Staphylococcus aureus Programme 2012 (SAP 2012) Community Survey Antimicrobial Susceptibility Report

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On behalf of the Australian Group on Antimicrobial Resistance (AGAR)

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Contents

1 Executive Summary

The Australian Group on Antimicrobial Resistance (AGAR) was established in 1986 and performs regular multicentre period-prevalence studies to monitor changes in antimicrobial resistance. Biennial community-onset *Staphylococcus aureus* antimicrobial surveillance programmes have been performed in Australia by AGAR since 2000.

In 2012, 29 laboratories participated in national surveillance of *S. aureus* resistance of community-onset infections. A total of 2,844 isolates of *S. aureus* causing infections were collected prospectively from hospital outpatients and general practice patients. Susceptibility testing was performed by Vitek 2® (bioMérieux). In the 2012 programme the percentage of *S. aureus* identified as MRSA ranged from 4.0% in the Australian Capital Territory to 26% in New South Wales. The proportion of MRSA in invasive and non-invasive isolates was not significantly different (p=0404). Approximately 40% of all MRSA were resistant to erythromycin and ciprofloxacin and approximately 15% were resistant to tetracycline and 10% were resistant to gentamicin and trimethoprim-sulphamethoxazole. Resistance to fusidic acid, mupirocin and rifampicin was uncommon. Two isolates were non susceptible to daptomycin. No resistance was detected to vancomycin, teicoplanin or linezolid. Significant differences in resistance across regions were evident for all antimicrobials except rifampicin and mupirocin. These differences may be explained by the different MRSA clones in circulation in each region.

Over the seven biennial AGAR community surveys (2000 to 2012) the percentage of *S. aureus* identified as MRSA increased significantly (p<0.0001) by 6 percentage points (11.5% in 2000 to 17.9% in 2012). However, in the same time period a significant decrease in resistance in MRSA to all the non-β-lactam antimicrobials except high-level mupirocin (which was only tested for in the last four surveys) was observed in Australia. This suggests that the increase in MRSA is due to the emergence and expansion of non-multiresistant clones in the community.

Among MSSA, resistance to non-β-lactams in 2012 was uncommon except for erythromycin (12.8%). Over the 7 AGAR surveys no trends in resistance, either increase or decrease, were evident for erythromycin, gentamicin or rifampicin. Small but significant increases were observed nationally for clindamycin, ciprofloxacin, fusidic acid, trimethoprim-sulphamethoxazole and high-level mupirocin resistance.

In conclusion, the MRSA rates continue to rise in strains causing infections in people in the community. The national rate is now 17.9%, with levels as high as 25.5% in New South Wales. This makes the empiric choice for the correct antibiotic therapy of community *S. aureus* infections increasingly difficult.

2 Introduction

2.1 Objective of the Program

The objective of the 2012 surveillance program was to determine the proportion of resistance to commonly used antimicrobials in *S. aureus* in the Australian community, in general practice patients and in hospital outpatients (excluding day-only patients but including emergency department patients).

2.2 Importance of Staphylococcus aureus

S. aureus continues to be the causative organism of a wide range of community-acquired infections ranging from relatively minor skin and soft tissue infections to serious and life threatening systemic sepsis with a high mortality [1] . In Australia, methicillin-resistant *S. aureus* (MRSA) were first detected in Sydney in the 1960s [2], but really became an endemic problem in hospitals, in particular the Eastern states, with the appearance of a multiresistant strain, an eastern-Australian MRSA strain (now divided into Aus-2 and Aus-3 EMRSA), in the 1970s and 80s [3,4]. Community MRSA strains, generally less resistant to a range of antibiotics and associated with skin and soft tissue infection, emerged in the 1990s, initially in Western Australia [5,6] and the Northern Territory [7], and subsequently in the Eastern states [8-10]. Strains harbouring the genes encoding Panton-Valentine leukocidin (PVL) were first detected in Australia in the late 1990s (the South Western Pacific or Oceania clone: ST30-IV) [11]. The PVL positive Queensland clone (ST93-IV) was characterized in 2000 [12] and is now the dominant CA-MRSA in Australia [13]. Importation of several overseas PVL positive clones has occurred: USA300 (ST8-IV), the Bengal Bay Clone (ST772-V), Taiwan CA-MRSA (ST59-V_T) and European CA-MRSA (ST80-IV) [14]. PVL is associated with recurrent furunculosis and more severe infections including osteomyelitis, septicaemia and necrotising pneumonia.

