Demographics, antimicrobial susceptibility and molecular epidemiology of *Staphylococcus aureus* in New Zealand, 2014

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LIST OF ABBREVIATIONS

ATCC	American Type Culture Collection
BURP	based upon repeat pattern
CC	multilocus sequence type clonal complex
CLSI	Clinical and Laboratory Standards Institute
EUCAST	European Committee on Antimicrobial Susceptibility Testing
lukS-PV	Panton Valentine leukocidin gene
MDR	multidrug resistant
MELAA	Middle Eastern/Latin American/African ethnic group
MIC	minimum inhibitory concentration
MIC_{50}	MIC at which at least 50% of isolates inhibited
MIC_{90}	MIC at which at least 90% of isolates inhibited
MLST	multilocus sequence typing
MRSA	methicillin-resistant *Staphylococcus aureus*
MSSA	methicillin-susceptible *Staphylococcus aureus*
nuc	thermostable nuclease gene
NZRM	New Zealand Culture Collection – Medical Section
PCR	polymerase chain reaction
PFGE	pulsed-field gel electrophoresis
PVL	Panton Valentine leukocidin
spa	staphylococcal protein A gene
Spa-CC	clonal complex of related *spa* types

SUMMARY

Recent studies have described significant increases in the incidence of *Staphylococcus aureus* infections in New Zealand over the past decade. These increases have been driven mainly by community-onset, methicillin-susceptible *S. aureus* (MSSA) skin and soft tissue infection (SSTI). This survey was undertaken to collect basic demographic data on patients with *S. aureus* infections; to provide information on antimicrobial resistance among *S. aureus*, including resistance to the topical agents fusidic acid and mupirocin; to determine the prevalence of the Panton Valentine leukocidin (PVL) toxin among *S. aureus*; and to identify and characterise the major MSSA clones.

Hospital and community diagnostic microbiology laboratories throughout New Zealand were requested to refer to ESR *S. aureus* (methicillin-susceptible and methicillin-resistant) isolated from clinical specimens during the 3 days, 18-20 March 2014. Patient demographic and hospitalisation history data was provided by referring laboratories or obtained from the Ministry of Health's national collections. Antimicrobial susceptibility to cefoxitin, ceftaroline, ciprofloxacin, clindamycin, co-trimoxazole, doxycycline, erythromycin, fusidic acid, gentamicin, mupirocin, rifampicin and vancomycin was determined by agar dilution; PVL genes detected by PCR; and *spa* typing, multilocus sequence typing (MLST), and DNA microarrays used to identify and characterise major *S. aureus* clones.

1185 *S. aureus* isolates were received for the survey. A subsample (stratified by referring laboratory and patient age) of 751 isolates was selected for the test panel. The results were weighted to allow for this subsampling. 83.7% of the isolates were from SSTI, with only 2.1% from invasive sites. The majority (74.1%) of patients with *S. aureus* infections were community patients who had not been in a healthcare facility in the previous 3 months.

The national point-prevalence rate of *S. aureus* infection was estimated to be 30.8 per 100 000 population. The highest age-specific prevalence rates occurred in the <5 year (56.2 per 100 000) and ≥65 year (62.3 per 100 000) age groups. The point-prevalence

continued

rates for the Māori and Pacific peoples ethnic groups (50.7 and 49.6 per 100 000, respectively) were approximately twice that for the European and Other ethnic group (25.7 per 100 000). Rates by deprivation index increased between each NZDep2006 quintile from the least deprived quintile 1 to the most deprived quintile 5.

The point-prevalence rates in Northland, Bay of Plenty, Hawke's Bay and Wairarapa District Health Boards were significantly ($p \leq 0.05$) higher than the national rate.

8.9% of *S. aureus* isolates were methicillin resistant (MRSA). Among MRSA, resistance to fusidic acid, erythromycin and ciprofloxacin was common at 57.6%, 25.3% and 16.1%, respectively. Resistance was uncommon among MSSA with the notable exceptions of 21.8% fusidic acid resistance and 8.7% mupirocin resistance. No MRSA or MSSA were resistant to ceftaroline, co-trimoxazole or vancomycin.

Methicillin resistance and fusidic acid resistance were both more prevalent among *S. aureus* isolated from patients in the youngest (<5 year) age group, and from patients in the Northern, Midland and Central regions. Methicillin resistance was also more prevalent among isolates from healthcare facility patients than isolates from community patients.

PVL genes were detected in a quarter (25.2%) of *S. aureus* isolates, and the prevalence among MSSA and MRSA was the same. PVL genes were significantly more prevalent among *S. aureus* isolated from patients in the 15-24 year age group and the Pacific people ethnic group, from community patients, and from SSTI than isolates from patients in other age and ethnic groups, healthcare facility patients or other types of infections. The prevalence of PVL was strongly associated with particular MSSA clones and MRSA strains.

MLST and DNA microarray testing of representative isolates of each of the most common *spa* types identified seven dominant MSSA clones. These seven clones collectively accounted for 44.7% of MSSA. Among MRSA, the AK3 MRSA strain was predominant and accounted for 59.4% of MRSA isolates. Both the most prevalent MSSA clone (CC1-MSSA) and AK3 MRSA are characterised by fusidic acid resistance.

continued

In conclusion, in New Zealand the vast majority of *S. aureus* infections are due to MSSA and are community-associated SSTI. There are significant demographic variations in the prevalence of *S. aureus* infections. Rates of multiresistance among both MSSA and MRSA are low. However, fusidic acid resistance is prevalent, associated with both the dominant MSSA clone and the dominant AK3 MRSA strain, and likely to be a result of the high usage of topical preparations of this agent.

RECOMMENDATIONS

- Future surveys should be undertaken at regular intervals and use similar methodologies to provide comparable data to monitor trends in *Staphylococcus aureus* infections and antimicrobial susceptibility in New Zealand.
- Establishment of a national system of ongoing, prospective surveillance of *S. aureus* bacteremia should be considered. Many countries and regions in the developed world (eg, Australia and Europe) base their national surveillance of *S. aureus* infections on bacteraemic isolates and a similar approach in New Zealand would facilitate international comparisons.
- Research into the reasons for the demographic disparities in *S. aureus* infections should be a priority.
- Further investigation of the genetic mechanisms of fusidic acid resistance would be useful given the high rate of fusidic acid resistance found in this and other recent New Zealand studies.
- The use of topical antimicrobials should be reviewed and, where warranted, should be restricted, due to the high rate of fusidic acid resistance which correlates with increases in the usage of topical preparations of this agent.

1 INTRODUCTION

Staphylococcus aureus is a major human pathogen causing infections that result in significant morbidity and mortality.[1-3] Although *S. aureus* is most commonly associated with skin and soft tissue infection (SSTI), it is also responsible for a range of serious invasive infections such as osteomyelitis, necrotizing pneumonia and bacteraemia. *S. aureus* infections commonly occur among patients in the community as well as patients in healthcare facilities.

