Australian Government
Department of Health and Aged Care

2022 · Volume 46

Communicable Diseases Intelligence

Australian Group on Antimicrobial Resistance (AGAR) Australian *Staphylococcus aureus* Surveillance Outcome Program (ASSOP)

Bloodstream Annual Report 2021

Geoffrey W Coombs, Denise A Daley, Princy Shoby, Shakeel Mowlaboccus, on behalf of the Australian Group on Antimicrobial Resistance

https://doi.org/10.33321/cdi.2022.46.76
Electronic publication date: 15/12/2022
http://health.gov.au/cdi

Communicable Diseases Intelligence
ISSN: 2209-6051 Online

This journal is indexed by Index Medicus and Medline.

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

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

Editor
Noel Lally

Deputy Editor
Simon Petrie

Design and Production
Kasra Yousefi

Editorial Advisory Board
David Durrheim,
Mark Ferson, John Kaldor,
Martyn Kirk and Linda Selvey

Website
http://www.health.gov.au/cdi

Contacts
CDI is produced by the Office of Health Protection and Response, Australian Government Department of Health and Aged Care, GPO Box 9848, (MDP 6) CANBERRA ACT 2601

Email:
cdi.editor@health.gov.au

Submit an Article
You are invited to submit your next communicable disease related article to the Communicable Diseases Intelligence (CDI) for consideration. More information regarding CDI can be found at: http://health.gov.au/cdi.

Further enquiries should be directed to:

cdi.editor@health.gov.au.

Annual report

Australian Group on Antimicrobial Resistance (AGAR) Australian *Staphylococcus aureus* Surveillance Outcome Program (ASSOP)

Bloodstream Annual Report 2021

Geoffrey W Coombs, Denise A Daley, Princy Shoby, Shakeel Mowlaboccus, on behalf of the Australian Group on Antimicrobial Resistance

Abstract

From 1 January to 31 December 2021, forty-eight institutions around Australia participated in the Australian *Staphylococcus aureus* Surveillance Outcome Programme (ASSOP). The aim of ASSOP 2021 was to determine the proportion of *Staphylococcus aureus* bacteraemia (SAB) isolates in Australia that were antimicrobial resistant, with particular emphasis on susceptibility to methicillin and on characterisation of the molecular epidemiology of the methicillin-resistant isolates. A total of 2,928 SAB episodes were reported, of which 78.4% were community-onset. Overall, 16.9% of *S. aureus* isolates were methicillin resistant. The 30-day all-cause mortality associated with methicillin-resistant SAB was 15.0%, which was not significantly different from the 14.4% all-cause mortality associated with methicillin-susceptible SAB ($p = 0.7$). With the exception of the β-lactams and erythromycin, antimicrobial resistance in methicillin-susceptible *S. aureus* was rare. However, in addition to the β-lactams, approximately 36% of methicillin-resistant *S. aureus* (MRSA) were resistant to ciprofloxacin; 30% to erythromycin; 15% to tetracycline; 16% to gentamicin; and 3% to co-trimoxazole. When applying the European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints, teicoplanin resistance was detected in three *S. aureus* isolates. Resistance to vancomycin or linezolid was not detected. Resistance to non-β-lactam antimicrobials was largely attributable to the healthcare-associated MRSA (HA-MRSA) clone ST22-IV [2B] (EMRSA-15), and the community-associated MRSA (CA-MRSA) clone ST45-V [5C2&5] which has acquired multiple antimicrobial resistance determinants including ciprofloxacin, erythromycin, clindamycin, gentamicin and tetracycline. The ST22-IV [2B] (EMRSA-15) clone is the predominant HA-MRSA clone in Australia. Nonetheless, 85% of methicillin-resistant SAB episodes were due to CA-MRSA clones. Although polyclonal, approximately 68% of CA-MRSA clones were characterised as ST93-IV [2B] (Queensland clone); ST45-V [5C2&5]; ST5-IV [2B]; ST1-IV [2B]; ST30-IV [2B]; and ST97-IV [2B]. As CA-MRSA is well established in the Australian community, it is important to monitor antimicrobial resistance patterns in community- and healthcare-associated SAB as this information will guide therapeutic practices in treating *S. aureus* bacteraemia.

Keywords: Australian Group on Antimicrobial Resistance (AGAR); antimicrobial resistance surveillance; *Staphylococcus aureus;* methicillin-susceptible *Staphylococcus aureus* (MSSA); methicillin-resistant *Staphylococcus aureus* (MRSA); bacteraemia

Background

Globally, *Staphylococcus aureus* is one of the most frequent causes of hospital-acquired and community-acquired bloodstream infections.[1] Although there are a wide variety of manifestations of serious invasive infection caused by *S. aureus,* in the majority of these 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] In 2009 the Infectious Diseases Society of America highlighted *S. aureus* as one of the key problem bacteria or ESKAPE pathogens[i] requiring new therapies.[3]

Although prolonged antimicrobial therapy and prompt source control are used to treat SAB,[4] mortality ranges from as low as 2.5% to as high as 40%.[5–8] Mortality rates, however, are known to vary significantly with patient age, clinical manifestation, comorbidities and methicillin resistance. A prospective study of SAB conducted in 27 laboratories in Australia and New Zealand found a 30-day all-cause mortality of 20.6%.[9] 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.

The Australian Group on Antimicrobial Resistance (AGAR), a network of laboratories located across Australia, commenced surveillance of antimicrobial resistance in *S. aureus* in 1986.[10] In 2013, AGAR commenced the Australian *Staphylococcus aureus* Sepsis Outcome Programme, now known as the Australian *Staphylococcus aureus* Surveillance Outcome Programme (ASSOP).[11] The primary objective of ASSOP 2021 was to determine the proportion of SAB isolates displaying antimicrobial resistance, with particular emphasis on:

1. susceptibility to methicillin; and
2. molecular epidemiology of methicillin-resistant *S. aureus* (MRSA).

Methodology

Participants

Thirty laboratories servicing 48 hospitals from all Australian states and mainland territories.

Collection period

From 1 January to 31 December 2021, the 30 laboratories collected all *S. aureus* isolated from blood cultures. When isolated from a patient's blood culture within 14 days of the first positive culture, *S. aureus* isolates with the same antimicrobial susceptibility profiles were excluded. A new SAB episode in the same patient was recorded if it was identified by a culture of blood collected more than 14 days after the last positive culture. Data were collected on age, sex, dates of admission and discharge (if admitted), and mortality at 30 days from date of first positive blood culture. To avoid interpretive bias, no attempt was made to assign attributable mortality. Each SAB episode was designated healthcare onset if the first positive blood culture(s) in an episode were collected > 48 hours after admission.

Laboratory testing

Participating laboratories performed antimicrobial susceptibility testing using the Vitek® 2 (bioMérieux, France) or the BD Phoenix™ (Becton Dickinson, USA) automated microbiology systems according to the manufacturer's instructions. Identification of *S. aureus* was achieved by matrix-assisted laser desorption ionization (MALDI) using either the Vitek MS® (bioMérieux, France) or the MALDI Biotyper® (Bruker Daltonics, Germany). Appropriate growth on chromogenic agar or polymerase chain reaction (PCR) for the presence of the *nuc* gene may have been performed for confirmation.

i ESKAPE: *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* species.