The Australian Group on Antimicrobial Resistance (AGAR) has conducted surveillance of antimicrobial resistance in *S. aureus* for over 20 years [15]. This surveillance role is very important given the ability of *S. aureus* strains to acquire new resistance and virulence determinants and to undergo rapid clonal expansion. Since the 1960s multiple waves of MRSA clones have occurred in Australia influencing the susceptibility profiles of the isolates seen in clinical practice. Results of previous AGAR surveys provide the only longitudinal record of the epidemiology of MRSA at a national level [16-18]. Given the emergence of hyper-virulent community MRSA strains, AGAR changed its methodology in 2000 to conduct surveys of community isolates biennially. The community-based surveys performed in 2000, 2002, 2004, 2006 and 2008 have been reported previously [19-21].

The results of the seventh community-based survey of *S. aureus* infection conducted in 2012 are reported here.

3 Methods

Up to 100 clinically significant consecutive isolates of *S. aureus* from different patients were collected by each laboratory. Isolates were collected from non-inpatients. Day surgery and dialysis patients were excluded. Isolates from nursing homes, long-term care facilities and hospice patients were included. Each *S. aureus* isolate was from an individual patient and was judged to have come from a potentially infected site.

3.1 Identification

The minimum requirements for identification of *S. aureus* were positive results for at least two of the following tests: slide coagulase test, tube coagulase test, demonstration of deoxyribonuclease production, appropriate growth on chromogenic agar, *mec* and *nuc* gene PCR and mass spectrometry. Fermentation of mannitol or growth on mannitol-salt agar may have been performed for confirmation.

3.2 Antimicrobial Susceptibility Testing

Participating laboratories performed antimicrobial susceptibility tests using the Vitek 2 AST-P612 card (bioMérieux) (Table 1). Penicillin susceptible strains were tested for β-lactamase production using nitrocefin or disc diffusion using a Penicillin 10 unit disc (CLSI) or Penicillin 1 unit disc (EUCAST). High-level mupirocin resistance was determined by disc diffusion (200 µg).

Table 1. Vitek 2 AST-P612 card

Antibiotic	MIC Range (mg/L)
Benzylpenicillin	0.03 – 0.5
Oxacillin	0.25 – 4
Cefoxitin screen	+/-
Vancomycin	0.5 – 32
Rifampicin	0.5 – 32
Fusidic acid	0.5 – 32
Gentamicin	0.5 – 16
Erythromycin	0.25 – 8
Clindamycin	0.25 – 8
Inducible clindamycin resistance	+/-
Tetracycline	1 – 16
Trimethoprim/Sulphamethoxazole	10 – 320
Ciprofloxacin	0.5 – 8
Teicoplanin	0.5 – 32
Linezolid	0.5 – 8
Nitrofurantoin	16 – 512
Mupirocin	2 – 8
Daptomycin	0.12 – 8

3.3 Quality Control

The quality control organism for this survey was *S. aureus* ATCC 29213. All participating laboratories are NATA accredited.

3.4 Statistical Analysis

The differences between proportions, adjusted for multiple comparisons, and 95% Confidence Intervals were calculated using GraphPad® Prism Software and EpiInfo version 6.0.

3.5 Participating Laboratories

Australian Capital Territory (1)
The Canberra Hospital

New South Wales (7)
Concord Hospital
Douglass Hanley Moir Pathology
Nepean Hospital
Royal North Shore Hospital
Royal Prince Alfred Hospital
Sydney South West Pathology Service – Liverpool
Westmead Hospital

Northern Territory (1)
Royal Darwin Hospital

Queensland (6)
Pathology Queensland, Princess Alexandra Hospital
Pathology Queensland Central Laboratory
Pathology Queensland, Prince Charles Hospital
Pathology Queensland, Gold Coast Hospital
Pathology Queensland, Cairns Base Hospital
Sullivan Nicolaides Pathology

South Australia (3)
SA Pathology - Flinders Medical Centre
SA Pathology - Institute of Medical Veterinary Science
SA Pathology - Women's and Children's Hospital

Tasmania (2)
Royal Hobart Hospital
Launceston General Hospital

Victoria (5)
Alfred Hospital
Austin Health
Monash Medical Centre
Royal Women's and Children's Hospital
St Vincent's Hospital

Western Australia (4)
PathWest, Fremantle Hospital
PathWest, QEII Medical Centre
PathWest, Royal Perth Hospital
Saint John of God Pathology

4 Demographics

4.1 Regional Source of Isolates

2,844 *S. aureus* were tested by the 29 institutions. Each state and mainland territory of Australia was represented. The contributions to the dataset from the 6 states and two territories ranged from 3.5% to 24.4% (Table 2).

Table 2. Number of institutions and *S. aureus* isolates collected in each state/territory

Region	Number of Institutions	Total	%
New South Wales (NSW)	7	693	24.4
Queensland (Qld)	6	599	21.0
Victoria (Vic)	5	500	17.6
Western Australia (WA)	4	397	14.0
South Australia (SA)	3	296	10.4
Tasmania (Tas)	2	159	5.6
Australian Capital Territory (ACT)	1	100	3.5
Northern Territory (NT)	1	100	3.5
Total	**29**	**2,844**	**100.0**

4.2 Age

Only 20% of isolates were received from patients 0 years to 16 years of age (Table 3) with 80% of isolates contributed by patients 17 years and older ($p<0.0001$).

