Annual survey of methicillin-resistant *Staphylococcus aureus* (MRSA), 2011

Helen Heffernan and Sarah Bakker

Nosocomial Infections Laboratory, Institute of Environmental Science and Research Limited (ESR)

Introduction

ESR conducts annual surveys of methicillin-resistant *Staphylococcus aureus* (MRSA). Each year, all hospital and community microbiology laboratories in New Zealand are asked to refer all MRSA isolated during a one-month period to ESR. Laboratories provide epidemiological information with each isolate referred. At ESR, MRSA are typed to identify MRSA strains. The purpose of these annual surveys is to provide information on the epidemiology of MRSA in New Zealand and to monitor changes over time.

The results of the 2011 MRSA survey are presented in this report, along with the trends in MRSA prevalence.

Previous reports on the annual MRSA surveys are available at http://www.surv.esr.cri.nz/antimicrobial/mrsa_annual.php.

Institute of Environmental Science & Research Limited
Kenepuru Science Centre
34 Kenepuru Drive, PO Box 50-348, Porirua 5240, New Zealand
Telephone: +64 4 914 0700, Facsimile: +64 4 914 0770

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Methods

MRSA isolates and data collection

Hospital and community microbiology laboratories in New Zealand were asked to refer all MRSA isolated during August 2011 to ESR. The Microbiology Department, Middlemore Hospital; Microbiology Department, Hawke's Bay Hospital; Microbiology Laboratory, Whakatane Hospital; and Diagnostic Medical Laboratory, Auckland, referred isolates during a 31-day period between mid-August and 31 October 2011. All remaining laboratories referred MRSA during August 2011.

When referring MRSA isolates, laboratories supplied epidemiological data including patient age, geographic location, hospitalisation status, MRSA isolation site, infection or colonisation status, and if MRSA was obtained from a screen or a diagnostic specimen. Laboratories also provided information on the susceptibility of the MRSA isolates to non-β-lactam antibiotics. Two community laboratories in the Auckland area, Labtests and Diagnostic Medlab, receive specimens from multiple district health boards (DHBs), Waitemata, Auckland and Counties Manukau, so these laboratories provided patient or staff addresses that were geocoded at ESR to assign people to a DHB.

People were classified as hospital patients or hospital staff if (i) they were inpatients or outpatients in a healthcare facility when MRSA was isolated, or had been in the previous three months; (ii) they were occupying a residential-care facility when MRSA was isolated, or had been in the previous three months; or (iii) they were employed by a healthcare or residential-care facility when MRSA was isolated. Patients or staff were classified as people in the community if (i) MRSA was isolated from patients while in the community and the patients had no history of occupying a healthcare or residential-care facility in the previous three months; (ii) MRSA was isolated on healthcare or residential-care facility admission-screening of patients who had no history of occupying such facilities in the previous three months; or (iii) MRSA was isolated from pre-employment swabs of healthcare staff with no employment history supplied.

All MRSA isolates received at ESR were assumed to be pure cultures of MRSA and methicillin/oxacillin resistance was not routinely confirmed.

spa *typing and based upon repeat pattern (BURP) analysis*

The polymorphic X region of the staphylococcal protein A gene (*spa*) was amplified as previously described.[1] PCR products were sequenced by the Sequencing Laboratory at ESR using an ABI 3130XL Sequencer. *spa* sequences were analysed using Ridom StaphType software version 2.0.3 (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.[2]

Pulsed-field gel electrophoresis (PFGE) and profile analysis

Where necessary to identify strains, PFGE of *Sma*I-digested genomic DNA was performed as previously described.[3] PFGE banding patterns were analysed using BioNumerics software version 5.1 (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. PFGE banding patterns were interpreted using the criteria proposed by Tenover et al.[4]

Multilocus sequence typing (MLST) and sequence analysis

Where necessary to characterise strains, MLST was performed as previously described.[5] Sequences were analysed using BioNumerics software version 5.1 and sequence types (STs) were assigned using the *S. aureus* database accessible at http://www.mlst.net.

