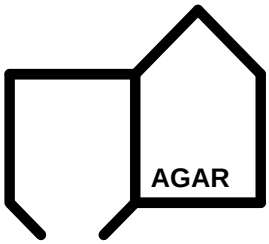

The Australian Group on Antimicrobial Resistance
http://antimicrobial-resistance.com

Staphylococcus aureus Survey
2011 Antimicrobial Susceptibility Report

Professor Graeme Nimmo
Division of Microbiology, Pathology Queensland Central Laboratory, Queensland

Ms Julie Pearson
Department of Microbiology and Infectious Diseases, PathWest Laboratory Medicine-WA,
Royal Perth Hospital, Western Australia

Professor Peter Collignon
Department of Microbiology and Infectious Diseases, The Canberra Hospital, Australian Capital Territory.
School of Clinical Medicine, Australian National University, Australian Capital Territory.

Clinical Professor Keryn Christiansen
Department of Microbiology and Infectious Diseases, PathWest Laboratory Medicine-WA,
Royal Perth Hospital, Western Australia

Mr Geoffrey Coombs
Department of Microbiology and Infectious Diseases, PathWest Laboratory Medicine-WA,
Royal Perth Hospital, Western Australia

Ms Jan Bell
Department of Microbiology and Infectious Diseases, SA Pathology, Women's and Children's Hospital,
South Australia

Professor Mary-Louise McLaws
Healthcare associated infection and infectious diseases control, The University of New South Wales,
New South Wales

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

Address correspondence to: Ms Julie Pearson

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

2011 Surveillance Report

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

Table of Contents

1 Executive Summary 4
2 Introduction 5
3 Methods 5
3.1 Species Identification 6
3.2 Susceptibility Testing Methodology 6
3.3 Quality Control 6
3.4 Statistical Analysis 6
4 Demographics 6
4.1 Regional Source of Isolates 6
4.2 Age 7
5 Specimen Source 7
6 Susceptibility Testing Results 8
6.1 Methicillin-resistant *S. aureus*, 2011 8
6.2 Trend data: methicillin-resistant *S. aureus*, 2005 - 2011 11
6.3 Methicillin-susceptible *S. aureus*, 2011 13
6.4 Trend data: methicillin-susceptible *S. aureus*, 2005 - 2011 13
6.5 Inducible clindamycin resistance 14
7 Discussion 14
8 References 15
9 Acknowledgements 18

1 Executive Summary

The Australian Group on Antimicrobial Resistance (AGAR) performs regular multicentre period-prevalence studies to monitor changes in antimicrobial resistance. In 2011, 29 laboratories from each state and mainland territory of Australia participated in national surveillance of *Staphylococcus aureus* resistance. The survey included only unique isolates from clinical specimens collected 48 hours or more after hospital admission. This is the fourth hospital-onset infections AGAR survey.

Regional prevalence of MRSA varied from 19.9% in Western Australia to 36.8% in New South Wales/Australian Capital Territory. The overall prevalence of MRSA in inpatients was 30.3%. Institutional prevalence ranged from 7.0% to 56.0%. MRSA resistance to ciprofloxacin (66.9%), erythromycin (64.0%), tetracycline (33.5%), co-trimoxazole (30.7%), gentamicin (30.4%) and clindamycin (constitutive resistance) (29.7%) was common and varied considerably between regions. Resistance levels were below 4% for fusidic acid, rifampicin, high-level mupirocin and daptomycin. Resistance was not detected for vancomycin, teicoplanin or linezolid. Regional variation in resistance is due to the differential distribution of MRSA clones between regions and particularly of the major health-care associated MRSA (HA-MRSA) clone, ST239-III (Aus 2/3 EMRSA) which is predominant in the eastern states and is resistant to multiple non-β-lactam antimicrobials. Resistance to non-β-lactam antimicrobials was uncommon in MSSA with the exception of erythromycin (13.2%) and no resistance was detected in MSSA for vancomycin, teicoplanin or linezolid. Inducible clindamycin resistance is still the norm for erythromycin resistant and clindamycin intermediate/susceptible *S. aureus* in Australia with 90.6% of MRSA and 83.1% of MSSA with this phenotype having a positive D-test.

The national proportion of *S. aureus* that are MRSA was similar in this 2011 survey to the three previous inpatient hospital surveys conducted by AGAR in 2005, 2007 and 2009. Yet, for the 2011 survey period resistance to many antimicrobials, in particular tetracycline, co-trimoxazole, erythromycin, ciprofloxacin and gentamicin, has significantly decreased. This suggests that non-multiresistant community-associated MRSA (CA-MRSA) clones are becoming more common in the hospital setting and may be replacing the long-established multiresistant clones such as ST239-III. Given hospital outbreaks of CA-MRSA in Australia are thought to be extremely rare it is most likely that patients colonised at admission with CA-MRSA have become infected with the colonising strain during their hospital stay.

There is ample and consistent evidence that infection control strategies based on screening, isolation and decolonisation are successful and highly cost effective. These strategies offer the best defence in preventing healthcare-acquired infections of colonising CA-MRSA in Australian hospitals.

2 Introduction

Staphylococcus aureus is a major pathogen both in the hospital environment and the wider community. In the hospital environment, the most common infections caused by *S. aureus* are skin and soft tissue, respiratory, bone, joint and sepsis. Invasive infections are frequently associated with life threatening bacteraemia infections. A study of *S. aureus* bacteraemia in this region reported all-cause 30-day mortality for *S. aureus* bacteraemia as 20.6%[1] with mortality increasing as resistance to the number of antimicrobials increased[2]. Hospital strains of methicillin-resistant *S.* aureus (MRSA) such at ST239-III (Aus 2/3 EMRSA) are frequently resistant to methicillin and multiple other antimicrobials[3]. Several studies have indicated that mortality is higher for patients infected with methicillin resistant *S. aureus* (MRSA) than methicillin susceptible *S. aureus* (MSSA)[4,5,6,7] and that MRSA infections are associated with increased cost due to increased length of stay and the necessity to treat with more costly antimicrobials[8,9,10].

