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Methicillin-resistant *Staphylococcus aureus* in Australia

MRSA bacteraemia - 2013 to 2018

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Summary

As part of the work of the Antimicrobial Use and Resistance in Australia (AURA) Surveillance System, analyses of methicillin-resistant *Staphylococcus aureus* (MRSA) bacteraemia data collected by the Australian Group on Antimicrobial Resistance (AGAR) from 2013 to 2018 identified important national and state and territory trends. These trends can be used to inform local therapeutic, quality improvement and infection prevention and control initiatives.

Staphylococcus aureus is the cause of many infections, including such things as boils, bullous impetigo cellulitis, acute and chronic osteomyelitis, infections of intravascular lines and other device infections, through to more life-threatening infections such as septicaemia and meningitis.

Between 2013 and 2018, the proportion of *S. aureus* bacteraemias caused by MRSA remained relatively stable at between 17% and 18%. However, there were variations in trends for MRSA bacteraemia by place of onset which need to be considered, with the emergence of community-acquired (CA) MRSA as the dominant clonal group causing MRSA bacteraemia. Community-onset (CO) MRSA bacteraemia increased and hospital-onset (HO) MRSA bacteraemia decreased during this period. There were similar trends in the proportions of CA MRSA and hospital-acquired (HA) MRSA clones, with increases in CA-MRSA and decreases in HA-MRSA clones. This is because of increases in CA-MRSA as a cause of HO-MRSA bacteraemia during this time.

One reason for the increase in CA-MRSA was changes in the clones that cause MRSA disease. Reductions in hospital-onset and healthcare-associated MRSA are likely attributable to concerted efforts in hospitals to control *S. aureus* bacteraemia. These include improvements in the management of invasive devices, national reporting of *S. aureus* bacteraemia and the National Hand Hygiene Initiative.

In 2018, ST93-IV, a community-associated clone, was the dominant MRSA clone across Australia, with disproportionate burden in the northern areas of Australia. Overall it caused 22% of all MRSA bacteraemias in Australia, and 1 in 4 community-onset infections. Notwithstanding the dominance of ST-93-IV, there is large variation in the burden of clones that cause community-onset disease by geographic regions.

While there is a diversity of clones by state, territory and region over time, it can no longer be assumed that MRSA clones are specific to either community or hospital environments; this is also the case internationally. This highlights the importance of AGAR genomic surveys to inform optimal prevention, control and treatment strategies.

The therapeutic implications of the changing spectrum of MRSA disease include lower reliability of with first-line agents for empiric treatment of skin and soft tissue infections; clindamycin has become unreliable as an empiric choice. Microbiological sampling and confirmatory antimicrobial susceptibility testing are increasingly important in some settings, both to identify whether MRSA is present and to confirm optimal oral therapeutic choices.

As MRSA types and clones will continue to evolve in Australia, and there is variation between clones in relation to their ability to spread and become a problem, it is likely that specific control and prevention measures will be required for both hospital and community settings. For example, in relation to surveillance, infection prevention and control including decolonisation, antimicrobial stewardship and antiseptic use practices. Control of emerging and dominant clones, such as ST93-IV and ST22-IV, is a priority in this regard. As such, the Commission will more work closely with AGAR, the states and territories and the Aged Care Commission for Quality and Safety to identify targeted prevention and response strategies.

Whilst trend analyses are important for system-based monitoring and strategy development, it is always important to remember that each case represents a person with severe clinical disease. These AGAR data, together with other analyses, suggest that the burden of MRSA invasive disease may disproportionately impact Australian indigenous communities and aged care residents. Prevention and control of MRSA in diverse community settings is a priority to address this situation and a focus for the states and territories.

In the One Health context, surveillance of livestock-associated clones is important in addressing antimicrobial resistance, overall. This report includes information regarding livestock-associated MRSA, In 2013, it was detected in a nasal swab from an Australian pig veterinarian, and subsequently detected at very low levels in pig herds across Australia. More recently, it has been identified in farm workers, pigs and their environments with the proportion of ST398 compared to other MRSA clones higher in pigs than farm workers.

Introduction

Staphylococcus aureus is a frequent coloniser of humans and a major human bacterial pathogen. It is the cause of a wide range of infections from benign self-limiting conditions (such as boils, bullous impetigo and folliculitis), to more serious infections (including cellulitis, post-surgical wound infection, acute and chronic osteomyelitis, septic arthritis, infections of intravascular lines, and prosthetic joint and other device infections), to life-threatening infections (including septicaemia, meningitis, post-viral pneumonia and endocarditis).[1] It is carried by about 30% of the population at any one time, and for the great majority of people it causes no harm.[2] Nevertheless, it has the capacity to cause outbreaks of infection in hospitals from a common source or through poor hand hygiene practices. Blood stream infections from this organism are a target for hospital surveillance and infection prevention initiatives due to its high morbidity and mortality and potentially preventable occurrence.

Soon after the introduction of (benzyl) penicillin into clinical medicine in the 1940s, strains of penicillin-resistant *S. aureus* emerged that produced penicillinase – the first β-lactamase enzyme to be described.[3] By the late 1950s, chemists began working on chemical modifications of the penicillin nucleus in the hope of finding a modification that would protect the antimicrobial medicine from degradation by penicillinase. The first successful modification was methicillin, which was marketed for the treatment of staphylococcal infection in 1960 in the United Kingdom. Other modifications followed (such as nafcillin, oxacillin, cloxacillin, flucloxacillin and dicloxacillin), each developed specifically for treating staphylococcal infection caused by penicillinase-producing strains.

Jevons[4] first reported resistance to methicillin in clinical isolates of *S. aureus* (methicillin-resistant *S. aureus* [MRSA]) from a London hospital in 1961. Of note, the isolates were also resistant to streptomycin and tetracycline, highlighting the staphylococcal propensity for accumulating resistance to multiple agents. Since that time, and slowly at first, MRSA has become a global phenomenon, and has taken many forms. The first report of MRSA in Australia was from Sydney in 1968.[5] By the late 1970s a particular type of multi-resistant MRSA had become established in public hospitals on the eastern Australian seaboard.[6] That clone, now called Aus-2/3 (multi-locus sequence type ST239-MRSA-III), became established in tertiary care hospitals in most parts of Australia. By the mid-1980s, community strains of MRSA started appearing in Western Australia, and since that time have developed into an Australia-wide problem.[6]

The mechanism of resistance to methicillin in staphylococci differs from resistance to penicillin. Rather than being mediated by a β-lactamase, methicillin resistance is due to the production of an additional so-called penicillin-binding protein, PBP2a, which is encoded by the *mecA* gene. This protein is a variant of one of the essential cell-wall synthetic enzymes, PBP2 (a transpeptidase). A methicillin-resistant isolate retains its original PBP2, but also produces PBP2a, which retains its transpeptidase function but has much lower affinity for β-lactams generally, including penicillins, cephalosporins and carbapenems. Because the resistance mechanism is not that of a β-lactamase, MRSA are also resistant to the combinations of β-lactamase inhibitors with β-lactams. A homologue of *mecA*, known as *mecC*, produces a novel PBP that has only approximately 63% homology at the amino acid level to the original PBP2a.[7] Although *mecA*- and *mecC*-encoded proteins possess different biochemical properties, *mecC* is able to confer methicillin resistance.[7] First reported in *mecA*- negative MRSA from humans and cattle in the UK and Europe, a *mecC*-positive MRSA was reported in Australian in 2016 from the mandible of a five-year-old domestic cat located in a semi-urban area of Melbourne.[8]

Treatment of MRSA infections depends on severity and phenotype of clinical presentation. Superficial skin infections can be managed with drainage and/or topical agents. More serious infections will require systemic antimicrobials: vancomycin is most commonly used when intravenous therapy is needed, and only a limited range of agents are effective when oral therapy is needed dependent on MRSA type. Recent evidence has confirmed that vancomycin is suboptimal treatment for staphylococcal infection compared to β-lactams when the infection is caused by strains susceptible to methicillin.[9] The implication is that vancomycin is suboptimal therapy for MRSA infections, but unfortunately there is no evidence that any alternative intravenous agent is superior.

Tracking MRSA emergence and spread through typing

There have been several systems for typing strains of *S. aureus*. Prior to the advent of multi-locus sequence typing (MLST), the most popular system was phage typing, which used a collection of different viruses (called bacteriophages) that attack and kill specific strains of this bacterial species. The patterns of killing by the different phages defined the 'phage type'. Phage typing was supplanted by pulse-field gel electrophoresis (PFGE) in the 1980s, a technique that created a 'bar code' of the bacterial DNA after fragmenting it with a specific enzyme. PFGE was valuable at the local level, but due to technical variation, could not easily be used to compare results from different laboratories locally or internationally.

MLST was developed in the late 1990s, and applied to a range of bacterial species, including *S. aureus*, soon after. MLST involves the DNA sequencing of seven so-called housekeeping genes, which are found in all strains of the species, and whose sequences are known not to vary significantly over time. Each unique gene sequence is called an 'allele', and the combination of the seven allelic sequences defines the allelic profile, which is considered to be a distinct clone. MLST has the advantage of being stable and readily portable, meaning that sequences are stored and can then be compared from anywhere in the world (MLST online database and analysis website). It can also provide information about the evolution of individual clones. The sequence type is designated by a number, preceded by 'ST'. Related sequence types belong to families called 'clonal complexes'.

The sequence type provides the base information of a clone, but an additional piece of genetic typing is required to identify an MRSA clone. This additional information is called the 'SCC*mec*' type (Staphylococcal Cassette Chromosome *mec*). The acquisition of SCC*mec* converts a methicillin-susceptible clone of *S. aureus* into an MRSA clone. It is a piece of mobile DNA (meaning it can be transferred to other staphylococci) that has been acquired by a staphylococcus and inserted into its chromosome. Possession of SCC*mec* makes the staphylococcus resistant to methicillin because it contains the *mec* gene, which codes for the additional penicillin-binding protein PBP2a, and the *mec* gene's associated regulatory genes. There are at least 12 varieties of SCC*mec*, which vary in size and content, and each type is designated by an upper case roman numeral. This is added to the sequence type to provide the full designation of a clone – for example, the Aus-2/3 clone is ST239-III, meaning it is sequence type 239 and SCC*mec* type III. Larger SCC*mecs* possess additional resistance genes besides *mec*, and are the main contributors to multi-resistance.

PFGE still plays a role in discriminating specific genetic lineages amongst strains with the sequence and SCC*mec* type. It forms the basis of the Western Australian typing nomenclature that has wide currency across Australia. For instance, at least five different clones have been identified in the ST5-IV type, only one of which (PFGE pattern WA-3) has become more common in recent years.

As costs reduced, whole genome sequencing (WGS) analysis is becoming more common for tracking clones of resistant bacteria. Sequencing of isolates within AGAR began in 2015. Slight changes in groupings has occurred because of this, mainly in the ST45-V and ST5-IV types (see Table 1).

MRSA surveillance: AGAR

The Australian Group on Antimicrobial Resistance (AGAR) has been tracking MRSA infections across the country since 1985. Despite the voluntary nature of AGAR, contribution of isolates from at least 24 laboratories has been maintained, with all states and mainland territories regularly represented.

In 2013, AGAR commenced the Australian Staphylococcal Sepsis Outcome Program (ASSOP), and switched from surveillance of isolates from any site to a blood culture isolate only continuous surveillance methodology. Infections were categorised as community-onset (from blood cultures collected prior to or within 48 hours of admission) and hospital-onset (from blood cultures collected more than 48 hours after admission) infections. In 2015, there was a transition from PFGE to WGS, resulting in slight changes in grouping across surveillance years (see Table 1). This report focusses on trends in MRSA bacteraemias from 2013 to 2018, the period relating to continuous blood culture surveillance.

Community- versus healthcare-associated clones

Prior to the 1990s, MRSA occurrence was an exclusively healthcare-associated multi-resistant organism. Patients with community onset MRSA had clear healthcare contact, and as such clonal delineation between community- versus healthcare-associated clones was not required. The first definitive reports worldwide of community-associated MRSA disease – that is isolation of MRSA in an individual without any healthcare risk factors – were noted as early as 1993 from an Aboriginal population in the Kimberly region of Western Australia.[10] Possibly community-associated MRSA had been reported overseas earlier but because of associated intravenous drug use or possible healthcare contact and true community-associated disease could not be confirmed with certainty.[11]

Throughout AGAR surveillance, classification of MRSA varied in line with available evidence of the time. Initially, SCC*mec* types were generally attributed to healthcare or community-onset disease with the larger SCC*mec*, types I, II and III, associated with healthcare, and types IV and V with the community. Healthcare clones were historically reliably multidrug resistant with only a small range of antimicrobials available for therapy including the glycopeptides, rifamycins and sodium fusidate.

The emergence of ST22-IV, a clone attributed to healthcare related outbreaks but harbouring SCC*mec* type IV, complicated previous groupings. The “epidemic” and “community” classification was present in the early 2000s, with epidemic strains being classified based on their ability to spread between and within hospitals. This accounted for the EMRSA nomenclature including the ST239-III and ST22-IV clones. In 2005[12], the Centre for Disease Control and Prevention (CDC) surveillance program formulated a MRSA definition as community-associated occurring without any of the following: history of hospital contact or long-term care facility residence within the year before infection, presence of a percutaneous device or indwelling catheter, dialysis within the previous year, hospitalization <48 hours (defined as three admission days) before MRSA culture, or previous MRSA infection or colonisation. Remaining cases were defined as healthcare-associated. Transition from the epidemic to healthcare-associated terminology occurred similarly across AGAR reports and remains today but specifically with <48 hours as the demarcation rather than calendar days.

The hospital versus community-onset classification in AGAR relates to the patient’s timing of onset of blood culture sampling in relation to healthcare. Community-onset bacteraemia is defined as a bacteraemia cultured from blood cultures collected prior to or within 48 hours of hospital admission. Hospital-onset bacteraemia occurs more than 48 hours after admission. It does not relate to specific MRSA clones.

MRSA: the clones

The introduction of MLST via whole genome sequencing in AGAR surveillance has enhanced understanding of MRSA epidemiology, or more correctly, epidemiologies. MRSA can be classified into three 'types': healthcare-associated, community-associated and livestock-associated; each with a range of different clones. Table 1 shows the key features of the healthcare-associated and the community-associated types and clones that have been tracked in Australia since 2000.

Healthcare-associated (HA-MRSA)

Two healthcare-associated clones have dominated healthcare-acquired MRSA infections in Australia: ST239-III (Aus-2/3) and ST22-IV (EMRSA-15) – the first possibly 'home-grown', bolstered by second clade importation, and the second likely only imported.