Antibiotic susceptibility testing

Antibiotic susceptibility testing was performed where necessary to identify strains and to supplement the susceptibility information provided by referring laboratories. Disc susceptibility testing was performed according to the methods of the Clinical and Laboratory Standards Institute (CLSI).[6] Except for fusidic acid and mupirocin, zones of inhibition were interpreted according to CLSI criteria.[7] Fusidic acid zones of inhibition were determined with a 10 µg disc and interpreted as ≥21 mm susceptible, 20 mm intermediate and ≤19 mm resistant.[8] Mupirocin zones of inhibition were determined with a 5 µg disc and interpreted as ≥14 mm susceptible and ≤13 mm resistant.[9]

PCR for staphylococcal-specific 16S rRNA, nuc *and* mecA

Isolates that were not able to be *spa* typed were tested for the genes encoding staphylococcal-specific 16S rRNA, *S. aureus*-specific thermostable nuclease (*nuc*) and methicillin resistance (*mecA*) by triplex PCR as previously described.[10]

Assigning MRSA strains

Isolates were characterised primarily based upon *spa* types and antibiotic susceptibility patterns, with PFGE as a supplementary typing tool where *spa* typing was inconclusive. There were three situations in which *spa* typing was considered inconclusive: (i) when a *spa* type correlated to a known MRSA strain but the antibiotic susceptibility pattern did not, (ii) when an isolate had a novel *spa* type, and (iii) when an isolate had a *spa* type ESR had not yet correlated to an MRSA strain.

Epidemiological analyses

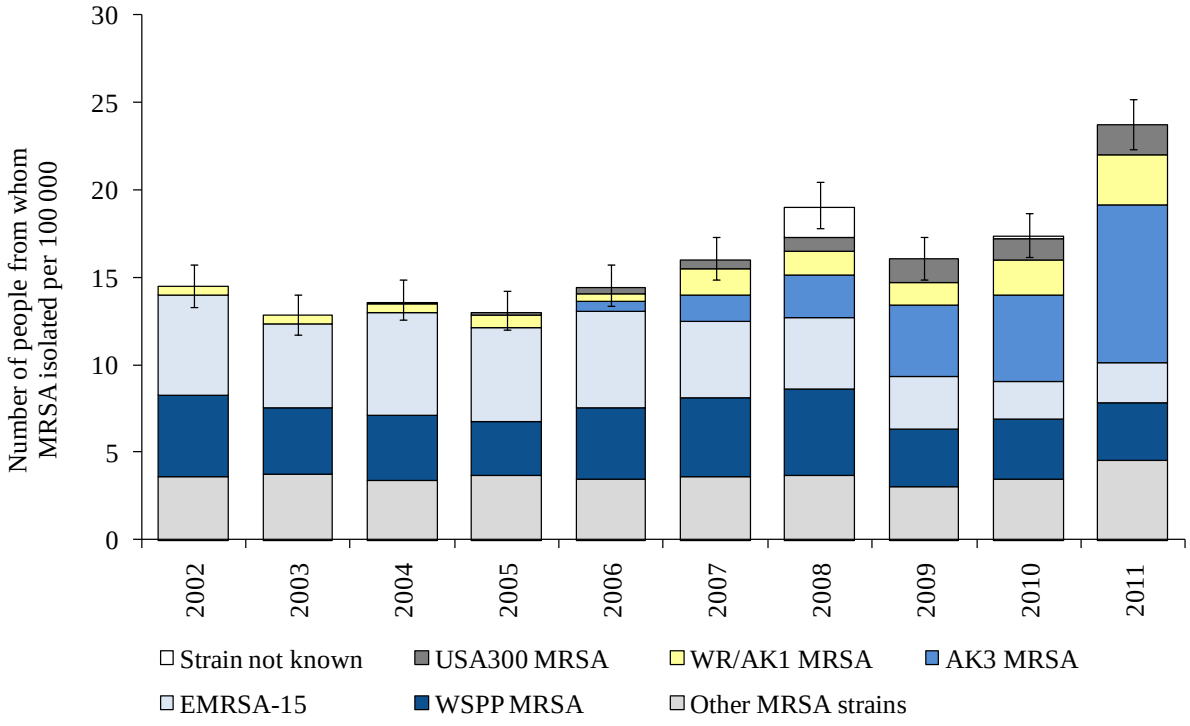
Epidemiological data and results were entered into ESR's laboratory information management system. Data and results were extracted and analysed using customised Microsoft Access 2003 queries. Point-prevalence rates were calculated based on the number of MRSA isolated per 100 000 population during the period of the survey. Mid-year New Zealand population estimates were used to calculate prevalence rates. 95% confidence intervals were calculated based on Poisson distribution. The statistical significance of time trends was calculated at a 95% confidence level using Poisson regression and the Mantel-Haenszel test for linear trend.