In recent years, community-associated MRSA (CA-MRSA) with origins in the community rather than the hospital setting are more frequently reported to be causing infections in hospitalised patients[11,12,13,14,15]. In many regions the most common CA-MRSA in the community is also the most common CA-MRSA in hospitals[15,16] suggesting that patients are either becoming infected in hospital with their colonising MRSA strains or that CA-MRSA are surviving and spreading in the hospital environment. CA-MRSA are generally more susceptible to the non-β-lactam antimicrobials than hospital-associated MRSA (HA-MRSA), however there are several reports of enhanced virulence amongst some genetic lineages of CA-MRSA[17,18,19]. Differences in infection types caused by HA-MRSA and CA-MRSA have been reported with CA-MRSA causing mostly skin and soft tissue infections, often in young, otherwise healthy individuals and HA-MRSA causing a range of infections in older patients with co-morbidities. However recent data suggests that CA-MRSA in the hospital environment has a similar disease profile to HA-MRSA; causing invasive disease in older patients[20,21,22]. Reducing HA-MRSA in the hospital environment will result in an overall reduction in antimicrobial resistance. However a corresponding increase in CA-MRSA does not reduce the burden of MRSA in the hospital environment and may lead to more severe infections because of the enhanced virulence of some CA-MRSA.

There are many strategies for reducing the incidence of MRSA in hospitals including staff and patient screening, contact precautions, patient isolation and decolonisation of positive patients[23] thereby reducing both patient mortality and the costs associated with a high burden of *S. aureus* disease. Limited success in reducing MRSA transmission has been achieved through enhanced hand hygiene programmes[24,25]. It is important to track the changing MRSA epidemiology in Australian hospitals in order to inform infection control management strategies and antimicrobial guidelines.

The Australian Group on Antimicrobial Resistance (AGAR) has performed antimicrobial resistance period-prevalence surveys in Australia since 1986[26]. Presently, 29 laboratories from all states and mainland territories of Australia contribute to AGAR surveys. Hospital inpatient surveys have been conducted biennially since 2005[27,28,29], alternating with biennial community surveys[30,31,32]. The findings of the 2011 AGAR hospital inpatients survey are presented here and results compared to the three previous hospital inpatients surveys.

3 Methods

From the 1st July to the 30th November 2011, each laboratory collected up to 100 consecutive *S. aureus* isolates from hospital inpatients (hospital stay >48 hours at the time of specimen collection). Only one isolate per patient was tested. Each *S. aureus* isolate was judged to come from a potentially infected site. Specimens received for the purpose of gathering surveillance data were excluded. Hospital laboratories collected only from one institution. The four private laboratories collected from institutions they serviced.

3.1 Species Identification

S. aureus was identified by morphology and positive results of at least two of the following tests: slide coagulase test, tube coagulase test, appropriate growth on chromogenic agar and demonstration of deoxyribonuclease production. Additional tests such as fermentation of mannitol, growth on mannitol-salt agar or polymerase chain reaction for the presence of the *nuc* gene may have been performed for confirmation.

3.2 Susceptibility Testing Methodology

Participating laboratories performed antimicrobial susceptibility tests using the Vitek2® AST-P612 card. Penicillin susceptible strains were tested for β-lactamase production using nitrocefin. A D-test was performed on all erythromycin resistant and clindamycin intermediate/susceptible strains and compared with the inducible clindamycin resistance (ICR) well of the AST-P612 card. CLSI breakpoints[33] were utilised for all antimicrobials excluding mupirocin and fusidic acid[34].

3.3 Quality Control

The quality control strains for this survey were *S. aureus* ATCC strains 29212, 29213 and BAA-1026. All participating laboratories are NATA accredited.

3.4 Statistical Analysis

The difference between proportions were tested using Chi-square test with alpha set at the 5% level and Fisher's exact test for 95% confidence limits (GraphPad® Prism Software). Relative risk and 95% confidence intervals (CI) were calculated using VassarStats (http://faculty.vassar.edu).

4 Demographics

Public (26) and private laboratories (3) participated in the study. Participants included New South Wales (7), Australian Capital Territory (1), Queensland (6), Victoria (5), Tasmania (2), Northern Territory (1), South Australia (3) and Western Australia (4). There were 2,357 isolates from 29 institutions (Table 1). To ensure institutional anonymity data from New South Wales and Australian Capital Territory, 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 1.

Table 1. *S. aureus* Isolates by region

Region	Number of Institutions	Total	%
New South Wales (NSW) Australian Capital Territory (ACT)	8	639	27.1
Queensland (Qld) Northern Territory (NT)	7	591	25.1
South Australia (SA)	3	254	10.8
Victoria (Vic) Tasmania (Tas)	7	541	22.9
Western Australia (WA)	4	332	14.1
Total	**29**	**2,357**	**100**

4.2 Age

Most (74.0%) *S. aureus* isolates were contributed by patients 41 years and older, while half (51.1%) of all isolates were contributed by patients ≥62 years of age (Table 2).

Table 2. Age of patients

Age Range (years)	n	%	Cumulative frequency
62-101	1206	51.1	51.1
41-61	515	21.8	74.0
17-40	344	14.6	88.6
2-16	96	4.1	92.7
0-1	196	8.3	100.0
Total	**2,357**	**100**	

5 Specimen Source

Skin and soft tissue infection specimens contributed the majority (70.5%) of isolates followed by respiratory specimens (17.1%). Blood culture isolates contributed 6.5% of the total with non-invasive isolates (91.3%, 95%CI 90.1%-92.4%) causing significantly (P<0.0001) more infection compared with invasive (8.7%, 95%CI 7.5%-9.9%) isolates (Table 3).