ST239-III: the first major Australian healthcare-associated multidrug-resistant clone

ST239-III encompasses the two PFGE types, Aus-2 and Aus-3. This clone is problematic clinically because it is multidrug-resistant with few available oral or intravenous agents for treatment. Historically, it was also the major cause of hospital-onset MRSA disease in Australia. Typically, it harbours resistance to macrolides, lincosamides, tetracyclines (genes located within SCC*mec* III), as well as trimethoprim and trimethoprim-sulfamethoxazole, plus gentamicin, and frequently acquired resistance to ciprofloxacin and rifampicin. Recent detailed genomic and phenotypic studies of ST239-III in Australia have shown that what was identified as Aus-2/3 may actually represent a mixture of two clades.[13] One clade represents the clade from the 1970s, whilst the second, which appeared in 2001 in Victoria, may have originated in Asia.[13]

The current evidence suggests that the first strains originated in Australia or possibly the United States.[14-16] The earliest known Australian strain was isolated in 1976.[16] By the late 1970s this clone had become established in many Melbourne teaching hospitals.[17] In 1985, when the first AGAR surveys were conducted, Aus-2/3 (as defined by PFGE performed at the time) was found to cause 12–25% of all *S. aureus* infections in large public capital-city hospitals along the eastern seaboard, in Brisbane, Sydney, Canberra and Melbourne, and to a lesser extent in Adelaide.[18] The only state that did not become a reservoir for ST239-III over time was Western Australia. This was likely due to intensive efforts at screening and segregating patients and staff from eastern states' hospitals.[19] It still remains very uncommon there.[20]

Biennial surveillance of hospital-onset *S. aureus* isolates collected from all sites from 2005 to 2012 demonstrated a decline in the proportion of the Aus-2/3 clone with the rate of decline increasing between 2007 and 2009.[21] Analysis of the trend prior to 2005 is difficult, due to inclusion of both community- and hospital-onset samples in the datasets. Notably, the decline in this clone in community-onset surveillance from 2002 to 2012 commenced in 2002.

Table 1: Important MRSA clones that have been identified in Australia 2013–18

Association	MRSA and SCC *mec**	Common PFGE included	Origin (year) [references]	First detected in Australia [reference]	Typical resistance pattern§	Panton-Valentine leucocidin	Major reservoir
Healthcare-associated	ST5-II	New York / Japan or USA100	Japan (1982)[22]	2005[23]	Macrolides/lincosamides Fluoroquinolones Tetracyclines Gentamicin variable	Negative	None
	ST22-IV	EMRSA-15	England (1991)[24]	1997[25]	Fluoroquinolones Macrolides/lincosamides variable	Negative	Long-term care facilities
	ST36-II	EMRSA-16 or USA200	Southern England (1991)[26]	2002[27]	Macrolides/lincosamides Fluoroquinolones Mupirocin	Negative	None
	ST239-III	Aus-2/3#	Australia or USA (1976)[14-16]	1976[16]	Macrolides/lincosamides Tetracyclines Trimethoprim-sulfamethoxazole Gentamicin Fluoroquinolones	Negative	Hospital 'frequent flyers'

continued

Table 1: Important MRSA clones that have been identified in Australia 2013–18 (continued)

Association	MRSA and SCC *mec**	Common PFGE included	Origin (year) [references]	First detected in Australia [reference]	Typical resistance pattern§	Panton-Valentine leucocidin	Major reservoir
Community-associated	ST1-IV	WA-1	Northern Western Australia[10, 28]	1989[10]	Fluoroquinolones, Macrolides/lincosamides variable Fusidic acid variable	Negative	Community
	ST5-IV	WA-3†, WA-21, WA-64, WA-71, WA-96, WA-105,	Western Australia	1999[28]	Macrolides/lincosamides Fluoroquinolones Tetracyclines Gentamicin variable	Negative	Community
	ST5-IV	WA-121	Western Australia	2010	Macrolides/lincosamides/ Trimethoprim Fluoroquinolones Tetracyclines Gentamicin variable	Positive	Community
	ST8-IV	USA300, WA-101, WA-5	United States (2000)[29]	2000[29]	Macrolides/lincosamides Fluoroquinolones (variable)	Positive	Community
	ST22-IV	Nil	Indian Subcontinent (2004)[30]	2005[20]	Trimethoprim/Gentamicin/ Fluoroquinolones	Positive	Community
	ST30-IV	Oceania/Southwest Pacific	New Zealand (1992)[31]	1997[32]	Macrolides Fluoroquinolone variable	Positive	Community
	ST45-V	WA-84† WA-4	Victoria	≤ 2004 [AGAR studies]	Fluoroquinolones Macrolides/lincosamides, Tetracyclines (variable)	Negative	Community
	ST78-IV	WA-2	Western Australia	≤ 2000 [AGAR studies]	Macrolides/lincosamides (variable)	Negative	Community
	ST93-IV	Queensland	South-eastern Queensland (2000)[33]	2000[33]	Typically no additional resistances	Positive	Community

* Staphylococcal Cassette Chromosome mec

† Dominant type in the MLST clone in the AGAR series

§ Apart from β-lactams

The 2/3 designation refers to different pulsed field electrophoresis types.

The decline of ST239-III, from at least 2005, is believed to reflect improved infection control efforts in all hospitals. These included the introduction of the National Hand Hygiene Initiative in June 2008[34], and national public reporting of healthcare-associated *S. aureus* bacteraemia.[35, 36] These initiatives were supported by implementation from 2013 of the National Safety and Quality Health Service (NSQHS) Standards (first edition) for accreditation of health service organisations, particularly the Preventing and Controlling Healthcare-Associated Infections Standard.[37] The requirements of the NSQHS Standards would have been complemented by local initiatives such as central line associated care bundles and intravascular device management processes more generally. Additionally, the antimicrobial stewardship requirements of the NSQHS Standards likely contributed to reduced use of intravenous antimicrobials and hence intravenous device requirements, as well as less reliance on fluoroquinolones.[38]

ST22-IV: a hospital and residential aged care facility healthcare clone

ST22-IV encompasses the Panton-Valentine leucocidin (PVL)-negative clone also known as EMRSA-15. Not all ST22-IV are considered healthcare-associated, as there is also a PVL-positive ST22-IV clone that is considered to be community-associated. Phylogenetic analyses of this sequence type suggest a distinct evolutionary pathway from the PVL-negative clone. The PVL-negative clone emerged in the United Kingdom (UK) in 1991[24, 39] where it was noted to cause hospital outbreaks. It was assigned its healthcare-associated status due to this characteristic, evidence based on phylogenetic analyses and epidemiological grouping of healthcare clones related to residential aged care or hospital settings.

PVL-negative ST22-IV can be suspected phenotypically by its distinct resistance profile and its lack of urease production.[25] It is consistently resistant to ciprofloxacin and often to macrolides/lincosamides as well as the β-lactam class. Data suggests that its susceptibility profile to antiseptics may differ to other clones[40] with elevated MICs to chlorhexidine. The emergence of fluoroquinolone resistance in this clone occurred in the mid-1980s, and was attributed to the first fluoroquinolone clinical trials in the UK that occurred during that time.[24]

The first Australian reports of EMRSA-15 were from Western Australia in 1997, in British healthcare workers who were screened as part of that state's MRSA containment policy. In Western Australia in 1997, 2.5% of all MRSA notifications were EMRSA-15; the proportion rose to 14.7% within three years. By 2001, it had been isolated from residents of 63 residential care facilities and 11 hospitals and caused four known outbreaks.[25] Healthcare workers migrating from outside Western Australia with positive screening tests were noted to be from the UK or the eastern Australian seaboard, demonstrating that it was already prevalent in Australian healthcare. By 2000, it was seen nationally in AGAR surveys in clinical samples, most prominently in Sydney. Its prevalence in AGAR surveillance has continued to grow steadily through all isolate (2000–2012) and blood culture only surveillance periods (2013 onwards).[21] This is in contrast to evidence that suggests aged care colonisation in some parts of the UK decreased between 2006 and 2009.[41]

Healthcare worker colonisation may continue to be a factor in the capacity for ST22-IV persistence and ongoing spread. Australian studies have demonstrated that it is four-fold more likely to colonise healthcare workers in an outbreak than other healthcare-associated strains such as ST239-III.[42] Despite strict pre-screening protocols in Western Australia, the proportion of colonised healthcare workers during localised outbreaks was found to be 3.4% for EMRSA-15, compared to 0.81% for Aus-2/3, despite Aus-2/3 being prevalent in Australian healthcare for many years. In contrast to healthcare workers, the proportions of patients colonised during the same outbreaks were 6.7% and 8.9% respectively.[42]

The reasons for higher colonisation is unknown however there are reports from the UK in the 1990s demonstrating ongoing persistence in healthcare workers during outbreak control efforts, which could only be interrupted with hospital-level cleaning of their home environment[43] and textiles. Apart from the first detection in UK healthcare workers in Western Australia, the link between foreign healthcare workers and the repeated introduction of EMRSA-15 remains speculative.

However, it is likely that the ST22-IV clone has a significant reservoir in residential aged-care facilities.[41, 44] In the UK, after emerging only a decade or so before, it was found to be the predominant MRSA clone isolated from nasal swabs in 65 nursing homes in Leeds.

Similarly, in Australia, a single centre study in Victoria found that 33% of ST22-IV infections occurred in patients admitted from residential aged-care facilities, compared to only 5% of cases caused by ST239-III.[44] Recent national phenotypic data also supports this finding. In 2017, one in three (33%) isolates from surveillance in aged care homes were methicillin resistant. The dominant resistance phenotype of MRSA isolates from aged care seen in this survey was consistent with the ST22-IV clone, with non-susceptibility to ciprofloxacin (46.1%), erythromycin (44.2%) and clindamycin (41.2%).[45] Although phenotypic differentiation between ST22-IV and other clones is not technically possible in these analyses, it may be that this may represents a burden of ST22-IV. Antibiograms compiled from samples referred from clinical settings in Queensland in 2018, suggest ST22-IV is three times higher in aged care compared to hospital settings, and more than ten times higher than in isolates referred from the community.[46] Although referral bias may be skewing these results, this adds support to the aged-care reservoir theory, which can only be confirmed on a national basis by further research.

Other healthcare-associated clones

Other healthcare-associated clones have remained rare in Australia. The AGAR surveys have regularly detected the New York/Japan clone (ST5-II, also called USA100) at very low levels since 2005 (1–6 isolates annually). This clone was first described in Australia in an outbreak in Western Australia, which was traced to an Australian healthcare worker who had been hospitalised in New York. This clone has subsequently remained uncommon in Western Australia.[23] ST5-II has not become established in Australia, despite its high prevalence in the US, Japan and Korea[47], and its high capacity for spread. The local situation for ST5-II is intermittent introduction from overseas, without local spread. ST5-II has a similar resistance profile to ST22-IV, including to macrolides/lincosamides and ciprofloxacin, but is less multi-resistant than ST239-III.

Similarly, EMRSA-16 (ST36-II and also called USA200), which is second only to ST22-IV in prevalence in the United Kingdom, has been seen intermittently in AGAR surveys, but shown no signs of becoming established.

Other healthcare-associated clones that have been found in the AGAR surveillance include ST250-I (so-called classical MRSA), ST247-I (EMRSA-17), ST8-VI (Irish 2), and ST228-I (Southern German). These fit the pattern of sporadic introduction into Australia, with no or very limited spread.

Community-associated MRSA

Community-associated MRSA (CA-MRSA) clones first emerged in Australia in the 1980s, and since that time they have diversified and increased in prevalence. In 2014, they were the most common cause of MRSA blood stream infection, causing 10.5% of all *S. aureus* blood stream infections, compared to 7.6% of healthcare-associated-MRSA (HA-MRSA) types.[21] The proportion of hospital-onset disease caused by CA-MRSA has been steadily rising. CA-MRSA clones now play a substantial role in hospital-onset *S. aureus* infections. This is not surprising, as a significant proportion of healthcare-associated staphylococcal infections are caused by strains that are carried by the patient at the time of the intervention that led to the infection. Higher prevalence of MRSA in the community increases the likelihood of MRSA-related complications when patients are admitted to hospital from the community.

CA-MRSA clones tend to be more susceptible to antimicrobials than HA-MRSA clones. They tend not to be resistant to the non-β-lactam antimicrobials, although with the passage of time, some CA-MRSA clones are accumulating more resistances. A characteristic frequently associated with the two dominant CA-MRSA clones, ST93-IV and ST30-IV, is the possession of the PVL-toxin (see Box 3). Other clones produce PVL at lower or variable rates (Table 2). In 2014, almost half of CA-MRSA (45%) bacteraemias were hospital-onset, that is they occurred more than 48 hours after hospital admission, as opposed to community-onset.[21]

Table 2: MRSA clones, association, place of onset and PVL carriage, 2018

Association	Clone	PVL positive, %
Healthcare-associated	ST22-IV (PVL negative)	0.0
	ST239-III	0.0
	ST5-II	–*
	ST8-II	–*
Community-associated	ST93-IV	96.0
	ST45-V	0.0
	ST5-IV	34.1
	ST1-IV	2.9
	ST30-IV	81.0
	ST97-IV	0.0
	ST78-IV	0.0
	ST5-V	–*
	ST8-IV	–*
	ST22-IV (PVL positive)	–*
	ST872 –IV	–*
	ST72-IV	–*
	ST953-IV	–*
	Other	14.0

* Insufficient numbers (<10)
Source: Australian Commission on Safety and Quality in Health Care AGAR Sepsis Outcome Programs 2018 Report[48]

ST1-IV (WA-1): the first established CA-MRSA in Australia

Community-associated strains of MRSA were first noted in Western Australia in 1984, and became a particular problem in the Kimberley region by 1989.[49] By 2004, it became clear that a number of new clones of CA-MRSA had emerged in Western Australia, and that one particular clone, ST1-IV (WA-1), dominated the CA-MRSA picture there, and spread to almost all other states and territories.[27, 28] It has been one of the most important CA-MRSA clones isolated across Australia by AGAR surveillance.

ST1-IV is usually susceptible to non-β-lactam agents. Around half of the strains harbour at least one additional resistance mechanism, most commonly to macrolides/lincosamides and/or fusidic acid. WA-1 does not usually produce PVL, although previous reports suggest that 2.8% of ST1-IV isolates possess this toxin.[48, 50]

ST30-IV (SWP): the Southwest Pacific clone – an introduced CA-MRSA

The SWP clone (ST30-IV) first appeared in Auckland, New Zealand, and was frequently isolated from patients of Western Samoan origin, leading to its original designation as WSPP (Western Samoan phage pattern).[51] The first descriptions were in 1998.[52] Soon after, it was recognised that ST30-IV was also present in Australia; and people of Pacific Island origin (Western Samoa and Tonga) were disproportionally affected.[32, 53] Recent studies have dated the SWP clone as far back as 1953[54], when its methicillin-susceptible and PVL-producing ancestor, then called 'phage type 80/81', was associated with major outbreaks of infections in Australian neonatal nurseries[55] and subsequently many other parts of the world.

The ST30-IV clone is almost always susceptible to non-β-lactam classes of antimicrobial; approximately 10% have additional resistance(s). The majority of these clones (70%) produce PVL (see Box 3).

ST93-IV (Qld): the Queensland clone – a home-grown and increasing problem

ST93-IV (Queensland) has become the dominant CA-MRSA in Australia. First recognised amongst Caucasians (and not Pacific Islanders) in southern Queensland in 2000.[33, 48]. At last review it had become the dominant CA-MRSA in Queensland, Northern Territory, and South Australia, on equal terms with WA-1 in New South Wales, and Victoria, and second only to WA-1 in Western Australia.[21, 50] AGAR surveys show that it was actually first detected in five states/territories in 2000, mostly notably in New South Wales.