Table 3. Age range of patients

Age Range (years)	n	%
0-1	174	6.1
2-16	392	13.8
17-40	788	27.7
41-60	585	20.6
61-108	905	31.8
Total	**2,844**	**100.0**

5 Specimen Source

The majority (96.3%) of isolates were from a non-invasive site (Table 4). Skin and soft tissue infection specimens contributed the majority (90.5%) of isolates followed by respiratory specimens (3.7%). Blood culture isolates contributed 3.1% of the total.

Table 4. Number and proportion of isolates associated with specimen types

Specimen Source	n	%	95%CI
Skin and Soft Tissue	2575	90.5	89.4 – 91.6
Respiratory	106	3.7	3.1 – 4.5
Blood	89	3.1	2.6 – 3.8
Urine	58	2.1	1.6 – 2.6
Sterile Body Cavity	16	0.6	0.4 – 0.9
Total	**2844**		
Invasive	104	3.7	3.0 – 4.4
Non-Invasive	2740	96.3	95.6 – 97.0

6 Susceptibility Testing Results

6.1 Methicillin-resistant S. aureus

The proportion of methicillin-resistant *S. aureus* was 17.9% (95%CI 16.6-19.4%) nationally (Table 5), ranging from 4.0% in the Australian Capital Territory to 25.5% in the New South Wales. The national proportion was similar for the 2010 survey but has increased slightly since 2006 (16.0%, 95%CI 14.7-17.3%, p=0.0405). At a regional level the proportions of MRSA have been stable since 2008 in all regions. Although the proportion of MRSA in the Northern Territory and the Australian Capital Territory appeared to have decreased over the test periods 2010 and 2012, 35.0% to 24% (p=0.0858) and 8% to 4% (p=0.2321) respectively, at this stage these decreases represent only random variation in proportions..

The proportion of invasive isolates (blood/sterile sites) that were MRSA was 21.2% (95%CI 14.4-30.0%) and were similar (p=0.4037) to the proportion of non-invasive isolates at 17.8% (95%CI 16.4-19.3%). The proportion of MRSA was highest in blood at 21.3% (95%CI 14.1-31.0%) (Table 6).

There were significant differences (p<0.0001) in the proportion of MRSA seen in different patient groups with patients from long term care facilities (46.7%, 95%CI 24.8-70.0%), patients attending emergency departments (20.9%, 95%CI 18.9-23.1%) and hospital outpatients (17.0%, 95%CI 14.2-20.1%), having high rates of MRSA.

Resistance in MRSA to non-β-lactam antimicrobials, with the exception of rifampicin, varied between states (Table 8).

There were differences in the proportion of resistance to non-β-lactam antimicrobials in MRSA associated with various patient types (Table 9). MRSA resistance for many antimicrobials was high in hospital outpatients, emergency and long-term care which is consistent with their having a higher proportion of healthcare-related acquisition.

No resistance was detected to vancomycin, teicoplanin or linezolid.

Table 5. Proportion of *S. aureus* that are MRSA by region and source

	ACT	NSW	NT	Qld	SA	Tas	Vic	WA	Aus	Aus 95%CI
All	**4.0** [4/100]	**25.5** [177/693]	**24.0** [24/100]	**17.2** [103/599]	**14.5** [43/296]	**5.7** [9/159]	**17.4** [87/500]	**15.9** [63/397]	**17.9** [510/2844]	**16.6 – 19.4**
Invasive	**0.0** [0/0]	**39.4** [13/33]	**50.0** [1/2]	**11.8** [2/17]	**20.0** [1/5]	**0.0** [0/11]	**13.0** [3/23]	**15.4** [2/13]	**21.2** [22/104]	**14.4 – 30.0**
Non-invasive	**4.0** [4/100]	**24.9** [164/660]	**23.5** [23/98]	**17.4** [101/582]	**14.4** [42/291]	**6.1** [9/148]	**17.6** [84/477]	**15.9** [61/384]	**17.8** [488/2740]	**16.4-19.3**

Table 6. Proportion of *S. aureus* that are MRSA by source

Specimen Source	MRSA	95%CI
Blood	**21.3** [19/89]	**14.1 – 31.0**
Sterile Body Cavity	**18.8** [3/16]]	**6.6 – 43.1**
Skin and Soft Tissue	**17.9** [462/2575]	**16.5 - 19.5**
Urine	**17.2** [10/58]	**9.6 – 28.9**
Respiratory	**15.1** [16/106]	**9.5 – 23.1**