Results

National point-prevalence rates of MRSA, 2002-2011

During the 2011 MRSA survey, MRSA were referred from 1042 people, 1020 of whom were patients and 22 of whom were staff. There was a 37.0% increase in the MRSA point-prevalence rate between 2010 and 2011, from 17.3 to 23.7 people with MRSA per 100 000 population (Figure 1). Overall, there was a statistically significant (P=0.0047) increase in the MRSA point-prevalence rate over the 10 years, 2002 to 2011 (Figure 1).

Figure 1. MRSA point-prevalence rates, 2002-2011



95% confidence intervals indicated by error bars. The category 'Strain not known' for 2008 and 2010 represents people identified with MRSA during the survey period but from whom no isolate was referred for strain identification.

MRSA infection status, strain prevalence, and strain association with healthcare facilities versus the community and with patient age

In 2011, of the 1020 patients with MRSA, 43.7% were categorised as hospital patients and 56.3% as community patients. MRSA was reported as causing infection in 78.2% of the 895 patients for whom this information was provided.

Six MRSA strains (AK3 MRSA, WSPP MRSA, WR/AK1 MRSA, EMRSA-15, USA300 MRSA and Queensland clone MRSA) were predominant in 2011 and collectively represented 86.2% of all MRSA isolations (Table 1). AK3 MRSA was the most prevalent MRSA strain, followed by the WSPP and WR/AK1 strains. The point-prevalence rates for these three strains were 9.0, 3.3 and 2.9 per 100 000 population, respectively (Figure 1).

Table 1. MRSA strain prevalence, association with healthcare facilities versus the community and association with patient age, 2011

Strain	Proportion (%) of all MRSA isolations[a]	Proportion (%) of each strain isolated from:		
		hospital patients or staff	people in the community	patients ≥60 years of age[b]
AK3 MRSA [ST5, SCC*mec* type IV][c]	38.0	43.8	56.2	16.2
WSPP MRSA [ST30, SCC*mec* type IV]	14.0	37.7	62.3	13.9
WR/AK1 MRSA [ST1, SCC*mec* type IV]	12.1	33.9	66.1	21.4
EMRSA-15 MRSA [ST22, SCC*mec* type IV]	9.6	65.0	35.0	78.1
USA300 MRSA [ST8, SCC*mec* type IV]	7.3	35.5	64.5	21.6
Queensland clone MRSA [ST93, SCC*mec* type IV]	5.4	37.5	62.5	17.9