Like the SWP clone, the Queensland clone tends to be susceptible to non-β-lactam classes of antimicrobial, and importantly it also produces PVL (see Box 3). The reasons for its success remain unclear, despite extensive molecular studies, and it harbours very few virulence factors besides the genes encoding PVL.[56]

It has been previously documented that the proportion of the PVL-producing clones, notably the Queensland and SWP clones, decreased with the change to bacteraemia-only surveillance in 2013.[21] This is consistent with the observation that PVL-producing strains are less likely to cause invasive infection.[57-59]

ST5-IV: an Australian clone with an international SCC*mec*

The ST5-IV clone is a varied clone comprising multiple PFGE types. WA-3, a largely PVL negative stain, was first documented in New South Wales and South Australia in 2000[27], but is now seen Australia wide. This is in contrast to a relatively newer strain, WA-121, a PVL positive ST5-IV clone that is typically urease positive. It has become increasingly common since it was first isolated from a 62 year old non-Aboriginal man from the Kimberley region of Western Australia. Although AGAR data does not differentiate between the varying types of ST5-IV, the PVL positive type within the clone carries the *edinA* epidermal cell differentiation inhibitor gene. Additionally it carries the SCC*mec* IVc, a SCC*mec* that is rarely documented in isolates attributed to Australian origin. It now accounts for an appreciable proportion of all MRSA in Western Australia.

ST45-V (WA-84, WA-4): a multidrug-resistant CA-MRSA

The ST45-V clone was first documented in Victoria in 2004. In 2010, it was found in NSW. It has now become successfully established in a number of states, and caused hospital outbreaks.[60] Although ST45-V is considered a CA-MRSA, based on the SCC*mec* type, it has been associated with multiple hospital outbreaks in New South Wales.[60] In a recent study from New South Wales, was reported that, of the 7,624 MRSA isolated in NSW from 2012–2017, ST45-V had increased significantly from <0.5% in 2012 to 14% of isolates in 2017 ($p<0.001$); 25% of isolates were for hospital-onset infection.[61] Unlike many CA-MRSA strains, ST45-V is multi-drug resistant, typically to erythromycin, gentamicin, tetracycline and the fluoroquinolones. It does not possess the PVL toxin; and it characteristically has a deletion in the *spa* gene which led to initial difficulties in identification when particular commercial MRSA gene detection kits were used.

Other CA-MRSA clones – ever increasing diversity

Since 2000, more than 100 clones on CA-MRSA have been detected in Australia. These are a mixture of both locally arising and international clones. For the locally arising clones, it suggests that although SCC*mec* is not believed to spread easily from MRSA to other methicillin-susceptible *S. aureus* clones, it does happen with some frequency. Previous longitudinal analyses have demonstrated that other CA-MRSA have collectively outnumbered WA-1, SWP and Queensland since 2006.[21] Thus, while SCC*mec* has the ability to be inserted into many chromosomal backgrounds, most of the resulting clones are not particularly well adapted for transmission and carriage compared to the dominant clones.

Following the introduction of molecular typing of MRSA, the AGAR surveys have shown an ever increasing number of new CA-MRSA clones across Australia. A few have become established are seen regularly. These include:

- WA-2 (ST78-IV): first documented in 2000, predominantly in Western Australia[27], but since spread Australian-wide; largely PVL negative
- PVL-positive ST22-IV: genetically distinct from the healthcare-associated ST22-IV clone, has been known to cause hospital outbreaks but considered a community-associated isolate.

Another clone of interest is USA300 (ST8-IV). This is a clone of CA-MRSA that has become a major cause of *S. aureus* infection in the community in the US, accounting for up to 50% of all community infections in many parts of country.[62] It was first recognised in 1999, and after spreading across the US, is an important cause of infection in some parts of the country.[63] This clone has been detected in AGAR surveys from at least 2000. However, numbers remain low, and it is another example of the sporadic introduction of a clone that has, to date, failed to become established in Australia, despite success elsewhere.[64] Like the Southwest Pacific and Queensland clones, USA300 produces PVL (see Box 3).

There have also been sporadic appearances of CA-MRSA from other countries, including the Taiwan clone (ST59-V), the Bengal Bay clone (ST772-V), and the European clone (ST80-IV)). To date, none of these are showing signs of becoming established.

The importance of Panton-Valentine leucocidin

Panton-Valentine leucocidin (PVL) was first described in 1932 by Panton and Valentine in *S. aureus* causing purulent infections.[65] Its importance was unrecognised until 2003, when a strong association was noted between certain clones of CA-MRSA and PVL[66] by French and other international investigators. Both the SWP and Queensland clones, as well as USA300, were identified as carrying PVL in that study. It has been shown subsequently that PVL is not confined to CA-MRSA, and can be found in methicillin-susceptible strains of *S. aureus*.[67]

PVL-producing strains of *S. aureus* are associated with a variety of distinctive clinical manifestations: excessively purulent skin and soft tissue infections that frequently require drainage/surgical intervention[68], recurrent furunculosis (boils)[69], multifocal osteomyelitis associated with early bone necrosis and deep vein thrombosis[70], and necrotising pneumonia.[71] By contrast, PVL-producing strains are less likely to cause bacteraemia or other invasive disease and the same or lower mortality than that caused by PVL negative *S. aureus*.[59, 72] Overall, PVL-producing *S. aureus* are not more life-threatening than other *S. aureus* but cause more morbidity, hospitalisation and infections that require surgical intervention. They appear to be over-represented in skin and soft tissue infections requiring hospital care, when compared to PVL-negative strains.[59, 72] The high degree of purulence of these infections may contribute to higher densities of organisms on the skin available for transmission to other susceptible individuals.

Infections caused by PVL-producing MRSA strains are more challenging to treat in the community, not just because of the frequent need for surgical invention, but also because the availability of effective antimicrobials in the community is limited. Currently 40.5% of all CA-MRSA in Australia are PVL-producing, found primarily in the Queensland and SWP clones.

Livestock-associated MRSA

There have been sporadic isolates of livestock-associated MRSA internationally for many years; but the first major problem emerged in Europe in 2003, with the description of ST398 in pigs and subsequently other livestock.[73] To date, this livestock-associated clone has not been detected in AGAR surveys. In 2013, it was detected in a nasal swab from an Australian pig veterinarian[74], and subsequently detected at very low levels in pig herds across Australia.[75] More recently, it has been identified in farm workers, pigs and their environments with the proportion of ST398 compared to other MRSA clones higher in pigs than farm workers.[76]

Another clone, ST612-IV, has been traditionally associated with equine reservoirs as well hospital environments outside of Australia. In Australia, this clone has been isolated from equine veterinarians and horses, as well as patients and healthcare workers identified secondary to mandatory screening processes in Western Australia. The lineages of these Australian isolates clustered to the reported reservoirs, either equine-associated or the South African healthcare lineage.[77] This clone (WA-20 – ST612-IV)[78], has been found only twice, in the 2013 and 2015 AGAR surveys, causing community-onset bloodstream infection.

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MRSA: hospital- versus community-onset disease

Figure 1 shows the combined incidence of healthcare- and community-associated clones from 2013 to 2018, as a proportion of all *S. aureus* bacteraemia reported to AGAR. In 2018, hospital-onset MRSA episodes comprised 4% of all *S. aureus* cases, compared to 7% in 2013.

Conversely, the incidence of community-onset MRSA disease fluctuated at around 11–14% from 2013 to 2018. Community clones caused 77% of all MRSA in 2018, compared to 59% in 2013. ST93-IV (Queensland clone), a community-associated clone, was the most common MRSA clone causing MRSA bacteraemia in Australia in 2018 (Figure 2). From 2013 to 2018, ST93-IV and ST22-IV (EMRSA-15), a healthcare-associated clone, were the largest contributors to episodes of bloodstream infection captured by AGAR. ST22-IV declined from 2014, and was overtaken by ST93-IV as the most common cause of all MRSA disease in Australia in 2016 (Figures 2 and 3). In 2018, ST93-IV caused one in four community-onset MRSA bacteraemias (Figure 4). Healthcare-associated clones, as a cause of hospital-onset MRSA disease, reduced from 2013 to 2018 from 55% to 37% (Figure 5), making community-associated clones the most common cause of hospital-onset disease.

The decreases in hospital-onset MRSA disease are attributed to ongoing reductions in ST239-III, followed later by ST22-IV. The expansion of ST93-IV accounted for the majority of increases in community-onset disease.

In 2014, at the end of the previous MRSA trend analysis, ST22-IV comprised 30% of all MRSA, and 5% of all *S. aureus* isolates[21]; it increased over the period 2000–2014 despite decreases in other parts of the world over the same period.[41] By the end of this analysis in 2018, the proportions had reduced to 18% and 3% respectively. In 2013, ST22-IV caused 50% more MRSA disease than ST239-III. Due to the decrease in cases of ST239-III, in 2018, ST22-IV was almost five times as common as the other main healthcare-associated clone in community- and hospital-onset disease, and has been superseded only by ST93-IV in terms of overall numbers of MRSA. It contributes significantly to both hospital- and community-onset bacteraemia.[50]

Figure 1: MRSA place of onset, percentage of all *S. aureus*, AGAR, 2013–2018

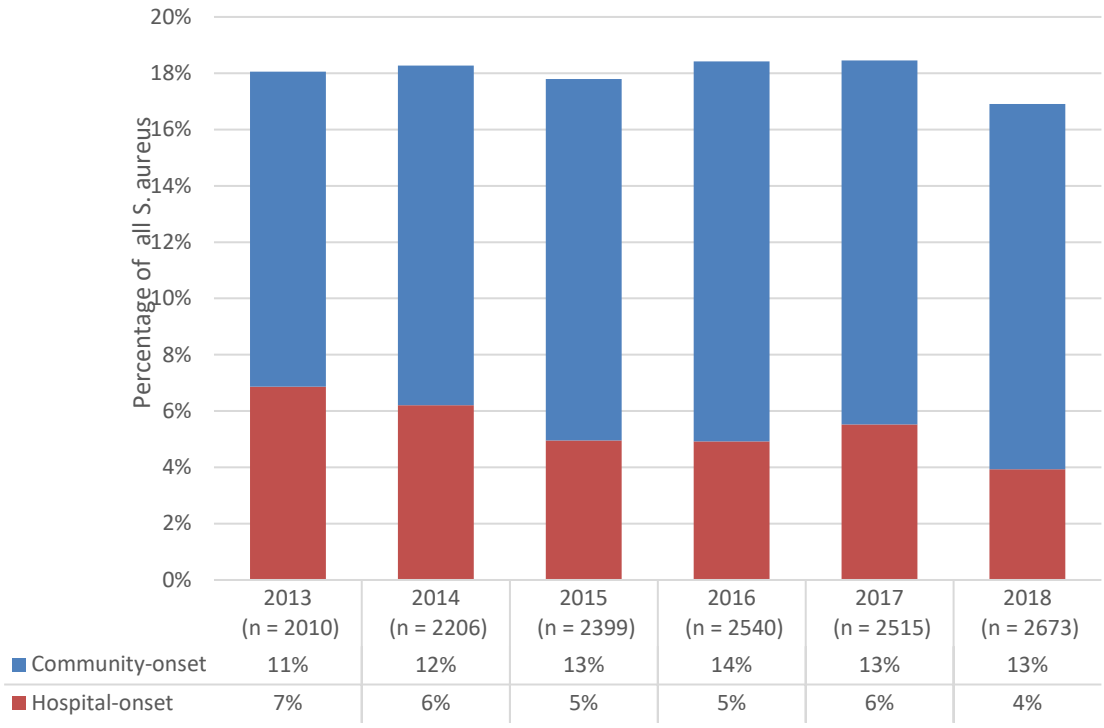
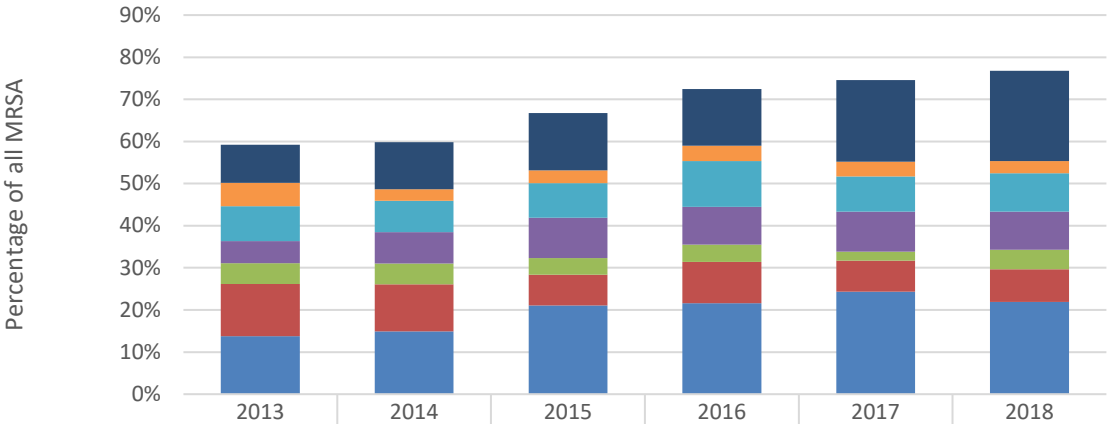
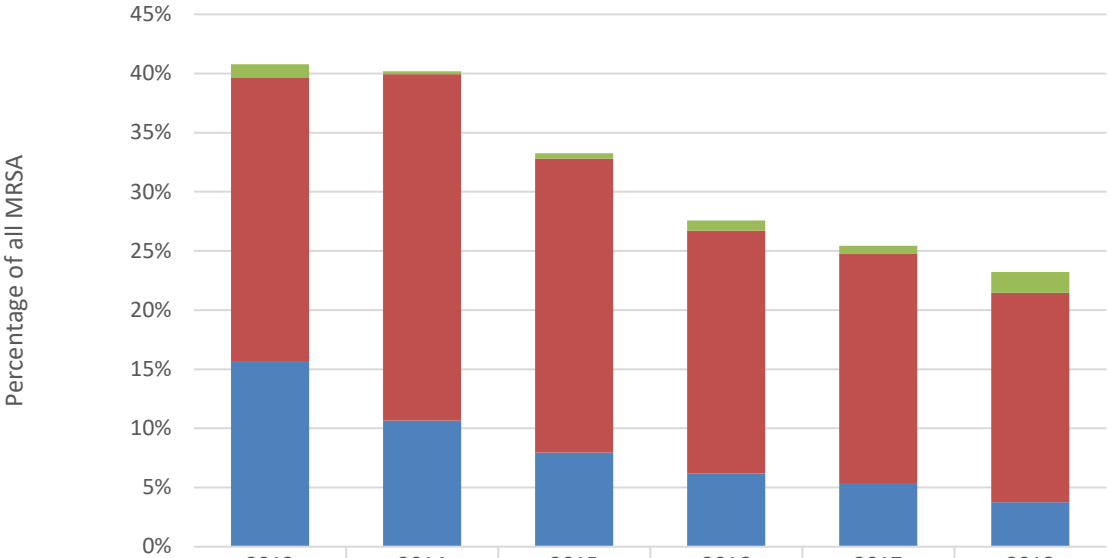


Figure 2: Community-associated MRSA clones, percentage of all MRSA, AGAR, 2013–2018