Minimum inhibitory concentration (MIC) data and isolates were referred to the Antimicrobial Resistance and Infectious Diseases (AMRID) Research Laboratory at Murdoch University. Clinical and Laboratory Standards Institute (CLSI)[12] and European Committee on Antimicrobial Susceptibility Testing (EUCAST)[13] MIC breakpoints were utilised for interpretation. Linezolid and daptomycin non-susceptible isolates were retested by Etest® (bioMérieux) using the Mueller-Hinton agar recommended by the manufacturer. The control strain used was *S. aureus* ATCC® 29213. High-level mupirocin resistance was determined by the BD Phoenix™ or by using a mupirocin 200 µg disk according to CLSI guidelines on all isolates with a mupirocin MIC > 8 mg/L by Vitek® 2. Multi-resistance was defined as resistance to three or more of the following non-β-lactam antimicrobials: vancomycin, teicoplanin, erythromycin/clindamycin, tetracycline, ciprofloxacin, gentamicin, co-trimoxazole, fusidic acid, rifampicin, high level mupirocin, and linezolid.

Molecular testing was performed by whole genome sequencing (WGS) using the NextSeq 500 platform (Illumina, USA). Sequence reads were analysed using the Nullarbor pipeline.[14] The SCC*mec* type was determined using KmerFinder v3.2,[15–17] and the SCC*mec* database curated from the Center for Genomic Epidemiology database.[18]

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 12.7 (MedCalc Software, Belgium).

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

Results

From 1 January to 31 December 2021, there were 2,928 unique episodes of SAB identified. A significant difference ($p < 0.0001$) was observed in patient sex, with 1,937 (66.2%) being male (95% confidence interval [95% CI]: 64.0–68.3). The mean age of patients was 58 years, ranging from 0 to 100 years, with a median age of 62 years. Overall, 2,296 episodes (78.4%) were community-onset (95% CI: 76.7–80.1). All-cause mortality at 30 days (where known) was 14.5% (95% CI: 11.0–18.7). Methicillin-resistant SAB mortality was 15.0% (95% CI: 7.1–26.5); methicillin-susceptible SAB mortality was 14.4% (95% CI: 10.5–19.0).

Methicillin-susceptible *Staphylococcus aureus* (MSSA) antimicrobial susceptibility

Overall, 2,433 of the 2,928 isolates (83.1%) were methicillin susceptible, of which 1,825/2,433 (75.3%) were penicillin resistant (MIC > 0.12 mg/L). All penicillin-susceptible isolates (MIC ≤ 0.12 mg/L) were tested either by *blaZ* PCR or penicillin disc diffusion (zone-edge test). On testing, a further 65 phenotypically penicillin-susceptible isolates were considered penicillin resistant. Fifty-two penicillin-susceptible isolates were not available for confirmation. Apart from erythromycin resistance (13.0% and 13.5% using CLSI and EUCAST breakpoints respectively), resistance to the non-β-lactam antimicrobials amongst MSSA was rare, ranging from 0% to 2.6% (Table 1). There were six isolates reported by Vitek® 2 as non-susceptible to daptomycin (MIC > 1.0 mg/L). By Etest®, all six isolates were considered daptomycin susceptible (MICs 0.38–1.0 mg/L).

By Vitek® 2 or BD Phoenix™, three isolates were reported as linezolid resistant (MIC > 4 mg/L). One isolate was unavailable for confirmation. By Etest®, the remaining two isolates had a linezolid MIC of 1.5 mg/L and were therefore considered susceptible. Using EUCAST interpretive criteria, 29 isolates were reported by Vitek® 2 as teicoplanin resistant (MIC > 2.0 mg/L). Fourteen isolates were unavailable for confirmation. By Etest®, 14 of the 15 referred isolates had a teicoplanin MIC of ≤ 2.0 mg/L. One isolate with an MIC of 3.0 mg/L was considered resistant. All MSSA were vancomycin susceptible. Only 1,849

Table 1: The number and proportion of methicillin-susceptible *Staphylococcus aureus* (MSSA) isolates non-susceptible to penicillin and the non-β-lactam antimicrobials, AGAR, 2021

		CLSI		EUCAST	
Antimicrobial	**Isolates (*n*)**	**Intermediate % (*n*)**	**Resistant % (*n*)**	**Susceptible, increased exposure % (*n*)**	**Resistant % (*n*)**
Benzylpenicillin	2,425	–[a]	75.3 (1,825)	–[a]	75.3 (1,825)
Benzylpenicillin[b]	2,381	–[a]	79.4 (1,890)	–[a]	79.4 (1,890)
Cefoxitin (methicillin)[c]	2,928	–[a]	16.9 (495)	–[a]	16.9 (495)
Ciprofloxacin	2,429	0.0 (0)	2.6 (64)	96.9 (505)	3.1 (16)
Clindamycin (constitutive)	2,427	0.0 (0)	1.2 (29)	–[a]	1.6 (39)
Clindamycin (inducible + constitutive resistance)	2,427	0.0 (0)	10.5 (254)	–[a]	11.4 (276)
Daptomycin	2,432	–[a]	0.0 (0)[d]	–[a]	0.0 (0)
Erythromycin	2,428	28.7 (697)	13.0 (315)	0.5 (12)	13.5 (328)
Fusidic acid	2,429	–[e]	–[e]	–[a]	2.1 (50)
Gentamicin	2,429	0.7 (17)	0.9 (21)	–[a]	2.6 (64)
Linezolid	2,432	–[a]	0.0 (0)	–[a]	0.0 (0)
Mupirocin (high-level)[f]	1,849	–[a]	1.2 (22)	–[a]	1.2 (22)
Rifampicin	2,426	0.1 (2)	0.1 (3)	–[g]	0.2 (6)
Teicoplanin	2,418	0.0 (0)	0.0 (0)	–[a]	0.0 (1)
Tetracycline/doxycycline[h]	2,429	0.1 (3)	2.2 (54)	0.5 (13)	2.4 (59)
Trimethoprim/sulfamethoxazole	2,418	–[a]	0.2 (6)	0.0 (0)	0.2 (6)
Vancomycin	2,432	0.0 (0)	0.0 (0)	–[a]	0.0 (0)

a No category defined.

b Beta-lactamase adjusted.

c Resistance as determined by cefoxitin screen (Vitek) or cefoxitin MIC (Phoenix).

d Non-susceptible; resistance not defined (DAP).

e No guidelines for indicated species (FUSc).

f Mupirocin.

g The rifampicin concentration range on cards restricts category interpretation to non-resistant or resistant.

h Doxycycline concentration range (Phoenix panel) restricts ability to accurately identify intermediate and resistant category.

of the 2,433 MSSA (76.0%) had mupirocin susceptibility testing performed, of which 22 (1.2%) were high-level mupirocin resistant. Fourteen of the 22 mupirocin resistant MSSA isolates were referred from Queensland; 13 of the 22 isolates were also resistant to fusidic acid. Of the 2,247 isolates tested, 39 (1.6%) were constitutively resistant to clindamycin; however, 276 (11.4%) were classified as having both constitutive and inducible clindamycin resistance. Only 2.5% of MSSA were multi-resistant. By Vitek® 2 or BD Phoenix™, fifty-two isolates were reported as non-susceptible to cotrimoxazole. Eight isolates were unavailable for confirmation. By disc susceptibility testing, 41/56 (73.2%) were susceptible by both CLSI and EUCAST criteria.