Table 7. Proportion of *S. aureus* that are MRSA by patient group

Specimen Source	MRSA	95%CI
Long Term Care Facility	**46.7** [7/15]	**24.8 – 70.0**
Emergency Department	**20.9** [305/1460]	**18.9 – 23.1**
Hospital Outpatient	**17.0** [104/613]	**14.2 – 20.1**
General Practice	**12.7** [94/740]	**10.5 – 15.3**
Other/Unknown	**0** [0/12]	**0.0 – 24.3**

Table 8. Proportion [and number] of MRSA non-susceptible to non-β-lactams

Drug	ACT [n=4]	NSW [n=177]	NT [n=24]	Qld [n=103]	SA [n=43]	Tas [n=9]	Vic [n=87]	WA [n=63]	Aus [n=510]	Aus 95%CI
Erythromycin	**75.0** [3]	**43.5** [77]	**29.2** [7]	**21.4** [22]	**30.2** [14]	**44.4** [4]	**58.6** [51]	**36.5** [23]	**39.2** [200]	**35.3 – 43.7**
Clindamycin*	**0.0** [0]	**15.8** [28]	**12.5** [3]	**9.7** [10]	**11.6** [5]	**0.0** [0]	**23.0** [20]	**3.2** [2]	**13.3** [68]	**10.7 – 16.6**
Tetracycline	**0.0** [0]	**15.8** [28]	**20.8** [5]	**8.7** [9]	**11.6** [5]	**0.0** [0]	**29.9** [26]	**1.6** [1]	**14.5** [74]	**11.7-17.8**
Trimethoprim-sulphamethoxazole	**0.0** [0]	**11.3** [20]	**12.5** [3]	**3.9** [4]	**7.0** [3]	**0.0** [0]	**21.8** [19]	**4.8** [3]	**10.2** [52]	**7.9 – 13.1**
Ciprofloxacin	**25.0** [1]	**51.4** [91]	**16.7** [4]	**19.4** [20]	**18.6** [8]	**44.4** [4]	**58.6** [51]	**20.6** [13]	**37.5** [191]	**33.4 – 41.7**
Gentamicin	**0.0** [0]	**12.4** [22]	**20.8** [5]	**2.9** [3]	**4.7** [2]	**0.0** [0]	**16.1** [14]	**3.2** [2]	**9.4** [48]	**7.2 – 12.3**
Fusidic Acid	**0.0** [0]	**4.5** [8]	**0.0** [0]	**6.8** [7]	**4.7** [2]	**0.0** [0]	**8.0** [7]	**3.2** [2]	**5.1** [26]	**3.5 – 7.4**
Mupirocin[#]	**0.0** [0]	**2.3** [4]	**0.0** [0]	**3.9** [4]	**0.0** [0]	**0.0** [0]	**0.0** [0]	**0.0** [0]	**1.6** [8]	**0.8 – 3.1**
Rifampicin	**0.0** [0]	**1.1** [2]	**0.0** [0]	**1.0** [1]	**0.0** [0]	**0.0** [0]	**2.3** [2]	**1.6** [1]	**1.2** [6]	**0.5-2.5**

* Constitutive resistance
[#] High level resistance

Table 9. Proportion [and number] of non-susceptible MRSA by patient type, Australia

Drug	Emergency Department [n=305]	Hospital Outpatient [n=104]	General Practice [n=94]	Long-term Care Facility [n=7]
Erythromycin	**36.4** [111]	**51.0** [53]	**36.2** [34]	**42.9** [3]
Clindamycin*	**15.4** [47]	**13.5** [14]	**7.4** [7]	**0.0** [0]
Tetracycline	**15.7** [48]	**17.3** [18]	**8.5** [8]	**0.0** [0]
Trimethoprim-Sulphamethoxazole	**11.5** [35]	**11.5** [12]	**5.3** [5]	**0.0** [0]
Ciprofloxacin	**35.1** [107]	**54.8** [57]	**25.5** [24]	**57.1** [4]
Gentamicin	**10.8** [33]	**11.5** [12]	**3.2** [3]	**0.0** [0]
Fusidic Acid	**4.9** [15]	**7.7** [8]	**3.2** [3]	**0.0** [0]
Mupirocin[#]	**1.0** [3]	**3.8** [4]	**1.1** [1]	**0.0** [0]
Rifampicin	**1.3** [4]	**1.9** [2]	**0.0** [0]	**0.0** [0]

* Constitutive resistance [#] High level resistance

6.2 Trends in Proportion of *S. aureus* that are MRSA 2000-2012

Significant increases in the proportion of *S. aureus* that are MRSA occurred in all regions except the ACT, Tasmania and Western Australia (Table 10).

