Australian Government
Department of Health

AGAR

AUSTRALIAN GROUP ON ANTIMICROBIAL RESISTANCE

Australian *Staphylococcus aureus* Sepsis Outcome (ASSOP)

Draft Final 2021 Report

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Contents

Key findings:

Staphylococcus aureus

- A total of 2,921 *Staphylococcus aureus* bacteraemia (SAB) episodes were reported to date, 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%. Mortality for methicillin-resistant *S. aureus* (MRSA) (15.0%) and methicillin-susceptible *S. aureus* (MSSA) (14.2%) were similar; and was higher in hospital-onset (HO) (15.8%) than CO (14.1%) bacteraemia
- The 30-day all-cause mortality for *S. aureus* was significantly lower among children (0.9%, 2/235) compared to adults (16.0%, 342/2,140) ($P < 0.01$)
- 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 (25.4% in MRSA, 23.3% in MSSA)
- In MRSA, resistance to erythromycin and clindamycin has continued to decline overall, largely due to the substantial decline in the multi-resistant ST239-III clone
- Community-associated methicillin-resistant *S. aureus* (CA-MRSA) strains were the dominant cause of MRSA bacteraemia
- Two healthcare-associated methicillin-resistant *S. aureus* (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
- The majority of EMRSA-15 bacteraemias were hospital-onset
- Forty one CA-MRSA clones were identified; the dominant CA-MRSA clone was ST93-IV (Queensland clone)
- Overall, 42.9% of CA-MRSA isolates harboured the PVL associated genes
- The Queensland clone of CA-MRSA (ST93-IV), which harbours the PVL associated genes, was seen in all states and territories except Tasmania; it is now the most common CA-MRSA clone in Queensland, South Australia, Western Australia and the Northern Territory
- The ST45-V MRSA clone remains prominent in New South Wales and the Australian Capital Territory and is associated with both CO and HO infections

1. Background and objectives

This report on the staphylococcal sepsis outcome program operated by the Australian Group on Antimicrobial Resistance (AGAR) presents analyses of antimicrobial resistance (AMR) associated with episodes of bacteraemia (blood stream infection) that were reported by 48 participating Australian public and private laboratories across Australia in 2021.

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, enabling benchmarking and trend projections. AGAR has collected ongoing data on the prevalence of antimicrobial resistance in Australia over a long period using standardised methods.

The 48 institutions across Australia that currently contribute to AGAR are listed in Table 1.

Historically, the main focus of AGAR was antimicrobial resistance 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 concentrated on the three groups of pathogens within the listed programs.

AGAR publishes detailed annual reports on each program on its website (www.agargroup.org.au), and also in the Communicable Diseases Intelligence (CDI) journal.

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, Sir Charles Gairdner Hospital
Microbiology services provided by PathWest Laboratory Medicine WA, Fiona Stanley Hospital

1.1. Australian Staphylococcal Sepsis Outcome Program

Globally *Staphylococcus aureus* is one of the most frequent causes of hospital-acquired and community-acquired blood stream infections.[1] Although there are a wide variety of manifestations of serious invasive infection caused by *S. aureus*, in the great majority of cases the organism can be detected in blood cultures. Therefore, *S. aureus* bacteraemia (SAB) is considered a very useful marker for serious invasive infection.[2]

Despite standardised treatment protocols for SAB, including prolonged antimicrobial therapy and prompt source control[3], mortality can range from as low as 2.5% to as high as 40%.[4-6] Mortality rates are known to vary significantly with patient age, clinical manifestation, co-morbidities and methicillin resistance.[7, 8] A prospective study of SAB conducted by 27 laboratories in Australia and New Zealand found a 30-day all-cause mortality of 20.6%. On univariate analysis, increased mortality was significantly associated with older age, European ethnicity, methicillin resistance, infections not originating from a medical device, sepsis syndrome, pneumonia/empyema and treatment with a glycopeptide or other non-β-lactam antibiotic.[9]

AGAR began surveillance of antimicrobial resistance in *S. aureus* in 1986.[10] In 2013, AGAR commenced the Australian Staphylococcal Sepsis Outcome Program (ASSOP).[11]

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

- Assessing susceptibility to methicillin
- Molecular epidemiology of methicillin-resistant *S. aureus* (MRSA).

2. Summary of methods

Forty-eight institutions, in each state and territory of Australia, were enrolled in the 2021 AGAR programs. The AGAR laboratories collected all isolates from unique patient episodes of bacteraemia 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.

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.

2.1 Data fields

Laboratory data collected for each episode included an accession number, the date the blood culture was collected, the organism isolated (genus and species), and the antimicrobial susceptibility test results (minimum inhibitory concentrations) for each species. The patient's date of birth, sex and postcode of residence were also provided. If the patient was admitted to hospital, the dates of admission and discharge were recorded. Depending on the level of participation, limited clinical and outcome data were also provided. These included the principal clinical manifestation, and the outcome (died, all-cause or survived) at seven and 30 days.

2.2 Species identification

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).

2.3 Susceptibility testing

Susceptibility testing of isolates is described in Appendix B. The analysis used breakpoints from the Clinical and Laboratory Standards Institute (CLSI) M100–A32[12] and the European Committee on Antimicrobial Susceptibility Testing (EUCAST) v12.0.[13]

2.4 PCR screening and whole genome sequencing

All methicillin-resistant *S. aureus* (MRSA) were subjected to whole genome sequencing using the Illumina NextSeq™ 500 platform. Data were analysed using the Nullarbor bioinformatic pipeline.[14] The pipeline was used to identify the multi-locus sequence type, SCC*mec* (MRSA) and Panton-Valentine leucocidin (MRSA).

2.5 Statistical analysis

Confidence intervals for proportions, Fisher's exact test for categorical variables, and chi-square test for trend were calculated, if appropriate, using MedCalc for Windows, version 19.7.4 (MedCalc Software, Ostend Belgium).

3 Results

3.1 Isolates recovered

There were 2,921 SAB episodes reported, 494 (16.9%; 95% confidence interval [CI] 15.6-18.3) were methicillin resistant, ranging from 7.9% (95% CI 3.6-14.7) in Tasmania to 43.0% (95% CI: 32.4-54.1) in the Northern Territory (Table 2). There was no significant difference in the proportion of MRSA among children (12.0%, 95% CI: 8.5-16.4) and adults (17.4%, 95% CI: 16.0-18.9)

Table 2: Number of each species recovered, by state and territory, AGAR, 2021

Organism	NSW	Vic	Qld	SA	WA	Tas	NT	ACT	Total
Staphylococcus aureus	768	615	495	228	513	114	86	102	2,921
methicillin resistant, percent	19.8	12.7	13.1	18.0	19.1	7.9	43.0	13.7	16.9
methicillin susceptible, percent	80.2	87.3	86.9	82.0	80.9	92.1	57.0	86.3	83.1

3.2 Place of onset of bacteraemia

Almost all patients with bacteraemia were admitted to hospital: 2,875, 98.4%.

Information on place of onset of bacteraemia was available for all *S. aureus* episodes (Table 3).

Most SABs were community onset (78.4%; 95% CI 76.9-80.0). The proportion of MRSA episodes that were community onset was lower among children (67.6%, 23/34) than adults (78.7%, 361/460).

Table 3: Species recovered, by place of onset, AGAR, 2021

Organism	Community onset % (*n*)	Hospital onset % (*n*)	Total, 100%
Staphylococcus aureus	78.4 (2,290)	21.6 (631)	2,921
Methicillin resistant	77.7 (384)	22.3 (110)	494
Methicillin susceptible	78.5 (1,906)	21.5 (521)	2,427

3.3 Onset versus 30-day all-cause mortality

Information on 30-day all-cause mortality, when place of onset was known, 2,375 (81.3%).

The 30-day all-cause mortality for *S. aureus* was significantly lower among children (0.9%, 2/235) compared to adults (16.0%, 342/2,140) ($P < 0.01$). There was no significant difference in 30-day all-cause mortality between methicillin-susceptible *S. aureus* (MSSA) (14.2%) and MRSA (15.0%) episodes, or between healthcare-associated MRSA (HA-MRSA) (18.6%) and community-associated MRSA (CA-MRSA) (13.5%) clones.

