

The Australian Group on Antimicrobial Resistance
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***Staphylococcus aureus* Survey**

2007 Antimicrobial Susceptibility Report

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Antimicrobial Susceptibility Report of *Staphylococcus aureus* Isolates from the Australian Group on Antimicrobial Resistance (AGAR)

2007 Surveillance Report

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The AGAR group has been partially funded by the Commonwealth of Australia, Department of Health and Ageing since 2001

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1 Executive Summary

The Australian Group on Antimicrobial Resistance (AGAR) performs regular multicentre period-prevalence studies to monitor changes in antimicrobial resistance. In 2007, 31 laboratories participated in national surveillance of *Staphylococcus aureus* resistance. Two thousand seven hundred and five isolates of *S. aureus* were collected prospectively and tested by Vitek2[®], disc diffusion and Etest[®].

The survey included only unique isolates from clinical specimens collected 48 hours or more after hospital admission. This is the second hospital-acquired infections AGAR survey, the first being in 2005. Previous surveys from 1986 to 1999 and for 2001 and 2003 included all unique clinical isolates received by the participating laboratories. Those for 2000, 2002, 2004 and 2006 included only outpatient isolates in order to estimate the prevalence of methicillin-resistant *S. aureus* (MRSA) in community staphylococcal infections.

Regional prevalence of MRSA varied from 19.0% in WA to 41.3% in NSW/ACT. The overall prevalence of MRSA in inpatients was 32.9%. Resistance to non-beta-lactam antimicrobials with the exception of erythromycin was uncommon in MSSA. Resistance to erythromycin (77.2%), clindamycin (37.9%), tetracycline (54.9%), cotrimoxazole (55.9%), ciprofloxacin (76.7%) and gentamicin (55.5%) was common in MRSA and varied considerably between regions. Regional variation is due to the differential distribution of MRSA clones between regions and particularly of the major health-care associated MRSA (HA-MRSA) clone, ST239-MRSA-III. The latter clone is predominant in the eastern states and is resistant to multiple non-beta-lactam antimicrobials.

Prevalence of MRSA in individual hospitals varied markedly from 4.2% to 58.6%. Increasing age was associated with risk for MRSA. However, the association between institutional prevalence and institutional mean age was only weak. The weakness of the association may have been related to sample size or to other factors, such as activity, acuity and infection control practice, beyond the scope of this survey. MRSA infection is associated with increased mortality, morbidity and healthcare costs. It is generally accepted that the prevalence of MRSA in an institution reflects the effectiveness of infection control practice. Furthermore, there is ample and consistent evidence that infection control strategies based on screening, isolation and decolonisation are successful and highly cost effective.

2 Introduction

2.1 Objective of the Programme

The objective of the 2007 surveillance program was to determine the prevalence of antimicrobial resistance in clinical isolates of *S. aureus* throughout Australia in hospital inpatients admitted for 48 hours or more.

2.2 Importance of *Staphylococcus aureus*

S. aureus is one of the major pyogenic bacteria and causes a wide variety of infections in man which are associated with considerable morbidity and significant mortality. Manifestations of *S. aureus* infection range from skin and soft tissue infections such as impetigo and furunculosis to invasive infections such as osteomyelitis, necrotising pneumonia and infective endocarditis. Invasive infections are frequently associated with bacteraemia. In the pre-antibiotic era the mortality of staphylococcal bacteraemia was as high as 90%¹. With antibiotic treatment, estimates of mortality for staphylococcal bacteraemia vary considerably: 0.0% to 83.3% for methicillin-resistant *S. aureus* (MRSA) and 3.6% to 51.7% for methicillin-susceptible *S. aureus* (MSSA)². In Australia, as in most of the world, antimicrobial resistance in *S. aureus* is a major impediment to effective treatment. A study of 3,430 cases of *S. aureus* bacteraemia by the Australia New Zealand Cooperative on Staphylococcal Sepsis (ANZCOSS) has shown that 30-day mortality varies significantly for isolates with different susceptibility patterns: mortality for MSSA was 16.5%, for AUS-2/3-like MRSA 31.7%, for EMRSA-15-like 24.4% and for non-multiresistant MRSA 19.4%³. Hospital strains are frequently resistant to methicillin and multiple other antimicrobials⁴.