MRSA antimicrobial susceptibility

The proportion of *S. aureus* that were MRSA was 16.9% (95% CI: 13.7–20.5). Of the 495 MRSA identified, 438 were cefoxitin-screen positive by Vitek® 2 and 57 had a cefoxitin MIC > 4 mg/L by BD Phoenix™. All MRSA isolates were penicillin resistant. Amongst the MRSA isolates, resistance to non-β-lactam antimicrobials was common, except for rifampicin, cotrimoxazole and fusidic acid where resistance ranged from 0% to 5.5% (Table 2). All MRSA were susceptible to vancomycin and linezolid. Four isolates were reported by Vitek® 2 as daptomycin non-susceptible (MIC > 1.0 mg/L). One isolate was unavailable for confirmation. By Etest®, two of the three isolates were considered daptomycin susceptible (MICs 0.75 and 1.0 mg/L). The remaining isolate was confirmed as non-susceptible by CLSI and resistant by EUCAST criteria (MIC 1.5 mg/L). Polymorphisms in genes encoding *mprF, walK, walR, cls, rpoB, rpoC, pgsA* and *agrA* were investigated. No known mutations were detected.

By Vitek® 2, nine isolates were reported as teicoplanin resistant when using the EUCAST resistant breakpoint of > 2 mg/L (MICs = 4.0 mg/L). However, using the CLSI resistant breakpoint of > 8 mg/L, the isolates were classified as susceptible. By Etest®, seven of the nine isolates were considered susceptible (MICs 1.5 and 2.0 mg/L) and the remaining two isolates, each with MIC of 4.0 mg/L, were resistant by EUCAST criteria. Three of 330 MRSA isolates tested (0.9%) had high-level mupirocin resistance.

Of the 493 isolates tested, 39 (7.9%) and 46 (9.3%) were constitutively resistant to clindamycin by CLSI and EUCAST criteria respectively while 112 (22.7%) and 120 (24.3%) were classified as having both constitutive and inducible clindamycin resistance by CLSI and EUCAST criteria respectively.

By Vitek® 2 or BD Phoenix™, 58 isolates were reported as non-susceptible to cotrimoxazole. Two isolates were unavailable for confirmation. By disc susceptibility testing, 41/56 (73.2%) were susceptible by both CLSI and EUCAST criteria. Multi-resistance was identified in 21.6% of MRSA.

MRSA molecular epidemiology

Whole genome sequencing was performed on 472 of the 495 MRSA (95.4%). Based on molecular typing, 71 (15.0%) and 401 (85.0%) of isolates were identified as healthcare-associated MRSA (HA-MRSA) and community-associated MRSA (CA-MRSA) clones respectively (Table 3).

Healthcare-associated methicillin-resistant *Staphylococcus aureus*

For the 71 HA-MRSA isolates, 23 (32.4%) were classified as hospital-onset and 48 (67.6%) were classified as community-onset. Based on the multilocus sequence type (MLST) and the *SCCmec* type, three HA-MRSA clones were identified: 64 isolates of ST22-IV [2B] (EMRSA-15) (13.6 % of MRSA typed and 2.2% of *S. aureus*); six isolates of ST239-III [3A] (Aus-2/3 EMRSA) (1.3% and 0.2%), and one isolate of ST5-I [1B] (Cordoba strain) (Table 3).

The dominant HA-MRSA clone in Australia in 2021 was ST22-IV [2B] (EMRSA-15), accounting for 90.1% of HA-MRSA; it was identified in all states and territories (Table 4). ST22-IV [2B] (EMRSA-15) is Panton-Valentine Leucocidin toxin (PVL) negative and, using CLSI breakpoints, 95.3% and 59.4% were ciprofloxacin and erythromycin non-susceptible respectively. Overall, 31.3% of ST22-IV [2B] (EMRSA-15) were hospital-onset.

ST239-III [3A] (Aus-2/3 EMRSA) accounted for 8.5% of HA-MRSA and was only identified in New South Wales and South Australia (Table 4). PVL negative ST239-III [3A] (Aus-2/3 EMRSA) were typically resistant to erythromycin (100%); cotrimoxazole (100%); ciprofloxacin (100%); gentamicin (100%); tetracycline (100%); and clindamycin (66.7%). Overall, 33.3% of ST239-III [3A] (Aus-2/3 EMRSA) were hospital-onset.

Table 2: The number and proportion of methicillin-resistant *Staphylococcus aureus* (MRSA) isolates non-susceptible to penicillin and the non-β-lactam antimicrobials, AGAR, 2021

		CLSI		EUCAST	
Antimicrobial	**Isolates (*n*)**	**Intermediate % (*n*)**	**Resistant % (*n*)**	**Susceptible, increased exposure % (*n*)**	**Resistant % (*n*)**
Benzylpenicillin	494	–[a]	100.0 (494)	–[a]	100.0 (494)
Benzylpenicillin[b]	495	–[a]	100.0 (495)	–[a]	100.0 (495)
Cefoxitin (methicillin)[c]	2,928	–[a]	16.9 (495)	–[a]	16.9 (495)
Ciprofloxacin	494	0.8 (4)	34.8 (172)	64.4 (318)	35.6 (176)
Clindamycin (constitutive)	493	0.4 (2)	7.9 (39)	–[a]	9.3 (46)
Clindamycin (inducible + constitutive resistance)	494	0.4 (2)	22.7 (112)	–[a]	24.3 (120)
Daptomycin	494	–[a]	0.2 (1)[d]	–[a]	0.2 (1)
Erythromycin	494	20.0 (99)	29.6 (146)	1.0 (5)	30.2 (149)
Fusidic acid	495	–[e]	–[e]	–[a]	5.5 (27)
Gentamicin	494	5.7 (28)	8.1 (40)	–[a]	16.2 (80)
Linezolid	495	–[a]	0.0 (0)	–[a]	0.0 (0)
Mupirocin (high-level)[f]	330	–[a]	0.9 (3)	–[a]	0.9 (3)
Rifampicin	494	0.0 (0)	0.4 (2)	–[g]	0.8 (4)
Teicoplanin	495	0.0 (0)	0.0 (0)	–[a]	0.4 (2)
Tetracycline/doxycycline[h]	494	0.8 (4)	12.8 (63)	1.6 (8)	14.8 (73)
Trimethoprim/sulfamethoxazole	488	–[a]	2.7 (13)	0.4 (2)	2.7 (13)
Vancomycin	495	0.0 (0)	0.0 (0)	–[a]	0.0 (0)

a No category defined.

b Beta-lactamase adjusted.

c Resistance as determined by cefoxitin screen (Vitek) or cefoxitin MIC (Phoenix).

d Non-susceptible; resistance not defined (DAP).

e No guidelines for indicated species (FUSc).

f Mupirocin.

g The rifampicin concentration range on cards restricts category interpretation to non-resistant or resistant.

h Doxycycline concentration range (Phoenix panel) restricts ability to accurately identify intermediate and resistant category.