Table 3. Source of *S. aureus* isolates

Specimen Source	n	%	95%CI
Skin and Soft Tissue	1661	70.5	68.6-72.3
Respiratory	404	17.1	15.6-18.7
Blood	153	6.5	5.5-7.6
Urine	88	3.7	3.0-4.6
Sterile Body Cavity	49	2.1	1.5-2.7
CSF	2	0.1	0.01-0.3
Total	**2,357**	**100**	
Invasive	204	8.7	7.5-9.9
Non-Invasive	2,153	91.3	90.1-92.4

6 Susceptibility Testing Results

6.1 Methicillin-resistant *S. aureus*, 2011

Cefoxitin was used to test for methicillin-resistance. The proportion of MRSA was 30.3% (95%CI 28.4%–32.1%) nationally (Table 4) with significantly different (P<0.0001) proportions across Australia ranging from 19.9% (95%CI 15.9%–24.5%) in WA to 36.8% (95%CI 33.1%–40.6%) in NSW/ACT. The proportion of invasive *S. aureus* that were MRSA (30.9%) was not significantly higher than for non-invasive isolates (30.2%) (P=0.8998).

Table 4. Proportion of MRSA by region and source

	All isolates			Invasive*			Non-invasive		
Region	n/N	%	95%CI	n/N	%	95%CI	n/N	%	95%CI
NSW/ACT	235/639	36.8	33.1-40.6	29/65	44.6	33.2-56.7	206/574	35.9	32.1-39.9
Qld/NT	180/591	30.5	26.9-34.3	11/41	26.8	15.7-41.9	169/550	30.7	27.0-34.7
SA	55/254	21.7	17.0-27.1	10/28	35.7	20.7-54.2	45/226	19.9	15.2-25.6
Vic/Tas	177/541	32.7	28.9-36.8	9/42	21.4	11.7-35.9	168/499	33.7	29.7-37.9
WA	66/332	19.9	15.9-24.5	4/28	14.3	5.7-31.5	62/304	20.4	16.2-25.3
Aus	713/2357	30.3	28.4-32.1	63/204	30.9	24.9-37.5	650/2153	30.2	28.3-32.2

* Blood, CSF and sterile body cavity
n=number of MRSA isolates, N=number of *S. aureus* isolates

Within regions, the proportion of MRSA in the different institutions also varied (Table 5). The difference in MRSA proportions by institution varied by 12 percentage points (PP) in WA, 24 PP in SA, 28 PP in Qld/NT, 32 PP in Vic/Tas and 41 PP in NSW/ACT.

Table 5. Proportion of MRSA by institution

Region	Lab Code	% MRSA
NSW/ACT	1	15.0
	2	35.5
	3	23.6
	4	36.0
	5	41.0
	6	56.0
	7	50.0
	8	43.0
Qld/NT	10	51.0
	11	25.0
	12	25.0
	13	24.2
	28	29.5
	29	31.5
	30	23.0
SA	14	31.3
	15	24.0
	16	7.0
Vic/Tas	18	18.2
	19	42.0
	21	10.4
	22	34.2
	23	36.7
	31	37.0
	32	38.6
WA	24	22.1
	25	16.0
	26	25.0
	27	13.0
Aus		30.3

The proportion of MRSA isolated in the five sources of infection was similar (P=0.2427) with MRSA ranging from 29.0% in skin and soft tissue infections to 36.4% in urine (Table 6).

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

	All isolates		
Source of Infection	**n/N**	**%**	**95%CI**
Skin and soft tissue	482/1661	29.0	26.8-31.3
Respiratory	136/404	33.7	29.1-38.5
Blood/CSF	46/155	29.7	22.6-37.5
Urine	32/88	36.4	26.4-46.7
Sterile Body Cavity	17/49	34.7	17-49.6

In 2011, as in past AGAR hospital-onset surveys, increasing age was a risk factor for methicillin resistance (Table 7). Inpatients ≥41 years of age were 1.8 times more likely (OR 95%CI 1.5-2.3) to have an MRSA not MSSA infection compared with younger patients.

Table 7. Age by methicillin susceptibility of *S. aureus*

	MRSA			MSSA		
Age (y)	**n**	**Row %**	**Column %**	**n**	**Row %**	**Column %**
0-1	22	11.2	3.1	174	88.8	10.6
2-16	15	15.6	2.1	81	84.4	4.9
17-40	100	29.1	14.0	244	70.9	14.8
41-61	146	28.3	20.5	369	71.7	22.4
62-101	430	35.7	60.3	776	64.3	47.2
Total	713	30.3	100	1,644	69.7	100

Resistance in MRSA to non-β-lactam antimicrobials varied significantly between states. Amongst the MRSA, resistance to the non-β-lactam antimicrobials was common except for fusidic acid, rifampicin, high-level mupirocin and daptomycin where resistance was below 4% (Table 8). Resistance was not detected for vancomycin, teicoplanin or linezolid. Resistance levels varied between regions with Vic/Tas having the highest proportions for the top six antimicrobials for resistance. This is in contrast with previous AGAR hospital-onset surveys where NSW/ACT had the highest levels for resistance. WA once again had the lowest levels of resistance for these antimicrobials. Compared with Vic/Tas, WA had lower levels of resistance by 29 to 54 PP: for erythromycin (29 PP), clindamycin (35 PP), gentamicin (36 PP), co-trimoxazole (36 PP), tetracycline (41 PP) and ciprofloxacin (54 PP). 291/713 (40.8%) MRSA were multiresistant (resistant to 3 or more non-β-lactams). The proportion of MRSA that were multiresistant ranged from 7.6% in WA to 54.2% in Vic/Tas.