MRSA was first reported in Australia in 1968⁵. This archaic strain of MRSA was not usually resistant to other non-beta-lactam antimicrobials. The emergence of MRSA resistant to gentamicin and other classes of antimicrobials was first noted in eastern Australia in 1976 and outbreaks of hospital infection due to multiresistant MRSA (mMRSA) occurred in the state of Victoria and in Sydney in the late 1970s and early 1980s⁶⁻⁸. mMRSA became endemic in hospitals in the eastern Australian states in the late 1980s and the 1990s with some spread to hospitals in South Australia, the Northern Territory and Tasmania^{4, 9}. However, these strains did not become established in Western Australian hospitals due to active screening and infection control policies^{4, 10}. Using multilocus sequence typing (MLST) Eastern Australian MRSA has been shown to be a single clone – ST239-MRSA-III¹¹. This is one of the most successful MRSA clones and is now found extensively in Europe, Asia, and South America. MRSA clones of overseas origin have also been found in Australia. Most notably the United Kingdom strain, EMRSA-15, has spread widely in Australia to become a major endemic cause of hospital sepsis.

Vancomycin has been the mainstay of treatment for serious infections due to MRSA. However, there is evidence that vancomycin is less effective in the treatment of MSSA than anti-staphylococcal beta-lactams^{12, 13}. Failure of vancomycin treatment of MRSA has been associated with the emergence of strains with MICs to vancomycin in the intermediate range (VISA)^{14, 15}. These strains have been described in many parts of the world including Australia¹⁶. Isolation of VISA follows failure of prolonged treatment with vancomycin. One recent study has suggested that treatment failure is related to slightly higher vancomycin MICs (1.0 to 2.0 mg/L versus ≤ 0.5 mg/L) in pre-treatment isolates of MRSA¹⁷. Few treatment options remain for mMRSA and resistance to linezolid, one of the few new anti-staphylococcal agents of recent years, is already being reported¹⁸.

While it is well known that *S. aureus* is a major cause of severe sepsis, few population based estimates of its incidence or prevalence are available. A recent Australian survey of *S. aureus* bacteraemia from 1999 to 2002 documented 3,129 episodes².

Approximately 51% of bacteraemic episodes had their onset in hospitals. MRSA caused 40% of hospital-onset and 12% of community-onset episodes. The authors estimated that approximately 6,900 episodes of *S. aureus* bacteraemia occur in Australia annually. This equates to 35/100,000 of population. Meta-analysis of the outcomes of *S. aureus* bacteraemia has shown that the relative risk of death due to MRSA bacteraemia is at least twice that due to MSSA¹⁹. It is widely acknowledged that nosocomial MRSA infection represents an additional burden of disease not just replacement of MSSA infection²⁰. The cost of these additional infections is substantial for hospitals, patients and society. While costs vary from country to country, annual additional hospital costs in the USA are estimated at between US\$1.5 billion and US\$4.2 billion²⁰. In Australia, the additional hospital costs associated with nosocomial *S. aureus* bacteraemia alone are estimated at approximately \$150 million². Effective infection control measures have been shown to substantially reduce nosocomial infection and to result in substantial savings²⁰.

3 Methods

Thirty one laboratories from the each state and two territories of Australia participated in the *S. aureus* AGAR survey. Commencing in June 2007, each laboratory collected up to 100 consecutive significant clinical isolates from hospital inpatients (hospital stay >48 hours at the time of specimen collection) of the largest hospital served by the laboratory. Only one isolate per patient was tested. Specimens collected for the purpose of gathering surveillance data were excluded.