Table 10. Trend data for proportion of *S. aureus* that are MRSA, 2000-2012

Year	ACT	NSW	NT	Qld	SA	Tas	Vic	WA	Aus	Aus 95%CI
2000	**5.0** [5/100]	**19.7** [138/700]	**7.0** [7/100]	**7.7** [23/300]	**7.5** [30/400]	**2.0** [2/100]	**9.6** [45/469]	**11.5** [46/400]	**11.5** [296/2569]	**10.3 -12.8**
2002	**8.0** [8/100]	**25.4** [175/689]	**21.0** [21/100]	**12.3** [37/300]	**9.0** [36/400]	**6.0** [6/100]	**11.5** [46/399]	**13.8** [55/398]	**15.4** [384/2486]	**14.1 - 16.9**
2004	**6.0** [6/100]	**21.6** [171/793]	**28.8** [17/59]	**18.0** [54/300]	**10.3** [41/399]	**3.0** [3/99]	**12.2** [61/500]	**13.0** [52/400]	**15.3** [405/2650]	**14.0 -16.7**
2006	**5.0** [5/100]	**25.3** [201/795]	**20.0** [20/100]	**13.8** [69/500]	**12.0** [36/299]	**6.8** [13/190]	**14.5** [87/598]	**11.3** [45/397]	**16.0** [476/2979]	**14.7 -17.3**
2008	**7.0** [7/100]	**27.2** [214/786]	**21.0** [21/100]	**17.4** [104/598]	**14.0** [42/300]	**3.0** [6/198]	**16.8** [100/597]	**14.6** [58/396]	**18.0** [552/3075]	**16.6 -19.4**
2010	**8.0** [8/100]	**24.0** [167/696]	**35.0** [35/100]	**17.7** [106/600]	**14.0** [42/299]	**5.0** [10/200]	**18.7** [112/599]	**14.8** [59/400]	**18.0** [539/2994]	**16.6-19.4**
2012	**4.0** [4/100]	**25.5** [177/693]	**24.0** [24/100]	**17.2** [103/599]	**14.5** [43/296]	**5.7** [9/159]	**17.4** [87/500]	**15.9** [68/397]	**17.9** [510/2844]	**16.6 - 19.4**
X^2 for trend	0.0248	**6.036**	**11.57**	**14.73**	**15.27**	0.5837	**25.73**	3.352	**52.23**	
P	0.8749	**0.014**	**0.0007**	**0.0001**	**<0.0001**	0.4449	**<0.0001**	0.0671	**<0.0001**	

6.3 Trends in MRSA non-susceptibility 2000-2012

Nationally, resistance to the non-β-lactam antimicrobials has significantly decreased for all agents except high-level mupirocin (Table 11). The biggest decreases were seen in resistances associated with ST239-III: gentamicin (32 percentage points (PP)), tetracycline (29PP) and erythromycin (27PP). Trimethoprim-sulphamethoxazole resistance (also associated with ST239-III) has decreased by 14PP since it was first tested in 2006. Ciprofloxacin resistance, associated with ST239-III but also many other HA- and CA-MRSA, has decreased by 14PP since 2000.

Regionally, the largest significant decreases in resistance occurred for gentamicin and tetracycline in Victoria (64 and 41PP respectively), NSW (38 and 37PP) and South Australia (32 and 42PP), for erythromycin in Victoria (35PP), for ciprofloxacin in South Australia (40PP) and for fusidic acid in Tasmania (50PP).

Table 11. Trend data (%) for non-susceptibility in MRSA, 2000-2012.

	ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Aus
Erythromycin									
2000	20.0	70.3	57.1	52.2	66.7	0.0	93.3	45.7	66.6
2002	62.5	72.6	61.9	40.5	36.1	33.3	89.1	60.0	64.8
2004	66.7	60.2	41.2	31.5	41.5	33.3	83.6	48.1	55.6
2006	60.0	53.2	25.0	40.6	30.6	53.8	60.9	37.8	48.5
2008	28.6	48.6	47.6	30.8	28.6	66.7	59.0	32.8	43.8
2010	50.0	52.1	37.1	27.4	40.5	10.0	47.3	37.3	41.9
2012	75.0	43.5	29.2	21.4	32.6	44.4	58.6	36.5	39.4
X^2 for trend	0.2317	43.2	3.98	11.49	4.973	0.0098	43.61	6.539	110.1
p	0.6303	**<0.0001**	**0.0460**	**0.0007**	**0.0257**	0.9213	**<0.0001**	**0.0106**	**<0.0001**
Clindamycin									
2000	0.0	32.6	0.0	17.4	13.3	0.0	80.0	2.2	30.4
2002	12.5	52.6	47.6	16.2	2.8	16.7	50.0	7.3	35.9
2004	0.0	31.6	17.6	9.3	7.3	0.0	32.8	5.8	21.7
2006	20.0	22.4	5.0	17.4	0.0	30.8	24.1	2.2	17.9
2008	0.0	18.2	23.8	11.5	2.4	16.7	24.0	1.7	15.0
2010	25.0	27.5	5.7	12.3	2.4	10.0	22.3	5.1	17.3
2012	0.0	15.8	12.5	9.7	11.6	0.0	23.0	3.2	13.3
X^2 for trend	0.3587	42.65	5.151	1.286	0.0653	0.6894	45.39	0.2189	79.37
p	0.5492	**<0.0001**	**0.0232**	0.2568	0.7984	0.4064	**<0.0001**	0.6399	**<0.0001**
Tetracycline									
2000	0.0	52.9	14.3	30.4	53.3	0.0	71.1	2.2	43.9
2002	62.5	53.7	52.4	35.1	19.4	33.3	87.0	5.5	45.6
2004	50.0	41.5	23.5	14.8	14.6	33.3	70.5	0.0	33.6
2006	40.0	30.8	20.0	20.3	2.8	46.2	42.5	0.0	26.5
2008	14.3	17.8	28.6	11.5	4.8	16.7	42.0	5.2	19.0
2010	25.0	19.2	11.4	19.8	4.8	0.0	29.5	5.1	18.0
2012	0.0	15.8	20.8	8.7	11.6	0.0	29.9	1.6	14.5
X^2 for trend	1.642	114.9	4.442	10.28	23.08	4.518	65.86	0.0283	186.4
p	0.2000	**<0.0001**	**0.0351**	**0.0013**	**<0.0001**	**0.0335**	**<0.0001**	0.2000	**<0.0001**
Trimethoprim-sulphamethoxazole									
2006	40.0	27.4	15.0	20.3	2.8	38.5	42.5	0.0	24.6
2008	14.3	16.3	28.6	11.5	4.8	16.7	38.0	1.7	17.4
2010	25.0	19.8	11.4	17.0	4.8	0.0	25.9	1.7	16.5
2012	0.0	11.3	12.5	3.9	7.0	0.0	21.8	4.8	10.2
X^2 for trend	1.329	12.39	0.6341	7.231	0.6678	7.693	11.57	2.589	33.44
p	0.249	**0.0004**	0.4258	**0.0072**	0.4138	**0.0055**	**0.0007**	0.1076	**<0.0001**
Ciprofloxacin									
2000	0.0	68.1	14.3	26.1	56.7	0.0	68.9	8.7	51.7
2002	62.5	70.3	52.4	37.8	33.3	16.7	84.8	23.6	56.8
2004	50.0	64.9	29.4	35.2	39.0	66.7	90.2	19.2	54.6
2006	40.0	55.7	20.0	26.1	27.8	76.9	63.2	11.1	45.4
2008	42.9	52.1	28.6	22.1	23.8	66.7	69.0	19.0	43.0
2010	50.0	53.9	8.6	24.5	26.2	40.0	67.0	10.2	40.6
2012	25.0	51.4	16.7	19.4	18.6	44.4	58.6	20.6	37.6
X^2 for trend	0.0878	22.97	7.319	5.295	11.73	0.3574	9.702	0.0529	48.01
p	0.7670	**<0.0001**	**0.0068**	**0.0214**	**0.0006**	0.5500	**0.0018**	0.8180	**<0.0001**

	ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Aus
Gentamicin									
2000	0.0	50.0	14.3	17.4	36.7	0.0	80.0	2.2	41.2
2002	62.5	54.9	47.6	32.4	16.7	0.0	80.4	3.6	43.8
2004	50.0	40.9	23.5	14.8	17.1	33.3	68.9	0.0	33.3
2006	40.0	28.4	20.0	24.6	2.8	38.5	39.1	0.0	25.2
2008	14.3	16.3	28.6	9.6	0.0	16.7	36.0	0.0	16.1
2010	25.0	19.2	11.4	19.8	7.1	0.0	26.8	1.7	17.3
2012	0.0	12.4	20.8	2.9	4.7	0.0	16.1	3.2	9.4
X^2 for trend	1.642	125.8	3.442	11.87	20.36	1.129	101.6	0.00004	221.8
p	0.2	**<0.0001**	**0.0635**	**0.0006**	**<0.0001**	0.2879	**<0.0001**	0.9948	**<0.0001**
Fusidic acid									
2000	0.0	2.9	28.6	17.4	16.7	50.0	8.9	15.2	9.1
2002	0.0	4.6	4.8	5.4	25.0	50.0	2.2	5.5	7.0
2004	0.0	5.3	11.8	5.6	9.8	33.3	1.6	13.5	6.7
2006	0.0	3.0	10.0	8.7	11.1	0.0	2.3	11.1	5.3
2008	0.0	1.4	9.5	5.8	14.3	0.0	3.0	8.6	4.5
2010	0.0	4.2	5.7	0.9	9.5	0.0	6.3	13.6	5.4
2012	0.0	4.5	0.0	6.8	4.7	0.0	8.0	3.2	5.1
X^2 for trend	-	0.00972	3.0600	2.0743	4.835	12.71	1.051	1.317	6.766
p	-	0.9214	0.08	**0.0977**	**0.0279**	**0.0004**	0.3053	0.2512	**0.0093**
High-level mupirocin									
2006	0.0	0.5	0.0	5.8	0.0	0.0	3.4	0.0	1.7
2008	0.0	0.9	0.0	2.9	0.0	0.0	1.0	1.7	1.3
2010	0.0	0.6	0.0	1.9	0.0	0.0	0.9	0.0	0.7
2012	0.0	1.1	0.0	3.9	0.0	0.0	0.0	0.0	1.6
X^2 for trend	-	0.2929	-	0.3624	-	-	3.688	0.03199	0.1352
p	-	0.5884	-	0.5472	-	-	0.0548	0.5717	0.7131
Rifampicin									
2000	0.0	2.9	0.0	0.0	3.3	0.0	8.9	0.0	3.0
2002	12.5	2.3	0.0	10.8	0.0	0.0	4.3	3.6	3.4
2004	0.0	5.3	0.0	3.7	0.0	33.3	1.6	0.0	3.2
2006	0.0	2.5	0.0	7.2	0.0	0.0	2.3	0.0	2.5
2008	0.0	0.9	4.8	1.9	2.4	0.0	2.0	0.0	1.4
2010	0.0	0.6	0.0	2.8	0.0	0.0	2.7	0.0	1.3
2012	0.0	1.1	0.0	1.0	0.0	0.0	2.3	1.6	1.2
X^2 for trend	1.064	5.052	0.0549	3.777	0.7426	0.9046	2.67	0.19	10.17
p	0.3023	**0.0246**	0.8161	0.0520	0.3888	0.3416	0.1022	0.6629	**0.0014**

6.4 Methicillin-susceptible S. aureus

Susceptibility testing of MSSA (Table 12) show resistance to non-β-lactam agents remains uncommon except for erythromycin where overall resistance is 12.8% (95%CI 11.5-14.2%). All isolates were susceptible to vancomycin, teicoplanin, linezolid and daptomycin. Resistance to penicillin was high and in similar proportions ranging from 82.3% to 90.8% across all regions.

Table 12. Proportion [and number] of MSSA non-susceptible

Drug	ACT [n=96]	NSW [n=516]	NT [n=76]	Qld [n=496]	SA [n=253]	Tas [n=150]	Vic [n=413]	WA [n=334]	Aus [n=2334]	Aus 95%CI
Penicillin	**84.4** [81]	**87.4** [451]	**90.8** [69]	**87.9** [436]	**84.2** [213]	**83.3** [125]	**87.9** [363]	**82.3** [275]	**86.2** [2013]	**84.3 – 87.6**
Erythromycin	**14.6** [14]	**12.4** [64]	**15.8** [12]	**12.3** [61]	**15.4** [39]	**12.0** [18]	**14.3** [59]	**9.6** [32]	**12.8** [299]	**11.5 – 14.2**
Clindamycin*	**1.0** [1]	**2.3** [12]	**0.0** [0]	**1.6** [8]	**2.0** [5]	**0.7** [1]	**1.7** [7]	**1.2** [4]	**1.6** [38]	**1.2 – 2.2**
Tetracycline	**5.2** [5]	**2.7** [14]	**0.0** [0]	**1.6** [8]	**3.2** [8]	**3.3** [5]	**4.1** [17]	**4.8** [16]	**3.1** [73]	**2.5 – 3.9**
Trimethoprim-Sulphamethoxazole	**5.2** [5]	**4.1** [21]	**0.0** [0]	**1.0** [5]	**4.7** [12]	**2.0** [3]	**5.8** [24]	**2.1** [7]	**3.7** [87]	**3.0 – 4.6**
Ciprofloxacin	**2.1** [2]	**2.1** [11]	**1.3** [1]	**2.6** [13]	**3.2** [8]	**5.3** [8]	**5.1** [21]	**2.7** [9]	**2.8** [65]	**2.2 – 3.5**
Gentamicin	**1.0** [1]	**0.6** [3]	**0.0** [0]	**0.6** [3]	**1.2** [3]	**0.0** [0	**0.7** [3]	**0.0** [0]	**0.6** [13]	**0.3 – 1.0**
Fusidic Acid	**7.3** [7]	**6.4** [33]	**2.6** [2]	**11.3** [56]	**1.2** [3]	**6.7** [10]	**3.1** [13]	**3.3** [11]	**5.8** [135]	**4.9 – 6.8**
Mupirocin#	**2.1** [2]	**1.6** [8]	**1.3** [1]	**9.5** [47]	**0.8** [2]	**0.0** [0]	**1.0** [4]	**1.2** [4]	**2.9** [68]	**2.3 – 3.7**
Rifampicin	**0.0** [0]	**0.6** [3]	**0.0** [0]	**0.4** [2]	**0.0** [0]	**0.0** [0]	**0.5** [2]	**0.0** [0]	**0.3** [7]	**0.1 –0.6**