Table 3: Proportion of healthcare-associated and community-associated methicillin-resistant *Staphylococcus aureus* (MRSA), AGAR, 2021 by clone, onset, and Panton-Valentine leucocidin (PVL) carriage

Clone	Clonal complex	Total, *n*	Community onset, % (*n*)[a]	Hospital onset, % (*n*)[a]	PVL positive, % (*n*)[a]
Healthcare-associated					
ST22-IV (EMRSA-15)	22	64	68.8 (44)	31.3 (20)	0.0 (0)
ST239-III (Aus2/3 EMRSA)	8	6	–[b] (4)	–[b] (2)	–[b] (0)
ST5-I (Cordoba)	5	1	–[b] (0)	–[b] (1)	–[b] (0)
Total HA-MRSA		71	67.6 (48)	32.4 (23)	0.0 (0)
Community-associated					
ST93-IV	93	99	91.9 (91)	8.1 (8)	94.9 (94)
ST45-V	45	62	80.6 (50)	19.4 (12)	0.0 (0)
ST5-IV	5	48	81.3 (39)	18.8 (9)	37.5 (18)
ST1-IV	1	28	75.0 (21)	25.0 (7)	7.1 (2)
ST30-IV	30	20	85.0 (17)	15.0 (3)	80.0 (16)
ST97-IV	97	15	66.7 (10)	33.3 (5)	0.0 (0)
ST22-IV	22	9	–[b] (5)	–[b] (4)	–[b] (9)
ST88-IV	88	8	–[b] (5)	–[b] (3)	–[b] (0)
ST59-IV	59	7	–[b] (1)	–[b] (6)	–[b] (0)
ST6-IV	6	7	–[b] (6)	–[b] (1)	–[b] (3)
ST8-IV	8	7	–[b] (6)	–[b] (1)	–[b] (0)
ST953-IV	97	7	–[b] (6)	–[b] (1)	–[b] (0)
ST72-IV	8	5	–[b] (4)	–[b] (1)	–[b] (0)
ST78-IV	8	5	–[b] (3)	–[b] (2)	–[b] (0)
ST188-IV	188	4	–[b] (3)	–[b] (1)	–[b] (0)
ST6145-V	45	4	–[b] (3)	–[b] (1)	–[b] (0)
ST872-IV	1	4	–[b] (3)	–[b] (1)	–[b] (0)
ST5-V	5	3	–[b] (2)	–[b] (1)	–[b] (0)
ST5-VI	5	3	–[b] (1)	–[b] (2)	–[b] (0)
ST149-IV	5	2	–[b] (1)	–[b] (1)	–[b] (2)
ST2250-IV	2250	2	–[b] (2)	–[b] (0)	–[b] (0)
ST45-IV	45	2	–[b] (1)	–[b] (1)	–[b] (0)
ST59-V	59	2	–[b] (1)	–[b] (1)	–[b] (0)
ST5-unk	5	2	–[b] (1)	–[b] (1)	–[b] (0)
ST7696-V	45	2	–[b] (2)	–[b] (0)	–[b] (0)
ST7709-IV	97	2	–[b] (2)	–[b] (0)	–[b] (0)
ST8-novel	8	2	–[b] (2)	–[b] (0)	–[b] (0)
ST121-V	121	1	–[b] (1)	–[b] (0)	–[b] (0)
ST1232-V	398	1	–[b] (1)	–[b] (0)	–[b] (0)
ST1524-IV	5	1	–[b] (1)	–[b] (0)	–[b] (1)
ST188-V	188	1	–[b] (0)	–[b] (1)	–[b] (0)

Clone	Clonal complex	Total, *n*	Community onset, % (*n*)[a]	Hospital onset, % (*n*)[a]	PVL positive, % (*n*)[a]
ST1-novel	1	1	–[b] (1)	–[b] (0)	–[b] (0)
ST2048-IV	395	1	–[b] (0)	–[b] (1)	–[b] (0)
ST2884-V	88	1	–[b] (1)	–[b] (0)	–[b] (0)
ST3628-V	5	1	–[b] (1)	–[b] (0)	–[b] (1)
ST3921-IV	30	1	–[b] (1)	–[b] (0)	–[b] (0)
ST398-V	398	1	–[b] (1)	–[b] (0)	–[b] (0)
ST4301-IV	22	1	–[b] (1)	–[b] (0)	–[b] (0)
ST508-IV	45	1	–[b] (0)	–[b] (1)	–[b] (0)
ST5213-IV	1	1	–[b] (0)	–[b] (1)	–[b] (0)
ST5662-IV	5	1	–[b] (1)	–[b] (0)	–[b] (0)
ST6149-IV	97	1	–[b] (1)	–[b] (0)	–[b] (1)
ST6151-IV	93	1	–[b] (1)	–[b] (0)	–[b] (0)
ST672-V	672	1	–[b] (1)	–[b] (0)	–[b] (1)
ST6963-IV	22	1	–[b] (1)	–[b] (0)	–[b] (0)
ST72-V	8	1	–[b] (1)	–[b] (0)	–[b] (0)
ST73-IV	5	1	–[b] (1)	–[b] (0)	–[b] (0)
ST7684-IV	6	1	–[b] (0)	–[b] (1)	–[b] (1)
ST7685-V	Singleton	1	–[b] (1)	–[b] (0)	–[b] (0)
ST7697-IV	5	1	–[b] (1)	–[b] (0)	–[b] (1)
ST7698-IV	5	1	–[b] (1)	–[b] (0)	–[b] (0)
ST7699-V	45	1	–[b] (1)	–[b] (0)	–[b] (0)
ST7700-IV	1	1	–[b] (0)	–[b] (1)	–[b] (1)
ST7701-IV	5	1	–[b] (1)	–[b] (0)	–[b] (0)
ST7702-IV	1	1	–[b] (0)	–[b] (1)	–[b] (0)
ST7703-IV	1	1	–[b] (1)	–[b] (0)	–[b] (0)
ST7704-novel	398	1	–[b] (1)	–[b] (0)	–[b] (0)
ST7705-IV	22	1	–[b] (1)	–[b] (0)	–[b] (0)
ST7706-IV	398	1	–[b] (1)	–[b] (0)	–[b] (0)
ST7707-IV	1	1	–[b] (0)	–[b] (1)	–[b] (0)
ST7708-IV	93	1	–[b] (1)	–[b] (0)	–[b] (0)
ST7711-IV	1	1	–[b] (1)	–[b] (0)	–[b] (1)
ST7-IV	7	1	–[b] (1)	–[b] (0)	–[b] (0)
ST80-IV	80	1	–[b] (0)	–[b] (1)	–[b] (0)
ST834-IV	Singleton	1	–[b] (1)	–[b] (0)	–[b] (0)
ST87-IV	59	1	–[b] (1)	–[b] (0)	–[b] (0)
ST88-novel	88	1	–[b] (1)	–[b] (0)	–[b] (0)
Total CA-MRSA		401	79.6 (319)	20.4 (82)	37.9 (152)
MRSA typed		472	77.8 (367)	22.2 (105)	32.2 (152)

a Percentage of the clone.

b Insufficient numbers (<10) to calculate percentage.