3.1 Species Identification

The minimum tests for identification of *S. aureus* were two positive test results from the following:

1. Slide coagulase test
2. Tube coagulase test
3. Demonstration of deoxyribonuclease production

Additional tests such as fermentation of mannitol or growth on mannitol-salt agar may have been performed for confirmation.

3.2 Susceptibility Testing Methodology

Participating laboratories performed antimicrobial susceptibility tests using the Vitek2[®] AST-P545 card (Table 1). Penicillin susceptible strains were tested for β -lactamase production using nitrocefin. Mupirocin and ceftiofur were tested by disc diffusion using the CLSI or CDS methods²¹⁻²³. Tigecycline MIC was determined by Etest[®] as was the MIC of mupirocin resistant isolates (AB Biodisk, Solna, Sweden). CLSI breakpoints²³ were utilised for all antimicrobials excluding mupirocin²⁴, fusidic acid²⁵ and tigecycline²⁶.

Table 1: Vitek 2® AST-P545 card

Antibiotic	MIC Range (mg/L)	
Benzyloxyphenoxymethyl penicillin	0.03	0.5
Oxacillin	0.25	4.0
Cefazolin	4.0	64.0
Vancomycin	1.0	32.0
Rifampicin	0.5	32.0
Fusidic acid	0.5	32.0
Gentamicin	0.5	16.0
Erythromycin	0.25	8.0
Clindamycin	0.25	8.0
Tetracycline	1.0	16.0
Trimethoprim/Sulphamethoxazole	10.0	320.0
Ciprofloxacin	0.5	8.0
Quinupristin/dalfopristin (Synercid®)	0.25	16.0
Teicoplanin	0.5	32.0
Linezolid	0.5	8.0
Imipenem	1.0	16.0
Nitrofurantoin	16.0	152.0

3.3 Quality Control

Additional quality control was not performed for this survey. As all participating laboratories are NATA accredited, routine QC testing of antimicrobial susceptibility test methods is an integral part of routine procedures.

3.4 Statistical Analysis

P values were calculated for the difference between proportions using Fisher exact test with alpha set at the 5% level (GraphPad® Prism Software). EpiInfo version 6.0 (CDC, Atlanta, GA) software was used to calculate rates with 95% confidence intervals (CI) and χ^2 test.

4 Demographics

Both public (27) and private laboratories (4) participated in the study. Participants included New South Wales (8), ACT (1), Queensland (6), Victoria (6), Tasmania (2), Northern Territory (1), South Australia (3) and Western Australia (4). There were 2,705 isolates from 31 institutions (Table 2). To ensure institutional anonymity data from NSW and ACT, from Tasmania and Victoria and from Queensland and Northern Territory have been combined.

4.1 Regional Source of Isolates

The number of participating institutions and the number of isolates collected from each region is shown in Table 2.

Table 2. Isolates by Region

Region	Number of Institutions	Total	%
New South Wales (NSW)	9	806	29.8
Australian Capital Territory (ACT)			
Queensland (Qld)	7	684	25.3
Northern Territory (NT)			
South Australia (SA)	3	261	9.6
Victoria (Vic)	8	639	23.6
Tasmania (Tas)			
Western Australia (WA)	4	315	11.6
Total	31	2,705	100

4.2 Age

Half (50.2%) of all isolates were contributed by the elderly, 62-106 years of age (Table 3).

Table 3. Age of Patients

Age Range (years)	n	% (95%CI)
0-1	185	6.8 (5.9-7.8)
2-16	88	3.3 (2.6-4.0)
17-40	428	15.8 (14.5-17.2)
41-61	645	23.8 (22.2-25.5)
62-106	1358	50.2 (48.3-52.1)
Total	2,704	100

Age data not provided for one isolate.

5 Specimen Source

The majority of isolates (65.7%) were from skin and soft tissue infections (Table 4). Blood culture isolates made up 7.0% of the total while all invasive isolates accounted for 11.5%. Respiratory specimens were the second most common source (19.2%).

