to adults (7.4%, 88/1,182) (P < 0.01).
- Fluoroquinolone resistance in *E. coli* decreased in 2021 (2020 16.1%, 2021 12.3%, down 23.3%), most notably in New South Wales (12.1%, 155/1,281, down 30.8%) and Victoria (13.2% 143/1,085, down 34.2%).
- Fluoroquinolone resistance is commonly linked to cephalosporin resistance caused by ESBLs of the CTX-M type. Just over three-quarters (256/321, 79.8%) of *E. coli* that were ciprofloxacin resistant and had confirmed β-lactamase genes belonged to ST131 (210, 65.4%) or ST1193 (*n* = 46, 14.3%).
- The low rates of carbapenemase-producing *Enterobacterales* (CPE) bacteraemia are encouraging (0.2% overall, mostly carrying $bla_{\text{IMP-4}}$). For *Enterobacter cloacae* complex the figure is higher at 1.8% overall (CO 1.2%, HO 2.6%).
- No *mcr* genes other than *mcr-9* or *mcr-10* were found among all referred isolates
- The impact of COVID-19 on the reduction in antimicrobial resistance remains unclear, as it may be due to several contributing factors.

2021 Reports

AGAR publishes detailed annual reports on each program on its website (www.agargroup.org.au), and also in the Communicable Diseases Intelligence (CDI) journal. The 2021 AGAR Surveillance Outcome Report will be available by end of December 2022 on the Australian Commission on Safety and Quality in Health Care website (Australian Group on Antimicrobial Resistance | Australian Commission on Safety and Quality in Health Care). For further information on AGAR and the AGAR programs please contact Denise Daley (denise.daley@health.wa.gov.au).

Table 1: Hospitals that contributed to AGAR, by state and territory, AGAR, 2021

State or territory	Hospital
New South Wales	Children's Hospital Westmead
	Concord Repatriation General Hospital
	John Hunter Hospital
	Liverpool Hospital
	Nepean Hospital
	Royal North Shore Hospital
	St Vincent's Hospital, Sydney*
	Sydney Children's Hospital
	Westmead Hospital
	Wollongong Hospital
Victoria	Alfred Hospital
	Austin Hospital (Austin Health)
	Monash Children's Hospital†
	Monash Medical Centre (Dandenong Hospital) †
	Monash Medical Centre (Monash Health)
	Royal Melbourne Hospital
	Royal Women's and Children's Hospital
	St Vincent's Hospital*
Queensland	Gold Coast Hospital
	Prince Charles Hospital§
	Princess Alexandra Hospital§
	Royal Brisbane and Women's Hospital
	Greenslopes Private Hospital#, ††
South Australia	Flinders Medical Centre
	Royal Adelaide Hospital
	Women's and Children's Hospital**
Western Australia	Fiona Stanley Hospital
	Joondalup Hospital*
	North-west regional Western Australia (Broome, Carnarvon, Derby, Exmouth, Fitzroy Crossing, Halls Creek, Karratha, Kununurra, Newman, Port Hedland,, Wyndham) §§
	Perth Children's Hospital§§
	Royal Perth Hospital##
	Sir Charles Gairdner Hospital
	St John of God Hospital, Murdoch††
Tasmania	Launceston General Hospital
	Royal Hobart Hospital
Northern Territory	Alice Springs Hospital
	Royal Darwin Hospital
Australian Capital Territory	Canberra Hospital

* Public/private hospital
† Microbiology services provided by Monash Medical Centre (Monash Health)
§ Microbiology services provided by Pathology Queensland Central Laboratory
# Microbiology services provided by Sullivan Nicolaides Pathology
** Microbiology services provided by SA Pathology, Royal Adelaide Hospital
†† Private hospital
§§ Microbiology services provided by PathWest Laboratory Medicine WA, Queen Elizabeth II Medical Centre
Microbiology services provided by PathWest Laboratory Medicine WA, Fiona Stanley Hospital

Acknowledgments

- Participating members of AGAR in 2021

Institution	AGAR members
Alfred Hospital, Vic	Adam Jenney and Jacqueline Williams
Alice Springs Hospital, NT	James McLeod
Austin Hospital, Vic	Marcel Leroi and Elizabeth Grabsch
Canberra Hospital, ACT	Peter Collignon and Susan Bradbury
Children's Hospital Westmead, NSW	Alison Kesson and Andrew Jarrett
Concord Hospital, NSW	Thomas Gottlieb and John Huynh
John Hunter Hospital, NSW	Hemalatha Varadhan and Bree Harris
Joondalup Hospital, WA	Shalinie Perera and Ian Meyer
Launceston General Hospital, Tas	Pankaja Kalukottege and Kathy Wilcox
Liverpool Hospital, NSW	Michael Maley and Helen Ziochos
Monash Children's Hospital, Vic	Tony Korman and Despina Kotsanas
Monash Health (Dandenong Hospital), Vic	Tony Korman and Kathryn Cisera
Monash Health (Monash Medical Centre), Vic	Tony Korman and Despina Kotsanas
Nepean Hospital, NSW	James Branley and Linda Douglass
Pathology Queensland Central Laboratory, Qld	Graeme Nimmo and Narelle George
Pathology Queensland Gold Coast University Hospital, Qld	Petra Derrington and Cheryl Curtis
Pathology Queensland Prince Charles Hospital, Qld	Robert Horvath and Laura Martin
Pathology Queensland Princess Alexandra Hospital, Qld	Naomi Runnegar and Joel Douglas
PathWest Laboratory Medicine – north-west regional WA	Michael Leung
PathWest Laboratory Medicine – WA, Fiona Stanley Hospital	Denise Daley
PathWest Laboratory Medicine – WA, Perth Children's Hospital	Chris Blyth
PathWest Laboratory Medicine – WA, Queen Elizabeth II Medical Centre	Ronan Murray and Jacinta Bowman
PathWest Laboratory Medicine – WA, Royal Perth Hospital	Owen Robinson and Geoffrey Coombs
Royal Darwin Hospital, NT	Rob Baird and Jann Hennessy
Royal Hobart Hospital, Tas	Louise Cooley and David Jones
Royal Melbourne Hospital	Katherine Bond and Rose Cotronei
Royal North Shore Hospital, NSW	Angela Wong
Royal Women's Hospital, Vic	Andrew Daley and Gena Gonis
SA Pathology, Flinders Medical Centre, SA	Kelly Papanaoum and Xiao Chen,
SA Pathology, Royal Adelaide Hospital, SA	Morgyn Warner and Kija Smith
SA Pathology, Women's and Children's Hospital, SA	Morgyn Warner and Kija Smith
St John of God Hospital, Murdoch, WA	Sudha Pottumarthy-Boddu and Jacqueline Foster
St Vincent's Hospital, Melbourne, Vic	Amy Crowe and Lisa Brenton
St Vincent's Hospital, Sydney, NSW	David Lorenz
Sullivan Nicolaides Pathology, Qld	Jennifer Robson and Marianne Allen
Sydney Children's Hospital, NSW	Monica Lahra and Peter Huntington
Westmead Hospital, NSW	Jon Iredell and Andrew Ginn
Wollongong Hospital, NSW	Peter Newton and Melissa Hoddle

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