The incidence of invasive and non-invasive *S. aureus* infections in New Zealand is among the highest reported in the developed world.[4] Moreover, recent studies have described significant increases in the incidence of *S. aureus* infections, particularly SSTI, in New Zealand over the past decade.[4,5] A national study found that hospital admissions for *S. aureus* SSTI rose from 81 to 140 cases per 100 000 between 2000 and 2011.[4] Similarly an Auckland hospital- and laboratory-based study over much the same time period reported a significant increase in non-invasive *S. aureus* infections, largely driven by community-onset methicillin-susceptible *S. aureus* (MSSA) infections.[5]

Perhaps not unexpectedly, as has been observed for infectious diseases generally in New Zealand, there are also distinct ethnic disparities in rates of *S. aureus* infections. A recent Auckland study found that, compared with European children, Māori children were twice as likely, and Pacific children almost three times as likely, to be admitted to hospital with *S. aureus* SSTI.[6]

During the past two decades, the epidemiology of *S. aureus* infections has changed considerably in several parts of the world, particularly due to the spread of community-associated methicillin-resistant *S. aureus* (MRSA).[3] In New Zealand, the majority of *S. aureus* disease is due to MSSA, with recent aggregate national antimicrobial susceptibility data showing a stable MRSA prevalence of approximately 8–10%, although the prevalence of MRSA differs between regions.[7,8]

The molecular epidemiology of MRSA in New Zealand is relatively well described due to the annual national surveys of MRSA.[8] However, comparatively little is known about the molecular epidemiology of MSSA. Furthermore, there are notable gaps in current national information about the susceptibility of *S. aureus* to commonly prescribed antimicrobial agents, in particular topical agents such as fusidic acid and mupirocin. The last national survey of antimicrobial susceptibility among *S. aureus*, undertaken in 1999, found high rates

of fusidic acid resistance (17%) and mupirocin resistance (14%).[9] A 2013 Auckland study found an alarming 29% of *S. aureus* tested were fusidic acid resistant and hypothesized the increase in fusidic acid resistance had been driven by concurrent increases in community prescribing of topical preparations of this antimicrobial. Moreover, this study found that fusidic acid resistance was highly clonal and was associated with MSSA belonging to multilocus sequence type clonal complex 1 (CC1) and CC5 MRSA (ie, the AK3 MRSA strain).[10]

Clinical isolates of *S. aureus* harbor an array of virulence factors involved in adhesion, invasion and immune evasion. Over the past decade there has been considerable attention paid to one particular toxin produced by some strains of *S. aureus* – the Panton Valentine leukocidin (PVL). This attention first focused on the association of PVL with severe necrotizing pneumonia and then on PVL as a virulence determinant carried by emerging strains of community-associated MRSA. While there is still considerable uncertainty about the role of PVL in disease, colonisation and clinical outcome, PVL-producing strains of *S. aureus* appear to be strongly associated with SSTI and with community-onset infections.[11] Previous studies in Auckland have suggested that *S. aureus* isolates in New Zealand have a high prevalence of the genes encoding PVL, with a 2009 study reporting a rate of 37% and a 2013 study of isolates from children describing a rate of 56%.[12,13]

To provide contemporary information on antimicrobial resistance patterns and the molecular epidemiology of *S. aureus* in New Zealand, the Institute of Environmental Science and Research (ESR) collected and analysed a nationally representative sample of clinical *S. aureus* isolates in March 2014. Specifically, the aims of this survey were to:

- collect basic demographic data on patients with *S. aureus* infections;
- provide information on antimicrobial resistance among *S. aureus*, including resistance to agents such as ceftaroline (a new-generation cephalosporin active against MRSA), and the topical antimicrobials fusidic acid and mupirocin;
- determine the prevalence of PVL among *S. aureus* and whether PVL-producing strains are associated with particular types of infections and patients; and
- identify and characterise the major MSSA clones.

2 METHODS

2.1 Isolates and patient information

All hospital and community diagnostic microbiology laboratories in New Zealand, except Labtests, were requested to refer to ESR all *S. aureus* (methicillin-susceptible and methicillin-resistant) isolated from clinical specimens during the 3 days, 18-20 March 2014 inclusive. *S. aureus* isolated from screening specimens were not collected. Because of the high numbers of *S. aureus* isolated by Labtests, which provides community laboratory services for the greater Auckland area, this laboratory was requested to refer only a representative sample of approximately 40 isolates for each day of the 3-day collection period. To enable an allowance to be made for this sampling when analysing the results, Labtests also provided information on their total *S. aureus* isolations during the 3-day collection period.

When referring isolates for the survey, diagnostic laboratories supplied epidemiological data including the patient's NHI number and date of birth, whether the patient was a resident of a long-term care facility, the source or site of the specimen from which *S. aureus* was isolated, and the penicillin susceptibility of the isolate. The options laboratories were asked to use when specifying the source or site of the specimen were 'SSTI', 'blood', 'other invasive site' or 'other site', with the latter two options to be further specified.

The target number of isolates for the survey was 750. A total of 1185 *S. aureus* isolates were actually referred. Therefore, a subsample of the 1185 isolates was selected to compile a test panel for the survey. The following criteria were used to select the test panel:

- Any isolates for which a patient NHI was not provided were excluded.
- All non-duplicate isolates referred by Labtests were included.
- All non-duplicate isolates referred by Nelson Hospital Laboratory were included as these isolates were received after the subsampling was undertaken.
- All non-duplicate isolates from laboratories that referred ≤30 isolates were included.
- Non-duplicate isolates from all other laboratories were subsampled. The subsample was stratified by referring laboratory and patient age group, using a sampling frame that included all non-duplicate isolates except those from Nelson Hospital Laboratory. The age groupings used for this stratification were 0–4 years, 5–19 years, 20–64 years and ≥65 years.

Information on the patient's district health board location, ethnicity, NZDep2006 deprivation index score and recent hospitalisation history was obtained from the Ministry of Health's national collections of data. Approval to obtain the hospitalisation history information was granted by the Northern Regional Ethics Committee.

Ethnic groups presented are based on a prioritised classification of ethnicity, with the Māori ethnic group at the top of the hierarchy, followed by Pacific peoples, Asian, Middle Eastern/Latin American/African (MELAA), and European or Other (including New Zealander) ethnic groups. More information about ethnicity classification is available on the Ministry of Health website: http://www.health.govt.nz/publication/ethnicity-data-protocols-health-and-disability-sector.

Patients were categorised as healthcare facility patients if they had any admission to a healthcare facility in the 3 months prior to the date the specimen yielding *S. aureus* was taken, but not if their only admission within these 3 months was <48 hours prior to their specimen being collected. Patients with no history of any hospitalisation in the previous 3 months and who were not reported to be residents of a long-term care facility were categorised as community patients.