Table 4. Source of Isolates

Specimen Source	n	% (95%CI)
Skin and Soft Tissue (Deep Tissue/Bone)	64	2.4 (1.8-3.0)
Skin and Soft Tissue (Other)	1,714	63.4 (61.5-65.2)
Respiratory (Invasive)	15	0.6 (0.3-0.9)
Respiratory (Other)	503	18.6 (17.1-20.1)
Blood	190	7.0 (6.1-8.0)
Eye	85	3.1 (2.5-3.9)
Urine	82	3.0 (2.4-3.7)
Sterile Cavity	39	1.4 (1.0-2.0)
Ear	7	0.3 (0.1-0.5)
CSF	5	0.2 (0.1-0.4)
Total	2,704	100
Invasive	312	11.5 (10.3-12.8)
Non-Invasive	2,392	88.5 (87.2-89.6)

Source data not provided for one isolate.

6 Susceptibility Testing Results: 2007 Study

6.1 Methicillin-resistant *S. aureus*

Cefoxitin was used to test for methicillin-resistance for the 2,705 isolates of which 32.9% (95%CI 31.1%-34.7%) were methicillin-resistant *S. aureus* (MRSA). The proportion of MRSA varied significantly between states/territories ($X^2 = 58.28$, $p < 0.0001$) (Table 5). The proportion of MRSA in NSW/ACT hospitals was significantly higher ($p < 0.0001$) than the Australian average. Although the proportion of *S. aureus* that were MRSA was higher amongst non-invasive isolates than invasive isolates this was not statistically significant. The proportion of MRSA varied markedly between institutions (Table 6).

Resistance in MRSA to non-beta-lactam antimicrobials varied significantly between states (Table 7). Resistance with the widest range was identified for gentamicin (5.0% to 64.8%, $p < 0.0001$), tetracycline (3.3% to 67.1%, $p < 0.0001$), cotrimoxazole (3.3% to 65.3%, $p < 0.0001$), rifampicin (0% to 15.1%, $p = 0.004$), clindamycin (8.3% to 49.5%, $p < 0.0001$) and tigecycline (0% to 25.4%, $p < 0.0001$). Resistance to ciprofloxacin was also common ranging from 26.7% to 88.7% ($p < 0.0001$). Resistance to fusidic acid was less common ranging from 1.4% to 8.4% ($p = 0.0243$). Mupirocin resistance was low ranging from 0% to 3.8%. Overall 13/18 (72.2%) mupirocin resistant isolates exhibited high-level resistance (MIC >256mg/L). No resistance was detected for vancomycin, teicoplanin, quinupristin-dalfopristin or linezolid. Differences in resistance profiles are due to differences in the carriage of resistance determinants by prevalent clones of MRSA which in turn vary in their geographic distribution. A full description of clonal prevalence is provided in the SAP 2007 Epidemiology and Typing Report.

Table 5: Proportion of MRSA by Region and Source

	NSW/ACT	Qld/NT	SA	Vic/Tas	WA	Aus	Difference across regions χ^2 P
All	333/806 (41.3%)	212/684 (31.0%)	71/261 (27.2%)	213/639 (33.3%)	60/315 (19.0%)	889/2705 (32.9%)	58.28 <0.0001
Invasive	45/124 (36.3%)	15/65 (23.1%)	5/26 (19.2%)	23/56 (41.1%)	3/41 (7.3%)	91/312 (29.2%)	18.77 0.0009
Non- invasive	287/681 (42.1%)	197/619 (31.8%)	66/235 (28.1%)	190/583 (32.6%)	57/274 (20.8%)	797/2392 (33.3%)	46.85 <0.0001

When the proportions of MRSA isolates resistant to non-beta-lactam antibiotics in the 2005 and 2007 surveys were compared significant changes were found in the following:

- erythromycin resistance decreased from 86.3% to 80.5% in NSW/ACT ($p=0.04$);
- clindamycin resistance decreased from 86.7% to 49.5% in NSW/ACT ($p<0.0001$) and from 41.2% to 30.5% in Vic/Tas ($p=0.0224$);
- tetracycline resistance decreased from 83.0% to 67.1% in Vic/Tas ($p=0.0002$);
- trimethoprim/sulphamethoxazole resistance decreased from 70.1% to 62.2% in NSW/ACT ($p=0.03$) and from 80.8% to 65.3% in Vic/Tas ($p=0.0002$);
- gentamicin resistance decreased from 69.8% to 62.5% in NSW/ACT ($p=0.04$) and from 79.5% to 64.8% in Vic/Tas ($p=0.0006$).