Table 4: The number and proportion of healthcare-associated methicillin-resistant *Staphylococcus aureus* (MRSA) clones, AGAR, 2021, by state and territory

	Percentage (*n*)[a]								
Clone	**ACT**	**NSW**	**NT**	**Qld**	**SA**	**Tas.**	**Vic.**	**WA**	**Australia**
ST22-IV (EMRSA-15)	–[b] (3)	79.3 (23)	–[b] (2)	–[b] (2)	–[b] (5)	–[b] (2)	100.0 (17)	100.0 (10)	90.1 (64)
ST239-III (Aus2/3 EMRSA)	–[b] (0)	17.2 (5)	–[b] (0)	–[b] (0)	–[b] (1)	–[b] (0)	0.0 (0)	0.0 (0)	8.5 (6)
ST5-1 (Cordoba)	–[b] (0)	3.4 (1)	–[b] (0)	–[b] (0)	–[b] (0)	–[b] (0)	0.0 (0)	0.0 (0)	1.4 (1)
Total	**3**	**29**	**2**	**2**	**6**	**2**	**17**	**10**	**71**

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

b Insufficient numbers (<10) to calculate percentage.

Community-associated methicillin-resistant *Staphylococcus aureus*

For the 401 CA-MRSA isolates, 82 episodes (20.4%) were classified as hospital-onset and 319 (79.6%) as community-onset. Based on the MLST and the *SCCmec* type, 67 CA-MRSA clones were identified (Table 3). Overall, 67.8% of CA-MRSA were classified into six clones each having ten or more isolates: 99 isolates of ST93-IV [2B] (Queensland clone) (24.7% of MRSA typed and 3.4% of *S. aureus*); 62 isolates of ST45-V [5C2&5] (15.5% and 2.1%); 48 isolates of ST5-IV [2B] (12.0% and 1.7%); 28 isolates of ST1-IV [2B] (7.0% and 1.0%); 20 isolates of ST30-IV [2B] (5.0% and 0.7%) and 15 isolates of ST97-IV [2B] (3.7% and 0.5%).

ST93-IV [2B] (Queensland CA-MRSA) accounted for 24.7% of CA-MRSA, ranging from 0% in Tasmania to 60.6% in the Northern Territory (Table 5). Typically PVL positive, 91.9% of ST93-IV [2B] were community-onset.

ST45-V [5C2&5] accounted for 15.5% of CA-MRSA and was isolated primarily in New South Wales and Victoria (Table 5). All isolates were PVL negative. Overall, 80.6% of ST45-V [5C2&5] were community-onset.

ST5-IV [2B] accounted for 12.0% of CA-MRSA and was isolated in all regions of Australia except the Australian Capital Territory, ranging from 7.0% in New South Wales to 17.2% in Western Australia (Table 5). Overall, 37.5% of ST5-IV [2B] were PVL positive and 81.3% of ST5-IV [2B] were community-onset.

ST1-IV [2B] accounted for 7.0% of CA-MRSA and was isolated in all regions of Australia, ranging from 1.8% in Victoria to 14.7% in South Australia (Table 5). Overall, 7.1% of ST1-IV [2B] were PVL positive and 75.9% of ST1-IV [2B] were community-onset.

ST30-IV [2B] accounted for 5.0% of CA-MRSA and was isolated in all regions of Australia except South Australia, the Northern Territory and the Australian Capital Territory, ranging from 3.4% in Queensland and Western Australia to 8.7% in New South Wales (Table 5). Overall, 80.0% of ST30-IV [2B] were PVL positive and 85.0% of ST30-IV [2B] were community-onset.

ST97-IV [2B] accounted for 3.7% of CA-MRSA and was isolated in all regions except South Australia, Tasmania, the Northern Territory and the Australian Capital Territory, ranging from 1.1% in Western Australia to 7.3% in

Victoria (Table 5). All isolates of ST97-IV [2B] were PVL negative and 66.7% of ST97-IV [2B] were community-onset.

Overall, 65.1% of CA-MRSA were non-multi-resistant, including 52.9% isolates resistant to the β-lactams only. A significant increase was seen in multi-resistant CA-MRSA isolates in ASSOP 2021 (34.9%) from 9.2% in ASSOP 2013.[11] Multi-resistance was primarily due to the ST45-V [5C2&5] clone.

Resistance profiles for the six predominant CA-MRSA clones are shown in Table 6.

Panton-Valentine leucocidin

Overall, 152 MRSA (32.2%) were PVL positive. All were CA-MRSA (Table 3).

Discussion

The AGAR surveillance programmes collect data on antimicrobial resistance, focussing on bloodstream infections caused by *S. aureus*, *Enterococcus* and gram-negative bacilli including the *Enterobacterales*, *Pseudomonas aeruginosa* and *Acinetobacter* species. All data collected in the AGAR programmes are generated as part of routine patient care in Australia, with most data available through laboratory and hospital bed management information systems. Isolates are referred to a central laboratory where strain and antimicrobial resistance determinant characterisation is performed. As the programmes are similar to those conducted in Europe,[19] comparison of Australian antimicrobial resistance data with other countries is possible.

In ASSOP 2021, methicillin resistance was found in 16.9% (95% CI: 13.7–20.5) of the 2,928 SAB episodes. In the 2021 European Centre for Disease Prevention and Control (ECDC) SAB surveillance programme, the European Union/European Economic Area (EU/EEA) population-weighted mean percentage of *S. aureus* resistant to methicillin was 14.3% (95% CI: 14.1–14.6), ranging from 0.9% (95% CI: 0.5–1.5) in Norway to 42.9% (95% CI: 35.5–50.5) in Cyprus.[19]

In Europe, the EU/EEA population-weighted mean percentage has significantly decreased from 23.2% in 2009 to 14.3% in 2021. A decrease in methicillin-resistant SAB has been reported in several parts of the world,[20,21] and is believed to be due to the implementation of antimicrobial stewardship and a package of improved infection control procedures including hand hygiene;, MRSA screening and decolonisation;, patient isolation; and infection prevention care bundles.[22–26] The percentage of methicillin-resistant SAB in Australia, however, has not decreased significantly over the nine years of ASSOP, ranging from 18.8% in 2013 to 17.2% in 2021 (X^2 for linear trend = 2.46; $p = 0.11$).[ii] Nonetheless, while a significant decrease in MRSA bacteraemia has not been seen in Australia, significant decreases in HA-MRSA from 41.0% to 15.0% ($p < 0.0001$) and in hospital-onset MRSA from 38.0% to 21.6% ($p < 0.0001$) have been observed over the nine ASSOP surveys.[11,27–33] Over the same time period, significant increases in CA-MRSA from 59.0% to 85.0% ($p < 0.0001$) and in community-onset MRSA from 61.1% to 78.4% ($p < 0.0001$) have been observed. Because of the increased burden of CA-MRSA bacteraemia in Australia, a significant reduction in the overall proportion of SAB due to MRSA may prove problematic.

In ASSOP 2021, the all-cause mortality at 30 days was 14.5% (95% CI: 11.0–18.7). No significant difference in mortality was observed between methicillin-resistant SAB and methicillin-susceptible SAB ($p = 0.8$).

ii Rates include only those laboratories that participated in all years 2013–2021.