Table 4: Onset setting and 30-day all-cause mortality (blood culture isolates), AGAR, 2021

	Community onset		Hospital onset		Total	
Organism	Number	Deaths % (*n*)	Number	Deaths % (*n*)	Number	Deaths % (*n*)
Staphylococcus aureus	1,843	14.1 (260)	532	15.8 (84)	2,375	14.5 (344)
Methicillin resistant	318	12.9 (41)	89	22.5 (20)	407	15.0 (61)
CA-MRSA	212	12.7 (27)	28	46.4 (13)	270	14.8 (40)
HA-MRSA	40	20.0 (8)	17	29.4 (5)	57	22.8 (13)
Methicillin susceptible	1,520	14.3 (218)	442	13.8 (61)	1,962	14.2 (279)

CA-MRSA = community-associated methicillin-resistant *Staphylococcus aureus*; HA-MRSA = healthcare-associated methicillin-resistant *S. aureus*

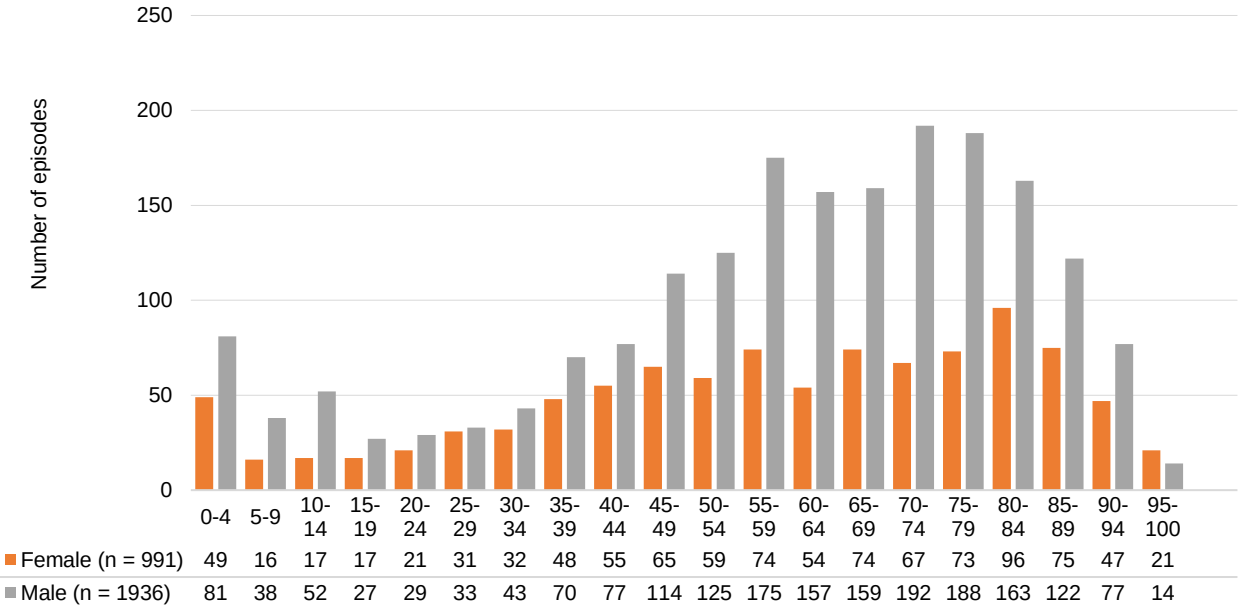
Notes:
Eighty methicillin-resistant *Staphylococcus aureus* were not available for whole genome sequencing at this time

3.4 Patient age and sex

Age and sex were available for all patients staphylococcal bacteraemia. The proportion of males was 66.1%.

Increasing age was a surrogate risk factor for bacteraemia (Figure 1); 20.9% of *S. aureus* episodes were in patients aged less than 40 years. The proportion of patients aged 0–19 years was 10.8% (*n* = 261).

Figure 1:
Number of episodes of bacteraemia due to *Staphylococcus aureus*, by patient age group and sex, AGAR, 2021



3.5 Principal clinical manifestation

The principal clinical manifestations, which represent the most likely primary site or source for the origin of the blood stream infection, are described below.

The principal clinical manifestation was known for 2,684 (91.7%) episodes of SAB (Table 5). Overall, the most frequent principal clinical manifestation was osteomyelitis/septic arthritis (22.6%) followed by skin and skin structure infection (19.0%). Almost half (42.7%, 117/274) of the clinical manifestations in children were due to osteomyelitis/septic arthritis.

Of the hospital-onset SABs where data were available, the most common principal clinical manifestation was device-related infection without metastatic focus (34.8%, 202/581). Of the community-onset SABs where data were available, the most common principal clinical manifestation was osteomyelitis/septic arthritis (26.3%, 553/2,103).

Table 5: Principal clinical manifestation for *Staphylococcus aureus* bacteraemia, by patient sex, AGAR, 2021

Principal clinical manifestation	Female % (*n*)	Male % (*n*)	Total % (*n*)
Osteomyelitis/septic arthritis	20.2 (183)	23.8 (423)	22.6 (606)
Skin and skin structure infection	17.0 (154)	20.0 (355)	19.0 (509)
Device-related infection without metastatic focus	18.4 (167)	16.0 (285)	16.8 (452)
No identifiable focus	15.1 (137)	11.9 (212)	13.0 (349)
Other clinical syndrome	6.5 (59)	7.9 (140)	7.4 (199)
Endocarditis left-sided	5.0 (45)	6.0 (107)	5.7 (152)
Pneumonia/empyema	4.4 (40)	3.7 (65)	3.9 (105)
Deep abscess(es) excluding those in the CNS	2.9 (26)	4.0 (71)	3.6 (97)
Device-related infection with metastatic focus	2.1 (19)	2.3 (40)	2.2 (59)
Febrile neutropenia	3.3 (30)	1.3 (23)	2.0 (53)
CNS infection (meningitis, abscess(es))	1.8 (16)	2.0 (36)	1.9 (52)
Endocarditis right-sided	3.4 (31)	1.1 (20)	1.9 (51)
Total	907	1,777	2,684

CNS = central nervous system

The most common principal clinical manifestation for methicillin-susceptible *S. aureus* was osteomyelitis/septic arthritis (23.7%, 528/2,228), whereas for methicillin-resistant *S. aureus* it was skin and skin structure infection (26.4%, 119/450) (Table 6).

Table 6: Principal clinical manifestation for *Staphylococcus aureus* bacteraemia, by methicillin susceptibility, AGAR, 2021

Principal clinical manifestation	Methicillin-resistant % (*n*)	Methicillin-susceptible % (*n*)	Total % (*n*)
Osteomyelitis/septic arthritis	16.4 (74)	23.7 (528)	22.5 (602)
Skin and skin structure infection	26.4 (119)	17.5 (390)	19.0 (509)
Device-related infection without metastatic focus	13.8 (62)	17.5 (390)	16.9 (452)
No identifiable focus	11.1 (50)	13.4 (298)	13.0 (348)
Other clinical syndrome	8.7 (39)	7.2 (160)	7.4 (199)
Endocarditis left-sided	6.2 (28)	5.5 (123)	5.6 (151)
Pneumonia/empyema	4.9 (22)	3.7 (83)	3.9 (105)
Deep abscess(es) excluding those in the CNS	6.0 (27)	3.1 (70)	3.6 (97)
Device-related infection with metastatic focus	1.3 (6)	2.4 (53)	2.2 (59)
Febrile neutropenia	1.3 (6)	2.1 (47)	2.0 (53)

CNS infection (meningitis, abscess(es))	2.2 (10)	1.9 (42)	1.9 (52)
Endocarditis right-sided	1.6 (7)	2.0 (44)	1.9 (51)
Grand Total	450	2,228	2,678

CNS = central nervous system

3.6 Length of hospital stay following bacteraemic episode

Information on length of hospital stay following bacteraemia was available for 2,660 (90.9%) episodes. Overall, 23.6% of patients remained in hospital for more than 30 days (Table 7).

Table 7: Length of hospital stay following *Staphylococcus aureus* bacteraemia, by methicillin susceptibility and place of onset, AGAR, 2021

Species	Length of stay following bacteraemia				Total
	<7 days % (*n*)	7–14 days % (*n*)	15–30 days % (*n*)	>30 days % (*n*)	
Staphylococcus aureus	16.0 (73)	25.4 (116)	33.1 (151)	25.4 (116)	456
Methicillin resistant	17.0 (61)	26.0 (93)	34.6 (124)	22.3 (80)	358
Community onset	12.2 (12)	23.5 (23)	27.6 (27)	36.7 (36)	98
Hospital onset	18.7 (412)	27.8 (612)	30.3 (667)	23.3 (513)	2,204
Methicillin susceptible	20.6 (354)	29.6 (510)	28.9 (497)	20.9 (360)	1,721
Community onset	12.0 (58)	21.1 (102)	35.2 (170)	31.7 (153)	483
Hospital onset	16.0 (73)	25.4 (116)	33.1 (151)	25.4 (116)	456

3.7 Susceptibility testing results

The following sections present the results of susceptibility testing in priority indicator species, and the findings for antimicrobial resistance by place of onset and multi-drug resistance. Susceptibility testing methods are described in Appendix B.