Table 8. MRSA: number and proportion non-susceptible

	NSW/ACT (n=235)		Qld/NT (n=180)		SA (n=55)		Vic/Tas (n=177)		WA (n=66)		Aus (n=713)		Difference across regions	
Drug	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	***P***	***X*²**
Erythromycin	164	69.8	103	57.2	28	50.9	131	74.0	30	45.5	456	64.0	**<0.0001**	28.63
Clindamycin*	89	37.9	43	23.9	10	18.2	68	38.4	2	3	212	29.7	**<0.0001**	42.82
Tetracycline	91	38.7	59	32.8	12	21.8	76	42.9	1	2	239	33.5	**<0.0001**	43.66
Co-trimoxazole	87	37.0	50	27.8	11	20.0	69	39.0	2	3	219	30.7	**<0.0001**	37.54
Ciprofloxacin	188	80.0	85	47.2	34	61.8	150	84.7	20	30.3	477	66.9	**<0.0001**	115.7
Gentamicin	85	36.2	58	32.2	7	12.7	66	37.3	1	2	217	30.4	**<0.0001**	42.07
Fusidic Acid	5	2	12	7	1	2	6	3	2	3	26	4	0.1444	6.844
Rifampicin	3	1	7	4	0	0	3	2	1	2	14	2	0.2598	5.279
Mupirocin†	4	2	5	3	0	0	0	0	0	0	9	1	0.1121	7.492
Daptomycin	0	0	2	1	0	0	0	0	0	0	2	1	0.2038	5.939

* Constitutive resistance
† High-level resistance

6.2 Trend data: methicillin-resistant *S. aureus*, 2005 - 2011

The national proportion of MRSA in 2011 was 30.3% which was not significantly different from the proportions identified in 2005, 2007 or 2009 (31.9%, 32.9% and 33.6% respectively, P=0.3856). Apart from NSW/ACT which had a significant reduction in the proportion of MRSA since 2005 (from 43.4% to 36.8%, P=0.0172), the proportions were stable across regions (Table 9).

Table 9. Proportion (%) of *S. aureus* that are MRSA, 2005 to 2011

	NSW/ACT	QLD/NT	SA	Vic/Tas	WA	Aus
2005	43.4	26.7	24.7	31.6	22.5	31.9
2007	41.3	31.0	27.2	33.3	19.0	32.9
2009	41.4	30.7	27.3	34.6	28.2	33.6
2011	36.8	30.5	21.7	32.7	19.9	30.3
P	**0.0172**	0.1627	0.5235	0.5108	0.8577	0.3856
X^2 for trend	5.673	1.949	0.4070	0.4325	0.03215	0.7527

Some significant improvements in resistance to the non-β-lactams have occurred since the first AGAR hospital inpatients survey in 2005 (Table 10). Nationally, resistance has decreased for erythromycin (80.0% in 2005 to 64.0% in 2011, P<0.0001), clindamycin (44.2% to 29.7%, P<0.0001), tetracycline (59.4% to 33.5%, P<0.0001), co-trimoxazole (60.3% to 30.7%, P<0.0001), ciprofloxacin (76.8% to 66.9%, P<0.0001), gentamicin (60.6% to 30.4%, P<0.0001) and rifampicin (5.2% to 2.0%, P=0.0003) while resistance has remained stable for fusidic acid (4.3% to 3.6%, P=0.2623) and high-level mupirocin (0.6% to 1.3%, P=0.4754). The national decreases in resistance may primarily be the result of significant regional decreases in NSW/ACT and Vic/Tas particularly for erythromycin, tetracycline, co-

trimoxazole and gentamicin. Significant falls in ciprofloxacin resistance occurred in NSW/ACT and Qld/NT, for rifampicin in Qld/NT and SA, and for fusidic acid in SA.

Table 10. Proportion (%) of MRSA resistant to the non-β-lactams, 2005 to 2011

	NSW/ACT	QLD/NT	SA	Vic/Tas	WA	Aus
Erythromycin						
2005	86.5	72.9	60.7	90.4	57.5	80.0
2007	80.5	75.0	70.4	86.4	41.7	77.2
2009	78.2	67.1	72.7	74.4	50.0	70.9
2011	69.8	57.2	50.9	74.0	45.5	64.0
P	**<0.0001**	**0.0003**	0.5435	**<0.0001**	0.2538	**<0.0001**
X^2 for trend	24.04	12.9	0.3691	26.9	1.302	61.22
Clindamycin						
2005	68.7	41.8	8.3	41.2	10.0	44.2
2007	49.5	44.3	11.3	30.5	8	37.9
2009	50.9	37.6	11.7	33.6	10.2	35.0
2011	37.9	23.9	18.2	38.4	3	29.7
P	**<0.0001**	**0.0001**	0.1021	0.5697	0.2388	**<0.0001**
X^2 for trend	42.3	14.4	2.672	0.3232	1.388	36.3
Tetracycline						
2005	69.0	44.6	35.7	83.0	6	59.4
2007	62.8	49.1	42.3	67.1	3	54.9
2009	55.4	50.0	46.8	47.6	3	45.1
2011	38.7	32.8	21.8	42.9	2	33.5
P	**<0.0001**	0.0382	0.3296	**<0.0001**	0.1132	**<0.0001**
X^2 for trend	54.14	4.297	0.9503	88.22	2.509	121.7
Co-trimoxazole						
2005	70.1	51.4	32.1	80.8	8	60.3
2007	62.2	56.6	40.8	65.3	3	55.9
2009	54.2	42.9	36.4	45.6	2	41.6
2011	37.0	27.8	20.0	39.0	3	30.7
P	**<0.0001**	**<0.0001**	0.2037	**<0.0001**	0.0975	**<0.0001**
X^2 for trend	64.99	27.1	1.616	92.47	2.746	172.4
Ciprofloxacin						
2005	89.4	62.7	54.8	88.2	42.5	76.8
2007	85.9	67.0	69.0	88.7	26.7	76.7
2009	83.0	60.5	68.8	86.0	29.6	71.2
2011	80.0	47.2	61.8	84.7	30.3	66.9
P	**0.0009**	**0.001**	0.2784	0.219	0.1211	**<0.0001**
X^2 for trend	11.08	10.8	1.175	1.511	2.403	25.24
Gentamicin						
2005	69.8	55.4	33.3	79.5	5	60.6
2007	62.5	57.1	38.0	64.8	5	55.5
2009	55.4	49.1	42.9	44.4	3	43.7
2011	36.2	32.2	12.7	37.3	2	30.4
P	**<0.0001**	**<0.0001**	0.0838	**<0.0001**	0.1932	**<0.0001**
X^2 for trend	65.3	22.02	2.991	93.84	1.693	168.1
Fusidic acid						
2005	4	6	11.9	2	4	4
2007	3	7	9	1	5	4
2009	2	5	4	3	3	3
2011	2	7	2	3	3	4
P	0.1248	0.8575	**0.0099**	0.1846	0.6501	0.2623
X^2 for trend	2.356	0.03224	6.649	1.76	0.2057	1.257
Rifampicin						
2005	1	17.5	6	3	1	5
2007	1	15.1	4	2	0	5
2009	1	8	0	4	2	3
2011	1	4	0	2	2	2
P	0.7686	**<0.0001**	**0.0099**	0.9458	0.6559	**0.0003**
X^2 for trend	0.08653	22.08	6.646	0.004622	0.1985	13.3