Table 5: The number and proportion of the major community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) clones (> 10 isolates), AGAR, by state and territory and Panton-Valentine leucocidin (PVL) carriage, 2021

	Percentage (*n*)[a]								
Clone	**ACT**	**NSW**	**NT**	**Qld**	**SA**	**Tas.**	**Vic.**	**WA**	**Australia**
ST93-IV (Qld CA-MRSA)	9.1 (1)	10.4 (12)	60.6 (20)	30.5 (18)	23.5 (8)	–[b] (0)	12.7 (7)	37.9 (33)	24.7 (99)
Number PVL positive	0	12	20	17	7	0	7	31	94
Number PVL negative	1	0	0	1	1	0	0	2	5
ST45-V	36.4 (4)	31.3 (36)	0.0 (0)	5.1 (3)	2.9 (1)	–[b] (0)	29.1 (16)	2.3 (2)	15.5 (62)
Number PVL positive	0	0	0	0	0	0	0	0	0
Number PVL negative	4	36	0	3	1	0	16	2	62
ST5-IV	0.0 (0)	7.0 (8)	15.2 (5)	16.9 (10)	8.8 (3)	–[b] (3)	7.3 (4)	17.2 (15)	12.0 (48)
Number PVL positive	0	0	3	0	1	2	2	10	18
Number PVL negative	0	8	2	10	2	1	2	5	30
ST1-IV	9.1 (1)	7.0 (8)	6.1 (2)	10.2 (6)	14.7 (5)	–[b] (2)	1.8 (1)	3.4 (3)	7.0 (28)
Number PVL positive	0	0	0	2	0	0	0	0	2
Number PVL negative	1	8	2	4	5	2	1	3	26
ST30-IV	0.0 (0)	8.7 (10)	0.0 (0)	3.4 (2)	0.0 (0)	–[b] (1)	7.3 (4)	3.4 (3)	5.0 (20)
Number PVL positive	0	9	0	1	0	1	3	2	16
Number PVL negative	0	1	0	1	0	0	1	1	4
ST97-IV	0.0 (0)	6.1 (7)	0.0 (0)	5.1 (3)	0.0 (0)	–[b] (0)	7.3 (4)	1.1 (1)	3.7 (15)
Number PVL positive	0	0	0	0	0	0	0	0	0
Number PVL negative	0	7	0	3	0	0	4	1	15
Other clones (n = 61)	45.5 (5)	29.6 (34)	18.2 (6)	28.8 (17)	50.0 (17)	–[b] (1)	34.5 (19)	34.5 (30)	32.2 (129)
Number PVL positive	1	5	1	4	4	0	6	1	22
Number PVL negative	4	29	5	13	13	1	13	29	107
Total	**11**	**115**	**33**	**59**	**34**	**7**	**55**	**87**	**401**
PVL positive	1	26	24	24	12	3	18	44	152
PVL negative	10	89	9	35	22	4	37	43	249

a ACT: Australian Capital Territory; NSW: New South Wales; NT: Northern Territory; Qld: Queensland; SA: South Australia; Tas.: Tasmania; Vic.: Victoria; WA: Western Australia.
b Insufficient numbers (<10) to calculate percentage.

Table 6: Resistance combinations for the most predominant CA-MRSA clones,[a] AGAR, 2021

Resistance pattern[b]	ST93-IV	ST45-V	ST5-IV	ST1-IV	ST30-IV	ST97-IV
Single resistance						
β-lactams only	85		29	16	19	13
Resistance to methicillin and one antimicrobial						
Cip		8			1	
Dap				1		
Ery			1	1		2
Fus			2	3		
Sxt			1			
Tet				1		
Tei			1			
Resistance to methicillin and two antimicrobials						
CipFus		1				
CipGen		4				
CipTet		7				
Ery Tet			1	1		
EryCip		1	1	1		
EryClin	13		8			
Resistance to methicillin and three antimicrobials						
CipTetGen		14				
EryCipGen		1				
EryClinFus			1	3		
EryClinTet			1	1		
EryClinCip		1	1			
Resistance to methicillin and four antimicrobials						
CipTetGenFus		1				
CipTetGenRif		1				
EryClinSxtCip			1			
EryClinCipTet		6				
Resistance to methicillin and five antimicrobials						
EryClinCipTetGen		15				
Total	**98**	**60**	**48**	**28**	**20**	**15**

a Note: Only data from isolates tested against all antimicrobial groups were included (*n* =269).

b Cip: ciprofloxacin; Dap: daptomycin; Ery: erythromycin; Clin: clindamycin; Fus: fusidic acid; Sxt: cotrimoxazole; Tet: tetracycline; Tei: teicoplanin; Gen: gentamicin; Rif: rifampicin.

With the exception of the β-lactams and erythromycin, antimicrobial resistance in MSSA remains rare. However, for MRSA, in addition to the β-lactams, approximately 30% of isolates were resistant to erythromycin; 35% to ciprofloxacin; 15% to tetracycline; and 16% to gentamicin. Antimicrobial resistance was identified in the two predominant HA-MRSA clones: ST22-IV [2B] (EMRSA-15), which is typically ciprofloxacin and erythromycin resistant, and ST239-III [3A] (Aus-2/3 EMRSA) which is typically erythromycin, clindamycin, ciprofloxacin, cotrimoxazole, tetracycline and gentamicin resistant. In the early 1980s, the multi-resistant ST239-III [3A] (Aus-2/3 EMRSA) was the dominant HA-MRSA clone in Australian hospitals. However, in 2013 the first ASSOP survey showed ST22-IV [2B] (EMRSA-15) was replacing ST239-III [3A] (Aus-2/3 EMRSA) as the most prevalent HA-MRSA, and this change has occurred throughout most of the country. In ASSOP 2021, 13.6% of MRSA were characterised as ST22-IV [2B] (EMRSA-15).

In ASSOP 2021, ST93-IV [2B] (Queensland clone) remained the predominant CA-MRSA clone (24.7% of CA-MRSA) in Australia. CA-MRSA, in particular the ST45-V [5C2&5] clone (13.1% of MRSA), has acquired multiple antimicrobial resistance determinants including ciprofloxacin, erythromycin, clindamycin, gentamicin and tetracycline.

Approximately 20.4% of SAB caused by CA-MRSA was hospital-onset. As transmission of CA-MRSA in Australian hospitals is thought to be rare,[34,35] it is likely that many of the hospital-onset CA-MRSA SAB infections reported in ASSOP 2021 were caused by the patient's own colonising strains acquired prior to admission. In Australia, CA-MRSA clones such as PVL-positive ST93-IV [2B] (Queensland clone) are well established in the community and therefore it is important to monitor antimicrobial resistance patterns in both community- and healthcare-associated SAB, as this information will guide therapeutic practices in treating *S. aureus* sepsis.

In conclusion, ASSOP 2021 has demonstrated antimicrobial resistance in SAB in Australia continues to be a significant problem and is associated with a high mortality. This may be due, in part, to the high prevalence of community-associated methicillin-resistant SAB in Australia, which is higher than most EU/EEA countries. Consequently, MRSA must remain a public health priority; continuous surveillance of SAB and its outcomes and the implementation of comprehensive MRSA strategies targeting hospitals and long-term care facilities are essential.