These decreases are consistent with the reduced prevalence of AUS-2/3 MRSA seen in these regions (Refer to the SAP 2007 MRSA Epidemiology and Typing report).

Table 6: Proportion of MRSA by Institution

Region	Lab Code	% MRSA
NSW/ACT	1	28.0
	2	44.0
	3	31.3
	4	46.0
	5	57.0
	6	50.0
	7	41.7
	8	58.6
	9	17.5
Qld/NT	10	38.0
	11	28.0
	12	22.0
	13	26.6
	28	20.0
	29	33.3
	30	49.0
SA	14	29.5
	15	37.0
	16	11.0
Vic/Tas	18	4.2
	19	40.0
	20	41.7
	21	11.9
	22	34.8
	23	46.5
	31	40.0
	32	38.0
WA	24	23.7
	25	18.0
	26	17.5
	27	12.0
Australia		32.9

Table 7: MRSA: Number and Proportion Non-Susceptible

Drug	NSW/ACT	Qld/NT	SA	Vic/Tas	WA	Aus	Difference across regions χ^2 P
Erythromycin	268/333 (80.5%)	159/212 (75.0%)	50/71 (70.4%)	184/213 (86.4%)	25/60 (41.7%)	686/889 (77.2%)	57.66 <0.0001
Clindamycin*	165/333 (49.5%)	94/212 (44.3%)	8/71 (11.3%)	65/213 (30.5%)	5/60 (8.3%)	337/889 (37.9%)	71.55 <0.0001
Tetracycline	209/333 (62.8%)	104/212 (49.1%)	30/71 (42.3%)	143/213 (67.1%)	2/60 (3.3%)	488/889 (54.9%)	93.14 <0.0001
Trimethoprim-Sulphamethoxazole	207/333 (62.2%)	120/212 (56.6%)	29/71 (40.8%)	139/213 (65.3%)	2/60 (3.3%)	497/889 (55.9%)	86.69 <0.0001
Ciprofloxacin	286/333 (85.9%)	142/212 (67.0%)	49/71 (69.0%)	189/213 (88.7%)	16/60 (26.7%)	682/889 (76.7%)	130.6 <0.0001
Gentamicin	208/333 (62.5%)	121/212 (57.1%)	27/71 (38.0%)	138/213 (64.8%)	3/60 (5.0%)	497/889 (55.5%)	85.02 <0.0001
Fusidic Acid	11/333 (3.3%)	14/212 (6.6%)	6/71 (8.4%)	3/213 (1.4%)	3/60 (5.0%)	37/889 (4.2%)	11.21 0.024
Mupirocin	5/333 (1.5%)	8/212 (3.8%)	0/71 (0%)	6/213 (2.8%)	1/60 (1.7%)	18/889 (2.0%)	5.125 0.275
Rifampicin	3/333 (0.9%)	32/212 (15.1%)	3/71 (4.2%)	5/213 (1.9%)	0/60 (0%)	43/889 (4.8%)	65.64 <0.0001
Tigecycline	0/333 (0%)	10/212 (4.7%)	18/71 (25.4%)	39/213 (18.3%)	0/60 (0%)	67/889 (7.5%)	102.3 <0.0001