Percentages of non-susceptibility

Overall percentages of resistance or non-susceptibility using both CLSI breakpoints and EUCAST breakpoints are shown in Table 8. Resistance (as defined by EUCAST) by state and territory to methicillin is shown in Figure 2. Detailed resistance by state and territory can be found in Appendix C.

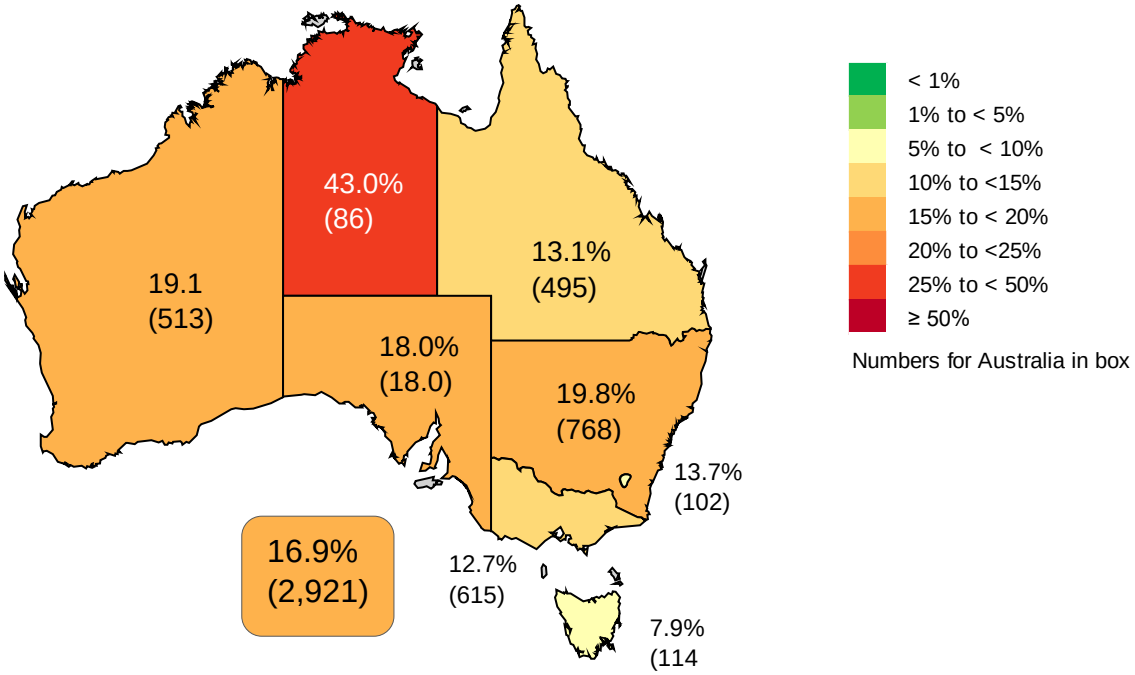
Supplementary data on percentages susceptible, susceptible – increased exposure (EUCAST), intermediate (CLSI), and resistant for each antimicrobial and all species, and the antimicrobial profiles by state and territory can be found in the 2021 report on the AGAR website. This report provides summary susceptibility data (number and percentage for species if more than 10 isolates were tested) using both CLSI and EUCAST interpretive guidelines.

Table 8: Antimicrobial resistances (CLSI and EUCAST), AGAR, 2021

Species and antimicrobial	Isolates (*n*)	CLSI		EUCAST	
		Intermediate % (*n*)	Resistant % (*n*)	Susceptible, increased exposure % (*n*)	Resistant % (*n*)
Staphylococcus aureus					
Benzylpenicillin[##]	2,874	–[†]	17.0 (490)	–[†]	17.0 (490)
Cefoxitin (methicillin)***	2,921	–[†]	16.9 (494)	–[†]	16.9 (494)
Ciprofloxacin	2,922	0.6 (18)	8.1 (236)	91.3 (2,668)	8.7 (254)
Clindamycin (constitutive)	2,919	0.1 (2)	2.3 (68)	0.0 (0)	2.9 (85)
Clindamycin (constitutive + inducible resistance)	2,920	0.1 (2)	12.5 (366)	0.0 (0)	14.5 (396)
Daptomycin	2,919	0.0 (0)[#]	–[†]	–[†]	0.0 (0)
Erythromycin	2,921	27.3 (796)	15.8 (461)	0.7 (20)	16.4 (449)
Fusidic acid	2,922	–**	–**	–[†]	2.6 (77)
Gentamicin	2,922	1.5 (45)	2.1 (61)	–[†]	4.9 (144)
Linezolid	2,923	–[†]	0.0 (0)	–[†]	0.0 (0)
Mupirocin (high-level)[§§§]	2,179	–[†]	1.1 (25)	–[†]	1.1 (25)
Rifampicin	2,919	0.1 (2)	0.2 (5)	–[§§]	0.3 (10)
Teicoplanin	2,907	0.0 (0)	0.0 (0)	–*	0.1 (3)
Tetracycline/doxycycline****	2,922	0.2 (7)[##]	4.0 (117)	0.7 (21)	4.5 (132)
Trimethoprim/sulfamethoxazole[‡‡]	2,903	0.1 (2)	0.6 (18)	0.1 (2)	0.6 (18)
Vancomycin	2,924	0.0 (0)	0.0 (0)	–[†]	0.0 (0)

CLSI = Clinical and Laboratory Standards Institute; EUCAST = European Committee on Antimicrobial Susceptibility Testing
* Beta-lactamase adjusted
† No category defined
§ Resistance as determined by cefoxitin screen (Vitek) or cefoxitin MIC (Phoenix)
# Non-susceptible; resistance not defined (DAP)
** No guidelines for indicated species (FUSc)
‡ Mupirocin high-level resistance screen
§§ The rifampicin concentration range on cards restricts category interpretation to non-resistant or resistant
Doxycycline concentration range (Phoenix panel) restricts ability to accurately identify intermediate and resistant category

Figure 2. Percentage of *Staphylococcus aureus* from patients with bacteraemia with resistance as defined by EUCAST to methicillin, Australia, AGAR, 2021



Antimicrobial resistance by place of onset

Antimicrobial resistances (CLSI and EUCAST) by place of onset, are shown in Table 9.

Table 9: Antimicrobial resistances (CLSI, EUCAST), by place of onset, AGAR, 2021

Species and antimicrobial	Number	Community onset		Hospital onset	
		% intermediate	% resistant	% susceptible, increased exposure	% resistant
Staphylococcus aureus					
Benzylpenicillin	2,247	–*	76.3 (1,714)	–*	75.3 (1,825)
Benzylpenicillin†	2,375	–*	79.5 (1,888)	–*	79.5 (1,888)
Cefoxitin (methicillin)§	2,921	–*	16.9 (494)	–*	16.9 (494)
Ciprofloxacin	2,427	0.0 (0)	2.6 (64)	96.9 (505)	3.1 (16)
Clindamycin (constitutive)	2,426	0.0 (0)	1.2 (29)	0.0 (0)	1.6 (276)
Clindamycin (inducible + constitutive resistance)	2,426	0.0 (0)	10.5 (254)	0.0 (0)	11.4 (276)
Daptomycin	2,425	–*	0.0 (0)	–*	0.0 (0)
Erythromycin	2,426	28.7 (697)	13.0 (315)	0.5 (12)	13.5 (328)
Fusidic acid	2,427	–**	–**	–*	2.1 (50)
Gentamicin	2,427	0.7 (17)	0.9 (21)	–*	2.6 (64)
Linezolid	2,425	–*	0.0 (0)	–*	0.0 (0)
Mupirocin (high-level)‡	1,848	–*	1.2 (22)	–*	1.2 (22)
Rifampicin	2,425	0.1 (2)	0.1 (3)	–§§	0.2 (6)
Teicoplanin	2,412	0.0 (0)	0.0 (0)	–*	0.0 (1)
Tetracycline/doxycycline##	2,427	0.1 (3)	2.2 (54)	0.5 (13)	2.4 (59)
Trimethoprim/sulfamethoxazole	2,414	–*	0.2 (6)	0.0 (0)	0.2 (6)
Vancomycin	2,427	0.0 (0)	0.0 (0)	–*	0.0 (0)

CLSI = Clinical and Laboratory Standards Institute; EUCAST = European Committee on Antimicrobial Susceptibility Testing
* No category defined
† Beta-lactamase adjusted
§ Resistance as determined by cefoxitin screen (Vitek) or cefoxitin MIC (Phoenix)
** No guidelines for indicated species (FUSc)
‡ Mupirocin high-level resistance screen
§§ The rifampicin concentration range on cards restricts category interpretation to non-resistant or resistant
Doxycycline concentration range (Phoenix panel) restricts ability to accurately identify intermediate and resistant category

3.8 Multidrug resistance

The most problematic pathogens are those with multiple acquired resistances. The definitions defined by Magiorakos et al.[15] were applied in this survey; where multi-drug resistance was defined as resistance to one or more agent in three or more antimicrobial categories. For each species, antimicrobials were excluded from the count if they were affected by natural resistance mechanisms.