2.2 Antimicrobial susceptibility testing

Susceptibility to cefoxitin, ceftaroline, ciprofloxacin, clindamycin, co-trimoxazole, doxycycline, erythromycin, fusidic acid, gentamicin, mupirocin, rifampicin and vancomycin was determined by agar dilution according to the methods of the Clinical and Laboratory Standards Institute (CLSI).[14] The ceftaroline pure substance used to prepare agar dilution plates was donated by AstraZeneca (via International Health Management Associates Inc, Schaumburg, Illinois, United States). The mupirocin pure substance used was donated by GlaxoSmithKline (Reference Materials Group, GlaxoSmithKline, Durham, United Kingdom). All other antibiotic pure substances used for agar dilution were purchased from Sigma-Aldrich (Saint Louis, Missouri, United States).

Isolates that tested as erythromycin-resistant and clindamycin-susceptible by agar dilution were tested for inducible clindamycin resistance by the CLSI disc diffusion method.[15]

Minimum inhibitory concentrations (MICs) were interpreted according to CLSI guidelines, except for fusidic acid and mupirocin MICs which were interpreted according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints.[15,16]

The MIC_{50} and MIC_{90} values were defined as the MICs at which at least 50% and 90%, respectively, of isolates were inhibited. The MICs given for co-trimoxazole refer to the trimethoprim component.

Penicillin susceptibility was not tested at ESR by agar dilution, but was reported, where available, by diagnostic laboratories as part of the dataset collected on each isolate referred for the survey.

Isolates were defined as multidrug-resistant (MDR) if they were resistant to ≥3 of the following antibiotics/antibiotic classes: cefoxitin, ceftaroline, ciprofloxacin, co-trimoxazole, doxycycline, erythromycin/clindamycin, fusidic acid, gentamicin, mupirocin, rifampicin or vancomycin.

2.3 Preparation of DNA template

Boiled lysis cell suspensions were used as a source of DNA template in all polymerase chain reactions (PCRs). Plate cultures were used to prepare cell suspensions, approximately equivalent to a 0.5 McFarland standard, in DNase/RNase free water. Suspensions were heated at 99˚C for 20 minutes. The heated suspensions were centrifuged to pellet cellular debris and then stored at 4˚C. The neat supernatants were used as a source of DNA template.

2.4 PVL toxin testing

A real-time duplex PCR assay was used to detect the PVL gene, *lukS*-PV, and the *S. aureus* species-specific thermostable nuclease gene, *nuc*, simultaneously.[17] The assay was performed in 25 µL reaction volumes using AmpliTaq Gold 360 PCR Master Mix (ATG360, Applied Biosystems, Carlsbad, California, United States), 0.5 µM of each primer (Table 1), 0.5 µM of each dual-labelled probe (Table 1), an additional 2.5 mM $MgCl_2$, and 1.5 µL of DNA template. Probes and primers were synthesized by BioSearch Technologies (Novato, California, United States). The cycling conditions used were: 95°C for 5 minutes followed by 40 cycles of 20 seconds denaturation at 94°C and 40 seconds annealing at 58°C.

Controls used were a water-only, no-template control; *Enterococcus faecalis* (ATCC 29212, NZRM 2244) as a negative control for both *lukS*-PV and *nuc*; EMRSA-15 MRSA (NZRM 4393) as a negative control for *lukS*-PV and a positive control for *nuc*; and WSPP MRSA (NZRM 3534) as a positive control for both *lukS*-PV and *nuc*.

Table 1. Primers and probes used for the PVL/*nuc* real-time PCR assay

Primer name	Target gene	Primer sequence (5´-3´)
*nuc*_F		CATCCTAAAAAAGGTGTAGAGA
*nuc*_R	*nuc*	TTCAATTTTMTTTGCATTTTCTACCA
*nuc*_CFR610[1]		CFR610-TTTTCGTAAATGCACTTGCTTCAGGACCA-BHQ2
PVL_F		ACCCCCATTAGTACACAGTG
PVL_R	*lukS*-PV	CTTCTAGTAGCATGAGTAACATC
PVL_FAM		FAM-TTCACTTGTATCTCCTGAGCCTTTTTCATGAG-BHQ1

1 Cal Fluoro Red 610.

2.5 *spa* typing and based-upon-repeat-pattern analysis

The polymorphic X region of the staphylococcal protein A gene (*spa*) was amplified as previously described.[18] PCR products were sequenced by the Sequencing Laboratory at ESR using an ABI 3130XL Sequencer. *spa* sequences were analysed using Ridom StaphType software version 2.2.1 (Ridom GmbH, Würzburg, Germany). Sequences were automatically assigned repeats and *spa* types using the software. Clustering of clonal complexes of related *spa* types (Spa-CCs) was performed using the based-upon-repeat-pattern (BURP) algorithm of the Ridom StaphType software and the default settings of the software which exclude *spa* types with less than five repeats and allow a maximum four costs to cluster *spa* types into the same Spa-CC.[19]

The identity of isolates that were not able to be *spa* typed was checked by a PCR targeting the *S. aureus* species-specific *nuc* gene as previously described.[20]

2.6 Pulsed-field gel electrophoresis typing

S. aureus isolates that were not *spa* typable were typed by pulsed-field gel electrophoresis **(**PFGE) using *Sma*I-digested genomic DNA as previously described.[21] In addition, PFGE was performed on any MRSA isolates when required to definitively identify the MRSA strain. PFGE banding patterns were analysed using BioNumerics software version 6.6 (Applied Maths, St-Martens-Latem, Belgium), with the Dice coefficient and unweighted-pair group method with arithmetic averages, at settings of 0.5% optimisation and 1.5% position tolerance.

2.7 Multilocus sequence typing

Isolates representing the more common *spa* types found among MSSA, as defined by the *spa* type being common to ≥10 of the isolates in the test panel, were further characterized using multilocus sequence typing (MLST). MLST was carried out using protocols and conditions described on the *S. aureus* MLST website.[22] The loci assessed were *arcC, aroE, glpF, gmk, pta, tpi* and *yqiL*. Sequences were analysed using the BioNumerics software and sequence types were assigned using the *S. aureus* MLST website interface.

2.8 DNA microarray

Isolates representing the more common *spa* types found among MSSA, as defined by the *spa* type being common to ≥10 of the isolates in the test panel, were also characterized using the Alere *S. aureus* Genotyping Kit 2.0 DNA microarray (Alere Technologies, Jena, Germany). This microarray detects 336 target sequences in the *S. aureus* genome, corresponding to 186 genes and allelic variants. The results enable the (1) broad classification of *S. aureus* into major clonal complexes, (2) detection of genes associated with antimicrobial resistance, virulence and adhesion, and (3) classification of SCC*mec* complex into distinct allotypes. The microarray was performed as per the manufacturer's instructions.[23,24]

2.9 Data analysis

Each of the isolates included in the test panel was assigned a weight based on the reciprocal of the probability the isolate had of being selected for inclusion in the subsample that comprised the test panel. This weight was used to produce unbiased weighted estimates of all results, including all patient demographics; antimicrobial susceptibilities; and the frequencies of *spa* types, PVL genes, and MSSA clones and MRSA strains. The weighting process resulted in weighted estimates that were usually not whole numbers. In this report weighted estimates have been rounded to the nearest whole number. Because of this rounding, any totals may not be exactly the sum of component subtotals. For example, the number of MSSA isolates plus MRSA isolates does not equal exactly the number of all *S. aureus* isolates.