* Constitutive resistance

6.2 Methicillin-susceptible *S. aureus*

The majority, 67.1% (95%CI 65.3-68.9%) of *S. aureus* isolates were MSSA. MSSA isolates were generally susceptible to most non-beta-lactam antimicrobials (Table 8). Resistance to erythromycin was most common but regional proportions were similar with proportions in resistance ranging from 7.8% to 10.5% ($p=0.589$). The only significant difference in proportion across all regions was for mupirocin ($p=0.006$) with Qld/NT and Vic/Tas having the highest level at 2.1%. Two-thirds of mupirocin resistant isolates (14/21, 66.7%) exhibited high-level resistance (MIC > 256mg/L). No resistance was detected for vancomycin, teicoplanin or linezolid. One isolate from Vic/Tas was resistant to quinupristin-dalfopristin.

Table 8: MSSA: Number and Proportion Non-Susceptible

Drug	NSW/ACT	Qld/NT	SA	Vic/Tas	WA	Aus	Difference across regions χ^2 P
Penicillin	407/473 (86.0%)	411/472 (87.1%)	160/190 (84.2%)	361/426 (84.7%)	223/255 (87.5%)	1562/1816 (86.0%)	1.968 0.742
Erythromycin	49/473 (10.4%)	44/472 (9.3%)	20/190 (10.5%)	33/426 (10.1%)	20/255 (7.8%)	176/1816 (9.7%)	2.818 0.589
Clindamycin*	2/473 (0.4%)	5/472 (1.1%)	0/190 (0%)	6/426 (0.9%)	0/255 (0%)	13/1816 (0.7%)	7.439 0.114
Tetracycline	14/473 (3.0%)	17/472 (3.6%)	4/190 (2.1%)	17/426 (4.0%)	6/255 (2.4%)	58/1816 (3.2%)	2.524 0.640
Trimethoprim- Sulphamethoxazole	6/473 (1.3%)	7/472 (1.5%)	2/190 (1.1%)	3/426 (0.7%)	1/255 (0.4%)	19/1816 (1.0%)	2.631 0.621
Ciprofloxacin	4/473 (0.8%)	7/472 (1.5%)	2/190 (1.0%)	7/426 (1.6%)	3/255 (1.2%)	23/1816 (1.3%)	1.416 0.922
Gentamicin	6/473 (1.3%)	8/472 (1.7%)	0/190 (0%)	2/426 (0.5%)	0/255 (0%)	16/1816 (0.9%)	9.175 0.057
Fusidic Acid	14/473 (3.0%)	13/472 (2.8%)	11/190 (5.8%)	10/426 (2.4%)	5/255 (2.0%)	53/1816 (2.9%)	6.891 0.142
Rifampicin	0/473 (0%)	1/472 (0.2%)	1/190 (0.5%)	2/426 (0.5%)	0/255 (0%)	4/1816 (0.2%)	3.624 0.459
Mupirocin	1/473 (0.2%)	10/472 (2.1%)	0/190 (0%)	9/425 (2.1%)	1/255 (0.4%)	21/1816 (1.2%)	14.45 0.006
Tigecycline	2/473 (0.4%)	1/472 (0.2%)	0/190 (0%)	1/425 (0.2%)	0/255 (0%)	4/1815 (0.2%)	1.870 0.760

6.3 Relationship of Age to Methicillin Susceptibility of *S. aureus*

Ages ranged from <1 years to 106 years (Table 9). The mean age for MRSA isolates was 56.1 years with a skewed distribution towards the older patient with 25th percentile at 40 years, 50th at 62 years and 75th 77 years of age. Age data were categorised into neonatal (<1-1 years), paediatric (2-16), adult (17-40), middle-age (41-61) and the older (62-106). The distribution of MSSA and MRSA across the five age groups was significantly different ($z=4.12$, $p<0.0001$).