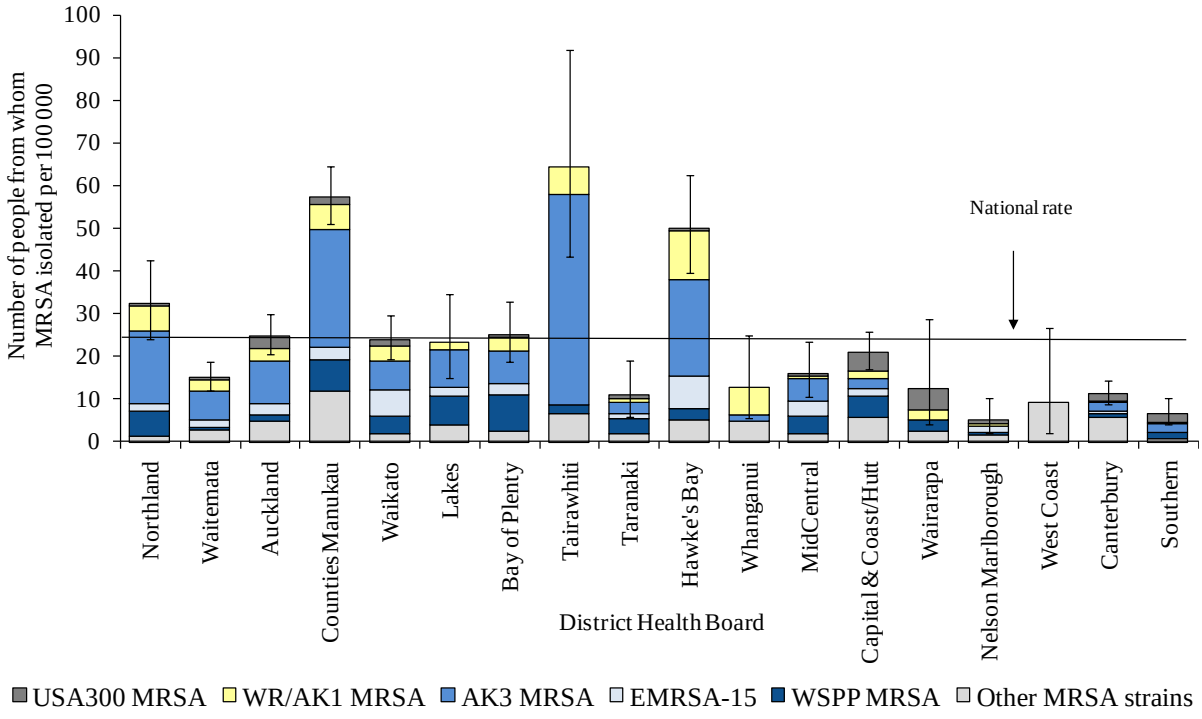
a Other strains accounted for the remaining 13.6% of MRSA.
b Age distribution for patients only, staff not included.
c ST, multilocus sequence type; SCC*mec*, staphylococcal cassette chromosome *mec*.

Geographic distribution of MRSA

There were significant geographical differences in the point-prevalence rates of MRSA isolations in 2011, with rates above the national rate of 23.7 MRSA per 100 000 population in the Tairawhiti (64.4 per 100 000), Counties Manukau (57.4), Hawke's Bay (50.1), Northland (32.2), Bay of Plenty (25.0), Auckland (24.7) and Waikato (23.9) DHBs (Figure 2). Similar geographical differences were evident in the point-prevalence rates of MRSA isolated only from infection, with the same seven DHBs having rates above the national point-prevalence rate of 15.9 MRSA infections per 100 000 population (Figure 3).