The population data used in this report was derived from the 2013 mid-year population estimates published by Statistics New Zealand, except for the NZDep2006 population data which was derived from the 2006 Census data. The point-prevalence rates of *S. aureus*

infection presented in this report are based on the number of people from whom a clinical isolate of *S. aureus* was received for this survey per 100 000 population.

Geographic analyses were by district health board (DHB) and by the Northern, Midland, Central and Southern regions. The Northern region includes Northland, Waitemata, Auckland and Counties Manukau DHBs; the Midland region includes Waikato, Lakes, Bay of Plenty, Tairawhiti and Taranaki DHBs; the Central region includes Hawke's Bay, Whanganui, MidCentral, Hutt, Capital and Coast, Wairarapa and Nelson Marlborough DHBS; and the Southern region includes West Coast, Canterbury, South Canterbury and Southern DHBs.

Statistical analyses were performed with SAS software v.9.3 (SAS Institute Inc, Cary, NC, United States).[25] The chi-square test was used to determine the significance of any observed differences. A p value of ≤ 0.05 was considered significant.

3 RESULTS

3.1 Isolates and patients

A total of 1185 *S. aureus* isolates were referred to ESR by diagnostic laboratories throughout New Zealand for the survey. A subsample of 751 isolates was selected from these 1185 isolates for the final test panel (Table 7 in the Appendix). Unless otherwise stated, the results presented have been weighted to allow for this subsampling and the subsampling undertaken at Labtests (note: Labtests was requested to only refer approximately one-third of the *S. aureus* they isolated during the 3-day collection period – see Section 2.1). The weighted total number of isolates was 1377 which represents the 1185 isolates referred for the survey plus the *S. aureus* isolated by Labtests over the 3-day collection period which were not referred.

The majority (83.7%) of the isolates were from SSTI. Only 2.1% of isolates were from blood or other invasive (ie, normally sterile) sites (Table 2).

The national point-prevalence rate of *S. aureus* infection was estimated to be 30.8 per 100 000 population. The highest age-specific prevalence rates occurred in the <5 year and ≥65 year age groups, with rates in both these age groups being significantly higher than the all-age rate (Table 2). The point-prevalence rates for the Māori and Pacific peoples ethnic groups (50.7 and 49.6 per 100 000, respectively) were approximately twice that for the European and Other ethnic group (25.7 per 100 000) (Table 2). Rates by deprivation index increased between each NZDep2006 quintile from the least deprived quintile 1 to the most deprived quintile 5 (Table 2).

An analysis by geographic area showed that the point-prevalence rates in Northland, Bay of Plenty, Hawke's Bay and Wairarapa DHBs were significantly higher than the national rate (Table 8 in the Appendix).

The majority (74.1%) of patients were community patients who had not been in a healthcare facility in the previous 3 months (Table 2). A further 3.4% of the patients were reported to be residents of a long-term care facility who had not been hospitalised in the last 3 months.

Table 2. Demographics of patients from whom *S. aureus* isolated and type of infection (weighted data)

	Percent (number) of patients or isolates[1]		Point-prevalence rate of *S. aureus* infection per 100 000 population (95% confidence interval)	
Age (years)				
<5	12.6	(173)	56.2	(48.2-65.3)
5-14	11.8	(163)	27.9	(23.8-32.6)
15-24	14.1	(194)	30.3	(26.2-34.9)
25-64	32.8	(452)	19.6	(17.8-21.5)
≥65	28.7	(396)	62.3	(56.3-68.8)
All ages	100.0	(1377)	30.8	(29.2-32.5)
Ethnicity[2]				
European and Other	58.7	(761)	25.7	(23.9-27.6)
Māori	26.1	(339)	50.7	(45.5-56.4)
Pacific peoples	10.6	(137)	49.6	(41.6-58.6)
Asian	4.1	(53)	10.3	(7.7-13.5)
MELAA	0.5	(6)	12.0	(4.4-26.1)
NZDep2006 quintile[3]				
1	11.5	(153)	18.5	(15.7-21.7)
2	15.0	(200)	24.7	(21.4-28.3)
3	19.1	(254)	31.9	(28.1-36.0)
4	23.6	(314)	39.7	(35.4-44.3)
5	30.7	(409)	51.2	(46.4-56.5)
Hospitalisation history of patients[4]				
HCF patient in last 3 months	22.5	(276)		
LTCF resident	3.4	(42)		
Community patient	74.1	(909)		
Site of isolation[5]				
Skin and soft tissue infection	83.7	(1151)		
Blood	0.7	(10)		
Other invasive sites	1.4	(19)		
Other sites[6]	14.2	(195)		

1 All numbers presented in this table are rounded from weighted frequencies, with the result that the sum of numbers in any one category may not equal exactly the total of 1377 *S. aureus.*

2 Patient ethnicity only available for 94.9% (713/751) of the isolates tested. Percentages given are the proportions among the patients for whom ethnicity known.

3 Patient NZDep2006 data only available for 96.9% (728/751) of the isolates tested. Percentages given are the proportions among the patients for whom NZDep2006 index score known.

footnotes continued on next page

footnotes for Table 2 continued:

4 Patients were categorised as healthcare facility (HCF) patients if they had any admission to a HCF in the 3 months prior to the date the specimen yielding *S. aureus* was taken, but not if their only admission within these 3 months was <48 hours prior to their specimen being collected. Patients with no history of any hospitalisation in the previous 3 months and who were not reported to be residents of a long-term care facility (LTCF) were categorised as community patients. In this analysis, hospitalisation in the last 3 months is prioritised over LTFC residency. Patient hospitalisation history data only available for 90.4% (679/751) of the isolates tested, and information on LTCF residency only reported for 96.5% (725/751) of the isolates tested.
5 Site of infection only available for 99.9% (750/751) of the isolates tested. Percentages given are the proportions among the isolates for which site known.
6 Other sites included isolates from respiratory sites, eyes, urinary sites and genital sites.

3.2 Antimicrobial susceptibility

Based on cefoxitin susceptibility, 8.9% of *S. aureus* isolates were categorised as methicillin resistant. Among MSSA, a fusidic acid resistance rate of 21.8% was observed. No MSSA were resistant to co-trimoxazole, doxycycline or vancomycin, and rates of resistance to ciprofloxacin, gentamicin and rifampicin were low (Table 3). Only 1.0% of MSSA were multidrug resistant to ≥3 antibiotic classes. The most common resistance pattern among MSSA was mono-resistance to fusidic acid, followed by fusidic acid + mupirocin resistance (Table 10 in the Appendix).