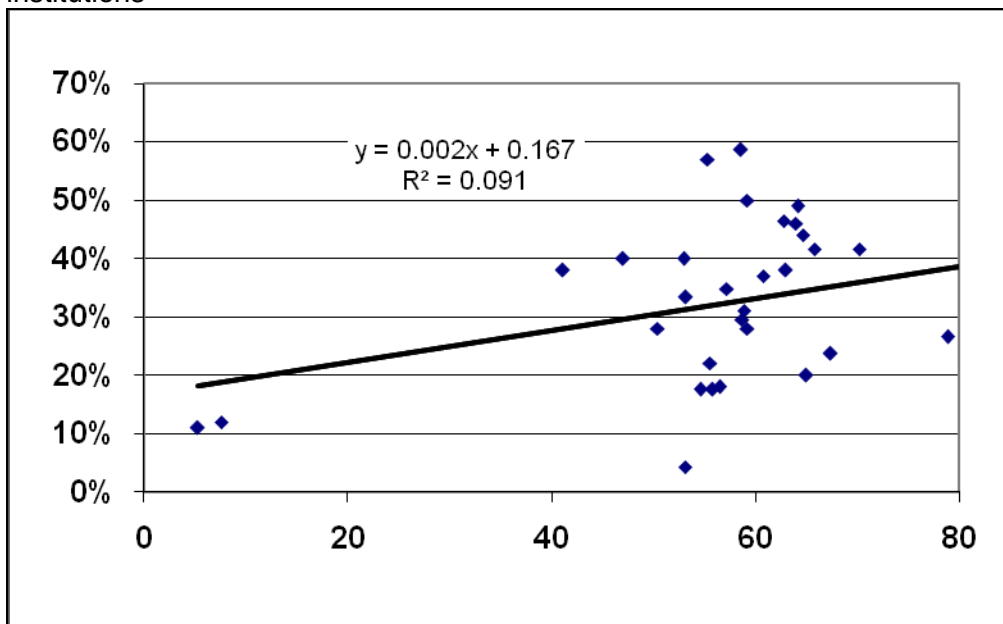
When the relationship between mean age and proportion of MRSA in institutions was examined, a weak trend was identified (Figure 1). The sample sizes contributed by the member hospitals were small resulting in a wide dispersion of the mean age across the 31 facilities which resulted in the poor association between mean age and MRSA.

Table 9: Age by methicillin susceptibility of *S. aureus*

Age	MRSA	MSSA
	N	N
	Row %	Row %
	[Col %]	[Col %]
0-1	14	171
	7.6%	92.4%
	[1.6%]	[9.4%]
2-16	15	73
	17.0%	83.0%
	[1.7%]	[4.0%]
17-40	116	312
	27.1%	72.9%
	[13.0%]	[17.2%]
41-61	210	435
	32.6%	67.4%
	[23.6%]	[24.0%]
62-106	534	824
	39.3%	60.7%
	[60.1%]	[45.4%]
Total	889	1,815
	32.9%	67.1%
	[100.0%]	[100.0%]

Age data not provided for one isolate

Figure 1: Relationship of mean age and proportion of MRSA for 31 institutions



7 Discussion

Surveys conducted by AGAR from 1986 to 1999 included all consecutive clinical isolates of *S. aureus* during the survey period regardless of acquisition^{4, 9, 27}. Participating laboratories did not need to acquire any additional information to distinguish between inpatients and outpatients and so an overall MRSA prevalence was derived. Compliance with methodology was a potential issue particularly in the early days of the surveys but this simple data collection was reliably achieved. It also allowed for comparison of results over a prolonged period. The advent of community clones of MRSA during the 1990s^{28, 29} led to interest in studying the prevalence of MRSA in outpatient infections alone. AGAR responded by conducting biennial outpatient surveys from 2000 onwards^{11, 30}. Since then evidence has emerged that clones that initially were acquired almost exclusively in the community were now being acquired in the healthcare setting with increasing frequency³¹. Therefore, in 2005 a survey of hospital-acquired *S. aureus* infection was undertaken³². The second hospital-acquired *S. aureus* infection survey was conducted in 2007 and is the subject of this report. Future surveys are planned biennially. The results provide us with accurate estimates at a national level of the proportion of hospital-acquired *S. aureus* infection that are due to MRSA and over time will reveal resistance trends.