Only isolates for which the full range of antimicrobial categories was tested were included for determination of multi-drug resistance. EUCAST breakpoints were primarily used in the analysis.

Multiple acquired resistances for key species are shown in Tables 10 and11. The agents included are listed in the notes after each table.

Table 10: Multiple acquired resistance in *Staphylococcus aureus* (methicillin resistant), by state and territory, AGAR, 2021

State or territory	Number of categories (non-MDR)					Number of categories (MDR)									
	Total	0	1	2	%	3	4	5	6	7	8	9	10	11	%
NSW	149	50	17	23	60.4	27	15	14	3	0	0	0	0	0	39.6
Vic	78	27	25	14	84.6	6	6	0	0	0	0	0	0	0	n/a
Qld	64	36	9	11	87.5	5	2	1	0	0	0	0	0	0	n/a
SA	38	13	13	7	86.8	4	0	1	0	0	0	0	0	0	n/a
WA	98	70	9	9	89.8	6	1	3	0	0	0	0	0	0	n/a
Tas	9	3	1	2	n/a	3	0	0	0	0	0	0	0	0	n/a
NT	36	20	5	8	91.7	3	0	0	0	0	0	0	0	0	n/a
ACT	13	4	2	3	n/a	1	1	2	0	0	0	0	0	0	n/a
Total	**485**	**223**	**81**	**77**	**78.6**	**55**	**25**	**21**	**3**	**0**	**0**	**0**	**0**	**0**	**21.4**

MDR = multi-drug resistant; resistant to one or more agent in three or more antimicrobial categories;

n/a = not applicable, insufficient numbers (<30) to calculate percentage

Note: Antimicrobials were aminoglycosides (gentamicin), ansamycins (rifampicin), fluoroquinolones (ciprofloxacin), folate pathway inhibitors (trimethoprim–sulfamethoxazole), fucidanes (fusidic acid), glycopeptides (vancomycin or teicoplanin), lincosamides (clindamycin), lipopeptides (daptomycin), macrolides (erythromycin), oxazolidinones (linezolid), and tetracyclines (tetracycline, Vitek®; doxycycline, Phoenix™).

Table 11: Multiple acquired resistance in *Staphylococcus aureus* (methicillin susceptible), by state and territory, AGAR, 2021

State or territory	Number of categories (non-MDR)					Number of categories (MDR)									
	Total	0	1	2	%	3	4	5	6	7	8	9	10	11	%
NSW	615	489	47	65	97.7	9	2	2	1	0	0	0	0	0	n/a
Vic	537	431	41	46	96.5	16	3	0	0	0	0	0	0	0	n/a
Qld	422	334	23	50	96.4	13	1	1	0	0	0	0	0	0	n/a
SA	181	145	18	16	98.9	2	0	0	0	0	0	0	0	0	n/a
WA	414	337	22	45	97.6	10	0	0	0	0	0	0	0	0	n/a
Tas	105	93	6	6	100.0	0	0	0	0	0	0	0	0	0	n/a
NT	49	39	1	6	93.9	3	0	0	0	0	0	0	0	0	n/a
ACT	88	73	5	9	98.9	1	0	0	0	0	0	0	0	0	n/a
Total	**2,411**	**1,941**	**163**	**243**	**97.3**	**54**	**6**	**3**	**1**	**0**	**0**	**0**	**0**	**0**	n/a

MDR = multi-drug resistant; resistant to one or more agent in three or more antimicrobial categories

n/a = not applicable, insufficient numbers (<30) to calculate percentage

Note: Antimicrobials were aminoglycosides (gentamicin), ansamycins (rifampicin), fluoroquinolones (ciprofloxacin), folate pathway inhibitors (trimethoprim–sulfamethoxazole), fucidanes (fusidic acid), glycopeptides (vancomycin or teicoplanin), lincosamides (clindamycin), lipopeptides (daptomycin), macrolides (erythromycin), oxazolidinones (linezolid), and tetracyclines (tetracycline, Vitek®; doxycycline, Phoenix™).

For *S. aureus*, the most common resistance combination was resistance to methicillin and fluoroquinolones (Table 12).

Table 12: Resistance combinations among *Staphylococcus aureus* tested against methicillin, fluoroquinolones and rifampicin, AGAR, 2021

Resistance pattern	N	% of total
Fully susceptible	2,331	80.6
Single resistance	388	13.4
Methicillin	311	10.8
Fluoroquinolones	72	2.5
Rifampicin	5	0.2
Resistance to two antimicrobial groups	173	6.0
Methicillin + fluoroquinolones	169	5.8
Methicillin + rifampicin	3	0.1
Fluoroquinolones + rifampicin	1	
Resistance to three antimicrobial groups	1	
Methicillin + fluoroquinolones + rifampicin	1	

Note: Only data from isolates tested against all five antimicrobial groups were included (*n* = 2,893).

Multidrug resistance by onset setting and 30-day all-cause mortality

Multi-drug resistances by onset setting (community or hospital) and 30-day all-cause mortality for the most common species are shown in Table 13.

Table 13: Multi-drug resistance, by onset setting and 30-day all-cause mortality, AGAR, 2021

Species	Category	Total		Community onset		Hospital onset	
		Number	Deaths, % (n)	Number	Deaths,% (n)	Number	Deaths, % (n)
Staphylococcus aureus	Total	2,347	14.5 (341)	1,820	14.1 (257)	527	15.9 (84)
	Non-MDR (≤2)	2,145	14.1 (303)	1,668	13.8 (230)	477	15.3 (73)
	MDR (>2)	600	16.2 (97)	463	14.3 (66)	137	22.6 (31)

MDR = multi-drug resistant; resistant to one or more agent in three or more antimicrobial categories

Notes:

1. Antimicrobial categories (agents) for each species are listed under Tables 10 and 11. For *Staphylococcus aureus,* anti-staphylococcal β-lactams (cefoxitin) is also included.

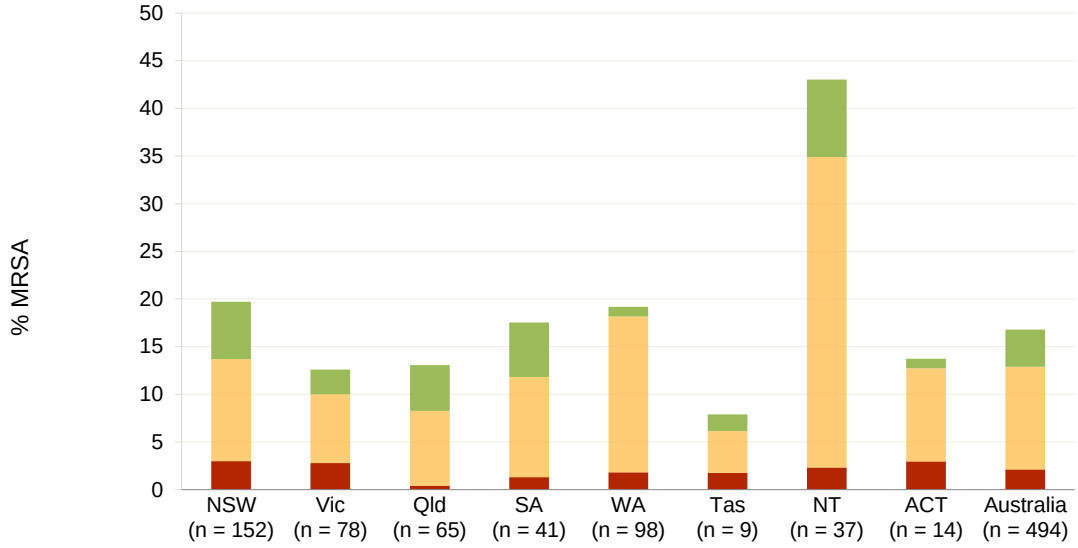
3.9 Whole genome sequencing

This section describes the results and the molecular epidemiology of MRSA. The benefits of molecular methods include increased accuracy in detecting the genetic mechanisms for AMR and clarifying the underlining epidemiology.

3.9.1 Molecular epidemiology of methicillin-resistant *Staphylococcus aureus*

Of the 494 MRSA reported, 355 (71.9%) were available for typing by whole genome sequencing to date. There were marked differences among the states and territories in the percentage and types of MRSA clones. Prevalence of MRSA ranged from 7.9% (9/114) in Tasmania to 43.0% (37/86) in the Northern Territory (Figure 3).