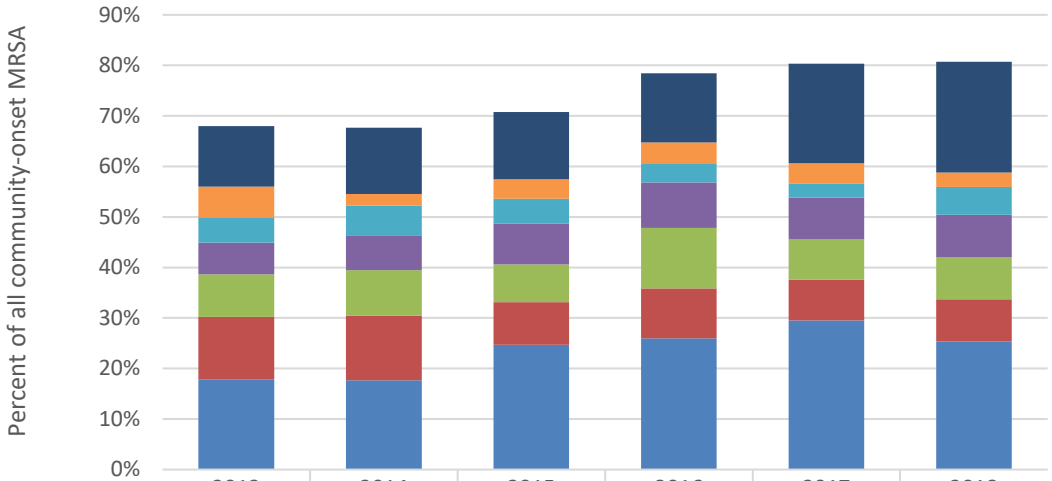
	2013 (n = 363)	2014 (n = 403)	2015 (n = 427)	2016 (n = 468)	2017 (n = 464)	2018 (n = 452)
Other CA	9%	11%	14%	13%	19%	21%
ST78-MRSA-IV	6%	3%	3%	4%	3%	3%
ST5-MRSA-IV	8%	7%	8%	11%	8%	9%
ST45-MRSA-V	5%	7%	10%	9%	9%	9%
ST30-MRSA-IV	5%	5%	4%	4%	2%	5%
ST1-MRSA-IV	12%	11%	7%	10%	7%	8%
ST93-MRSA-IV	14%	15%	21%	22%	24%	22%

Figure 3: Healthcare-associated MRSA clones, percentage of all MRSA, AGAR, 2013–2018



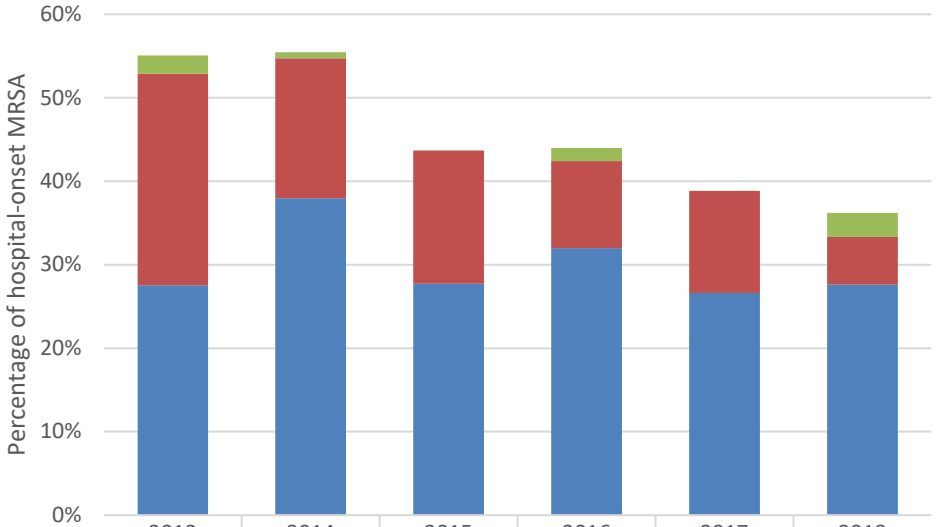
	2013 (n = 363)	2014 (n = 403)	2015 (n = 427)	2016 (n = 468)	2017 (n = 464)	2018 (n = 452)
Other HA	1%	0%	0%	1%	1%	2%
ST22-MRSA-IV	24%	29%	25%	21%	19%	18%
ST239-MRSA-III	16%	11%	8%	6%	5%	4%

Figure 4: Community-associated MRSA clones, percentage of all community-onset MRSA, AGAR, 2013–2018



	2013 (n = 225)	2014 (n = 266)	2015 (n = 308)	2016 (n = 343)	2017 (n = 325)	2018 (n = 347)
Other CA	12%	13%	13%	14%	20%	22%
ST78-MRSA-IV	6%	2%	4%	4%	4%	3%
ST30-MRSA-IV	5%	6%	5%	4%	3%	5%
ST45-MRSA-V	6%	7%	8%	9%	8%	8%
ST5-MRSA-IV	8%	9%	7%	12%	8%	8%
ST1-MRSA-IV	12%	13%	8%	10%	8%	8%
ST93-MRSA-IV	18%	18%	25%	26%	30%	25%

Figure 5: Healthcare-associated MRSA clones, percentage of all hospital-onset MRSA, AGAR, 2013–2018

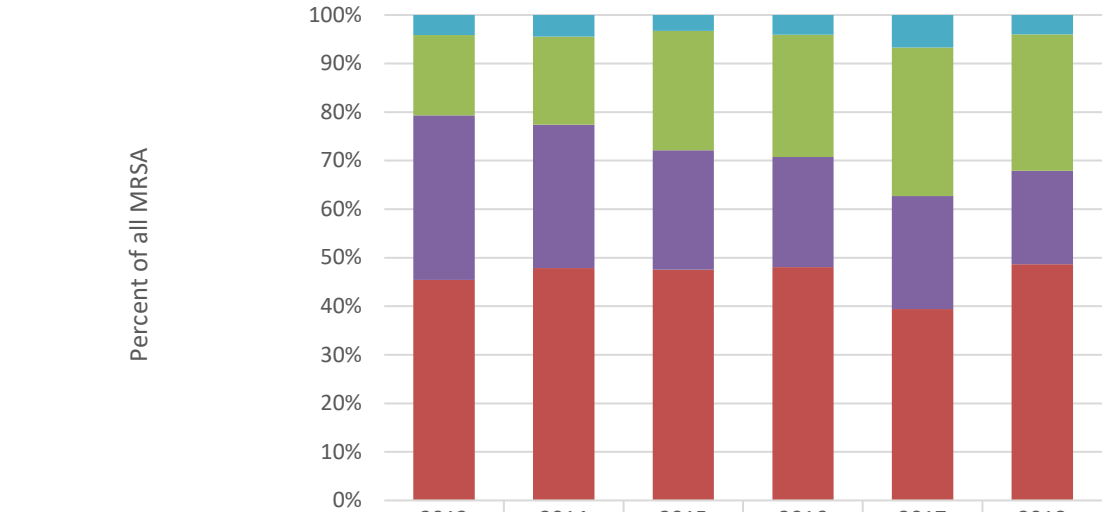


	2013 (n = 225)	2014 (n = 266)	2015 (n = 308)	2016 (n = 343)	2017 (n = 325)	2018 (n = 347)
Other HA	2%	1%	0%	2%	0%	3%
ST239-MRSA-III	25%	17%	16%	10%	12%	6%
ST22-MRSA-IV	28%	38%	28%	32%	27%	28%

PVL Status

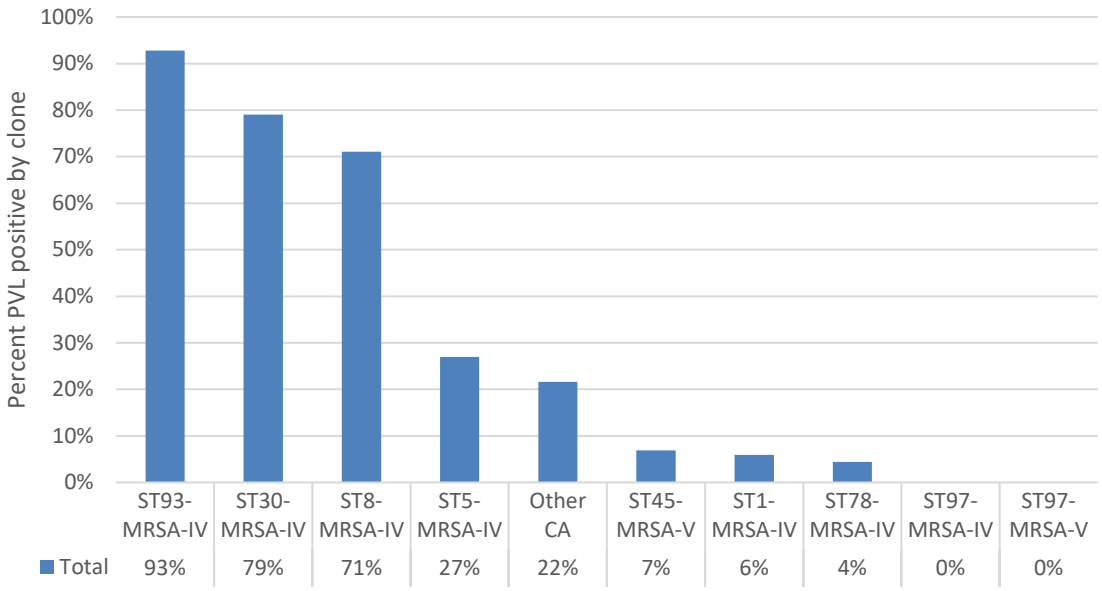
The treatment of severe disease due to MRSA differs when the presence of PVL is suspected. Therefore, knowledge of the frequency of PVL in the community and hospital is relevant for clinical care. PVL disease occurs more commonly in community-onset disease (37%), in comparison to hospital-onset disease (17%). In 2013, 80% of PVL-positive disease occurred in the community, rising to 88% in 2018 (Figure 6). ST93-IV, ST30-IV and ST8-IV harboured PVL most commonly during the last six years (Figure 7).

Figure 6: PVL status, community and hospital-onset disease, percentage of all MRSA, AGAR, 2013–2018



	2013	2014	2015	2016	2017	2018
Hospital-onset: PVL positive (n)	15	18	14	19	31	18
Community-onset: PVL positive (n)	60	73	105	118	142	127
Hospital-onset: PVL negative (n)	123	119	105	106	108	87
Community-onset: PVL negative (n)	165	193	203	225	183	220

Figure 7: Proportion of PVL positive community-associated clones, AGAR, 2013–2018

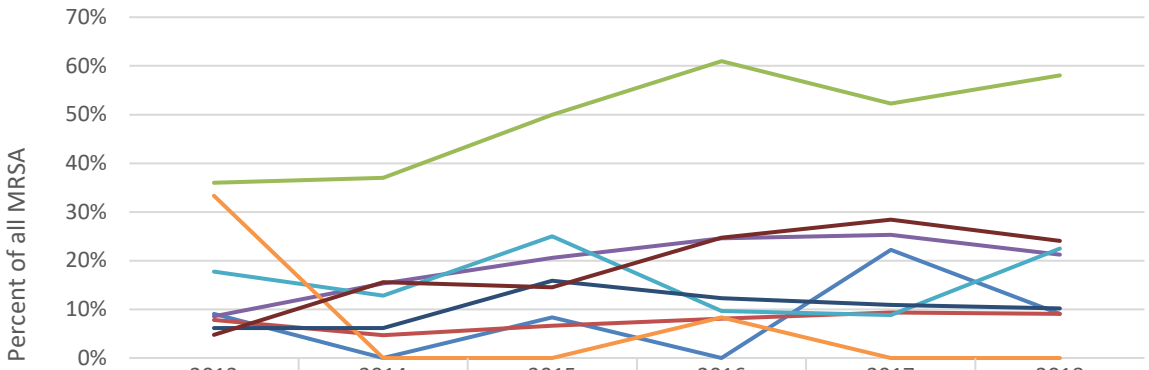


	ST93-MRSA-IV	ST30-MRSA-IV	ST8-MRSA-IV	ST5-MRSA-IV	Other CA	ST45-MRSA-V	ST1-MRSA-IV	ST78-MRSA-IV	ST97-MRSA-IV	ST97-MRSA-V
Total	93%	79%	71%	27%	22%	7%	6%	4%	0%	0%

Geographic variation

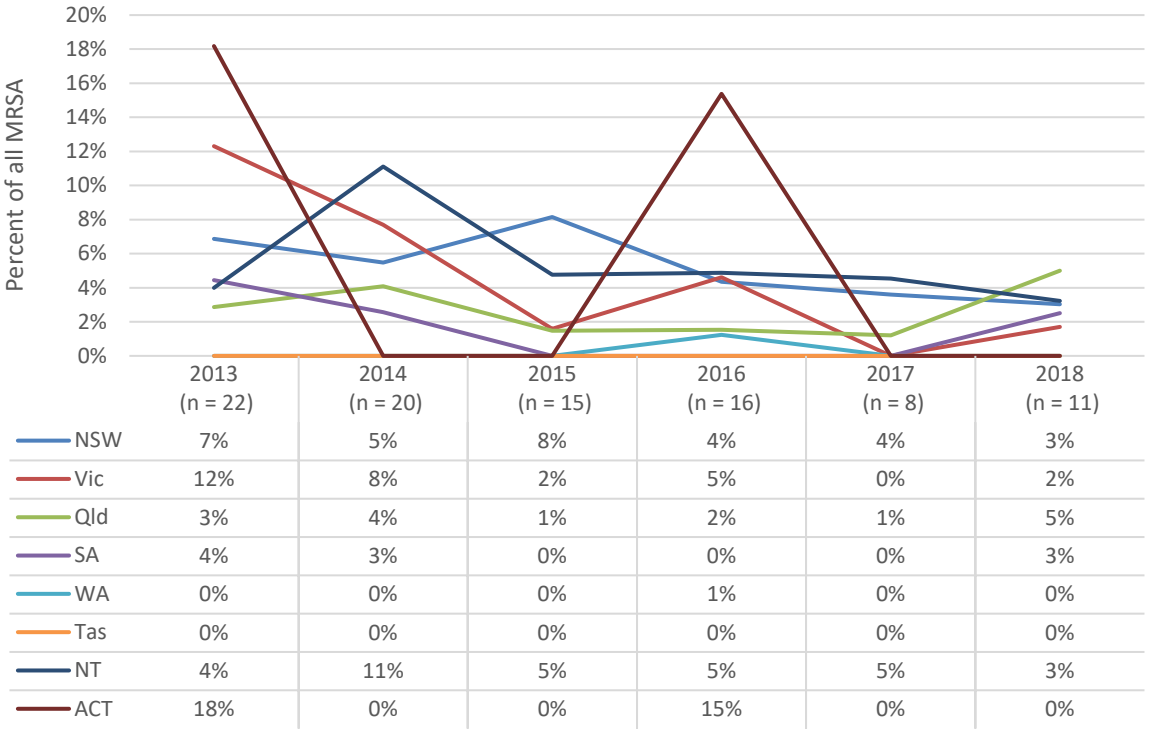
From 2013 to 2018, there were changes in a number of clones reported overall, and varying patterns by state and territory. However, there were consistent changes in most states and territories in two clones – ST93-IV and ST239-II. There were steady increases in the proportion of community-onset MRSA disease attributable to the community-associated clone ST93-IV in New South Wales, Queensland, Western Australia and the Northern Territory. Similar patterns have been seen in other state and territories, although without sustained increases in those clones. ST239-III has reduced as a proportion of all MRSA disease in both community- and hospital-onset disease over the same period (Figures 8–10) in most states and territories, coinciding with coordinated efforts to control *S. aureus* blood stream infection in healthcare settings. Differences in the other clones are shown in Figures 11–33.