Among MRSA, resistance to fusidic acid, erythromycin and ciprofloxacin was common at 57.6%, 25.3% and 16.1%, respectively. No MRSA were resistant to ceftaroline, co-trimoxazole, rifampicin or vancomycin (Table 3). Nearly one-quarter (23.1%) of MRSA were multidrug resistant to ≥2 antimicrobials classes in addition to β-lactams. The resistance patterns among MRSA varied according to the MRSA strain and were the patterns typically associated with the strain.[26] Notably, 84.7% of isolates of the AK3 MRSA strain were fusidic acid resistant.

Full MIC distribution data is presented in Table 9 in the Appendix.

There were some notable associations between patient demographics and antimicrobial susceptibility. In particular, methicillin resistance was significantly higher among *S. aureus* isolated from patients in the youngest age group (14.2% in the <5 year age group vs 8.1% in ≥5 year olds, *p* 0.006). Methicillin resistance was also significantly higher among *S. aureus* isolates from healthcare facility patients than isolates from community patients (13.9% vs 8.4%, *p* 0.008). Methicillin resistance was more prevalent in the Northern, Midland and Central regions than the Southern region (10.4%, 9.6%, 9.5% and 5.1%, respectively). Fusidic acid resistance was significantly higher among *S. aureus* isolated from patients in the youngest age group (39.6% in the <5 year age group vs 22.9% in ≥5 year olds, *p* <0.001). Fusidic acid resistance was also more prevalent in the Northern, Midland and Central regions than the Southern region (30.4%, 26.0%, 24.1% and 16.3%, respectively).

Table 3. Antimicrobial susceptibility among MSSA, MRSA and all *S. aureus* (weighted data)

Antimicrobial	Percent			mg/L	
	Susceptible	Intermediate	Resistant	MIC_{50}	MIC_{90}
MSSA (n=1255)[1]					
Cefoxitin	100	-	0.0	4	4
Ceftaroline	100	0.0	0.0	0.25	0.25
Ciprofloxacin	97.4	0.6	2.0	0.25	0.5
Clindamycin	99.9	0.0	0.1[2]	0.06	0.12
Co-trimoxazole	100	-	0.0	≤0.06	≤0.06
Doxycycline	99.8	0.2	0.0	0.12	0.12
Erythromycin	87.7	5.8	6.5	0.25	1
Fusidic acid	78.2	-	21.8	0.12	≥8
Gentamicin	99.5	0.3	0.2	0.5	0.5
Mupirocin	87.1	4.2	8.7	0.12	16
Penicillin[3]	17.5	-	82.5	NA	NA
Rifampicin	99.8	0.1	0.1	0.008	0.016
Vancomycin	100	0.0	0.0	1	1
MRSA (n=123)[1]					
Cefoxitin	0.0	-	100	≥32	≥32
Ceftaroline	100	0.0	0.0	0.5	1
Ciprofloxacin	83.0	0.8	16.1	0.25	8
Clindamycin	99.2	0.0	0.8[2]	0.06	0.12
Co-trimoxazole	100	-	0.0	≤0.06	≤0.06
Doxycycline	99.2	0.0	0.8	0.12	0.12
Erythromycin	74.7	0.0	25.3	0.25	≥32
Fusidic acid	42.4	-	57.6	≥8	≥8
Gentamicin	97.3	0.8	1.8	0.5	0.5
Mupirocin	95.6	0.0	4.4	0.12	0.25
Rifampicin	100	0.0	0.0	0.008	0.008
Vancomycin	100	0.0	0.0	1	1
All *S. aureus* (n=1377)[1]					
Cefoxitin	91.1	-	8.9	4	4
Ceftaroline	100	0.0	0.0	0.25	0.5
Ciprofloxacin	96.1	0.6	3.3	0.25	0.5
Clindamycin	99.9	0.0	0.1[2]	0.06	0.12
Co-trimoxazole	100	-	0.0	≤0.06	≤0.06
Doxycycline	99.8	0.2	0.1	0.12	0.12
Erythromycin	86.6	5.2	8.2	0.25	2
Fusidic acid	75.0	-	25.0	0.12	≥8
Gentamicin	99.3	0.4	0.3	0.5	0.5
Penicillin[3]	15.9	-	84.1	NA	NA
Mupirocin	87.8	3.8	8.3	0.12	16
Rifampicin	99.8	0.1	0.1	0.008	0.016
Vancomycin	100	0.0	0.0	1	1

1 The numbers presented are rounded from the weighted frequencies, with the result that the number of MSSA plus MRSA isolates does not equal exactly the number of all *S. aureus* isolates.

2 Constitutive clindamycin susceptibility. A further 5.5% of MSSA, 19.3% of MRSA and 6.7% of all *S. aureus* had inducible clindamycin resistance.

3 The penicillin susceptibility results are those reported by the referring laboratories when submitting isolates. Consequently MIC_{50} and MIC_{90} values are not available (NA).

3.3 *spa* types

Among MSSA, two *spa* types, t127 and t189, were prevalent (Table 4). Further characterization of the common MSSA clones, as initially identified by *spa* typing, is presented in Section 3.5 below. Nine MSSA isolates were non-typable by *spa* typing. PFGE typing indicated that three of these nine isolates were closely related, with their banding patterns sharing >90% similarity, but the banding patterns of the remaining six isolates indicated they were distinct strains.

Among MRSA, *spa* type t002 was predominant, and all *spa* type t002 MRSA were identified as the AK3 MRSA strain. The MRSA strain associated with any of the common *spa* types among MRSA is shown in Table 4. In total, 59.4% of the MRSA included in the survey were identified as the AK3 MRSA strain, 10.6% as WSPP MRSA, 9.8% as EMRSA-15, 4.1% as USA300 MRSA, 4.1% as WR/AK1 MRSA and 4.1% as Queensland clone MRSA.