Figure 3: Methicillin-resistant *Staphylococcus aureus* as a percentage of all *S. aureus* isolates, by state and territory, and nationally, AGAR, 2021



	NSW (n = 152)	Vic (n = 78)	Qld (n = 65)	SA (n = 41)	WA (n = 98)	Tas (n = 9)	NT (n = 37)	ACT (n = 14)	Australia (n = 494)
Not available (n = 114)	6.0	2.6	4.8	5.7	1.0	1.8	8.1	1.0	3.9
Community associated (n = 316)	10.7	7.2	7.9	10.5	16.4	4.4	32.6	9.8	10.8
Healthcare associated (n = 61)	3.0	2.8	0.4	1.3	1.8	1.8	2.3	2.9	2.1

MRSA = methicillin-resistant *Staphylococcus aureus*

Notes:
1. *S. aureus* were categorised as MRSA based on cefoxitin screen ((Vitek) or cefoxitin MIC (Phoenix).
2. Eighty MRSA were not available for whole genome sequencing at this time so association could not be determined

Healthcare-associated MRSA

Based on the MLST and SCC*mec* type, two HA-MRSA clones were identified: ST22-IV (EMRSA-15) and ST239-III (Aus 2/3 EMRSA) (Tables 14 -16).

PVL-associated genes were not identified in HA-MRSA. Nine PVL positive ST22-IV isolates were identified: three in South Australia, two in Victoria and Queensland, and one each in New South Wales and the Australian Capital Territory. PVL positive ST22-IV are frequently isolated in the South Asian subcontinent; they are not related to EMRSA-15, and are not considered to be a HA-MRSA clone.[16]

The most frequently isolated HA-MRSA clone, ST22-IV, was identified in all states and territories except Queensland (Table 16). ST239-III was identified in two states; New South Wales and South Australia.

Community-associated MRSA

Based on the MLST and SCC*mec* type, 34 CA-MRSA clones were identified. PVL was detected in 12 CA-MRSA clones. Overall, 42.9% (134/312) of CA MRSA were PVL positive (Table 14). The most frequently isolated CA-MRSA clone, ST93-IV (Qld CA-MRSA), was isolated in all states except Tasmania.

Of the hospital-onset MRSA, 77.6% (66/85) were caused by CA-MRSA.

Table 14: MRSA clones, association, place of onset and PVL carriage, AGAR, 2021

Clone	Clonal complex	Total, *n*	Community onset, % (*n*)*	Hospital onset, % (*n*)*	PVL positive, % (*n*)*
Healthcare-associated					
ST22-IV (EMRSA-15)	22	55	69.1 (38)	30.9 (17)	0.0 (0)
ST239-III (Aus2/3 EMRSA)	8	6	–† (4)	–† (2)	–† (0)
Total HA-MRSA		61	68.9 (42)	31.1 (19)	0.0 (0)
Community-associated					
ST93-IV (Qld CA-MRSA)	93	84	90.5 (76)	9.5 (8)	95.2 (80)
ST45-V	45	45	82.2 (37)	17.8 (8)	0.0 (0)
ST5-IV	5	41	78.0 (32)	22.0 (9)	41.5 (17)
ST1-IV (WA1 MRSA)	1	23	78.3 (18)	21.7 (5)	8.7 (2)
ST30-IV (SWP MRSA)	30	19	84.2 (16)	15.8 (3)	78.9 (15)
ST22-IV (PVL positive)	22	9	–† (5)	–† (4)	–† (9)
ST97-IV	97	9	–† (6)	–† (3)	–† (0)
ST88-IV		8	–† (5)	–† (3)	–† (0)
ST953-IV	8	7	–† (6)	–† (1)	–† (4)
ST8-IV	97	7	–† (6)	–† (1)	–† (0)
ST59-IV	59	6	–† (1)	–† (5)	–† (0)
ST6-IV	5	6	–† (6)	–† (0)	–† (0)
ST78-IV (WA2 MRSA)	78	5	–† (3)	–† (2)	–† (0)
Other (*n* = 28)		43	67.4 (29)	32.6 (14)	16.3 (7)
Total CA-MRSA		312	78.8 (246)	21.2 (66)	42.9 (134)
MRSA typed		373	77.2 (288)	22.8 (85)	35.9 (134)

MRSA = methicillin-resistant *Staphylococcus aureus*; PVL = Panton-Valentine leucocidin

* Percentage of the clone
† Insufficient numbers (<10) to calculate percentage

Table 15: Healthcare-associated MRSA clones, by state and territory, AGAR, 2021

Clone	Percentage (*n*)								
	NSW	Vic	Qld	SA	WA	Tas	NT	ACT	Australia
ST22-IV (EMRSA-15)	78.3 (18)	100.0 (17)	–* (2)	–* (2)	–* (9)	–* (2)	–* (2)	–* (3)	90.2 (55)
ST239-III (Aus2/3 EMRSA)	21.7 (5)	0.0 (0)	–* (0)	–* (1)	–* (0)	–* (0)	–* (0)	–* (0)	9.8 (6)
Total	23	17	2	3	9	2	2	3	61

MRSA = methicillin-resistant *Staphylococcus aureus*; n/a = not applicable (no isolates)
* Insufficient numbers (<10) to calculate percentage

Table 16: Major community-associated MRSA clones by state and territory and PVL carriage, AGAR, 2021

Clone	Percentage (*n*)								
	NSW	Vic	Qld	SA	WA	Tas	NT	ACT	Australia
ST93-IV (Qld CA-MRSA)	11.0 (9)	15.9 (7)	25.6 (10)	25.0 (6)	38.1 (32)	–* (0)	67.9 (19)	10.0 (1)	26.6 (84)
Number PVL positive	9	7	10	5	30	0	19	0	80
Number PVL negative	0	0	0	1	2	0	0	1	4
ST45-V	28.0 (23)	27.3 (12)	5.1 (2)	4.2 (1)	2.4 (2)	–* (0)	0.0 (0)	50.0 (5)	14.2 (45)
Number PVL positive	0	0	0	0	0	0	0	0	0
Number PVL negative									
ST5-IV	8.5 (7)	6.8 (3)	17.9 (7)	8.3 (2)	17.9 (15)	–* (3)	14.3 (4)	0.0 (0)	13.0 (41)
Number PVL positive	7	2	7	1	5	1	1		24
Number PVL negative		1		1	10	2	3		17
ST1-IV	8.5 (7)	2.3 (1)	12.8 (5)	16.7 (4)	3.6 (3)	–* (1)	3.6 (1)	10.0 (1)	7.3 (23)
Number PVL positive	7	1	3	4	3	1	1	1	21
Number PVL negative			2						2
ST30-IV	12.2 (10)	6.8 (3)	5.1 (2)	0.0 (0)	3.6 (3)	–* (1)	0.0 (0)	0.0 (0)	6.0 (19)
Number PVL positive	1	1	1		1				4
Number PVL negative	9	2	1		2	1			15
ST97-IV	4.9 (4)	6.8 (3)	2.6 (1)	0.0 (0)	1.2 (1)	–* (0)	0.0 (0)	0.0 (0)	2.8 (9)
Number PVL positive	4	3	1		1				9
Number PVL negative									
ST22-IV	1.2 (1)	4.5 (2)	5.1 (2)	12.5 (3)	0.0 (0)	–* (0)	0.0 (0)	10.0 (1)	2.8 (9)
Number PVL positive									
Number PVL negative	1	2	2	3				1	9
ST88-IV	3.7 (3)	0.0 (0)	0.0 (0)	8.3 (2)	3.6 (3)	–* (0)	0.0 (0)	0.0 (0)	2.5 (8)
Number PVL positive	3			2	3				8
Number PVL negative									
Other clones (n = 40)	22.0 (18)	22.7 (10)	25.6 (10)	20.8 (5)	29.8 (25)	–* (0)	14.3 (4)	20.0 (2)	23.4 (74)
Number PVL positive	14	7	9	5	23	0	3	2	63
Number PVL negative	4	3	1	0	2	0	1	0	11
Total	**121**	**54**	**57**	**24**	**87**	**3**	**36**	**5**	**387**
PVL positive	31	24	24	11	50	0	28	2	170
PVL negative	90	30	33	13	37	3	8	3	217

CA-MRSA = community-associated methicillin-resistant *Staphylococcus aureus*; MRSA = methicillin-resistant *Staphylococcus aureus*; PVL = Panton-Valentine leucocidin