Acknowledgments

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

Members of the AGAR in 2021 were:

Australian Capital Territory

Peter Collignon and Susan Bradbury, The Canberra Hospital

New South Wales

Thomas Gottlieb and John Huynh, Concord Hospital

James Branley and Linda Douglass, Nepean Hospital

Angela Wong, Royal North Shore Hospital

Jon Iredell and Andrew Ginn, Westmead Hospital

Bree Harris, John Hunter Hospital

Peter Newton and Melissa Hoddle, Wollongong Hospital

David Lorenz, St Vincent's Hospital

Michael Maley and Helen Ziochos, Liverpool Hospital

Monica Lahra and Peter Huntington, Sydney Children's Hospital

Alison Kesson and Andrew Jarrett, Children's Hospital Westmead

Northern Territory

Rob Baird and Jann Hennessy, Royal Darwin Hospital

James McLeod, Alice Springs Hospital

Queensland

Graeme Nimmo and Narelle George, Pathology Queensland Central Laboratory, Royal Brisbane and Women's Hospital

Petra Derrington and Cheryl Curtis, Pathology Queensland Gold Coast Hospital

Robert Horvath and Laura Martin, Pathology Queensland Prince Charles Hospital

Naomi Runnegar and Joel Douglas, Pathology Queensland Princess Alexandra Hospital

Jennifer Robson and Marianne Allen, Sullivan Nicolaides Pathology, Greenslopes Hospital

South Australia

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

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

Tasmania

Louise Cooley and David Jones, Royal Hobart Hospital

Pankaja Kalukottege and Kathy Wilcox, Launceston General Hospital

Victoria

Adam Jenney and Jacqueline Williams, The Alfred Hospital

Marcel Leroi and Elizabeth Grabsch, Austin Health

Tony Korman and Despina Kotsanas, Monash Medical Centre and Monash Children's Hospital

Tony Korman and Kathryn Cisera, Dandenong Hospital

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

Mary Jo Waters and Lisa Brenton, St Vincent's Hospital

Katherine Bond and Rose Cotronei, Royal Melbourne Hospital

Western Australia

Denise Daley, PathWest Laboratory Medicine, WA Fiona Stanley Hospital

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

Michael Leung, PathWest Laboratory Medicine, Northwest WA

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

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

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

Christopher Blyth, PathWest Laboratory Medicine, Perth Children's Hospital

Author details

Prof. Geoffrey W Coombs,[1,2,3]

Ms Denise A Daley,[2,3]

Ms Princy Shoby,[1]

Dr Shakeel Mowlaboccus,[1,2]

on behalf of the Australian Group on Antimicrobial Resistance

1. Antimicrobial Resistance and Infectious Disease (AMRID) Research Laboratory, Murdoch University, Murdoch, Western Australia, Australia

2. Department of Microbiology, PathWest Laboratory Medicine-WA, Fiona Stanley Hospital, Murdoch, Western Australia, Australia

3. Australian Group on Antimicrobial Resistance, Fiona Stanley Hospital, Murdoch, Western Australia, Australia

Corresponding author

Prof. Geoffrey Coombs

Antimicrobial Resistance and Infectious Disease (AMRID) Research Laboratory, Murdoch University, Murdoch, Western Australia, Australia

Telephone: +61 8 6152 2397

Email: g.coombs@murdoch.edu.au

References

1. Laupland KB. Incidence of bloodstream infection: a review of population-based studies. *Clin Microbiol Infect*. 2013;19(6):492–500. doi: https://doi.org/10.1111/1469-0691.12144.

2. Johnson AP, Pearson A, Duckworth G. Surveillance and epidemiology of MRSA bacteraemia in the UK. *J Antimicrob Chemother*. 2005;56(3):455–62. doi: https://doi.org/10.1093/jac/dki266.

3. Boucher HW, Talbot GH, Bradley JS, Edwards JE, Gilbert D, Rice LB et al. Bad bugs, no drugs: no ESKAPE! An update from the Infectious Diseases Society of America. *Clin Infect Dis*. 2009;48(1):1–12. doi: https://doi.org/10.1086/595011.

4. Thwaites GE, Edgeworth JD, Gkrania-Klotsas E, Kirby A, Tilley R, Török ME et al. Clinical management of *Staphylococcus aureus* bacteraemia. *Lancet Infect Dis*. 2011;11(3):208–22. doi: https://doi.org/10.1016/S1473-3099(10)70285-1.

5. van Hal SJ, Jensen SO, Vaska VL, Espedido BA, Paterson DL, Gosbell IB. Predictors of mortality in *Staphylococcus aureus* bacteremia. *Clin Microbiol Rev*. 2012;25(2):362–86. doi: https://doi.org/10.1128/CMR.05022-11.

6. Collignon P, Nimmo GR, Gottlieb T, Gosbell IB for the Australian Group on Antimicrobial Resistance. *Staphylococcus aureus* bacteremia, Australia. *Emerg Infect Dis*. 2005;11(4):554–61. doi: https://doi.org/10.3201/eid1104.040772.

7. Frederiksen MS, Espersen F, Frimodt-Møller N, Jensen AG, Larsen AR, Pallesen LV et al. Changing epidemiology of pediatric *Staphylococcus aureus* bacteremia in Denmark from 1971 through 2000. *Pediatr Infect Dis J*. 2007;26:398–405. doi: https://doi.org/10.1097/01.inf.0000261112.53035.4c.

8. Benfield T, Espersen F, Frimodt-Møller N, Jensen AG, Larsen AR, Pallesen LV et al. Increasing incidence but decreasing in-hospital mortality of adult *Staphylococcus aureus* bacteraemia between 1981 and 2000. *Clin Microbiol Infect*. 2007;13(3):257–63. doi: https://doi.org/10.1111/j.1469-0691.2006.01589.x.

9. Turnidge JD, Kotsanas D, Munckhof W, Roberts S, Bennett CM, Nimmo GR et al. *Staphylococcus aureus* bacteraemia: a major cause of mortality in Australia and New Zealand. *Med J Aust*. 2009;191(7):368–73. doi: https://doi.org/10.5694/j.1326-5377.2009.tb02841.x.

10. Nimmo GR, Bell JM, Collignon PJ for the Australian Group on Antimicrobial Resistance. Fifteen years of surveillance by the Australian Group for Antimicrobial Resistance (AGAR). *Commun Dis Intell Q Rep*. 2003;27(Suppl):S47–54.

11. Coombs GW, Nimmo GR, Daly DA, Le TT, Pearson JC, Tan HL et al. Australian *Staphylococcus aureus* Sepsis Outcome Programme annual report, 2013. *Commun Dis Intell Q Rep*. 2014;38(4):E309–19.

12. Clinical and Laboratory Standards Institute (CLSI). *Performance standards for antimicrobial susceptibility testing*. 32nd ed. CLSI supplement M100. Wayne, PA: CLSI; 16 February 2022.

13. The European Committee on Antimicrobial Susceptibility Testing (EUCAST). *Breakpoint tables for interpretation of MICs and zone diameters. Version 12.0*. Basel: EUCAST; 1 January 2022. Available from: https://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Breakpoint_tables/v_12.0_Breakpoint_Tables.pdf.

14. Seemann T, Goncalves da Silva A, Bulach DM, Schultz MB, Kwong JC, Howden BP. Nullarbor. San Francisco; Github. [Accessed on 3 Jun 2016.] Available from: https://github.com/tseemann/nullarbor.

15. Hasman H, Saputra D, Sicheritz-Ponten T, Lund O, Aaby Svendsen CA, Frimodt-Møller N et al. Rapid whole-genome sequencing for detection and characterization of microorganisms directly from clinical samples. *J Clin Microbiol*. 2014;52(1):139–46. doi: https://doi.org/10.1128/JCM.02452-13.