Table 4. Distribution of *spa* types among methicillin-susceptible and methicillin-resistant *S. aureus* (weighted data)

MSSA (n=1255)[1]			MRSA (n=123)[2]		
***spa* type (Spa-CC)[3]**	**Percent**	**(number)[4]**	***spa* type (MRSA strain)**	**Percent**	**(number)[4]**
t127 (CC 127)	15.3	(192)	t002 (AK3 MRSA)	47.7	(58)
t189 (CC 127)	10.2	(128)	t019 (WSPP MRSA)	8.0	(10)
t002 (CC 002)	4.6	(58)	t032 (EMRSA-15)	7.0	(9)
t1265 (CC 002)	4.0	(50)	t3949 (Queensland clone MRSA)	4.4	(5)
t645 (CC 876)	3.9	(50)	t127 (WR/AK1 MRSA)	4.4	(5)
t084 (CC 002)	2.8	(35)	t045 (AK3 MRSA)	3.5	(4)
t019 (CC 019)	1.9	(24)	t008 (USA300)	3.5	(4)
t659 (CC 876)	1.9	(24)	t311	3.1	(4)
t216 (CC 316)	1.7	(21)	t1062 (AK3 MRSA)	2.7	(3)
t065 (CC 019)	1.5	(19)	t375	2.7	(3)
t876 (CC 876)	1.4	(18)	t548 (AK3 MRSA)	2.6	(3)
t267 (CC 127)	1.4	(17)			
t159 (CC 876)	1.3	(16)			
t179 (CC 002)	1.3	(16)			
t701 (CC 008)	1.3	(16)			
t012 (CC 019)	1.0	(13)			
t078 (CC 078)	1.0	(12)			

1 *spa* types that accounted for ≥1% of MSSA are shown.

2 *spa* types that accounted for ≥2% of MRSA are shown. As this table does not include a full list of all the *spa* types identified among MRSA isolates, the total number of isolates of each MRSA strain may be greater than the number included in the table. The total number of each MRSA strain is included in a statement above in Section 3.3.

3 A Spa-CC (*spa* clonal complex) is a cluster of related *spa* types as determined by the based-upon-repeat-pattern (BURP) algorithm. The cluster is named according to the 'founder' *spa* type of the cluster.

4 The number is rounded from the weighted frequency, hence the same number may be associated with different percentage values and vice versa.

3.4 PVL prevalence

PVL genes were detected in a quarter (25.2%) of *S. aureus* isolates, and the prevalence among MSSA and MRSA was the same (Table 5). The prevalence of PVL was strongly associated with particular MSSA clones and MRSA strains. See Section 3.5 below for the associations with the most common MSSA clones identified in the survey. Among the common MRSA strains identified, all but one (98.3%) of the isolates of the AK3 MRSA strain were PVL negative, WSPP MRSA isolates were PVL positive and EMRSA-15 isolates were PVL negative.

S. aureus isolated from patients in the 15-24 year age group and patients in the Pacific peoples ethnic group were significantly more likely ($p < 0.001$) to contain PVL genes than *S. aureus* isolated from patients in other age groups and ethnic groups (Table 5). Similarly, *S. aureus* isolated from community patients and from SSTI were significantly more likely to contain PVL genes than *S. aureus* isolated from healthcare facility patients and from other types of infections, including invasive disease ($p < 0.05$) (Table 5).

Table 5. PVL prevalence among methicillin-susceptible and methicillin-resistant *S. aureus*, and by patient demographics and site of isolation (weighted data)[1]

	PVL positive isolates	
	Percent	**(number)**
All *S. aureus* (n=1377)	25.2	(348)
MSSA (n=1255)	25.2	(316)
MRSA (n=123)	25.2	(31)
Age group (years)		
<5 (n=173)	20.9	(36)
5-14 (n=163)	32.9	(54)
15-24 (n=194)	44.7	(87)
25-64 (n=452)	28.1	(127)
≥65 (n=396)	11.1	(44)
Ethnicity		
European and Other (n=761)	17.5	(133)
Māori (n=339)	28.9	(98)
Pacific peoples (n=137)	53.3	(73)
Asian (n=53)	39.6	(21)
MELAA (n=6)	50.0	(3)
Hospitalisation history of patients		
HCF patient in last 3 months (n=276)	17.7	(49)
LTCF patient (n=42)	9.0	(4)
Community patient (n=951)	26.8	(255)
Site of isolation		
Skin and soft tissue infection (n=1151)	26.3	(303)
Invasive sites (n=29)	20.8	(41)
Other sites (n=195)	18.1	(35)

1 All numbers presented in this table are rounded from weighted frequencies, with the result that the sum of numbers in any one category may not equal exactly the total of 1377 *S. aureus* isolates.

3.5 MSSA clones

MLST and DNA microarray testing of representative isolates of each of the most common *spa* types found among MSSA (ie, *spa* types that accounted for ≥10 of the isolates tested), identified seven dominant MSSA clones (Table 6). These seven clones collectively accounted for 44.7% of MSSA. When more than one MLST type was found among isolates belonging to the same clone, the MLST types were closely related and belonged to the same MLST clonal complex (CC). Similarly any *spa* types associated with the same MSSA clone were found to be closely related when analysed by the BURP algorithm and part of the same *spa* clonal complex.

With the exception the CC1-MSSA clone, all isolates belonging to the other dominant MSSA clones were uniformly either PVL positive or negative (Table 6). CC1-MSSA was characterised by fusidic acid resistance with 95.3% of the isolates of this clone being fusidic acid resistant. In addition, 41.7% of the fusidic acid-resistant CC1-MSSA isolates were also mupirocin resistant. None of the other dominant clones had a characteristic resistance pattern and most isolates belonging to these clones were fully susceptible.

Table 6. Dominant clones among the methicillin-susceptible *S. aureus* (weighted data)

DNA microarray strain assignment[1]	MLST types associated with clone	*spa* type(s) associated with clone	Percent PVL positive	Prevalence of clone (% of isolates in survey belonging to clone)
CC1-MSSA	ST1	t127	69.8	15.3
CC188-MSSA	ST188	t189	0.0	10.2
CC5-MSSA	ST5 and ST835[2]	t002, t1265[3]	0.0	8.6
CC121-MSSA [PVL+]	ST121	t645[4]	100	3.9
CC121-MSSA	ST2276[5]	t659[4]	0.0	1.9
CC15-MSSA	ST15	t084	0.0	2.8
CC30-MSSA [PVL+]	ST30	t019	100	1.9

1 Results using the Alere *S. aureus* Genotyping Kit 2.0 DNA microarray which defines MSSA strains by their MLST clonal complex (CC) affiliation as well as the presence or absence of PVL.

2 ST835 is a single-locus variant of ST5 and therefore belongs in MLST clonal complex 5 (CC5).

3 *spa* types t002 and t1265 are closely related when analysed by the BURP algorithm. The repeat sequence of t1265 (r26 r23 r17 r34 r17 r20 r17 r12 r12 r12 r16) differs by three repeats (as underlined) from that of t002 (r26 r23 r17 r34 r17 r20 r17 r12 r17 r16).

4 *spa* types t645 and t659, which belong to the same MLST clonal complex (CC121), are closely related when analysed by the BURP algorithm. The repeat sequence of t659 (r14 r44 r13 r12 r17 r17 r17 r23 r18) differs by three repeats (as underlined) from that of t645 (r14 r44 r13 r12 r17 r23 r18 r17).