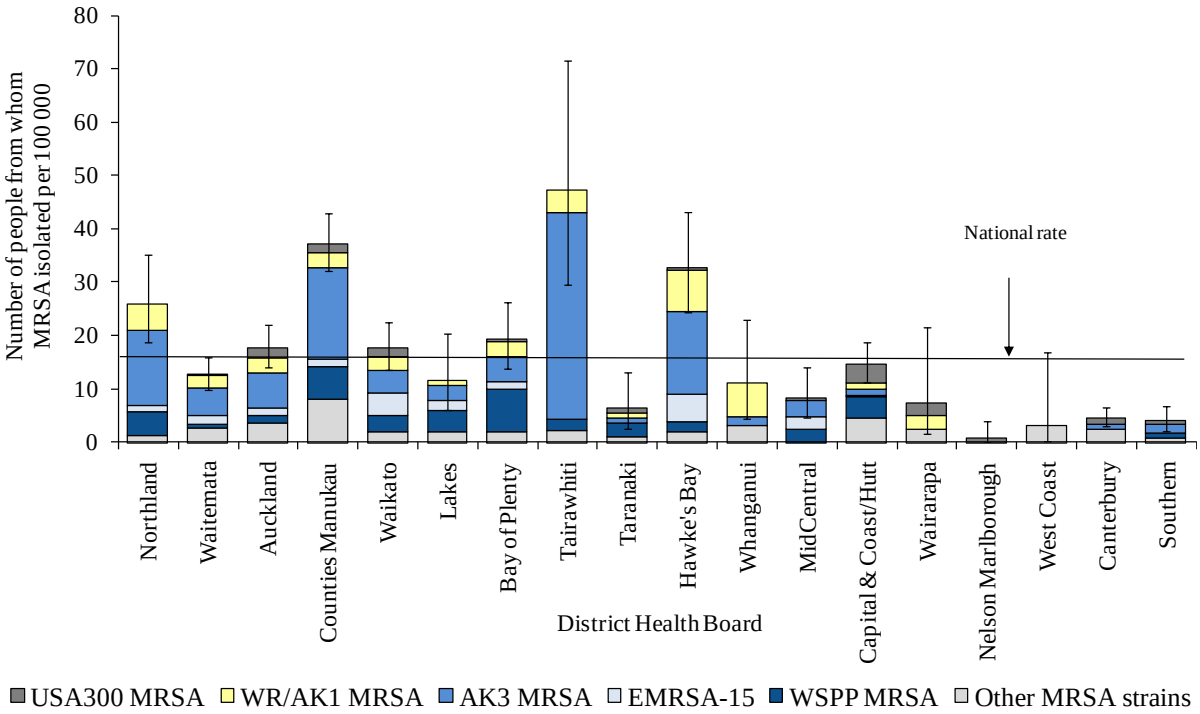
AK3 MRSA was the most prevalent MRSA strain in all North Island DHBs except Bay of Plenty, Taranaki, Whanganui and Capital & Coast/Hutt DHBs. This strain was particularly prevalent in Tairawhiti DHB where it represented 76.7% (23/30) of the MRSA isolated during the survey period.

Figure 2. MRSA point-prevalence rates by district health board, 2011



95% confidence intervals indicated by error bars. Data for the Capital & Coast and Hutt DHBs are combined as 'Capital & Coast/Hutt', and data for the Canterbury and South Canterbury DHBs are combined as 'Canterbury'.