	NSW/ACT	QLD/NT	SA	Vic/Tas	WA	Aus
Mupirocin (High level resistance)						
2005	1	0	1	1	1	1
2007	1	3	0	2	2	1
2009	1	1	0	1	1	1
2011	2	3	0	0	0	1
P	0.2723	0.1588	0.2138	0.3288	0.4142	0.4754
X^2 for trend	1.205	1.986	1.546	0.9537	0.6666	0.5094

6.3 Methicillin-susceptible *S. aureus*, 2011

The majority (69.7%) of *S. aureus* isolates were MSSA. Resistance to non-β-lactam antimicrobials with the exception of erythromycin (13.2%) was uncommon in MSSA (Table 11). No resistance was detected for vancomycin, teicoplanin or linezolid.

Resistance levels between regions varied significantly for penicillin and high-level mupirocin. SA had the highest rates of resistance for penicillin and Qld/NT was highest for high-level mupirocin.

Table 11. MSSA: number and proportion non-susceptible

	NSW/ACT (n=404)		Qld/NT (n=411)		SA (n=199)		Vic/Tas (n=364)		WA (n=266)		Aus (n=1644)		Difference across regions	
Drug	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	***P***	***X*²**
Penicillin	346	85.6	355	86.4	179	89.9	321	88.2	212	79.7	1413	85.9	**0.0121**	12.84
Erythromycin	49	12.1	64	15.6	25	12.6	52	14.3	27	10.2	217	13.2	0.2846	5.027
Clindamycin*	10	3	8	2	3	2	9	3	7	3	37	2	0.9065	1.022
Tetracycline	13	3	9	2	2	1	13	4	9	3	46	3	0.3658	4.309
Co-trimoxazole	9	2	8	2	3	2	8	2	5	2	33	2	0.9782	0.4494
Ciprofloxacin	15	4	12	3	5	3	15	4	8	3	55	3	0.8094	1.597
Gentamicin	5	1	7	2	1	1	3	1	2	1	18	1	0.2862	1.137
Fusidic Acid	11	3	24	6	8	4	3	1	9	3	55	3	0.1753	1.837
Rifampicin	0	0	0	0	1	1	0	0	0	0	1	1	0.1225	7.266
Mupirocin†	3	1	20	5	0	0	0	0	3	1	26	2	**0.0404**	4.201
Daptomycin	1	1	0	0	0	0	0	0	0	0	1	1	0.5460	3.071

* Constitutive resistance
† High-level resistance

6.4 Trend data: methicillin-susceptible *S. aureus*, 2005 - 2011

Nationally, there were small changes in the magnitude of resistance for MSSA in clindamycin (1.3% in 2005 to 2.3% in 2011, P=0.0057), ciprofloxacin (2.4% to 3.3%, P=0.0315), co-trimoxazole (1.4% to 2.0%, P=0.0475) and high-level mupirocin (0.3% to 1.6%, P=0.0001). In Vic/Tas, there were significant decreases in resistance in gentamicin (3.2% to 0.8%, P=0.0294) and fusidic acid (3.6% to 0.8%, P=0.0462). In WA, tetracycline resistance increased from 0.0% to 3.4% (P=0.0056) and high-level mupirocin resistance increased from 0.0% to 1.1% (P=0.0253). The greatest increase was for high-level mupirocin resistance in Qld/NT (0.4% to 4.9%, P<0.0001) (data not shown).

6.5 Inducible clindamycin resistance

There were 348 (15.8%) erythromycin resistant and clindamycin intermediate/susceptible isolates. Of these 306 (87.9%) were D-test positive indicating inducible clindamycin resistance. For MRSA the figure was 203/224 (90.6%) and for MSSA 103/124 (83.1%).

Results of the ICR well of the Vitek2® AST-P612 card were compared with the D-test results (Table 12). The positive predictive value of the ICR well was 98% with a lower negative predictive value (62%).

Table 12. Results of the D-test compared with the ICR well of the Vitek2® AST-P612 card

	AST-P612 ICR well	Positive	Negative
D-test	Positive	283	23
	Negative	5	37

7 Discussion

This survey demonstrates that MRSA remains a significant burden in Australian hospitals. However, the trends over 2005 to 2011 may be the result of several limitations of the data. The mix of laboratories has altered over time with one fewer NSW, one fewer SA and one fewer Vic laboratory participating in the 2011 survey compared with the 2005 survey. However, past analysis of results of only laboratories that participated in all surveys gave similar results[29].