5 ST2276 is a double-locus variant of ST121 and therefore belongs in MLST clonal complex 121 (CC121).

4 DISCUSSION

Over the past decade, there has been a change in the clinical and molecular epidemiology of *S. aureus* infections in New Zealand, with a significant increase in serious *S. aureus* SSTI,[4,5] the replacement of WSPP MRSA with AK3 MRSA as the predominant MRSA strain,[27] and reported high rates of resistance to topical antimicrobials.[7,10] In this context, the purpose of this survey was to provide contemporary information on the demographics, antimicrobial susceptibility patterns and molecular epidemiology of *S. aureus* infections in New Zealand.

Although our collection period only encompassed 3 days, we received nearly 1200 clinical isolates from diagnostic laboratories. As expected, the vast majority of isolates were from community-associated SSTI, a finding in keeping with a previous study in Auckland.[5] There were marked demographic differences in the rates of *S. aureus* infections, with the highest rates in the <5 year and ≥65 year age groups, in Māori and Pacific peoples, and in patients residing in areas of high socioeconomic deprivation. Previous New Zealand work has found that rates of *S. aureus* infections are highest in the <5 year age group.[4,5] Of particular concern was our finding of marked variations in the socioeconomic and ethnic distribution of *S. aureus* infections. The unequal burden of *S. aureus* infections in Māori and Pacific peoples is consistent with ethnic group disparities identified generally for infectious diseases in New Zealand.[28]

The MRSA rate of 8.9% was in keeping with aggregate susceptibility data from annual national surveillance.[7] In general, rates of antimicrobial resistance in MSSA were low, with the notable exception of fusidic acid (21.8%) and mupirocin (8.7%) resistance. In particular, the high rate of fusidic acid resistance is of concern, and is in keeping with recent data reported from the Auckland region.[10] This rate of fusidic acid resistance is one of the highest reported in the developed world, with only Ireland (19.9%) and Greece (52.5%) having comparably high rates in one previous study.[29] In New Zealand, topical fusidic acid remains a first-line recommended agent in many guidelines for the treatment of mild impetigo.[30] Our finding of an age-related stratification of fusidic acid resistance, with the highest rates in *S. aureus* isolated from patients in the <5 year group (39.6%) is therefore of particular concern. Furthermore, similar to previous work, we found that fusidic acid resistance was highly clonal, and was associated with the dominant MSSA clone (CC1-MSSA) and the dominant MRSA clone (the AK3 MRSA strain). It is highly likely that high population usage of topical fusidic acid has driven the emergence of these dominant *S. aureus* clones in

New Zealand.[10] In particular, the emergence of the AK3 MRSA strain over the past decade is likely to be due to the co-selection of strains harboring genes conferring both methicillin resistance and fusidic acid resistance.

However, in contrast to the increasing trend of fusidic acid resistance, mupirocin resistance among *S. aureus* has decreased to 8.3% from the rate of 14.2% found in the last national *S. aureus* survey in 1999.[9] Interestingly the 1999 survey was conducted at the end of a 9-year period during which mupirocin was available 'over the counter' without a prescription in New Zealand. Since 2000, mupirocin has been available only on prescription and community dispensing data shows that, in contrast to fusidic acid, mupirocin usage has been decreasing in recent years.[10]

Our finding of a strong association between PVL-positive *S. aureus* infections and SSTI and community-associated infections is in keeping with similar studies, both in New Zealand and overseas.[11,12] Interestingly, the PVL positivity rate of 25.2% in this survey was lower than that described in previous studies in New Zealand, in which PVL rates of 37% and 56% were described.[12,13] However, possible reasons for these differing rates include differing age distributions of patients, temporal shifts in circulating *S. aureus* clones, and geographic variation in PVL positivity, with both previous studies being confined to the Auckland region.

This study had several limitations. First, as the study was based on *S. aureus* isolates, the demographic analyses only represent the proportion of patients with a *S. aureus* infection who attended a doctor and also had a specimen taken for culture. This limitation is likely to mean that the differences in *S. aureus* infection rates we found between ethnic and socioeconomic groups could be greater than our data indicate, as access to medical care is likely to be more restricted for the ethnic and socioeconomic groups which we found had the highest rates of infection. This limitation could also affect the differences in age-specific rates of *S. aureus* infection we found if patients in some age groups are more likely than patients in other age groups to have specimens taken for culture. Second, the study design, both the point-prevalence methodology and scope of infection types included, limit the comparisons that can be made with rates of *S. aureus* infection in other countries. Third, the estimate that 3.4% of patients were long-term care facility residents may be an underestimate as the information on long-term care facility residency was only able to be obtained from referring laboratories which do not always have access to this information.

This survey has provided valuable current information on the antimicrobial susceptibility and epidemiology of *S. aureus* infections in New Zealand. To monitor trends, future surveys should be undertaken at regular intervals and use similar methodologies to provide comparable data. In addition, the establishment of a national system of ongoing, prospective surveillance of *S. aureus* bacteremia should be considered. Many countries and regions in the developed world (eg, Australia and Europe) base their national surveillance of *S. aureus* infections and antimicrobial susceptibility on bacteraemic isolates. A similar approach in New Zealand would facilitate international comparisons.[31,32]

The results of this survey also suggest several areas for future, more focused investigation and action. These areas include research to provide a better understanding of the demographic disparities in S. *aureus* infection rates. Given the high rate of fusidic acid resistance found in this and other recent New Zealand studies, further investigation of the genetic mechanisms of fusidic acid resistance would be useful. Previous work has suggested that most fusidic acid resistance among *S. aureus* in the Auckland area is due to the acquired *fusC* gene.[10] In addition, the high rate of fusidic acid resistance, which correlates with increases in the usage of topical preparations of this agent, along with an apparent decrease in mupirocin resistance which correlates with decreasing usage of this agent, suggest the use of topical antimicrobials needs to be reviewed and appropriately restricted.

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APPENDIX

Table 7. Number of isolates referred by each laboratory and number included in survey test panels (unweighted data)

Laboratory	Number of isolates	
	Referred	**Included in test panel**
Whangarei Hospital	31	30
Northland Pathology Laboratory	41	21
Dargaville Hospital	3	3
North Shore Hospital	22	20
Auckland City Hospital	30	14
Middlemore Hospital	41	19
Labtests[1]	120	114
Waikato Hospital	31	26
Pathlab Waikato	66	31
Laboratory Services, Rotorua	22	20
Pathlab Bay of Plenty	101	43
Tlab, Gisborne	23	23
Hawkes Bay Hospital	30	29
Southern Community Labs, Hastings	59	25
Taranaki Base Hospital	11	11
Taranaki Medlab	17	16
Medlab Central	67	29
Medlab Wairarapa	20	19
Hutt Hospital	19	19
Wellington Hospital	20	19
Aotea Pathology	115	47
Nelson Hospital	39	36
Medlab Blenheim	3	3
Greymouth Hospital	8	8
Canterbury Health Laboratories	52	26
Canterbury Southern Community Labs	89	36
Medlab Timaru	22	20
Southern Community Labs, Dunedin	64	26
Southern Community Labs, Invercargill	19	18
Total	**1185**	**751**