Figure 3. MRSA infection point-prevalence rates by district health board, 2011

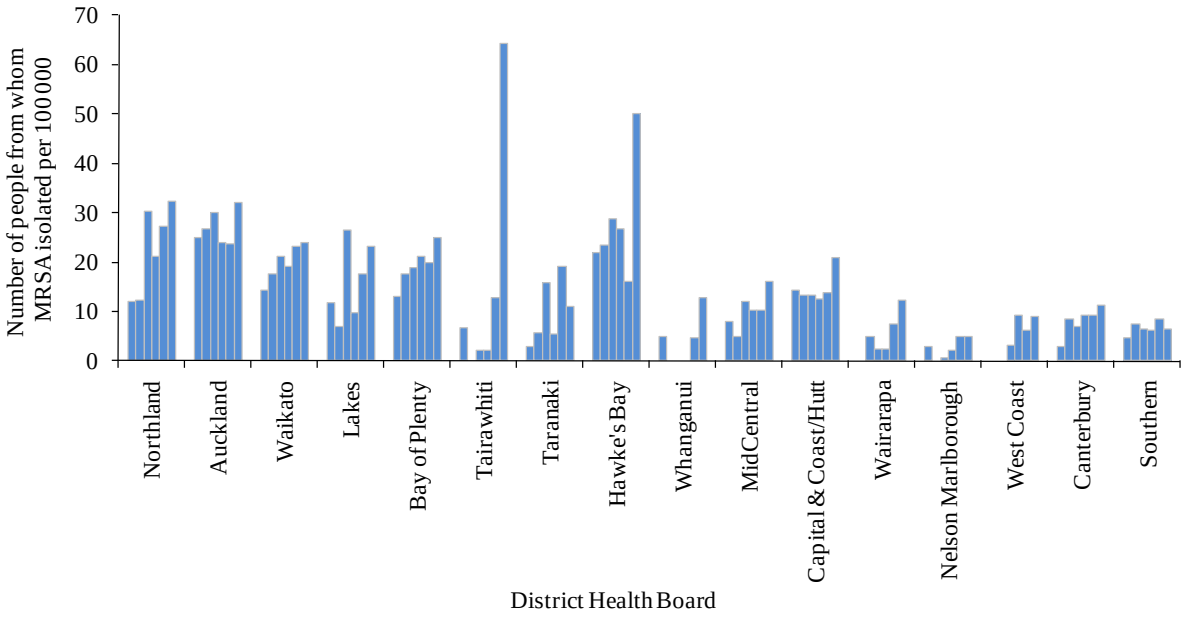


95% confidence intervals indicated by error bars. Data for the Capital & Coast and Hutt DHBs are combined as 'Capital & Coast/Hutt', and data for the Canterbury and South Canterbury DHBs are combined as 'Canterbury'.

Point-prevalence rates of MRSA by DHB, 2006-2011

Over the six-year period 2006 and 2011, there were statistically significant increases in MRSA point-prevalence rates in all DHBs except Auckland, Wairarapa, Nelson Marlborough and Southern (Figure 4). Notably, the prevalence of MRSA in Tairawhiti DHB was almost five times higher during the 2011 survey period compared with the 2010 survey period, and over three times higher in Hawke's Bay in 2011 compared with 2010.

Figure 4. MRSA point-prevalence rates by district health board, 2006-2011



The series of bars for each DHB represent the individual years 2006 to 2011 from left to right. Data for the Waitemata, Auckland and Counties Manukau DHBs are combined as 'Auckland', data for the Capital & Coast and Hutt DHBs are combined as 'Capital & Coast/Hutt', and data for the Canterbury and South Canterbury DHBs are combined as 'Canterbury'.

MRSA strain association with spa *types*

In 2011, the AK3 MRSA strain was most commonly associated with *spa* type t002, WSPP MRSA with t019, EMRSA-15 with t032, WR/AK1 MRSA with t127, USA300 MRSA with t008, and the Queensland clone MRSA with t3949 (Table 2). EMRSA-15 was associated with the greatest variety of *spa* types (Table 2).

MRSA belonging to multilocus sequence type (MLST) clonal complex 398 (CC398 MRSA), which has been described as a livestock-associated MRSA strain, was identified for the first time in New Zealand in 2011. CC398 MRSA were referred from three patients during the 2011 survey period. Two patients were from Canterbury DHB and the third from Southern DHB. The CC398 MRSA from both Canterbury patients were *spa* type t034, while that from the Southern DHB patient was *spa* type t011. *spa* types t011 and t034 are closely related and commonly associated with the CC398 MRSA strain. The isolates from all three patients were untypable by *Sma*I-digested PFGE typing, which is a characteristic trait of CC398 MRSA. All three isolates were tetracycline resistant.

There were 121 isolates that were not associated with a known MRSA strain and the most common *spa* types among these isolates were t1853 (15 isolates), t976 (8 isolates), t375 (7 isolates), t189 (6 isolates) and t437 (6 isolates). t1853 and t189 are in the same *spa* clonal complex (Spa-CC186), t976 and t437 are both in *spa* clonal complex Spa-CC316, while t375 is a 'singleton' (ie, does not cluster by BURP analysis with any other *spa* types).

Table 2. Frequency of MRSA strains and *spa* types, 2011

Strain	Number of isolates of the strain	*spa* clonal cluster	*spa* type	Number of isolates of the *spa* type
AK3 MRSA [ST5, SCC*mec* type IV][a]	396[b]	Spa-CC002	t002	347
			t045	19
			t548	7
			t062	4
			t105	3
			t306	3
			t088	2
			t179	2
			t010	1
			t067	1
			t311	1
			t539	1
			t985	1
			t1154	1
			t4323	1
			t5213	1
			t5677	1
WSPP MRSA [ST30, SCC*mec* type IV] Alternative names: Southwest Pacific clone and Oceania clone	146	Spa-CC019	t019	124
			t975	5
			t1752	3
			t1347	2
			t1836	2
			t021	1
			t138	1
			t685	1
			t1133	1
			t1273	1
			t3593	1
			t3723	1
			t5994	1
			t6653	1
		Excluded[c]	t779	1
WR/AK1 MRSA [ST1, SCC*mec* type IV] Alternative name: Western Australia (WA) MRSA-1	127	Spa-CC186	t127	106
			t267	6
			t1418	2
			t5100	2
			t224	1
			t1052	1
			t7136	1
		Spa-CC008	t701	5
		Excluded	t386	3