For 2011 the national proportion of *S. aureus* that were MRSA was 30.3% which was not significantly different to the proportions seen in past AGAR hospital-onset surveys (X^2 for trend 0.7527, P=0.3856). The only region to have a significant change over this time period was NSW/ACT which had a reduction in the proportion of MRSA of 7 PP from 2005 to 2011 (P=0.0172). Differences between regions in this survey were significant with SA and WA having a lower proportion than other regions. Differences between institutions within a region may be explained by the mean age of the different populations serviced by the institution (one institution in Vic and one in SA are children's hospitals) and by differences in infection control protocols. The proportion of MRSA amongst the different specimen types was similar. The high proportion of MRSA in invasive isolates is of concern as MRSA bacteraemia is associated with increased mortality compared with MSSA[4,5,6,7]. Direct comparison with prevalence in other countries is difficult due to methodological differences, however the European Centre for Disease Prevention and Control reports on antimicrobial resistance in healthcare-associated infections in *S. aureus* from nine countries[35]. In 2007, methicillin resistance in surgical site infections was 30.7% and ICU-acquired blood stream infections 41.7%. Targeted MRSA public health initiatives in several European countries appears to have been successful as methicillin resistance in *S. aureus* significantly decreased from 2004 to 2007 in Austria, France and Spain. Countries in our region report very high rates of MRSA. The Asian Network for Surveillance of Resistant Pathogens reported that from 2004-2006 the proportion of methicillin resistance in healthcare-associated *S. aureus* infections ranged from 38.1% in the Philippines to 86.5% in Sri Lanka[12].

More than 60% of the MRSA isolates for 2011 study were resistant to erythromycin and ciprofloxacin, and more than 30% were resistant to tetracycline, co-trimoxazole and gentamicin. Regional differences were again common due to different MRSA clones circulating in Australia. In the 1980s and 1990s multiresistant strains (later typed as ST239-III or Aus2/3 EMRSA) became epidemic in the eastern Australian states with some spread to hospitals in SA, NT and Tas[36]. In 1982, a state-wide MRSA policy was introduced in WA with the aim of preventing these strains from becoming established in WA hospitals. As a result, MRSA with tetracycline, co-trimoxazole and gentamicin resistance (characteristic of ST239-III) are rare in WA - 3% or lower in this survey. Erythromycin and ciprofloxacin resistance was more widespread in this survey with at least 30% of MRSA with this profile in any region. Erythromycin and ciprofloxacin resistance is common in ST239-III strains but is also characteristic of ST22-IV (EMRSA-15). ST22-IV is a common healthcare-associated MRSA (HA-MRSA) in Australia and is found in all regions[37]. Resistance was

not detected for vancomycin, teicoplanin or linezolid. Compared with previous AGAR hospital inpatient surveys in 2005, 2007 and 2009, the proportion of MRSA resistant to erythromycin, clindamycin, tetracycline, co-trimoxazole, ciprofloxacin, gentamicin and rifampicin has decreased nationally lead by significant decreases in NSW/ACT and Vic/Tas whilst the proportion of *S. aureus* that are MRSA has remained stable in most regions and nationally. This finding suggests that non-multiresistant community strains of MRSA are increasing in Australian hospitals at the expense of the long-established multiresistant ST239-III. Given reports of outbreaks of CA-MRSA in Australian hospitals are thought to be rare,[38,39] it is likely that many infections in hospital inpatients are caused by the patients' own colonising strains acquired prior to admission. It appears that current infection control procedures are successful in preventing their spread. Although at present in Australia there is no evidence of increasing resistance in local CA-MRSA[40], data from the United States of America show that previously non-multiresistant CA-MRSA can acquire multiple resistances over time[41]. With community clones such as the Qld clone (ST93-IV), South Western Pacific (ST30-IV) and WA 1 (ST1-IV) well established in Australia[32,42], it is important to monitor susceptibility patterns to MRSA over time as this information will guide therapeutic practices. In addition to this threat, virulent multiresistant overseas CA-MRSA have recently been isolated in Australia[43] and only time will tell if these difficult to treat clones become established in the Australian community or healthcare institutions.

This report should be read in conjunction with the SAP 2011 MRSA Epidemiology and Typing Report (www.agargroup.org/surveys).

8 References

1. Turnidge J, Kotsanas D, Munckhof W, Roberts S, Bennett C, Nimmo G, et al. *Staphylococcus aureus* bacteraemia: a major cause of mortality in Australia and New Zealand. MJA 2009;191:368-373.
2. Turnidge J. Australia New Zealand Cooperative on Outcomes in Staphylococcal Sepsis. Antimicrobials 2009, Melbourne, 26-28 February 2009.
3. Nimmo GR, Bell JM, Mitchell D, et al. Antimicrobial resistance in *Staphylococcus aureus* in Australian teaching hospitals 1989-1999. *Microb Drug Resis* 2003;9:155-60.
4. Whitby M, McLaws ML, Berry G. The risk of death from methicillin resistant *Staphylococcus aureus* bacteraemia: a meta-analysis. *Med J Aust* 2001; 175 (5): 264-267.
5. Lawes T, Edwards B, Lopez-Lozano J-M, 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:e000797.
6. Hanberger H, Walther S, Leone M, Barie P, Rello J, Lipman J et al. Increased mortality associated with methicillin-resistant *Staphylococcus aureus* (MRSA) infection in the intensive care unit: results from the EPIC II study. *Int J Antimicrob Agents* 2011;38:331-5.
7. De Kraker M, Wolkewitz M, Davey P, Grundmann H. Clinical impact of antimicrobial resistance in European hospitals: excess mortality and length of hospital stay related to methicillin resistant *Staphylococcus aureus* bloodstream infections. *Antimicrob Agents Chemother* 2011;55:1598-1605
8. Cosgrove S, Qi Y, Kaye K, Harbarth S, Karchmer A, Carmeli Y. The impact of methicillin resistance in *Staphylococcus aureus* bacteraemia on patient outcomes: mortality, length of stay, and hospital charges. *Infect Control Hosp Epidemiol* 2005;26:166-74.
9. Anderson D, Kaye K, Chen L, Schmader K, Choi Y, Sloane R et al. Clinical and financial outcomes due to methicillin resistant *Staphylococcus aureus* surgical site infection: a multi-center matched outcomes study. PLoS One 2009;15:e8305
10. Rubio-Terres C, Garau J, Grau S, Martinez-Martinez L. Cost of bacteraemia caused by methicillin-resistant vs. methicillin susceptible *Staphylococcus aureus* in Spain: a retrospective cohort study. *Clin Microbiol Infect* 2010;16:722-8
11. Joo E, Chung D, Ha Y, Park S, Kang S, Kim S et al. Community-associated Panton-Valentine leucocidin-negative methicillin resistant *Staphylococcus aureus* clone (ST72-