* Insufficient numbers (<10) to calculate percentage

3.10 Trend analysis (2013–2021)

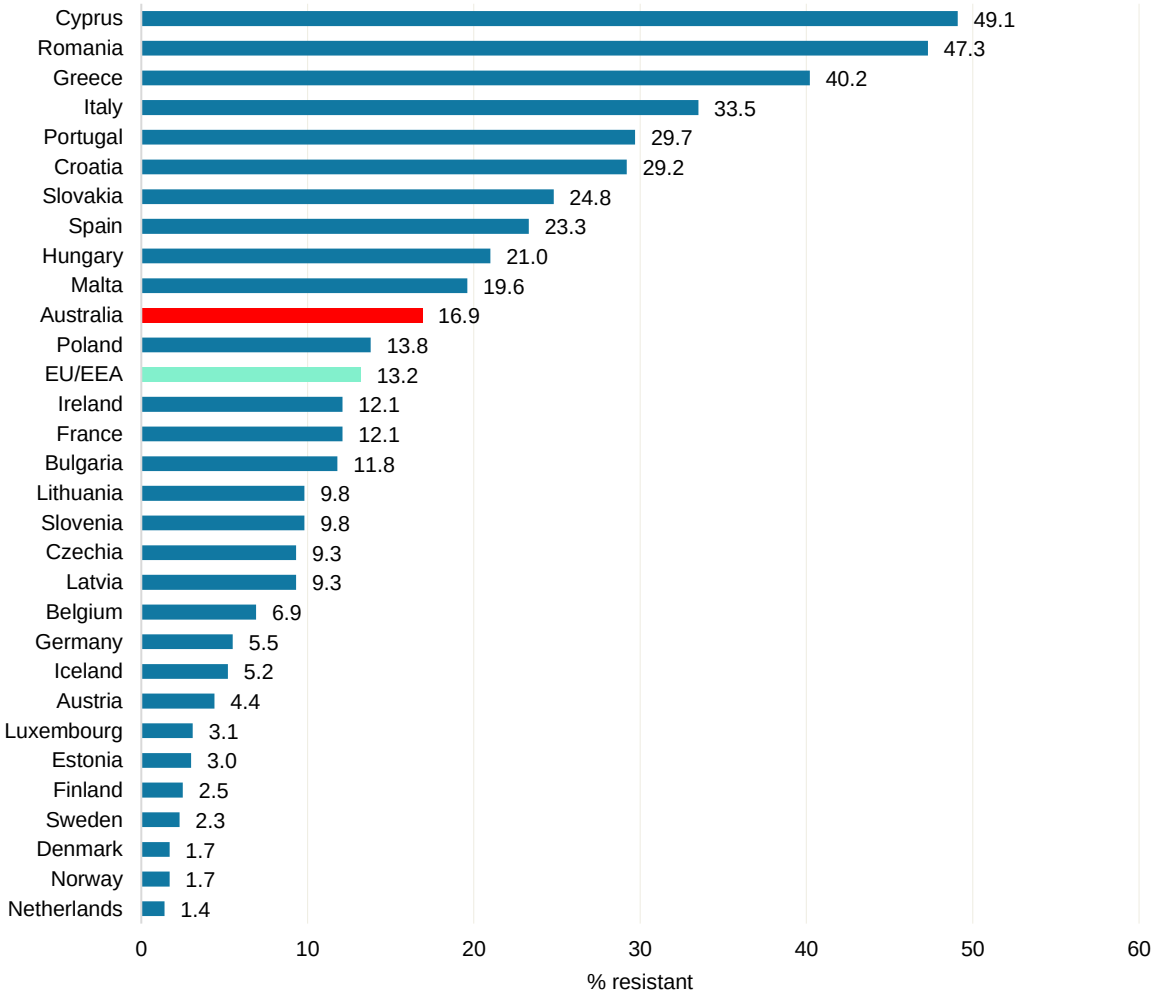
Trend data will be available for the final report.

4 International comparisons

Data from AGAR can be compared with data from the European Antimicrobial Resistance Surveillance Network (EARs-Net) program[17], as both programs examine resistance in bacterial pathogens found in blood cultures.

Australia ranked 11th in the rate of resistance to methicillin in *S. aureus* compared to all European countries (Figure 4), and has been consistent for the past three years.

Figure 4: Comparison of *Staphylococcus aureus* rates of resistance to methicillin in Australia and European countries, blood culture isolates, AGAR, 2021



EU/EEA = European Union (EU) and European Economic Area (EEA) countries population-weighted mean percentages

Source: EARS-Net (Europe)[18, 19]

5 Limitations of the study

Although this study is considered comprehensive in its coverage of Australia, and the methods follow international standards, the data and their interpretation have a number of limitations:

- The data are not denominator controlled, and there is currently no consensus on an appropriate denominator for such surveys; hospital size, patient throughput, patient complexity and local antibiotic use patterns all influence the types of resistance that are likely to be observed
- Although data have been collected from 48 large hospitals across Australia, it is not yet clear how representative the sample is of Australia as a whole, because the proportion of the population that is served by the laboratories that participate in AGAR is not accurately known. Further, it is likely that the proportion of the population served differs in each state and territory
- Concentration ranges of some antimicrobial agents in both the Vitek® and Phoenix™ cards limit the ability to accurately identify ‘susceptible’ for some combinations of antimicrobial agents and species
- Data is classified into hospital- and community-onset infections; healthcare-associated community-onset infections may be included in the community-onset group

Discussion and conclusions

AGAR data show that in 2021 episodes of bacteraemia in Australia had their onset overwhelmingly in the community. For the ASSOP, the most frequent principal clinical manifestations were osteomyelitis/septic arthritis and skin and skin structure. Strategies to reduce blood stream infections should take this information on clinical manifestation (sources of bacteraemia) into account.

The overall rates of MRSA fell slightly from 17.6% in 2020[20] to 16.9% in the 2021 study. This compares with the 2021 EU/EEA population-weighted mean MRSA percentage of 13.2%, ranging from 1.4% in the Netherlands to 49.1% in Cyprus.[19, 21, 22]

The rate of community-onset SABs that are methicillin resistant has remained steady. CA-MRSA clones are an increasing source of hospital-onset bacteraemia (particularly ST93-IV, ST5-IV ST45-V). The most common HA-MRSA strain (ST22-IV), was more frequently found in hospital-onset bacteraemia. The molecular characterisation of MRSA contained within this report aids in identifying opportunities for control of MRSA bacteraemia in the Australian setting.

The rapidly changing picture of MRSA in Australia, drawing from nine years of AGAR bacteraemia surveillance, is further explored in *Methicillin-resistant* Staphylococcus aureus *in Australia. MRSA bacteraemia – 2013 to 2018*.[16] This technical paper will be updated as appropriate by AGAR and the Commission to provide further information on the issue.

In this survey, multidrug resistance did not appear to play a contributory role in the rates of all-cause mortality *S. aureus* bacteraemia.

Abbreviations

Abbreviation	Term
AGAR	Australian Group on Antimicrobial Resistance
ANCU	*AURA National Coordinating Unit*
APAS	Australian Passive AMR Surveillance
AURA	Antimicrobial Use and Resistance in Australia
CI	Confidence interval
CLSI	Clinical and Laboratory Standards Institute
GLASS	Global Antimicrobial Resistance Surveillance System
EUCAST	European Committee on Antimicrobial Susceptibility Testing
MDR	Multi-drug resistant
MIC	Minimum inhibitory concentration
WGS	Whole genome sequencing
WHO	World Health Organization

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Participating members of AGAR:

Institution	AGAR members
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Austin Hospital, Vic	Marcel Leroi and Elizabeth Grabsch
Canberra Hospital, ACT	Peter Collignon and Susan Bradbury
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Concord Hospital, NSW	Thomas Gottlieb and John Huynh
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Appendix A. Study design

Forty-eight institutions participated in the 2021 survey, 42 adult and six children's hospitals. All states and territories were represented. The hospital peer group/type[23] represented were:

Principal referral hospitals (*n* = 25)
Public acute group A hospitals (*n* = 2)
Children's hospitals (*n* = 5)
Combined Women's and children's hospitals (*n* = 1)
Private acute group A hospitals (*n* = 2)
Regional and district hospitals from north-west regional Western Australia (*n* = 11)

- Public acute group C hospitals (*n* = 6)
- Public acute group D hospitals (*n* = 5)

The laboratories that participated in AGAR collected all isolates from different patient episodes of bacteraemia. 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 after admission, and as hospital onset if collected >48 hours after admission.

All laboratories that participated in AGAR obtained basic laboratory information for each patient episode plus varying demographic information, depending on the level at which they are enrolled in the program. There are two levels of enrolment: Bronze and Silver (Table A1). At Bronze level, participating laboratories provided date of collection, date of birth, sex, postcode and admission date. At Silver level, participating laboratories provided discharge date, device-related infection, principal clinical manifestation, intensive care unit admission, outcome at seven and 30 days, and date of death.

Table A1: Level of participation of laboratories that contributed data on *Staphylococcus aureus* bacteraemia, by state and territory, 2021

State or territory	Number of institutions	Level of participation	
		Bronze	Silver
New South Wales	10	1	9
Victoria	8	0	8
Queensland	5	0	5
South Australia	3	0	3
Western Australia	17*	2	15*
Tasmania	2	0	2
Northern Territory	2	1	1
Australian Capital Territory	1	0	1
Total	48	4	44

*Includes 11 regional and district hospitals from northwest Western Australia

Appendix B. Methods

Species identification

Isolates were identified using the routine methods for each institution. These included the Vitek® and Phoenix™ automated microbiology systems, and, if available, mass spectrometry (MALDI - TOF).