Table 2. Frequency of MRSA strains and *spa* types, 2011 *continued*

Strain	Number of isolates of the strain	*spa* clonal cluster	*spa* type	Number of isolates of the *spa* type
EMRSA-15 [ST22, SCC*mec* type IV]	98[d]	Spa-CC032	t032	63
			t022	7
			t1401	5
			t379	3
			t005	2
			t646	2
			t902	2
			t5538	2
			t557	1
			t578	1
			t718	1
			t852	1
			t910	1
			t1214	1
			t1370	1
			t3247	1
			t5501	1
			t7428	1
		Spa-CC3212	t3040	1
		Excluded	t605	1
USA300 MRSA [ST8, SCC*mec* type IV]	76	Spa-CC008	t008	64
			t024	7
			t622	2
			t711	1
			t1610	1
			t4919	1
Queensland clone MRSA [ST93, SCC*mec* type IV]	56	Spa-CC202	t3949	38
			t202	17
			t4178	1

a ST, multilocus sequence type; SCC*mec*, staphylococcal cassette chromosome *mec*.
b The total number of AK3 MRSA isolates was 397, but the *spa* type of one isolate could not be determined and therefore this isolate was identified solely by PFGE typing.
c *spa* types with less than five repeats are excluded from the BURP analysis to determine *spa* clonal clusters.
d The total number of EMRSA-15 isolates was 100, but the *spa* type of two isolates could not be determined and therefore these isolates were identified solely by PFGE typing.

Discussion

The prevalence of MRSA in New Zealand has increased significantly over the last 10 years (2002-2011), cumulating in a massive 37.0% increase between 2010 and 2011. This 37.0% increase was the largest single-year rise during the last 10 years. Concomitant with the national trend of increasing MRSA prevalence, there have also been significant increases in most DHBs in recent years. Of particular note, is the nearly five-fold increase in the Tairawhiti DHB in 2011, which was due almost entirely to the AK3 MRSA strain.

Consistent with earlier years, in 2011 there were large geographical differences in the prevalence of MRSA within New Zealand, with rates generally highest in DHBs in the upper half of the North Island. As MRSA from both diagnostic specimens and screening specimens were included in the survey, any apparent differences in MRSA rates between DHBs could be partly due to differences in screening policies. However, the relative rates of MRSA infections between DHBs were very similar to the rates of all MRSA isolations. Rates of MRSA infections may also be influenced by different policies for obtaining and processing diagnostic specimens.

Eight MRSA strains are currently recognised in New Zealand: AK3 MRSA [ST5, SCC*mec* type IV], AKh4 MRSA [ST239, SCC*mec* type III], EMRSA-15 [ST22, SCC*mec* type IV], EMRSA-16 [ST36, SCC*mec* type II], Queensland clone MRSA [ST93, SCC*mec* type IV], USA300 MRSA [ST8, SCC*mec* type IV], WR/AK1 MRSA [ST1, SCC*mec* type IV] and WSPP MRSA [ST30, SCC*mec* type IV]. Supplementary descriptions of these strains, including typical antibiotic susceptibility patterns, are available at http://www.esr.cri.nz/competencies/Health/Pages/MRSA%20strains.aspx.