MRSA-IV) causing healthcare associated pneumonia and surgical site infection in Korea. *J Hosp Infect* 2012;81:149-55.
12. Song J, Hseuh P, Chung D, Ko K, Kang C, Peck K et al. Spread of methicillin-resistant *Staphylococcus aureus* between the community and the hospitals in Asian countries: an ANSORP study. *J Antimicrob Chemother* 2011;66:1061-9.
13. Otter J, French G. Community-associated methicillin-resistant *Staphylococcus aureus* strains as a cause of healthcare-associated infection. *J Hosp Infect* 2011;79:189-93.
14. Green S, Marsh P, Ahmad N, Jefferies J, Clarke S. Characterization of community and hospital *Staphylococcus aureus* isolates in Southampton, UK. *J Med Microbiol* 2010;59:1084-8.
15. Seybold U, Kourbatova E, Johnson J, Halvosa S, Wang Y et al. Emergence of community-associated methicillin-resistant *Staphylococcus aureus* USA300 genotype as a major cause of health care-associated blood stream infections. *Clin Infect Dis.* 2006;42:647-656.
16. Sung J, Lee J, Choi E, Lee H. Changes in molecular epidemiology of community associated and healthcare-associated methicillin-resistant *Staphylococcus aureus* in Korean children. *Diagn Microbiol Infect Dis.* 2012;74:28-33.
17. Wu K, Zhang K, McClure J, Zhang J, Schrenzel J, Francois P et al. A correlative analysis of epidemiologic and molecular characteristics of methicillin-resistant *Staphylococcus aureus* clones from diverse geographic locations with virulence measured by *Caenorhabditis elegans* host model.
18. Coombs G, Georing R, Chua K, Monecke S, Howden B, Stinear T et al. The molecular epidemiology of the highly virulent ST93 Australian Community *Staphylococcus aureus* strain. PLos One. 2012;7:e43037.
19. Cheung G, Wang R, Khan B, Sturdevant D, Otto M. Role of the accessory gene regulator agr in community-associated methicillin-resistant *Staphylococcus aureus* pathogenesis. *Infect Immun.* 2011;79:1927-35.
20. Moore C, Hingwe A, Donabedian S, Perri M, Davis S, Haque N et al. Comparative evaluation of epidemiology and outcomes of methicillin-resistant *Staphylococcus aureus* (MRSA) USA300 infections causing community- and healthcare-associated infections. *Int J Antimicrob Agents.* 2009;34:148-155.
21. Davis S, Rybak M, Amjad M, Kaatz G, McKinnon P. Characteristics of patients with healthcare-associated infection due to SCCmec type IV methicillin-resistant *Staphylococcus aureus*. *Infect Control Hosp Epidemiol*. 2006;27:1025-1031.
22. Benoit S, Estivariz C, Mogdasy C, Pedreira W, Galiana A, Galiana A et al. Community strains of methicillin-resistant *Staphylococcus aureus* as a potential cause of healthcare-associated infections, Uruguay, 2002-2004. *Emerg Infect Dis*. 2008;14:1216-23.
23. Coombs G, Van Gessel H, Pearson J, Godsell M-R, O'Brien F, Christiansen K. Controlling a multicentre outbreak involving the New York/Japan methicillin resistant *Staphylococcus aureus* clone. *Infect Control Hosp Epidemiol*. 2007;28:845-852.
24. Grayson M, Jarvie L, Martin R, Johnson P, Jodoin M, 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. MJA 2008;188: 633-640.
25. McLaws ML, Pantle AC, Fitzpatrick KR, Hughes CF. More than hand hygiene is needed to affect methicillin resistant *Staphylococcus aureus* clinical indicator rates: clean hands save lives part IV. MJA 2009;19:S26-S31.
26. Nimmo G, Bell J, Collignon P. Fifteen years of surveillance by the Australian Group for Antimicrobial Resistance. *Comm Dis Intell*. 2003;27 Suppl:S47-S54.
27. Nimmo G, Pearson J, Collignon P, Christiansen K, Coombs G, Bell J et al. Prevalence of MRSA among *Staphylococcus aureus* isolated from hospital inpatients, 2005: Report from the Australian group for antimicrobial resistance. *Commun Dis Intell.* 2007;31:288-296.
28. Nimmo G, Collignon P, Coombs G, Christiansen K, Bell J, Pearson J et al. *Staphylococcus aureus* survey 2007 antimicrobial susceptibility report. www.agargroup.org/surveys.
29. Nimmo G, Pearson J, Collignon P, Christiansen K, Coombs G, Bell J et al. Antimicrobial susceptibility of *Staphylococcus aureus* isolated from hospital inpatients, 2009. *Commun Dis Intell.* 2011;35:237-243.