In the 2007 survey 2,705 isolates were collected from 31 laboratories covering all states and territories. The proportion of MRSA isolates in 2007, did not change significantly from the proportion in 2005, (32.9% and 31.9% respectively, $p=0.417$, $X^2=0.66$). The significant difference in proportions of MRSA between regions (from 19.0% in WA to 41.3% in NSW/ACT) may have been the result of different infection control strategies. The overall proportion of MRSA in invasive (mainly bacteraemia) isolates was similar to that of non-invasive isolates (29.2% and 33.3% respectively, $p=0.1600$). The high proportion of MRSA in invasive isolates is of concern as MRSA bacteraemia is associated with increased mortality compared with MSSA³³. Direct comparison with prevalence in other countries is difficult due to methodological differences. For example, the European surveillance system reports the proportion of MRSA in bacteraemia isolates in both inpatients and outpatients in 23 countries. Even so, the overall proportion in Europe in 2005 varied markedly from <1% in Denmark, Iceland, Norway and Sweden to 52% in Malta³⁴. The Netherlands and the Scandinavian countries have been consistently able to keep MRSA at very low levels in their hospitals over long periods.

Resistance to non-beta-lactams in MRSA was common for erythromycin, clindamycin, tetracycline, cotrimoxazole, ciprofloxacin and gentamicin and varied considerably from region to region. This regional variability is due to the differential distribution of MRSA clones in the major cities. For example, ST239-MRSA-III (AUS-2 and AUS-3 clones), which is resistant to multiple non-beta-lactams including gentamicin, erythromycin and tetracycline, is endemic in the eastern states but is less common in Western Australia and South Australia. ST22-MRSA-IV (EMRSA-15), which is resistant to ciprofloxacin and often erythromycin but susceptible to all other non-beta-lactams, is more common in Western Australia as are other non-multiresistant clones^{11, 30}. The lack of resistance to quinupristin-dalfopristin (one resistant isolate only detected) is in keeping with the low usage of this antibiotic. Resistance of MSSA to non-beta-lactam antimicrobials was uncommon except for erythromycin. There was little variability between regions in the low levels of resistance to other agents, with the exception of mupirocin, which once again may be due to regional variations in the prevalence of clones of MSSA carrying different combinations of resistance genes. The majority of mupirocin resistant MSSA were high-level resistant (MIC >256mg/L) suggesting the presence of the *mupA* gene usually encoded on a plasmid. This is of particular concern as this resistance can be transferred horizontally (between clones) and thus is likely to spread with selection pressure. Mupirocin is currently a mainstay of measures used for clearance of MRSA carriage.

The proportion of MRSA isolates varied between institutions from 4.2% to 58.6%. This is a cause for concern given the increased mortality, morbidity and cost associated with MRSA infection^{20, 35}. It is generally accepted that the prevalence of MRSA in an institution reflects the effectiveness of infection control practice³⁶, but it is also true that age remains a risk factor for MRSA infection³². Because MRSA data are statistically rare at the institution level the association between age and

MRSA will be weak. However, analysis of our 2007 survey data confirm that increasing age is a significant ($p < 0.0001$) risk of MRSA. Equally other factors such as variability in activity, acuity and infection control practice may also have contributed. Given the marked variability in prevalence between institutions it seems unlikely that mean age alone could explain the difference. The possibility of controlling MRSA in the healthcare setting was demonstrated quite early in Australia using the search and destroy approach employing screening, isolation and decolonisation¹⁰. More recently success in reducing nosocomial MRSA transmission has also been achieved by campaigns to increase compliance with hand hygiene standards³⁶⁻³⁸. The recent hand hygiene initiative sponsored by the Australian Commission on Safety and Quality in Healthcare is based on the latter approach. Should this initiative be successful, a reduction in the prevalence of MRSA in general and of specific healthcare-associated clones should be seen in future AGAR surveys of inpatient *S. aureus* infection.

8 References

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