Figure 8: Proportion of community-onset ST93-IV clones, percentage of all MRSA, by state and territory, AGAR, 2013–2018



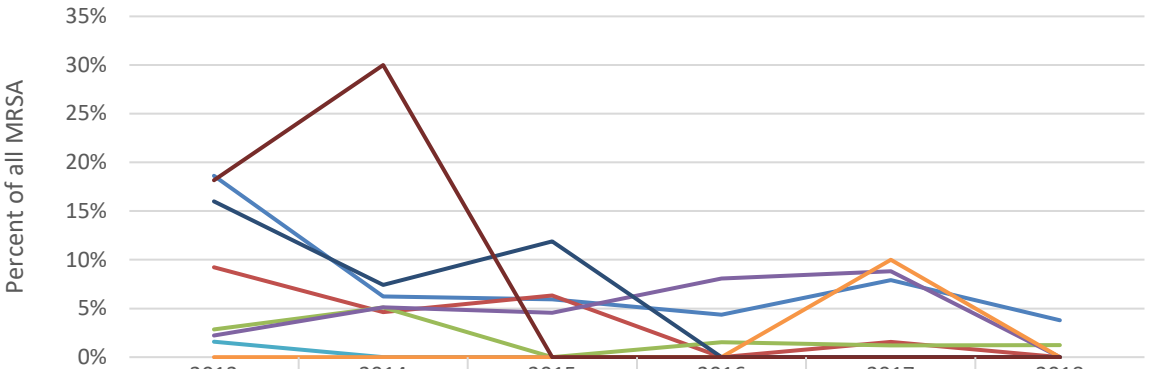
	2013 (n = 40)	2014 (n = 47)	2015 (n = 76)	2016 (n = 89)	2017 (n = 96)	2018 (n = 88)
NSW	9%	0%	8%	0%	22%	9%
Vic	8%	5%	7%	8%	9%	9%
Qld	36%	37%	50%	61%	52%	58%
SA	9%	15%	21%	25%	25%	21%
WA	18%	13%	25%	10%	9%	23%
Tas	33%	0%	0%	8%	0%	0%
NT	6%	6%	16%	12%	11%	10%
ACT	5%	16%	14%	25%	28%	24%

Figure 9: Proportion of community-onset ST239-III clones, percentage of all MRSA, by state and territory, AGAR, 2013–2018



	2013 (n = 22)	2014 (n = 20)	2015 (n = 15)	2016 (n = 16)	2017 (n = 8)	2018 (n = 11)
NSW	7%	5%	8%	4%	4%	3%
Vic	12%	8%	2%	5%	0%	2%
Qld	3%	4%	1%	2%	1%	5%
SA	4%	3%	0%	0%	0%	3%
WA	0%	0%	0%	1%	0%	0%
Tas	0%	0%	0%	0%	0%	0%
NT	4%	11%	5%	5%	5%	3%
ACT	18%	0%	0%	15%	0%	0%

Figure 10: Proportion of hospital-onset ST239-III clones, percentage of all MRSA, by state and territory, AGAR, 2013–2018

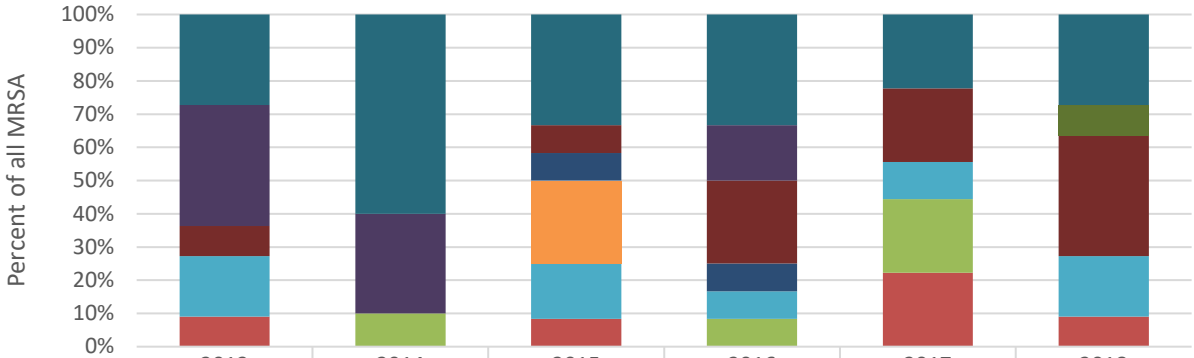


	2013 (n = 35)	2014 (n = 23)	2015 (n = 19)	2016 (n = 13)	2017 (n = 17)	2018 (n = 6)
NSW	19%	6%	6%	4%	8%	4%
Vic	9%	5%	6%	0%	2%	0%
Qld	3%	5%	0%	2%	1%	1%
SA	2%	5%	5%	8%	9%	0%
WA	2%	0%	0%	0%	0%	0%
Tas	0%	0%	0%	0%	10%	0%
NT	16%	7%	12%	0%	0%	0%
ACT	18%	30%	0%	0%	0%	0%

Australian Capital Territory

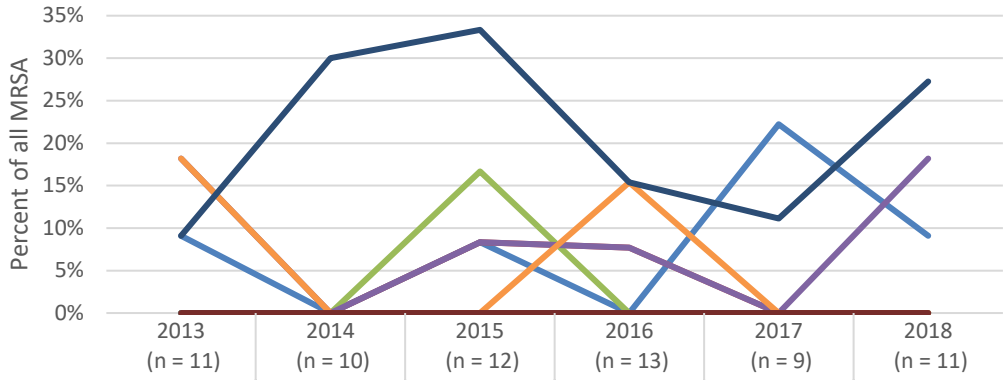
Community-onset disease and community-associated clones accounted for 68% and 52% of total MRSA disease respectively in the Australian Capital Territory from 2013–2018. A small number of blood stream isolates is reported to AGAR for the Australian Capital Territory, compared to other contributing states and territories. Consequently, there is more variation by year than in other states and territories, except Tasmania (Figure 11). However, it is clear that ST22-IV, a healthcare-associated clone, contributed the most burden of disease from 2013–2018, particularly in community-onset blood stream infections (Figure 11 and 12). ST22-IV is also very common in hospital-onset disease; and it appears that ST1-IV has increased over time (Figure 13).

Figure 11: MRSA clones, percentage of all MRSA, Australian Capital Territory, AGAR, 2013–2018



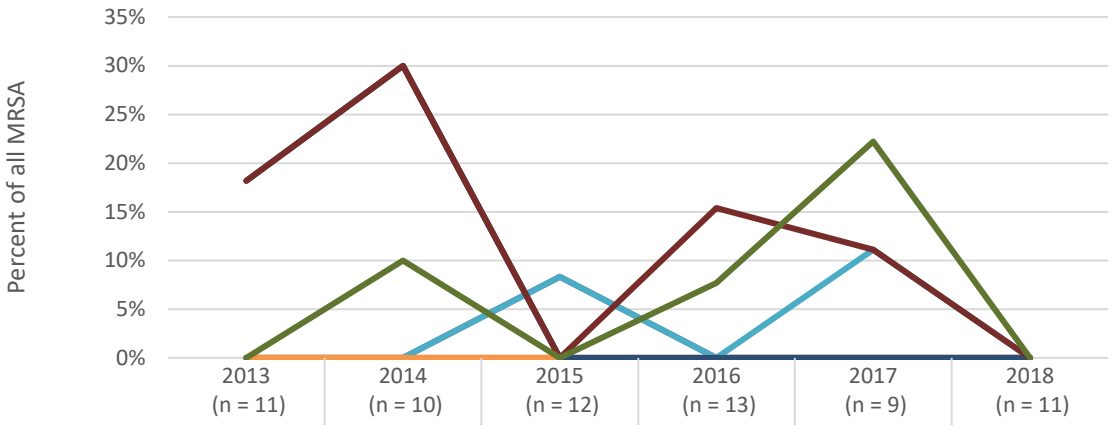
	2013 (n = 11)	2014 (n = 10)	2015 (n = 12)	2016 (n = 12)	2017 (n = 9)	2018 (n = 11)
ST22-IV	27.27%	60.00%	33.33%	33.33%	22.22%	27.27%
ST239-III	36.36%	30.00%	0.00%	16.67%	0.00%	0.00%
Other HA	0.00%	0.00%	0.00%	0.00%	0.00%	9.09%
Other CA	9.09%	0.00%	8.33%	25.00%	22.22%	36.36%
ST78-IV	0.00%	0.00%	8.33%	8.33%	0.00%	0.00%
ST5-IV	0.00%	0.00%	25.00%	0.00%	0.00%	0.00%
ST45-V	18.18%	0.00%	16.67%	8.33%	11.11%	18.18%
ST30-IV	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
ST1-IV	0.00%	10.00%	0.00%	8.33%	22.22%	0.00%
ST93-IV	9.09%	0.00%	8.33%	0.00%	22.22%	9.09%

Figure 12: Contribution of community-onset disease by major clones, percentage of all MRSA, Australian Capital Territory, AGAR, 2013–2018



	2013 (n = 11)	2014 (n = 10)	2015 (n = 12)	2016 (n = 13)	2017 (n = 9)	2018 (n = 11)
ST93-IV	9%	0%	8%	0%	22%	9%
ST78-IV	0%	0%	8%	8%	0%	0%
ST5-IV	0%	0%	17%	0%	0%	0%
ST45-V	18%	0%	8%	8%	0%	18%
ST30-IV	0%	0%	0%	0%	0%	0%
ST239-III	18%	0%	0%	15%	0%	0%
ST22-IV	9%	30%	33%	15%	11%	27%
ST1-IV	0%	0%	0%	0%	0%	0%

Figure 13: Contribution of hospital-onset disease by major clones, percentage of all MRSA, Australian Capital Territory, AGAR, 2013–2018

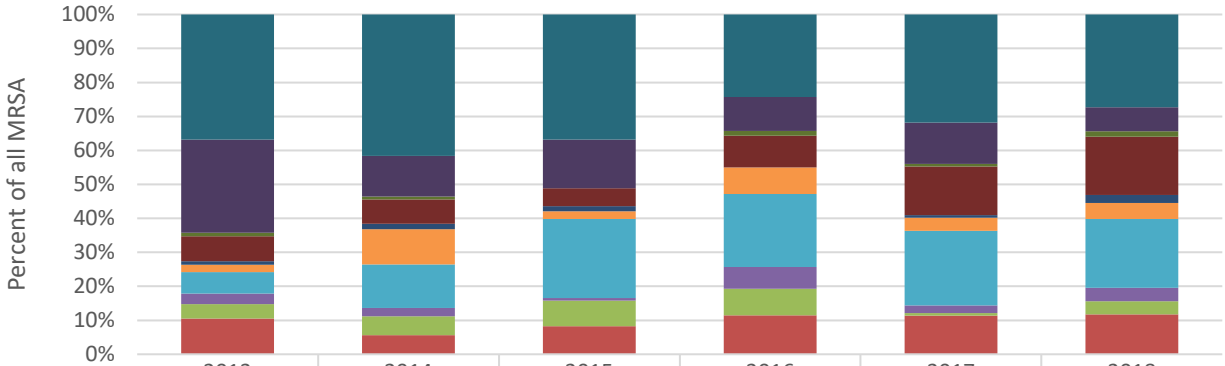


	2013 (n = 11)	2014 (n = 10)	2015 (n = 12)	2016 (n = 13)	2017 (n = 9)	2018 (n = 11)
ST93-IV	0%	0%	0%	0%	0%	0%
ST78-IV	0%	0%	0%	0%	0%	0%
ST5-IV	0%	0%	8%	0%	0%	0%
ST45-V	0%	0%	8%	0%	11%	0%
ST30-IV	0%	0%	0%	0%	0%	0%
ST239-III	18%	30%	0%	0%	0%	0%
ST22-IV	18%	30%	0%	15%	11%	0%
ST1-IV	0%	10%	0%	8%	22%	0%

New South Wales

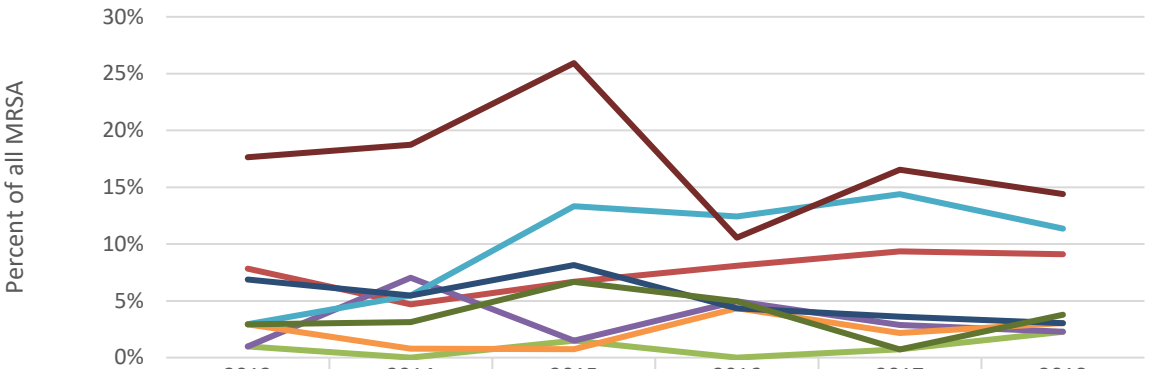
The proportion of community-associated clones has increased since 2014 (Figure 14) in New South Wales. Community-onset ST93-IV increased as a proportion of all MRSA blood stream infection, although at a lower rate than in some other states and territories. Whilst ST22-IV contributed the largest burden of community-onset MRSA blood stream infections in 2018, its proportional contribution to all MRSA disease in New South Wales has reduced over time (Figure 15). ST45-V increased substantially from 2013 to 2015. ST239-III has decreased since 2013, and now contributes less than 5% of all MRSA disease in New South Wales. The largest contributors to hospital-onset diseases are ST22-IV and ST45-V, which also cause the majority of community-onset blood steam infection, (Figure 16).