16. Larsen MV, Cosentino S, Lukjancenko O, Saputra D, Rasmussen S, Hasman H et al. Benchmarking of methods for genomic taxonomy. *J Clin Microbiol*. 2014;52(5):1529–39. doi: https://doi.org/10.1128/JCM.02981-13.

17. Clausen PTLC, Aarestrup FM, Lund O. Rapid and precise alignment of raw reads against redundant databases with KMA. *BMC Bioinformatics*. 2018;19(1):307. doi: https://doi.org/10.1186/s12859-018-2336-6.

18. International Working Group on The Classification of Staphylococcal Cassette Chromosome Elements (IWG-SCC). Classification of staphylococcal cassette chromosome mec (SCCmec): guidelines for reporting novel SCCmec elements. *Antimicrob Agents Chemother*. 2009;53(12):4961–7. doi: https://doi.org/10.1128/AAC.00579-09.

19. European Centre for Disease Prevention and Control (ECDC). Data from the ECDC Surveillance Atlas – Antimicrobial resistance. [Webpage.] Solna: ECDC; 2022. Available from: https://www.ecdc.europa.eu/en/antimicrobial-resistance/surveillance-and-disease-data/data-ecdc.

20. Johnson AP, Davies J, Guy R, Abernethy J, Sheridan E, Pearson A et al. Mandatory surveillance of methicillin-resistant *Staphylococcus aureus* (MRSA) bacteraemia in England: the first 10 years. *J Antimicrob Chemother*. 2012;67(4):802–9. doi: https://doi.org/10.1093/jac/dkr561.

21. de Kraker ME, Davey PG, Grundmann H, BURDEN study group. Mortality and hospital stay associated with resistant *Staphylococcus aureus* and *Escherichia coli* bacteremia: estimating the burden of antibiotic resistance in Europe. *PLoS Med*. 2011;8(10):e1001104. doi: https://doi.org/10.1371/journal.pmed.1001104.

22. Johnson PD, Martin R, Burrell LJ, Grabsch EA, Kirsa SW, O'Keeffe J et al. Efficacy of an alcohol/chlorhexidine hand hygiene program in a hospital with high rates of nosocomial methicillin-resistant *Staphylococcus aureus* (MRSA) infection. *Med J Aust*. 2005;183(10):509–14. doi: https://doi.org/10.5694/j.1326-5377.2005.tb07151.x.

23. Vos MC, Behrendt MD, Melles DC, Mollema FP, de Groot W, Parlevliet G et al. 5 years of experience implementing a methicillin-resistant *Staphylococcus aureus* search and destroy policy at the largest university medical center in the Netherlands. *Infect Control Hosp Epidemiol*. 2009;30(10):977–84. doi: https://doi.org/10.1086/605921.

24. Grayson ML, Jarvie LJ, Martin R, Johnson PD, Jodoin ME, McMullan C et al. Significant reductions in methicillin-resistant *Staphylococcus aureus* bacteraemia and clinical isolates associated with a multisite, hand hygiene culture-change program and subsequent successful statewide roll-out. *Med J Aust*. 2008;188(11):633–40. doi: https://doi.org/10.5694/j.1326-5377.2008.tb01820.x.

25. Kim YC, Kim MH, Song JE, Ahn JY, Oh DH, Kweon OM et al. Trend of methicillin-resistant *Staphylococcus aureus* (MRSA) bacteremia in an institution with a high rate of MRSA after the reinforcement of antibiotic stewardship and hand hygiene. *Am J Infect Control*. 2013;41(5):e39–43. doi: https://doi.org/10.1016/j.ajic.2012.12.018.

26. Lawes T, Edwards B, López-Lozano JM, Gould I. Trends in *Staphylococcus aureus* bacteraemia and impacts of infection control practices including universal MRSA admission screening in a hospital in Scotland, 2006–2010: retrospective cohort study and time-series intervention analysis. *BMJ Open*. 2012;2(3). pii: e000797. doi: https://doi.org/10.1136/bmjopen-2011-000797.

27. Coombs GW, Daley DA, Thin Lee Y, Pearson JC, Robinson JO, Nimmo GR et al. Australian Group on Antimicrobial Resistance Australian *Staphylococcus aureus* Sepsis Outcome Programme annual report, 2014. *Commun Dis Intell Q Rep*. 2016;40(2):E244–54.

28. Coombs GW, Daley DA, Lee YT, Pang S, Bell JM, Turnidge JD et al. Australian Group on Antimicrobial Resistance (AGAR) Australian *Staphylococcus aureus* Sepsis Outcome Programme (ASSOP) Annual Report 2015. *Commun Dis Intell (2018)*. 2018;42. pii: S2209-6051(18)00016-7.

29. Coombs GW, Daley DA, Lee YT, Pang S for the Australian Group on Antimicrobial Resistance. Australian Group on Antimicrobial Resistance (AGAR) Australian *Staphylococcus aureus* Sepsis Outcome Programme (ASSOP) annual report 2016. *Commun Dis Intell (2018)*. 2018;42. pii: S2209-6051(18)00021-0.

30. Coombs GW, Daley DA, Lee YT, Pang S. Australian Group on Antimicrobial Resistance (AGAR) Australian *Staphylococcus aureus* Sepsis Outcome Programme (ASSOP) annual report 2017. *Commun Dis Intell (2018)*. 2019;43. doi: https://doi.org/10.33321/cdi.2019.43.43.

31. Coombs GW, Daley DA, Mowlaboccus S, Lee YT, Pang S, Australian Group on Antimicrobial Resistance. Australian Group on Antimicrobial Resistance (AGAR) Australian *Staphylococcus aureus* Sepsis Outcome Programme (ASSOP) annual report 2018. *Commun Dis Intell (2018)*. 2020;44. doi: https://doi.org/10.33321/cdi.2020.44.18.

32. Coombs GW, Daley DA, Mowlaboccus S, Pang S, Australian Group on Antimicrobial Resistance. Australian Group on Antimicrobial Resistance (AGAR) Australian *Staphylococcus aureus* Sepsis Outcome Programme (ASSOP) Annual Report 2019. *Commun Dis Intell (2018)*. 2020;44. doi: 10.33321/cdi.2020.44.71.

33. Coombs GW, Daley DA, Yee NWT, Shoby P, Mowlaboccus S, Australian Group on Antimicrobial Resistance. Australian Group on Antimicrobial Resistance (AGAR) Australian *Staphylococcus aureus* Sepsis Outcome Programme (ASSOP) Annual Report 2020. *Commun Dis Intell (2018)*. 2022;46. doi: https://doi.org/cdi.2022.46.18.

34. O'Brien FG, Pearman JW, Gracey M, Riley TV, Grubb WB. Community strain of methicillin-resistant *Staphylococcus aureus* involved in a hospital outbreak. *J Clin Microbiol*. 1999;37(9):2858–

62. doi: https://doi.org/10.1128/JCM.37.9.2858-2862.

35. Schlebusch S, Price GR, Hinds S, Nourse C, Schooneveldt JM, Tilse MH et al. First outbreak of PVL-positive nonmultiresistant MRSA in a neonatal ICU in Australia: comparison of MALDI-TOF and SNP-plus-binary gene typing. *Eur J Clin Microbiol Infect Dis*. 2010;29(10):1311–4. doi: https://doi.org/10.1007/s10096-010-0995-y.