Susceptibility testing

Testing was performed using two commercial semi-automated methods: Vitek 2 (bioMérieux) (*n* = 34) and Phoenix (BD) (*n* = 4), which are calibrated to the ISO (International Organization for Standardization) reference standard method of broth microdilution. Commercially available Vitek 2 (AST-P612, AST-P643, or AST-P656) or Phoenix (PMIC-84) cards were used by all participants throughout the survey period.

The CLSI M100[12] and the EUCAST v12.0[24] breakpoints from January 2022 were used in the analysis.

S. aureus were classified as MRSA if cefoxitin screen positive (Vitek) or cefoxitin MIC > 4 mg/L (Phoenix). Cefoxitin screen negative isolates that were oxacillin resistant underwent mecA/nuc PCR. If mecA was detected, the isolate was reported as MRSA. All *S. aureus* with penicillin MIC ≤ 0.12 mg/L and no β-lactamase results provided were tested for penicillinase by disc diffusion. A sharp zone edge around a penicillin 10 unit disc was recorded as a penicillinase producer. [12]

Additional tests were performed on *S. aureus* to confirm unusual resistances or to provide additional information for antimicrobials where issues have been reported with Vitek/Phoenix panels[25-27]

- E-test MIC if:
  - Linezolid MIC >4 mg/L, or if MIC not provided
  - Daptomycin MIC > 1 mg/L or if MIC not provided
  - Vancomycin MIC > 2 mg/L or if MIC not provided
  - Teicoplanin MIC > 2 mg/L or if MIC not provided
- High-level mupirocin
  - Mupirocin > 2 mg/L (Vitek AST-P612)
- Trimethoprim/sulfamethoxazole disc (SXT 25 µg)
  - Trimethoprim/sulfamethoxazole resistant (Vitek or Phoenix)

Antimicrobials tested

The antimicrobials tested are shown in Table B1.

Table B1: Antimicrobials available on susceptibility testing cards and interpretive guidelines for CLSI and EUCAST

Antimicrobial agent	Breakpoint (mg/L)						
	CLSI M100*				EUCAST v12.0†		
	S	SDD	I	R	S, SD	S, IE	R
Benzylpenicillin							
	≤0.12		–§	≥0.25	≤0.125	–§	>0.125
Chloramphenicol (Phoenix card)							
	≤8		16	≥32	≤8	–§	>8
Ciprofloxacin							
	≤1		2	≥4	≤0.001	0.002–1	>1
Clindamycin							
	≤0.5		1–2	≥4	≤0.25	0.5	>0.5
Daptomycin							
	≤1		–#	–#	≤1	–§	>1
Doxycycline (Phoenix card)							
	≤4		8**	≥16**	≤1	2	>2
Erythromycin							
	≤0.5		1–4	≥8	≤1	2	>2
Fusidic acid							
	–#		–#	–#	≤1	–§	>1
Gentamicin							
	≤4		8	≥16	≤1	–§	>1
Linezolid							
	≤4		–§	≥8	≤4	–§	>4
Oxacillin							
	≤2		–§	≥4	–#	–#	–#
Rifampicin							
	≤1		2	≥4	≤0.06‡	0.12–0.5	>0.5
Teicoplanin							
	≤8		16	≥32	≤2	–§	>2
Tetracycline							
	≤4		8	≥16	≤1	2	>2
Trimethoprim							
	≤8		–§	≥16	–#	–#	–#
Trimethoprim–sulfamethoxazole							
	≤2/38		–§	≥4/76	≤2	4	>4
Vancomycin							
	≤2		4–8	≥16	≤2	–§	>2

CLSI = Clinical and Laboratory Standards Institute; EUCAST = European Committee on Antimicrobial Susceptibility Testing; I = intermediate (CLSI); R = resistant; S = susceptible (CLSI); S, IE = susceptible, increased exposure (EUCAST); S, SD = sensitive, standard dosing (EUCAST); SDD = sensitive dose dependent (CLSI)

* The breakpoints selected to identify resistance are described in the Performance Standards for Antimicrobial Susceptibility Testing. 31st ed. CLSI supplement M100, 2021
† EUCAST breakpoint tables for interpretation of MICs and zone diameters, version 11.0, 2021 (www.eucast.org)
§ No category defined
# No guidelines for indicated species
** The concentration range available on the current Vitek® card restricts the ability to identify the susceptible category. For analysis, breakpoints of ≤4 mg/L for susceptible and ≥8 mg/L for resistant were applied
‡ The rifampicin concentration on the cards restricts category interpretation to non-resistant or resistant

Molecular confirmation of resistance

WGS was performed by the Antimicrobial Resistance Infectious Diseases (AMRID) Research Laboratory at Murdoch University using the Illumina NextSeq™ 500 platform. The Nullarbor bioinformatic pipeline[14] was used to identify the multi-locus sequence type, and Panton-Valentine leucocidin (MRSA). SCC*mec* was determined using KmerFinder v3.2 and the SCCmec database curated from the Center for Genomic Epidemiology database (www.genomicepidemiology.org).

Quality control

Quality control strains used were those recommended by CLSI and EUCAST standards.

Data validation

Various checks were made to ensure that the data were valid. These included:

- Null values in the mandatory fields
- Missing MIC data
- Patient age if ≥100 or <0 years
- Confirm dates when:
  - Specimen collected after patient discharged or died
  - Patient discharged or died before admitted
  - Patient admitted before born
  - Patient admitted more than two days after specimen collected
  - Patient admitted more than six months before specimen collected

Appendix C. Susceptibility to antimicrobial agents

Overall percentages of resistance or non-susceptibility for *S. aureus* are shown in Table C1. For some antimicrobials, the concentration range tested did not distinguish between intermediate susceptibility (I) and resistant (R), and the term non- susceptible (NS) was used to describe these isolates.

Table C1: Susceptibility (CLSI and EUCAST) to antimicrobial agents in indicator species of national priority, by state and territory, 2021

Antimicrobial agent and species	Category*	CLSI and EUCAST percentage susceptibility at indicated category								
		NSW	Vic	Qld	SA	WA	Tas	NT	ACT	Australia
Benzylpenicillin										
Staphylococcus aureus	n	768	615	447	228	513	110	86	102	2,869
	%R†	83.5, 83.5	82.1, 82.1	88.6, 88.6	84.2, 84.2	80.9, 80.9	78.2, 78.2	86.0, 86.0	71.6, 71.6	83.0, 83.0
Ciprofloxacin										
Staphylococcus aureus	n	768	615	495	228	513	114	86	102	2,921
	%R	100.0, 13.4	100.0, 9.8	100.0, 4.6	100.0, 10.1	100.0, 5.1	100.0, 2.6	100.0, 5.8	100.0, 10.8	100.0, 8.7
Methicillin-resistant *S. aureus*	n	152	78	65	41	98	9	37	14	494
	%R	52.6, 53.9	53.8, 55.1	10.8, 10.8	36.6, 36.6	14.3, 14.3	n/a, n/a	8.1, 10.8	64.3, 64.3	34.8, 35.6
Methicillin-susceptible *S. aureus*	n	616	537	430	187	415	105	49	88	2,427
	%R	3.2, 3.4	2.4, 3.2	2.1, 3.7	3.7, 4.3	2.7, 2.9	1.0, 1.0	2.0, 2.0	2.3, 2.3	2.6, 3.2
Clindamycin (inducible + constitutive resistance)										
Staphylococcus aureus	n	768	615	495	228	512	114	86	102	2,920
	%R	13.3, 15.2	11.1, 11.7	15.2, 15.8	7.5, 9.2	12.5, 13.3	8.8, 8.8	17.4, 17.4	14.7, 14.7	12.5, 13.6
Methicillin-resistant *S. aureus*	n	152	78	65	41	98	9	37	14	494
	%R	26.3, 30.3	17.9, 17.9	23.1, 24.6	17.1, 17.1	18.4, 19.4	n/a, n/a	21.6, 21.6	35.7, 35.7	22.7, 24.3
Methicillin-susceptible *S. aureus*	n	616	537	430	187	414	105	49	88	2,426
	%R	10.1, 11.5	10.1, 10.8	14.0, 14.4	5.3, 7.5	11.1, 11.8	4.8, 4.8	14.3, 14.3	11.4, 11.4	10.5, 11.4
Daptomycin										
Staphylococcus aureus	n	766	615	494	227	513	114	86	102	2,917
	%NS§/R	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0
Methicillin-resistant *S. aureus*	n	151	78	64	41	98	9	37	14	492
	%NS§/R	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	n/a, n/a	0.0, 0.0	0.0, 0.0	0.0, 0.0
Methicillin-susceptible *S. aureus*	n	615	537	430	186	415	105	49	88	2,425
	%NS§/R	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0
Erythromycin										
Staphylococcus aureus	n	768	615	495	228	512	114	86	102	2,920
	%R	19.0, 19.8	12.8, 13.7	17.2, 17.4	17.5, 17.5	13.1, 13.9	11.4, 11.4	17.4, 17.4	15.7, 15.7	15.8, 16.3