1 Labtests isolated a total of 388 clinical *S. aureus* isolates during the 3-day collection period.

Table 8. District health board domicile of the patients (weighted data)

Region and District Health Board[1]	Percent (number) of patients from whom *S. aureus* isolated[2]		Point-prevalence rate of *S. aureus* infection per 100 000 population (95% confidence interval)	
Northern region	38.3	(509)	29.9	(27.3-32.6)
Northland	6.2	(82)	51.7	(41.1-64.1)
Waitemata	9.1	(122)	21.7	(18.0-25.9)
Auckland	9.4	(125)	26.7	(22.2-31.8)
Counties Manukau	13.6	(181)	35.1	(30.2-40.6)
Midland region	19.5	(260)	30.7	(27.1-34.7)
Waikato	7.4	(98)	26.3	(21.3-32.0)
Lakes	1.4	(18)	17.5	(10.4-27.6)
Bay of Plenty	7.0	(92)	43.2	(34.8-53.0)
Tairawhiti	1.7	(22)	47.1	(29.5-71.3)
Taranaki	2.2	(29)	26.2	(17.5-37.6)
Central region	26.0	(346)	34.1	(30.6-37.9)
Hawke's Bay	6.4	(85)	54.7	(43.7-67.6)
Whanganui	1.5	(21)	33.7	(20.8-51.4)
MidCentral	3.0	(41)	24.2	(17.3-32.8)
Hutt Valley	3.0	(40)	27.8	(19.9-37.8)
Capital and Coast	7.6	(101)	33.7	(27.4-40.9)
Wairarapa	1.7	(22)	54.1	(33.9-81.9)
Nelson Marlborough	2.7	(36)	25.5	(17.8-35.3)
Southern region	16.2	(216)	23.8	(20.8-27.2)
West Coast	0.8	(10)	30.6	(14.7-56.3)
Canterbury	8.7	(116)	22.9	(18.9-27.4)
South Canterbury	1.7	(22)	38.6	(24.2-58.4)
Southern	5.1	(68)	21.9	(17.0-27.8)

1 Patient's domicile only known for 96.9% (728/751) of the isolates tested.

2 All numbers presented in this table are rounded from weighted frequencies, with the result that the sum of numbers for the DHBs in any one region may not equal exactly the total for the region.

Table 9. Distribution of minimum inhibitory concentrations (MICs) among clinical isolates of *S. aureus* (weighted data)

Antimicrobial		Percent of isolates with an MIC (mg/L) of:[1]																			
		0.002	0.004	0.008	0.016	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024
Cefoxitin	MSSA										0.1	17.5	82.4								
	MRSA													4.6	17.2	78.2					
	All										0.1	15.9	75.1	0.4	1.5	7.0					
Ceftaroline	MSSA							5.0	85.3	9.5	0.2										
	MRSA								9.5	63.5	27.0										
	All							4.6	78.6	14.3	2.5										
Ciprofloxacin	MSSA						1.2	19.8	60.8	13.9	1.6	0.6	0.3	0.9	0.7						
	MRSA							9.9	69.0	3.4	0.8	0.8	0.0	7.4	8.8						
	All						1.1	18.9	61.6	13.0	1.5	0.6	0.3	1.5	1.5						
Clindamycin (constitutive)	MSSA					1.5	49.4	48.9	0.0	0.2	0.0	0.0	0.0	0.0	0.1						
	MRSA						70.7	28.5	0.0	0.0	0.0	0.0	0.0	0.0	0.8						
	All					1.3	51.3	47.1	0.0	0.1	0.0	0.0	0.0	0.0	0.1						
Co-trimoxazole	MSSA						96.7	1.0	1.0	0.7	0.3	0.3									
	MRSA						91.8	3.4	0.0	3.1	1.7										
	All						96.2	1.2	0.9	0.9	0.5	0.2									
Doxycycline	MSSA						16.1	80.3	1.1	0.3	0.8	0.6	0.7	0.2							
	MRSA						36.4	61.1	1.6	0.0	0.0	0.0	0.0	0.0	0.8						
	All						17.9	78.6	1.1	0.3	0.7	0.5	0.6	0.2	0.1						
Erythromycin	MSSA							31.5	55.7	0.6	2.5	1.8	1.5	0.7	0.3	5.5					
	MRSA							35.5	39.2	0.0	0.0	0.0	0.0	0.0	0.8	24.5					
	All							31.8	54.2	0.6	2.3	1.7	1.3	0.6	0.3	7.2					
Fusidic acid	MSSA						30.8	46.2	1.0	0.0	0.2	1.1	5.1	15.6							
	MRSA						13.2	23.1	3.5	0.8	1.8	0.0	6.3	51.3							
	All						29.2	44.1	1.2	0.1	0.3	1.0	5.2	18.8							
Gentamicin	MSSA							1.6	43.0	53.4	1.3	0.3	0.0	0.3	0.2						
	MRSA								33.2	64.2	0.0	0.0	0.0	0.8	0.0	1.8					
	All							1.4	42.1	54.4	1.2	0.2	0.0	0.4	0.1	0.2					
Mupirocin	MSSA						3.5	55.8	27.4	0.3	0.1	0.2	0.3	1.9	1.7	0.2	0.0	0.0	0.0	1.3	7.4
	MRSA						4.6	63.2	24.5	0.8	2.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.9	2.4
	All						3.5	56.5	27.1	0.4	0.3	0.2	0.2	1.7	1.5	0.2	0.0	0.0	0.0	1.4	7.0
Rifampicin	MSSA		8.4	80.0	11.4	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.1						
	MRSA		14.8	79.9	5.2																
	All		9.0	80.0	10.8	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.1						
Vancomycin	MSSA									25.9	74.1										
	MRSA									31.1	68.9										
	All									26.3	73.7										

footnote for Table 1:

1 The white fields represent the range of antibiotic concentrations tested. MIC values less than or equal to the lowest concentration tested are presented as this lowest concentration. MIC values greater than the highest concentration tested are presented as the next highest concentration after the highest concentration tested. The vertical bars indicate the breakpoints between the susceptibility categories. For antibiotics where there are two vertical lines, the first line represents the breakpoint between susceptible and intermediate, and the second line represents the breakpoint between intermediate and resistant. For antibiotics where there is one vertical line, the line represents the breakpoint between susceptible and resistant.

Table 10. Common antibiotic resistance patterns (weighted data)

Resistance pattern[1,2]	Percent (number) of isolates with resistance pattern			
	MSSA (n=1255)		MRSA (n=123)	
Fa	13.1	(165)	42.2	(52)
FaMu	6.9	(86)		
Em	3.7	(46)		

1 Only resistance patterns shared by ≥10 of the isolates tested are included in this table.
2 Em, erythromycin; Fa, fusidic acid; Mu, mupirocin.