Figure 14: MRSA clones, percentage of all MRSA, New South Wales, AGAR, 2013–2018



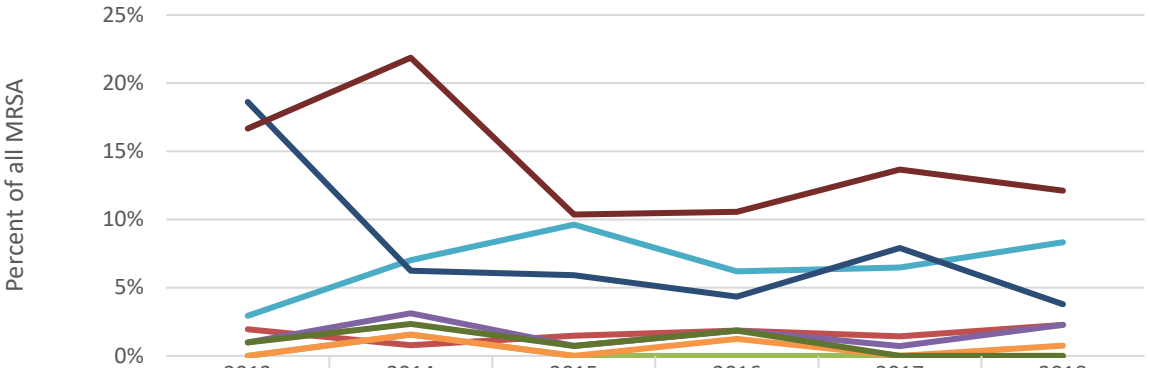
	2013 (n = 95)	2014 (n = 125)	2015 (n = 133)	2016 (n = 140)	2017 (n = 132)	2018 (n = 128)
ST22-IV	37%	42%	37%	24%	32%	27%
ST239-III	27%	12%	14%	10%	12%	7%
Other HA	1%	1%	0%	1%	1%	2%
Other CA	7%	7%	5%	9%	14%	17%
ST78-IV	1%	2%	2%	0%	1%	2%
ST5-IV	2%	10%	2%	8%	4%	5%
ST45-V	6%	13%	23%	21%	22%	20%
ST30-IV	3%	2%	1%	6%	2%	4%
ST1-IV	4%	6%	8%	8%	1%	4%
ST93-IV	11%	6%	8%	11%	11%	12%

Figure 15: Contribution of community-onset disease by major clones, percentage of all MRSA, New South Wales, AGAR, 2013–2018



	2013 (n = 95)	2014 (n = 125)	2015 (n = 133)	2016 (n = 140)	2017 (n = 132)	2018 (n = 128)
ST93-IV	8%	5%	7%	8%	9%	9%
ST78-IV	1%	0%	1%	0%	1%	2%
ST5-IV	1%	7%	1%	5%	3%	2%
ST45-V	3%	5%	13%	12%	14%	11%
ST30-IV	3%	1%	1%	4%	2%	3%
ST239-III	7%	5%	8%	4%	4%	3%
ST22-IV	18%	19%	26%	11%	17%	14%
ST1-IV	3%	3%	7%	5%	1%	4%

Figure 16: Contribution of hospital-onset disease by major clones, percentage of all MRSA, New South Wales, AGAR, 2013–2018

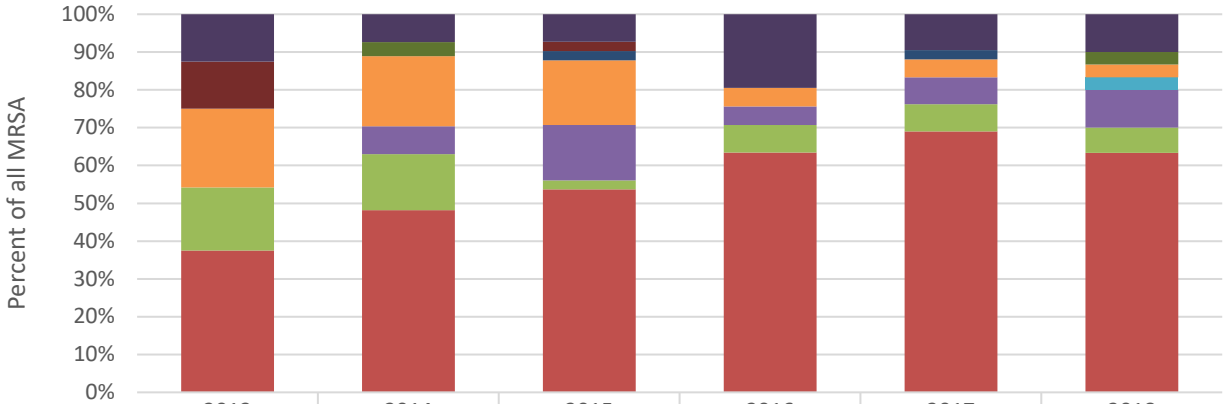


	2013 (n = 95)	2014 (n = 125)	2015 (n = 133)	2016 (n = 140)	2017 (n = 132)	2018 (n = 128)
ST93-IV	2%	1%	1%	2%	1%	2%
ST78-IV	0%	2%	0%	0%	0%	0%
ST5-IV	1%	3%	1%	2%	1%	2%
ST45-V	3%	7%	10%	6%	6%	8%
ST30-IV	0%	2%	0%	1%	0%	1%
ST239-III	19%	6%	6%	4%	8%	4%
ST22-IV	17%	22%	10%	11%	14%	12%
ST1-IV	1%	2%	1%	2%	0%	0%

Northern Territory

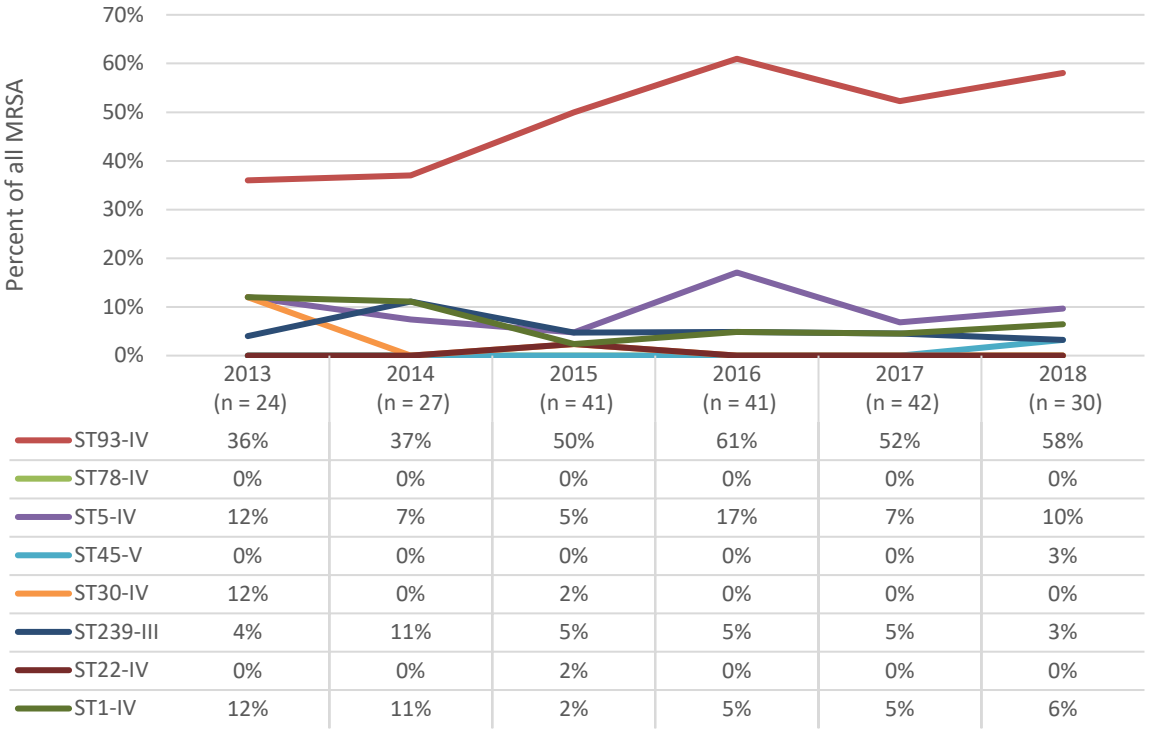
Community-onset disease (81%) and community-associated clones (88%) caused the vast majority of MRSA bacteraemia in the Northern Territory from 2013 to 2018. ST93-IV was the main community-associated clone causing both hospital- and community-onset disease (Figure 17-19). It overtook ST239-III as the most common cause of hospital-onset MRSA disease from 2013 to 2018. Other clones such as ST5-IV contributed considerable burden of disease in the community, as did ST30-IV in hospital-onset disease.

Figure 17: MRSA clones, percentage of all MRSA, Northern Territory, AGAR, 2013–2018



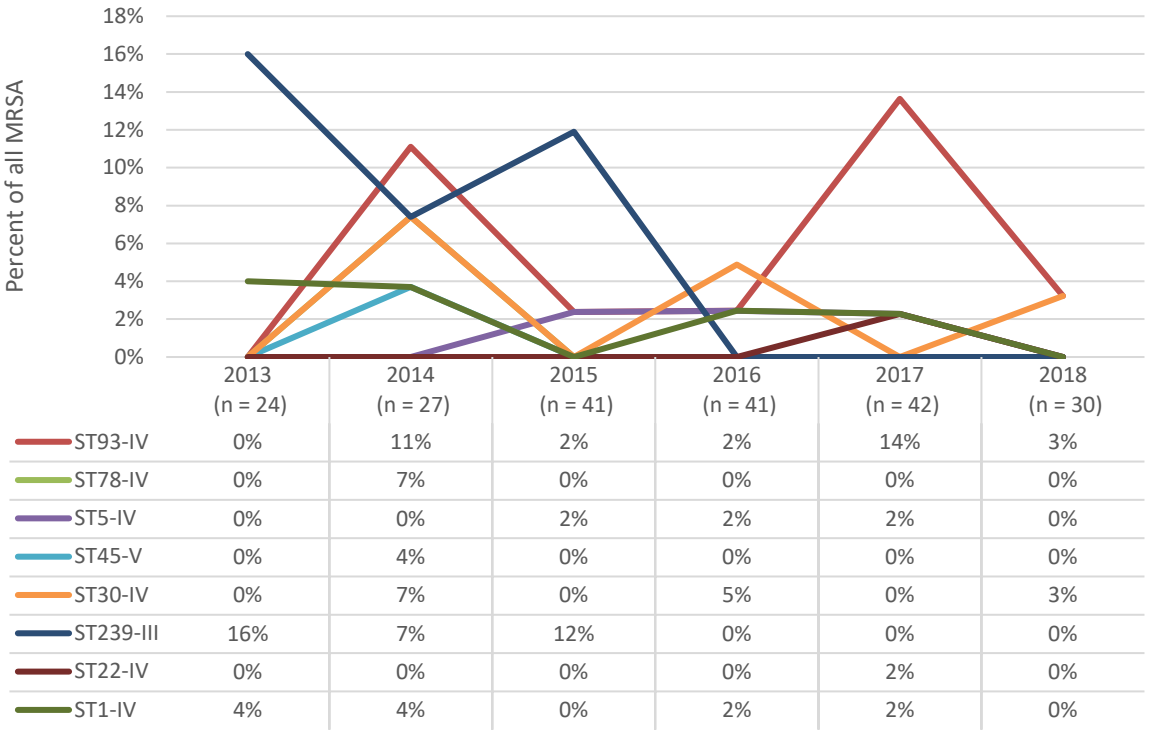
	2013 (n = 24)	2014 (n = 27)	2015 (n = 41)	2016 (n = 41)	2017 (n = 42)	2018 (n = 30)
ST5-IV	12.50%	7.41%	7.32%	19.51%	9.52%	10.00%
ST45-V	0.00%	3.70%	0.00%	0.00%	0.00%	3.33%
ST30-IV	12.50%	0.00%	2.44%	0.00%	0.00%	0.00%
ST22-IV	0.00%	0.00%	2.44%	0.00%	2.38%	0.00%
ST239-III	20.83%	18.52%	17.07%	4.88%	4.76%	3.33%
Other HA	0.00%	0.00%	0.00%	0.00%	0.00%	3.33%
Other CA	0.00%	7.41%	14.63%	4.88%	7.14%	10.00%
ST1-IV	16.67%	14.81%	2.44%	7.32%	7.14%	6.67%
ST93-IV	37.50%	48.15%	53.66%	63.41%	69.05%	63.33%

Figure 18: Contribution of community-onset disease by major clones, percentage of all MRSA, Northern Territory, AGAR, 2013–2018



	2013 (n = 24)	2014 (n = 27)	2015 (n = 41)	2016 (n = 41)	2017 (n = 42)	2018 (n = 30)
ST93-IV	36%	37%	50%	61%	52%	58%
ST78-IV	0%	0%	0%	0%	0%	0%
ST5-IV	12%	7%	5%	17%	7%	10%
ST45-V	0%	0%	0%	0%	0%	3%
ST30-IV	12%	0%	2%	0%	0%	0%
ST239-III	4%	11%	5%	5%	5%	3%
ST22-IV	0%	0%	2%	0%	0%	0%
ST1-IV	12%	11%	2%	5%	5%	6%

Figure 19: Contribution of hospital-onset disease by major clones, percentage of all MRSA, Northern Territory, AGAR, 2013–2018

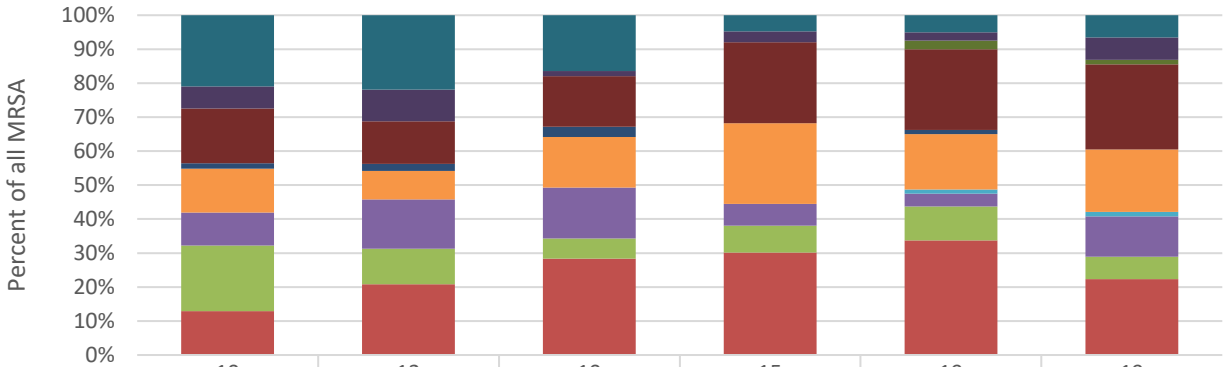


	2013 (n = 24)	2014 (n = 27)	2015 (n = 41)	2016 (n = 41)	2017 (n = 42)	2018 (n = 30)
ST93-IV	0%	11%	2%	2%	14%	3%
ST78-IV	0%	7%	0%	0%	0%	0%
ST5-IV	0%	0%	2%	2%	2%	0%
ST45-V	0%	4%	0%	0%	0%	0%
ST30-IV	0%	7%	0%	5%	0%	3%
ST239-III	16%	7%	12%	0%	0%	0%
ST22-IV	0%	0%	0%	0%	2%	0%
ST1-IV	4%	4%	0%	2%	2%	0%