Antimicrobial agent and species	Category*	CLSI and EUCAST percentage susceptibility at indicated category								
		NSW	Vic	Qld	SA	WA	Tas	NT	ACT	Australia
Methicillin-resistant *S. aureus*	n	152	78	65	41	98	9	37	14	494
	%R	36.8, 37.5	20.5, 21.8	33.8, 33.8	39.0, 39.0	18.4, 19.4	n/a, n/a	21.6, 21.6	35.7, 35.7	29.6, 30.2
Methicillin-susceptible *S. aureus*	n	616	537	430	187	414	105	49	88	2,426
	%R	14.6, 15.4	11.7, 12.5	14.7, 14.9	12.8, 12.8	11.8, 12.6	7.6, 7.6	14.3, 14.3	12.5, 12.5	13.0, 13.5
Fusidic acid										
Staphylococcus aureus	n	768	615	495	228	513	114	86	102	2,921
	%R	–[#], 2.5	–[#], 2.6	–[#], 3.6	–[#], 3.1	–[#], 2.1	–[#], 1.8	–[#], 4.7	–[#], 0.0	–[#], 2.6
Methicillin-resistant *S. aureus*	n	152	78	65	41	98	9	37	14	494
	%R	–[#], 7.2	–[#], 3.8	–[#], 4.6	–[#], 9.8	–[#], 2.0	–[#], n/a	–[#], 8.1	–[#], 0.0	–[#], 5.5
Methicillin-susceptible *S. aureus*	n	616	537	430	187	415	105	49	88	2,427
	%R	–[#], 1.3	–[#], 2.4	–[#], 3.5	–[#], 1.6	–[#], 2.2	–[#], 1.0	–[#], 2.0	–[#], 0.0	–[#], 2.1
Gentamicin										
Staphylococcus aureus	n	768	615	495	228	513	114	86	102	2,921
	%R	4.7, 8.6	0.5, 3.7	0.6, 2.8	3.9, 4.4	1.2, 2.7	0.0, 0.9	2.3, 10.5	2.0, 6.9	2.1, 4.9
Methicillin-resistant *S. aureus*	n	152	78	65	41	98	9	37	14	494
	%R	18.4, 32.2	0.0, 6.4	1.5, 7.7	14.6, 17.1	3.1, 4.1	n/a, n/a	0.0, 10.8	14.3, 42.9	8.1, 16.2
Methicillin-susceptible *S. aureus*	n	616	537	430	187	415	105	49	88	2,427
	%R	1.3, 2.8	0.6, 3.4	0.5, 2.1	1.6, 1.6	0.7, 2.4	0.0, 1.0	4.1, 10.2	0.0, 1.1	0.9, 2.6
Linezolid										
Staphylococcus aureus	n	805	461	473	239	448	127	82	97	2,251
	%R	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0
Methicillin-resistant *S. aureus*	n	152	78	65	41	98	9	37	14	494
	%R	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	n/a, n/a	0.0, 0.0	0.0, 0.0	0.0, 0.0
Methicillin-susceptible *S. aureus*	n	616	537	430	187	415	105	49	88	2,427
	%R	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0
Mupirocin (high-level)[**]										
Staphylococcus aureus	n	340	319	416	187	411	65	0	88	1,826
	%R	0.3, 0.3	0.9, 0.9	3.8, 3.8	0.5, 0.5	1.0, 1.0	0.0, 0.0	n/a, n/a	0.0, 0.0	1.4, 1.4
Methicillin-resistant *S. aureus*	n	152	78	65	41	98	9	37	14	494
	%R	44.7, 44.7	52.6, 52.6	96.9, 96.9	97.6, 97.6	100.0, 100.0	n/a, n/a	0.0, 0.0	100.0, 100.0	66.2, 66.2
Methicillin-susceptible *S. aureus*	n	0	0	2	1	0	0	0	0	3
	%R	n/a, n/a	n/a, n/a	n/a, n/a	n/a, n/a	n/a, n/a	n/a, n/a	n/a, n/a	n/a, n/a	n/a, n/a
Oxacillin/methicillin										
Staphylococcus aureus	n	768	615	495	228	513	114	86	102	2,921
	%R	19.8, 19.8	12.7, 12.7	13.1, 13.1	18.0, 18.0	19.1, 19.1	7.9, 7.9	43.0, 43.0	13.7, 13.7	16.9, 16.9
Rifampicin										
Staphylococcus aureus	n	768	615	495	226	513	114	86	102	2,919
	%R	0.1,	0.0,	0.4,	0.0,	0.2,	0.0,	0.0,	1.0,	0.2, 0.2

Antimicrobial agent and species	Category*	CLSI and EUCAST percentage susceptibility at indicated category								
		NSW	Vic	Qld	SA	WA	Tas	NT	ACT	Australia
		0.1	0.0	0.4	0.0	0.2	0.0	0.0	1.0	
Methicillin-resistant *S. aureus*	n	157	69	74	26	99	7	40	8	480
	%R	0.0, 0.7	0.0, 0.0	1.4, 1.5	0.0, 0.0	0.0, 0.0	n/a, n/a	0.0, 0.0	0.0, 0.0	0.2, 0.4
Methicillin-susceptible *S. aureus*	n	647	392	398	213	348	120	42	89	2,249
	%R	0.2, 0.0	0.0, 0.0	0.3, 0.2	0.0, 0.0	0.9, 0.2	0.0, 0.0	0.0, 0.0	0.0, 1.1	0.2, 0.1
Teicoplanin										
Staphylococcus aureus	n	768	615	479	227	513	114	86	102	2,904
	%R	0.0, 0.1	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.4	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.1
Tetracycline/doxycycline										
Staphylococcus aureus	n	768	615	495	228	513	114	86	102	2,921
	%NS/R	6.3, 7.6	5.0, 5.0	3.4, 3.4	0.4, 2.6	2.5, 2.5	2.6, 2.6	0.0, 0.0	3.9, 3.9	4.0, 4.5
Methicillin-resistant *S. aureus*	n	152	78	65	41	98	9	37	14	494
	%NS/R	24.3, 28.9	16.7, 16.7	9.2, 9.2	0.0, 7.3	3.1, 3.1	n/a, n/a	0.0, 0.0	21.4, 21.4	12.8, 14.8
Methicillin-susceptible *S. aureus*	n	616	537	430	187	415	105	49	88	2,427
	%NS/R	1.8, 2.3	3.4, 3.4	2.6, 2.6	0.5, 1.6	2.4, 2.4	1.9, 1.9	0.0, 0.0	1.1, 1.1	2.2, 2.4
Trimethoprim–sulfamethoxazole										
Staphylococcus aureus	n	765	615	487	220	513	114	85	102	2,901
	%R	1.0, 1.0	0.2, 0.2	0.0, 0.0	0.9, 0.9	0.4, 0.4	0.0, 0.0	4.7, 4.7	1.0, 1.0	0.6, 0.6
Methicillin-resistant *S. aureus*	n	149	78	65	38	98	9	36	14	487
	%R	3.4, 3.4	0.0, 0.0	0.0, 0.0	2.6, 2.6	2.0, 2.0	n/a, n/a	8.3, 8.3	7.1, 7.1	2.5, 2.5
Methicillin-susceptible *S. aureus*	n	616	537	422	182	415	105	49	88	2,414
	%R	0.5, 0.5	0.2, 0.2	0.0, 0.0	0.5, 0.5	0.0, 0.0	0.0, 0.0	2.0, 2.0	0.0, 0.0	0.2, 0.2
Vancomycin										
Staphylococcus aureus	n	805	461	473	239	448	127	82	97	2,732
	%R	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0

CLSI = Clinical and Laboratory Standards Institute; ECOFF = epidemiological cut-off value; EUCAST = European Committee on Antimicrobial Susceptibility Testing; I = intermediate (CLSI) or susceptible, increased exposure (EUCAST); n/a = insufficient numbers (<10) to calculate; NS = intermediate plus resistant; R = resistant; SDD = sensitive dose dependent (CLSI)

* Category analysed for each organism. If different for CLSI and EUCAST, they are separated by a comma
† Benzylpenicillin resistance including beta-lactamase producers
§ Resistance not defined
# No breakpoints defined for indicated species
** Mupirocin high-level resistance screen