30. Coombs G, Nimmo G, Pearson J, Christiansen K, Bell J, Collignon P, et al. Prevalence of MRSA strains among *Staphylococcus aureus* isolated from outpatients, 2006: Report from the Australian Group on Antimicrobial Resistance. *Comm Dis Intell*. 2009;33:10-20.
31. Nimmo G, Pearson J, Coombs G, Christiansen K, Collignon P, Bell J et al. *Staphylococcus aureus* programme 2008 (SAP 2008) community survey antimicrobial susceptibility report. www.agargroup.org/surveys.
32. Nimmo G, Pearson J, Coombs G, Christiansen K, Collignon P, McLaws M-L. *Staphylococcus aureus* programme 2010 (SAP 2010) community survey antimicrobial susceptibility report. www.agargroup.org/surveys.
33. Clinical and Laboratory Standards Institute (2012). Performance standards for antimicrobial susceptibility testing; twenty-second informational supplement. M100-S22. CLSI, Villanova, PA, USA.
34. Comite de L'antibiogramme de la Societe Francaise de microbiologie. Recommendations 2010 (www.sfm-microbiologie.org).
35. European Centre for Disease Prevention and Control. Surveillance of health-care associated infections in Europe, 2007. Stockholm: ECDC;2012.
36. Nimmo G, Bell J, Mitchell D, Gosbell I, Pearman J, Turnidge J. Antimicrobial resistance in *Staphylococcus aureus* in Australian teaching hospitals 1989-1999. *Microb Drug Resis*. 2003;9:155-60.
37. Coombs G, Pearson J, Nimmo G, Christiansen K. *Staphylococcus aureus* programme 2011 (SAP 2011) hospital-onset survey MRSA epidemiology and typing report. www.agargroup.org/surveys.
38. O'Brien F, Pearman J, Gracey M, Riley T, Grubb W. Community strain of methicillin-resistant *Staphylococcus aureus* involved in a hospital outbreak. *J Clin Microbiol* 1999;37:2858-2862.
39. Schlebusch S, Price G, Hinds S, Nourse C, Schooneveldt J, Tilse M, 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;29:1311-1314.
40. Chua K, Laurent F, Coombs G, Grayson M, Howden B. Not community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA)! A clinician's guide to community MRSA – its evolving antimicrobial resistance and implications for therapy. *Clin Infect Dis*. 2011;52:99-114.
41. Diep B, Chambers H, Graber C, Szumowski J, Miller L, Han L, et al. Emergence of multidrug-resistant, community associated, methicillin resistant *Staphylococcus aureus* clone USA300 in men who have sex with men. *Ann intern Med*. 2008;148:249-257.
42. Coombs G, Pearson J, Christiansen K, Nimmo G. Widespread dissemination of the Panton-Valentine leucocidin ST93-MRSA-IV (Qld CA-MRSA) clone in the Australian community. 20th European Congress on Clinical Microbiology and Infectious Diseases, Vienna, Austria, April 2010.
43. Pearson J, Coombs G, Tan H-L, Cramer S, Wilson L, Chew Y, et al. Introduction of a multi-resistant Panton-Valentine leucocidin positive community associated MRSA into Western Australia. International Symposium on Staphylococci and Staphylococcal Infections, Bath, UK, September, 2008

9 Acknowledgements

AGAR members:

Victoria	
Alfred Hospital	Denis Spelman, Michael Huysmans
Austin Hospital	Ben Howden, Peter Ward
Monash Medical Centre	Tony Korman, Despina Kotsanas
Royal Women's and Children's Hospital	Suzanne Garland, Gena Gonis
St Vincent's Hospital	Mary Jo Waters, Linda Joyce
New South Wales	
Concord Hospital	Thomas Gottlieb, Graham Robertson
Douglass Hanly Moir Pathology	Miriam Paul, Richard Jones
Nepean Hospital	James Branley, Donna Barbaro
Royal North Shore Hospital	George Kotsiou, Peter Huntington
Royal Prince Alfred Hospital	Colin MacLeod, Bradley Watson
Sydney South West Pathology Service, Liverpool	Iain Gosbell, Annabelle LeCordier
Westmead Hospital	David Mitchell, Lee Thomas
Australian Capital Territory	
The Canberra Hospital	Peter Collignon, Susan Bradbury
South Australia	
SA Pathology, Flinders Medical Centre	Kelly Papanaoum, Hendrik Pruul
SA Pathology, Royal Adelaide Hospital	Morgyn Warner, Fleur Manno
SA Pathology, Women's and Children's Hospital	John Turnidge, Jan Bell
Western Australia	
PathWest Laboratory Medicine-WA, Fremantle Hospital	David McGechie, Rebecca Wake
PathWest Laboratory Medicine-WA, QEII Medical Centre	Ronan Murray, Barbara Henderson
PathWest Laboratory Medicine-WA, Royal Perth Hospital	Keryn Christiansen, Geoffrey Coombs
St John of God Pathology, WA	Victoria D'Abrera, Sindy Budalich
Queensland	
Pathology Queensland, Cairns Base Hospital	Enzo Binotto, Bronwyn Thomsett
Pathology Queensland, Gold Coast Hospital	Petra Derrington, Sharon Dal-Cin
Pathology Queensland, Prince Charles Hospital	Chris Coulter, Sonali Coulter
Pathology Queensland, Princess Alexandra Hospital	Joan Faoagali, Joel Douglas
Pathology Queensland Central Laboratory	Graeme Nimmo, Narelle George
Sullivan Nicolaides Pathology	Jenny Robson, Georgia Peachy
Tasmania	
Launceston General Hospital	Mhisti Rele, Kathy Wilcox
Royal Hobart Hospital	Louise Cooley, Rob Peterson
Northern Territory	
Royal Darwin Hospital	Rob Baird, Jann Hennessy