Queensland

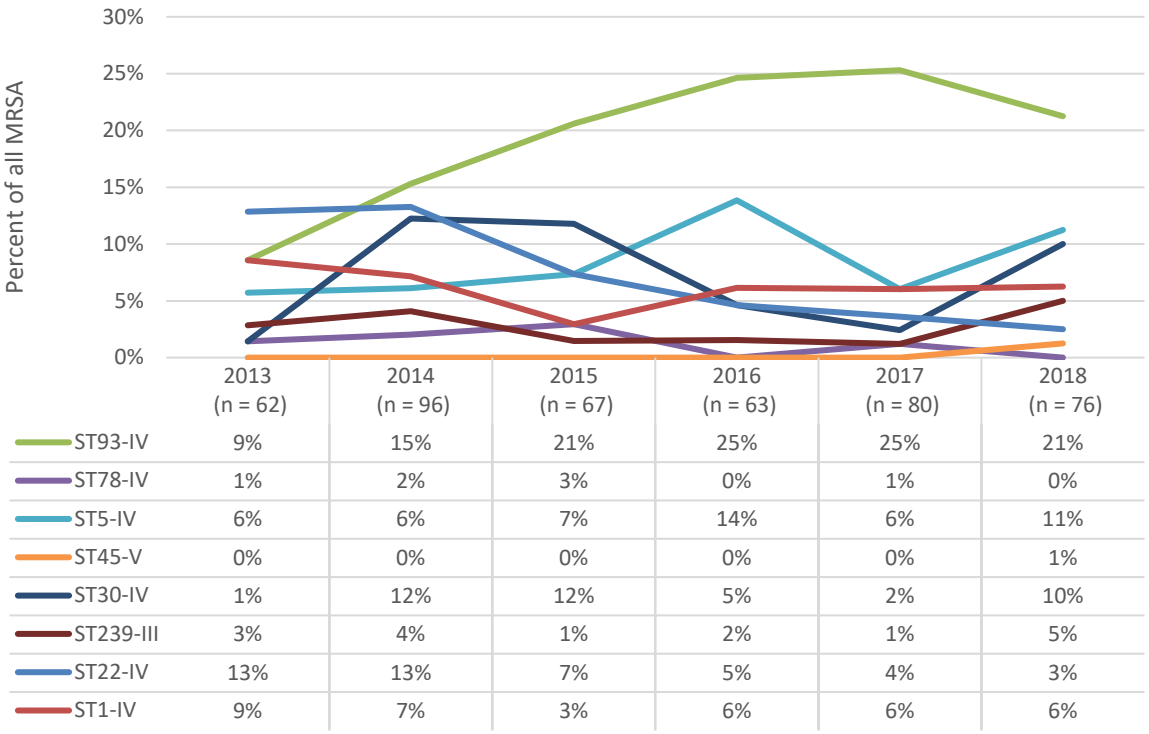
Community-associated clones caused 81% of blood stream infections in Queensland from 2013 to 2018. Community-onset disease accounted for 70% of all episodes. Dominant MRSA clones included ST93-IV and ST5-IV (Figure 20). There were increases in ST93-IV between 2013 and 2018; similar to the Northern Territory, these were mainly in community-onset disease, (Figure 21). In Queensland in 2018, community-onset ST93-IV disease accounts for 20% of all MRSA blood stream infection, compared to almost 60% in the Northern Territory. ST22-IV disease has substantially reduced over time in both community and hospital settings (Figure 21-22). Hospital-onset ST5-IV increased over the period; it accounted for 10% of all MRSA disease in 2017, and may also be increasing in community-onset disease (Figure 21-22). Most other clones contributed proportionately less MRSA disease from 2013 to 2018.

Figure 20: MRSA clones, percentage of all MRSA, Queensland, AGAR, 2013–2018,



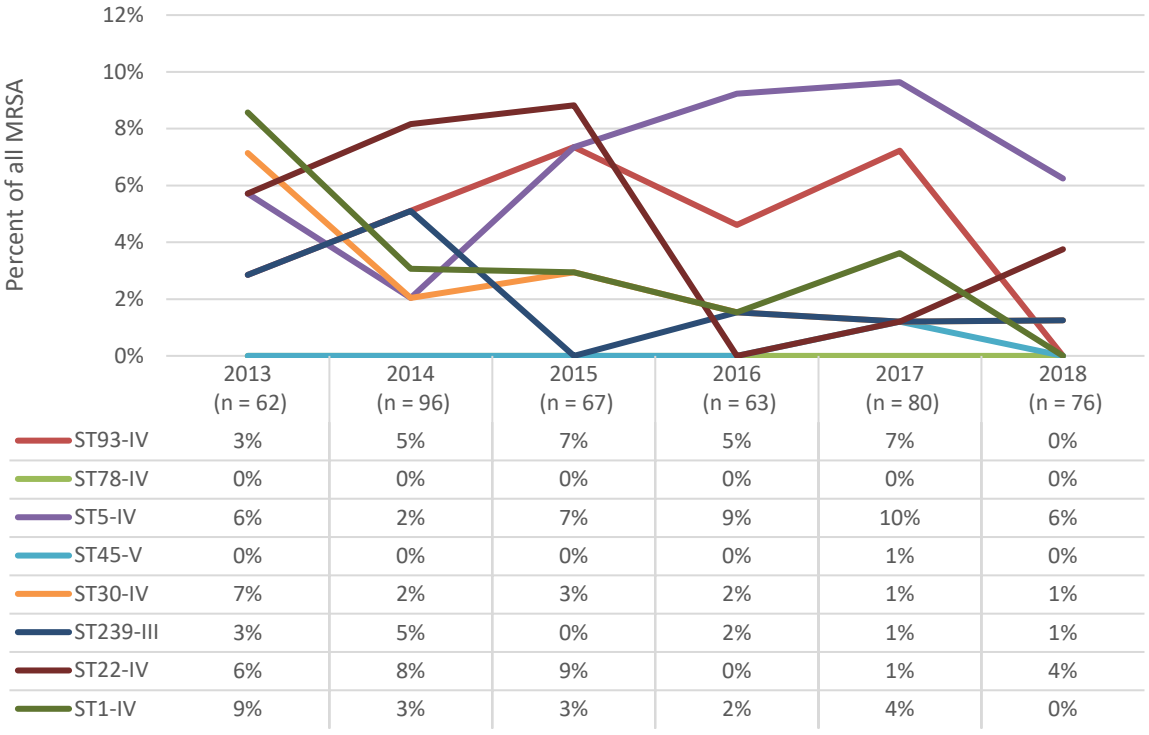
	10 (n = 62)	12 (n = 96)	10 (n = 67)	15 (n = 63)	19 (n = 80)	19 (n = 76)
ST22-IV	21%	22%	16%	5%	5%	7%
ST239-III	6%	9%	1%	3%	3%	7%
Other HA	0%	0%	0%	0%	3%	1%
Other CA	16%	13%	15%	24%	24%	25%
ST78-IV	2%	2%	3%	0%	1%	0%
ST5-IV	13%	8%	15%	24%	16%	18%
ST45-V	0%	0%	0%	0%	1%	1%
ST30-IV	10%	15%	15%	6%	4%	12%
ST1-IV	19%	10%	6%	8%	10%	7%
ST93-IV	13%	21%	28%	30%	34%	22%

Figure 21: Contribution to community-onset disease by major clones, percentage of all MRSA, Queensland, AGAR, 2013–2018



	2013 (n = 62)	2014 (n = 96)	2015 (n = 67)	2016 (n = 63)	2017 (n = 80)	2018 (n = 76)
ST93-IV	9%	15%	21%	25%	25%	21%
ST78-IV	1%	2%	3%	0%	1%	0%
ST5-IV	6%	6%	7%	14%	6%	11%
ST45-V	0%	0%	0%	0%	0%	1%
ST30-IV	1%	12%	12%	5%	2%	10%
ST239-III	3%	4%	1%	2%	1%	5%
ST22-IV	13%	13%	7%	5%	4%	3%
ST1-IV	9%	7%	3%	6%	6%	6%

Figure 22: Contribution of hospital-onset disease by major clones, percentage of all MRSA, Queensland, AGAR, 2013–2018

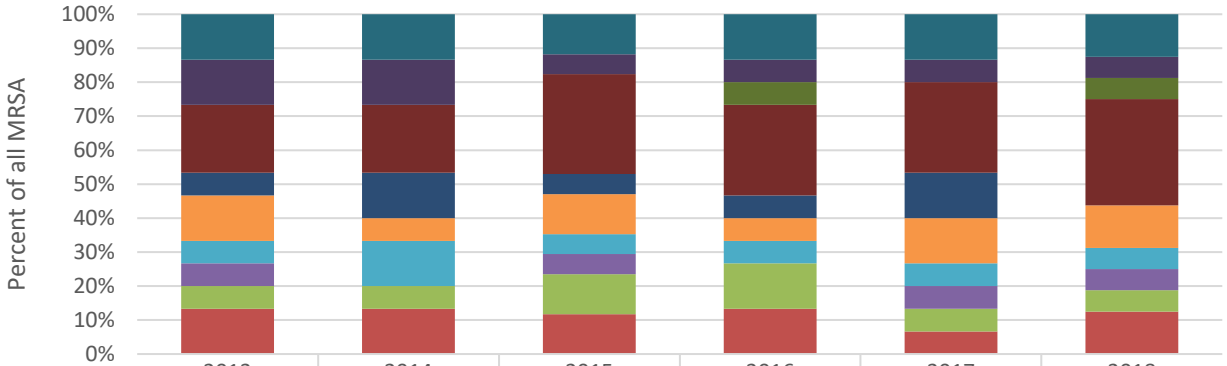


	2013 (n = 62)	2014 (n = 96)	2015 (n = 67)	2016 (n = 63)	2017 (n = 80)	2018 (n = 76)
ST93-IV	3%	5%	7%	5%	7%	0%
ST78-IV	0%	0%	0%	0%	0%	0%
ST5-IV	6%	2%	7%	9%	10%	6%
ST45-V	0%	0%	0%	0%	1%	0%
ST30-IV	7%	2%	3%	2%	1%	1%
ST239-III	3%	5%	0%	2%	1%	1%
ST22-IV	6%	8%	9%	0%	1%	4%
ST1-IV	9%	3%	3%	2%	4%	0%

South Australia

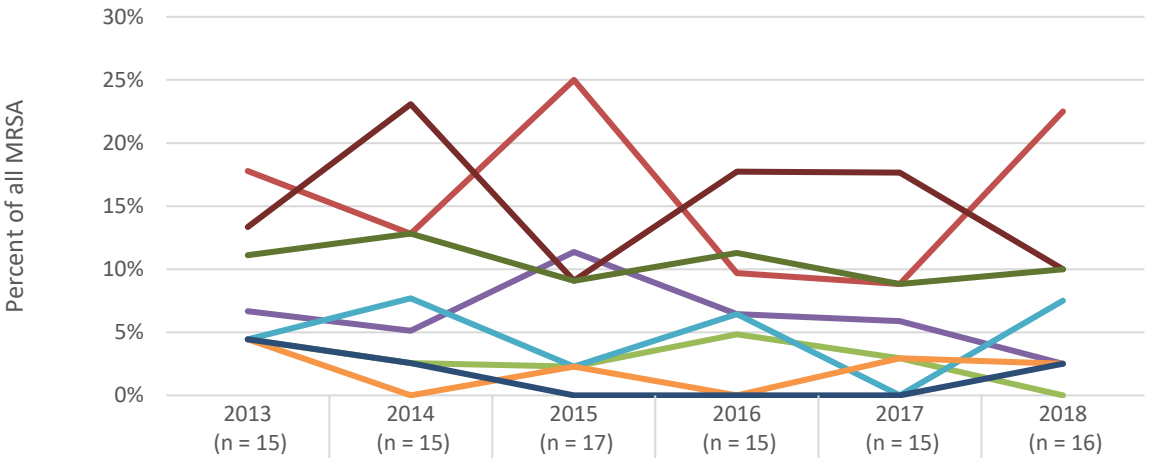
From 2013 to 2018, community-onset cases accounted for 78% of all MRSA bacteraemia in South Australia, whilst community-associated clones accounted for 72%. There were no clear patterns in the contribution of community-onset disease to total MRSA in South Australia, other than a possible trend of decreasing ST22-IV community-onset cases (Figures 23 and 24).There were decreasing trends in hospital-onset ST1-IV, ST30-IV and ST22-IV, and the burden of ST5-IV disease increased between 2014 and 2017 (Figure 25).

Figure 23: MRSA clones, percentage of all MRSA, South Australia, AGAR, 2013–2018



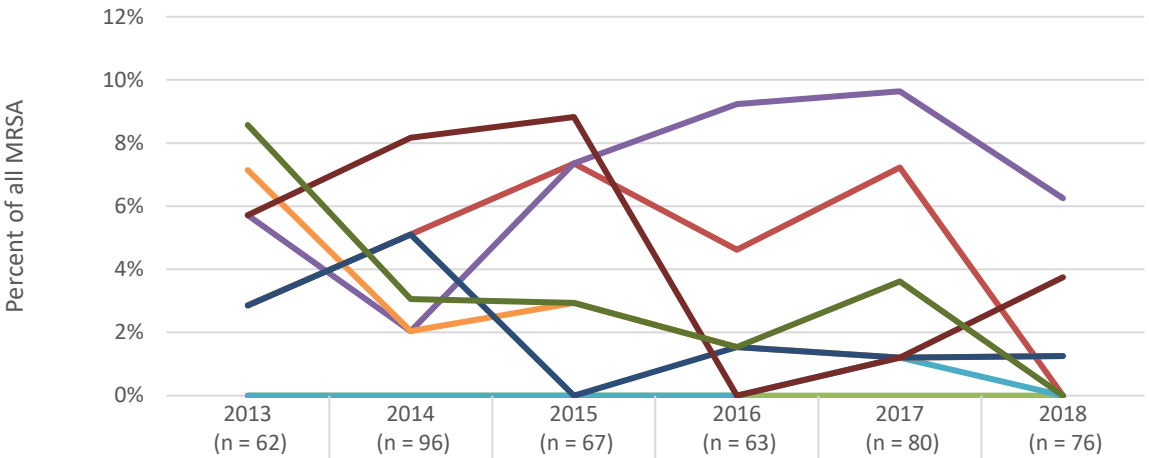
	2013 (n = 15)	2014 (n = 15)	2015 (n = 17)	2016 (n = 15)	2017 (n = 15)	2018 (n = 16)
ST22-IV	13.33%	13.33%	11.76%	13.33%	13.33%	12.50%
ST239-III	13.33%	13.33%	5.88%	6.67%	6.67%	6.25%
Other HA	0.00%	0.00%	0.00%	6.67%	0.00%	6.25%
Other CA	20.00%	20.00%	29.41%	26.67%	26.67%	31.25%
ST78-IV	6.67%	13.33%	5.88%	6.67%	13.33%	0.00%
ST5-IV	13.33%	6.67%	11.76%	6.67%	13.33%	12.50%
ST45-V	6.67%	13.33%	5.88%	6.67%	6.67%	6.25%
ST30-IV	6.67%	0.00%	5.88%	0.00%	6.67%	6.25%
ST1-IV	6.67%	6.67%	11.76%	13.33%	6.67%	6.25%
ST93-IV	13.33%	13.33%	11.76%	13.33%	6.67%	12.50%

Figure 24: Contribution of community-onset disease by major clones, percentage of all MRSA, South Australia, AGAR, 2013–2018



	2013 (n = 15)	2014 (n = 15)	2015 (n = 17)	2016 (n = 15)	2017 (n = 15)	2018 (n = 16)
ST93-IV	18%	13%	25%	10%	9%	23%
ST78-IV	4%	3%	2%	5%	3%	0%
ST5-IV	7%	5%	11%	6%	6%	3%
ST45-V	4%	8%	2%	6%	0%	8%
ST30-IV	4%	0%	2%	0%	3%	3%
ST239-III	4%	3%	0%	0%	0%	3%
ST22-IV	13%	23%	9%	18%	18%	10%
ST1-IV	11%	13%	9%	11%	9%	10%

Figure 25: Contribution of hospital-onset disease by major clones, percentage of all MRSA, South Australia, AGAR, 2013–2018