* Constitutive resistance
# High level resistance

6.5 Trends in MSSA non-susceptibility 2000-2012

In spite of some survey-to-survey variability there were no long term trends for either an increase or decrease in resistance to the non-β-lactams either within regions or nationally for erythromycin, tetracycline, gentamicin or rifampicin. Clindamycin resistance remains low but increased significantly in Australia from 0.7% in 2000 to 1.6% in 2012 (p=0.0001), ciprofloxacin resistance increased from 1.4% to 2.8% (p=0.0042) and fusidic acid increased from 3.7% to 5.8% (p<0.0001). High-level mupirocin and trimethoprim-sulphamethoxazole were first tested in 2006. From 2006 to 2012, mupirocin resistance increased from 0.0% in 2006 to 2.9% (p<0.0001) and trimethoprim-sulphamethoxazole resistance increased from 2.0% to 3.7% (p=0.0005). The increases in resistance for fusidic acid and high-level mupirocin were due to significant increases in resistance to these antimicrobials in Queensland (5.8% to 11.3%, p<0.0001 and 0.0% to 9.5%, p<0.0001 respectively). The national increase in ciprofloxacin resistance was largely due to an increase in Victoria (1.4% to 5.1%, p=0.0073).

7 Summary

Biennial community-based *S. aureus* antimicrobial surveillance programmes have been performed in Australia by AGAR since 2000.

In the 2012 programme the percentage of *S. aureus* identified as MRSA ranged from 4.0% in the Australian Capital Territory to 25.5% in New South Wales. Isolates from blood were more likely to be MRSA than isolates from skin and soft tissue infections. More than one in ten *S. aureus* infections in patients attending general practice are MRSA. For patients attending emergency departments or outpatient clinics the figure is 1 in 5, and for patients residing in long term care facilities is 1 in 2.

Resistance in MRSA to the non-β-lactams was: erythromycin 39.4%, ciprofloxacin 37.6%, tetracycline 14.5%, gentamicin 9.4%, clindamycin 13.3%, trimethoprim-sulphamethoxazole 10.2%, fusidic acid 5.1%, rifampicin 1.2% and high-level mupirocin resistance 1.6%. No resistance was detected to vancomycin, teicoplanin or linezolid. Significant differences in resistance across regions were evident for all antimicrobials except mupirocin and rifampicin. These differences may be explained by the different MRSA clones in circulation in each region, for example Aus 2/3 EMRSA (ST239-III) which are reliably resistant to gentamicin, erythromycin, tetracycline, ciprofloxacin and trimethoprim-sulphamethoxazole are commonly found in the ACT, NSW and Victoria.

There were significant differences in the proportion of resistance to non-β-lactam antimicrobials in MRSA associated with various patient types with gentamicin, tetracycline, ciprofloxacin, clindamycin, trimethoprim-sulphamethoxazole and fusidic acid resistance higher in hospital outpatients that other patient types. This is consistent with their having a higher proportion of healthcare-related acquisition.

Over the 7 AGAR community surveys (2000, 2002, 2004, 2006, 2008, 2010 and 2012) the percentage of *S. aureus* identified as MRSA increased significantly ($p<0.0001$) by 6 percentage points (11.5% in 2000 to 17.9% in 2012). However, in the same time period a significant decrease in resistance in MRSA to all the non-β-lactams except high-level mupirocin (which was only tested for in the last three surveys) was observed in Australia. This suggests that the increase in MRSA is due to the emergence and expansion of non-multiresistant clones in the community. The PVL-positive Queensland clone (ST93-IV), typically susceptible to all the non-β-lactam antimicrobials, is of particular concern as numbers are increasing in several regions of Australia [22,23].

Resistance to non-β-lactams among the MSSA in 2012 was: erythromycin 12.8%, fusidic acid 5.8%, tetracycline 3.1%, ciprofloxacin 2.8%, trimethoprim-sulphamethoxazole 3.7%, high-level mupirocin resistance 2.9%, clindamycin 1.6%, gentamicin 0.6% and rifampicin 0.3%. Over the 7 AGAR surveys, no trends in resistance, increase or decrease, were evident for erythromycin, tetracycline, gentamicin or rifampicin. Nationally, small but significant increases were seen for clindamycin, ciprofloxacin, fusidic acid, high level mupirocin and trimethoprim-sulphamethoxazole.

In summary, resistance in MSSA remains uncommon with the exception of erythromycin. Resistance in MRSA appears dynamic due to the success or decline of MRSA clones circulating in Australia.

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