The MRSA strains associated with community-acquired infections often belong to lineages distinct from MRSA associated with hospital-acquired infections,[11] although this distinction is blurring with some community-associated MRSA (CA-MRSA) strains now also causing hospital-acquired infections.[12,13] In 2011, six strains, AK3 MRSA, WSPP MRSA, WR/AK1 MRSA, EMRSA-15, USA300 MRSA and Queensland clone MRSA, were collectively responsible for 86.2% of MRSA isolations in New Zealand. Five of these six most common strains - AK3 MRSA, WSPP MRSA, WR/AK1 MRSA, USA300 MRSA and Queensland clone MRSA - are usually considered CA-MRSA. The EMRSA-15 strain was the only healthcare-associated MRSA (HA-MRSA) strain represented among the six most common strains in 2011 and accounted for just 9.6% of MRSA.

The current predominance of CA-MRSA strains indicates that once again MRSA may be more commonly transmitted and acquired in the community in New Zealand than in our healthcare facilities. This was also the situation in the 1990s when New Zealand was one of the first countries to experience CA-MRSA, with the emergence of the WSPP MRSA strain in 1992 and its increasing prevalence throughout the rest of the decade.[14] As a consequence, by the late 1990s almost two-thirds of MRSA were isolated from people categorised as community patients. However, the introduction and spread of the healthcare-associated EMRSA-15 strain changed the epidemiology of MRSA from about 2000, with the EMRSA-15 strain being the most prevalent MRSA in each of the annual surveys conducted between 2002 and 2006, after which time its prevalence has steadily decreased.

The most notable change in MRSA strains in recent years has been the emergence in 2005 and subsequent spread of the AK3 MRSA. In 2011, AK3 MRSA was the most prevalent strain and accounted for 38.0% of MRSA isolations – up from 29.0% the previous year. AK3 MRSA was the most prevalent strain in most DHBs in the upper and central North Island and was particularly dominant in Tairawhiti. AK3 MRSA has been considered primarily a CA-MRSA strain in New Zealand, with the majority (56.2% in 2011) of patients from whom it is isolated being categorised as 'community' patients by our criteria. In addition, the relatively young age profile of the patients from whom AK3 MRSA is isolated is characteristic of CA-MRSA. Like most CA-MRSA, the AK3 MRSA strain has type IV SCC*mec* and it is not multiresistant – being most commonly resistant to only fusidic acid in addition to β-lactams. However, atypically for a CA-MRSA strain, it does not produce Panton-Valentine leukocidin (PVL). AK3 MRSA is multilocus sequence type 5 (ST5). Based on its MLST and SCC*mec* type, AK3 MRSA appears to belong to the globally widespread 'Paediatric Clone' (CC5-MRSA-IV). This clone has achieved pandemic spread and is a major cause of MRSA infections, but is considered a HA-MRSA clone.[15]

The CC398 MRSA strain was first identified among pigs and veal calves in the Netherlands, and it was already highly prevalent among these animals at the time it was first identified in 2003. Initial isolations of CC398 MRSA from humans were from people who had contact with pig farms. The strain quickly spread to other countries in Europe, North America and Asia, and also to other animal species. Consequently, CC398 MRSA is referred to as a 'livestock-associated' MRSA (LA-MRSA) strain.[16] While the transmissibility of this strain among humans may be lower than that of other widespread MRSA strains, CC398 MRSA clearly has the ability to become widespread among herds of animals, which creates a substantial reservoir and therefore risk for human MRSA colonisation and infection.[17]

Follow-up of the three patients from whom CC398 MRSA was isolated during the 2011 survey period, which represented the first isolations of this strain in New Zealand, failed to identify any of the risk factors associated with this MRSA strain: contact with livestock, especially pigs, or travel to Europe. However, one of the patients had travelled in the previous eight months to Vietnam and Cambodia. Interestingly, the MLST type of the isolate from this patient was ST1232, which belongs to clonal complex 398. There is just one entry for ST1232 in the international MLST database and it is from Cambodia, so this patient is likely to have acquired their MRSA there. Little is known about the prevalence and types of MRSA among pigs and other food-producing animals in New Zealand.

In conclusion, the prevalence of MRSA is continuing to increase in most DHBs in New Zealand, although there are still large variations in prevalence between DHBs. CA-MRSA strains are predominant, with AK3 MRSA now the most common MRSA strain. In the 2011 survey, the AK3 MRSA strain was almost three times as prevalent as any other strain.

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