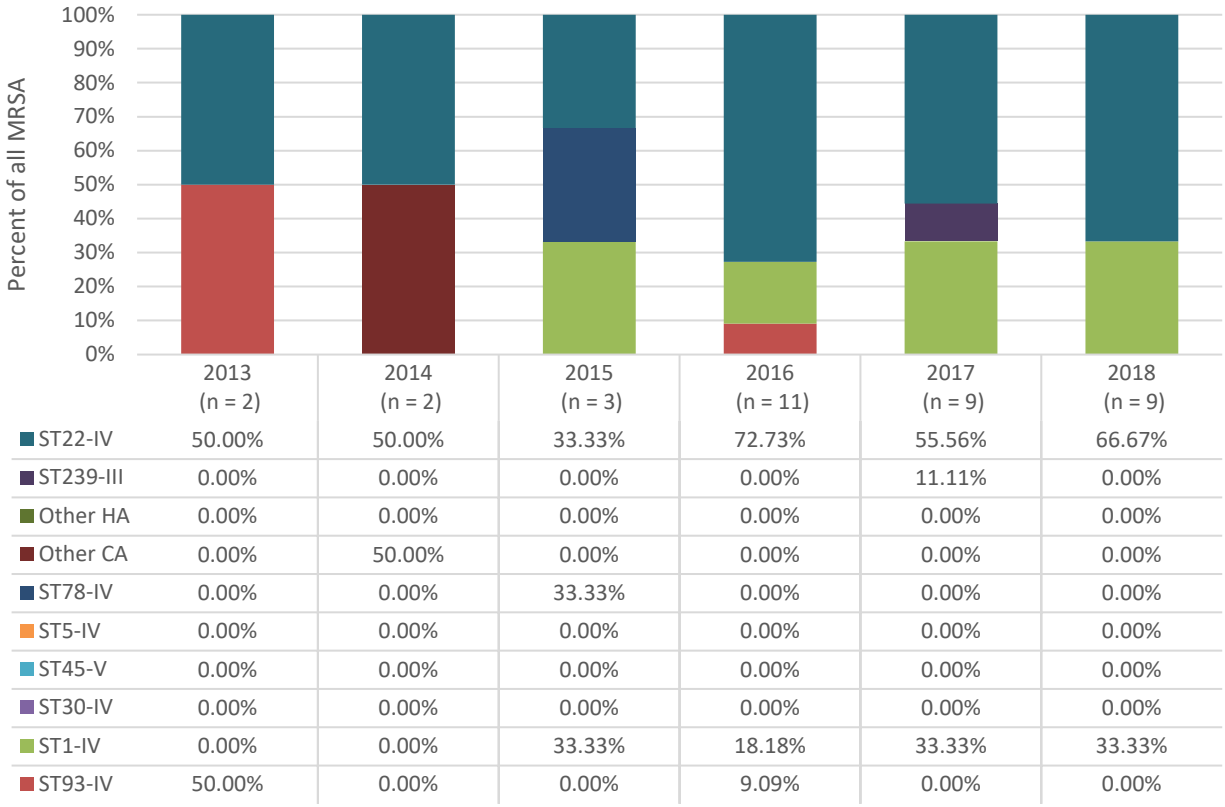


	2013 (n = 62)	2014 (n = 96)	2015 (n = 67)	2016 (n = 63)	2017 (n = 80)	2018 (n = 76)
ST93-IV	3%	5%	7%	5%	7%	0%
ST78-IV	0%	0%	0%	0%	0%	0%
ST5-IV	6%	2%	7%	9%	10%	6%
ST45-V	0%	0%	0%	0%	1%	0%
ST30-IV	7%	2%	3%	2%	1%	1%
ST239-III	3%	5%	0%	2%	1%	1%
ST22-IV	6%	8%	9%	0%	1%	4%
ST1-IV	9%	3%	3%	2%	4%	0%

Tasmania

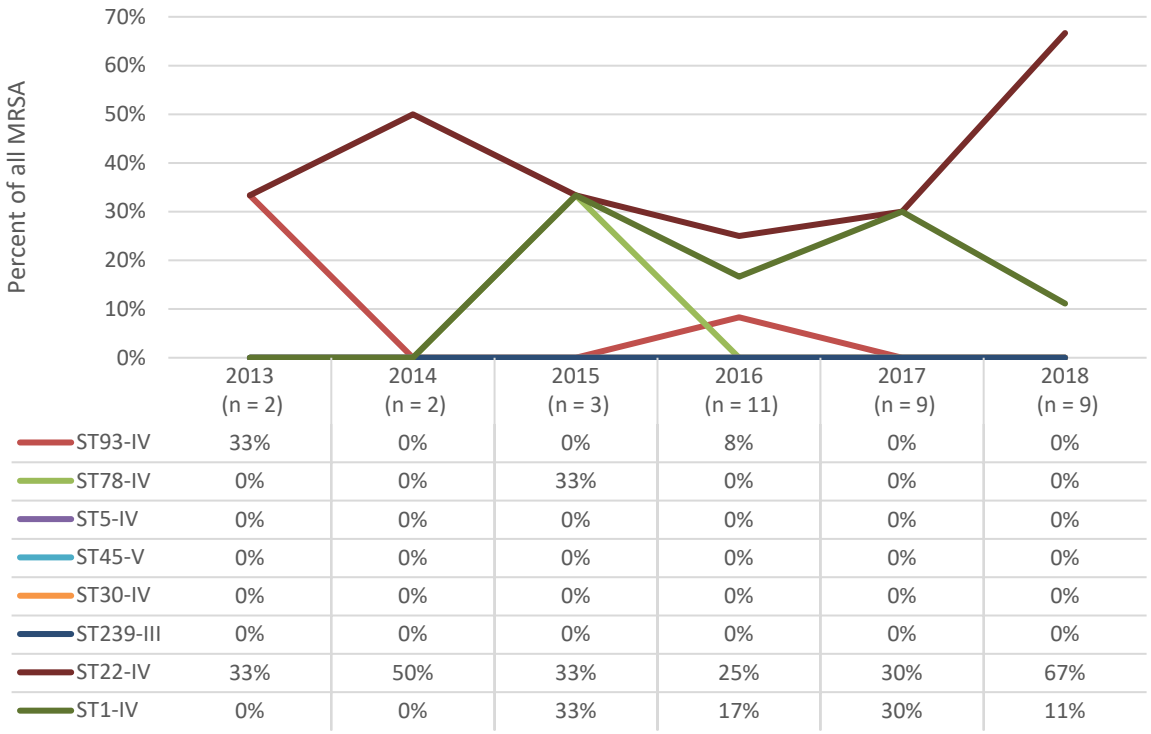
Interpretation of trends in Tasmania, is limited by small sample size. The majority of MRSA disease from 2013 to 2018 was community-onset disease (72%). Despite this, healthcare-associated clones comprised the majority of all causative clones (66%), with ST22-IV predominating (Figures 26–28).

Figure 26: MRSA clones, percentage of all MRSA, Tasmania, AGAR, 2013–2018



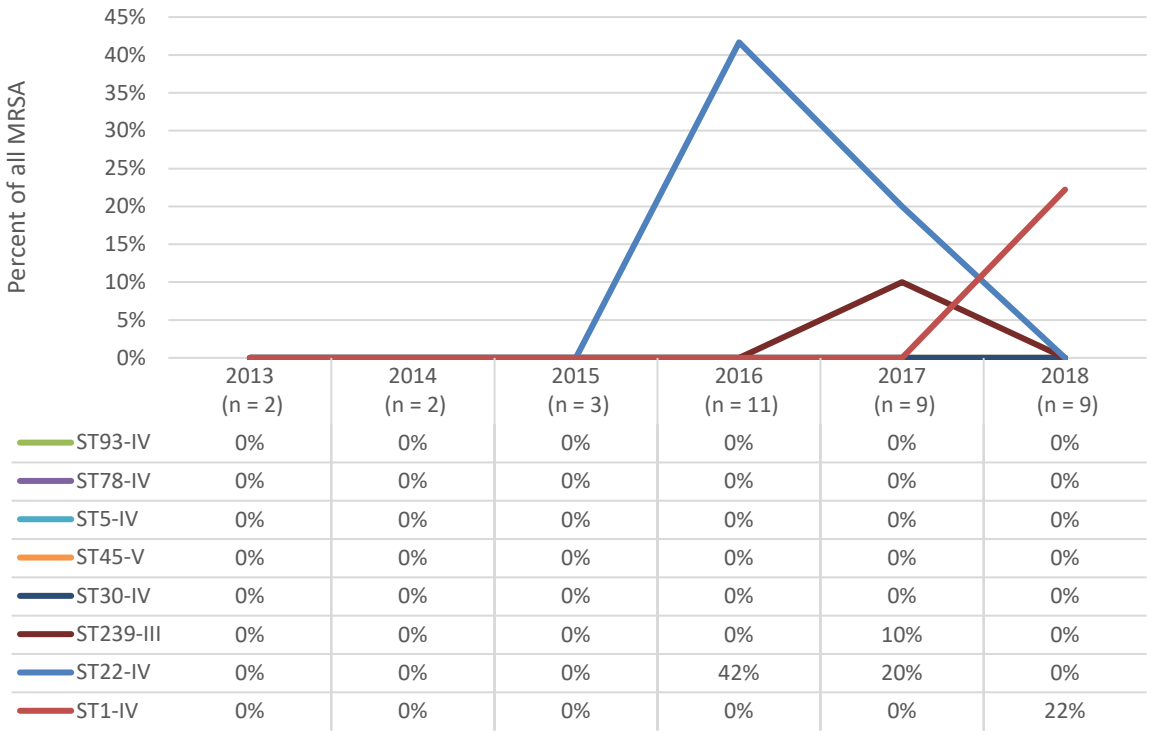
	2013 (n = 2)	2014 (n = 2)	2015 (n = 3)	2016 (n = 11)	2017 (n = 9)	2018 (n = 9)
ST22-IV	50.00%	50.00%	33.33%	72.73%	55.56%	66.67%
ST239-III	0.00%	0.00%	0.00%	0.00%	11.11%	0.00%
Other HA	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
Other CA	0.00%	50.00%	0.00%	0.00%	0.00%	0.00%
ST78-IV	0.00%	0.00%	33.33%	0.00%	0.00%	0.00%
ST5-IV	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
ST45-V	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
ST30-IV	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
ST1-IV	0.00%	0.00%	33.33%	18.18%	33.33%	33.33%
ST93-IV	50.00%	0.00%	0.00%	9.09%	0.00%	0.00%

Figure 27: Contribution of community-onset disease by major clones, percentage of all MRSA, Tasmania, AGAR, 2013–2018



	2013 (n = 2)	2014 (n = 2)	2015 (n = 3)	2016 (n = 11)	2017 (n = 9)	2018 (n = 9)
ST93-IV	33%	0%	0%	8%	0%	0%
ST78-IV	0%	0%	33%	0%	0%	0%
ST5-IV	0%	0%	0%	0%	0%	0%
ST45-V	0%	0%	0%	0%	0%	0%
ST30-IV	0%	0%	0%	0%	0%	0%
ST239-III	0%	0%	0%	0%	0%	0%
ST22-IV	33%	50%	33%	25%	30%	67%
ST1-IV	0%	0%	33%	17%	30%	11%

Figure 28: Contribution of hospital-onset disease by major clones, percentage of all MRSA, Tasmania, AGAR, 2013–2018

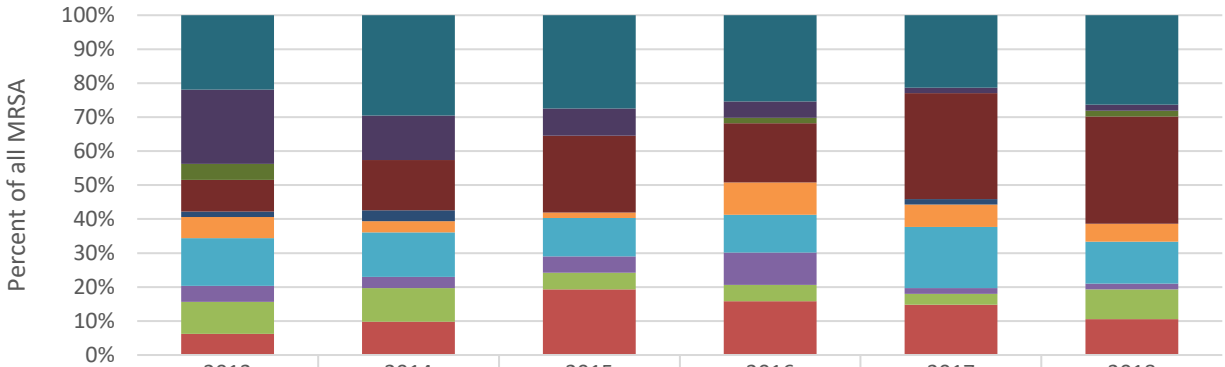


	2013 (n = 2)	2014 (n = 2)	2015 (n = 3)	2016 (n = 11)	2017 (n = 9)	2018 (n = 9)
ST93-IV	0%	0%	0%	0%	0%	0%
ST78-IV	0%	0%	0%	0%	0%	0%
ST5-IV	0%	0%	0%	0%	0%	0%
ST45-V	0%	0%	0%	0%	0%	0%
ST30-IV	0%	0%	0%	0%	0%	0%
ST239-III	0%	0%	0%	0%	10%	0%
ST22-IV	0%	0%	0%	42%	20%	0%
ST1-IV	0%	0%	0%	0%	0%	22%

Victoria

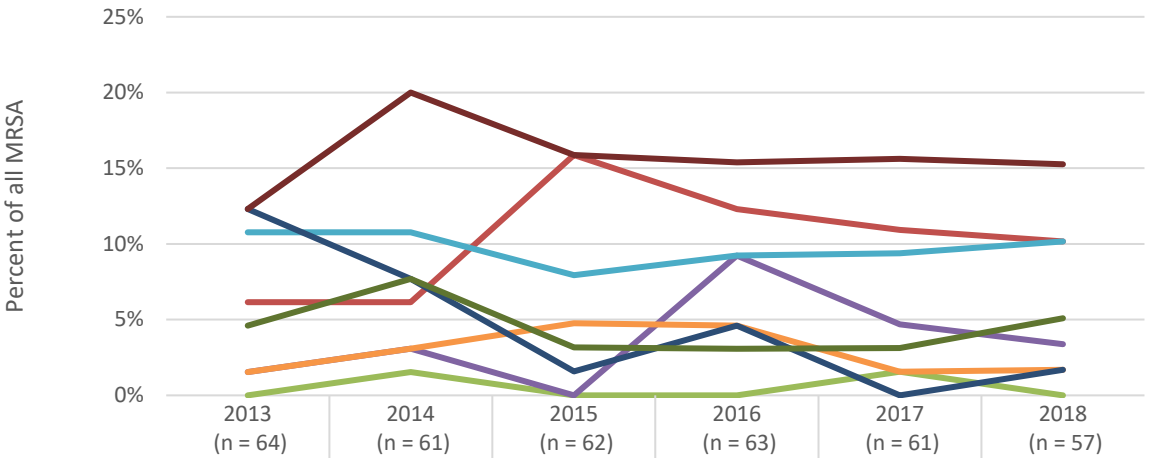
From 2013 to 2018, community-onset MRSA bacteraemia accounted for 70% of all MRSA episodes sampled from Victorian laboratories that contribute to AGAR. Community-associated clones accounted for two out of three (64%) of these episodes (Figure 29). Community-onset ST22-IV disease increased in 2014 to become the most common cause of community-onset MRSA disease; it accounted for 15% of all MRSA episodes in 2018 (Figure 30). Community-onset ST93-IV episodes also increased from 2013 to 2018, and caused approximately 10% of MRSA episodes in Victoria in 2018. There were striking reductions in hospital-onset ST239-III episodes 2013 to 2018, from almost 9% of all MRSA episodes to 0–2% from 2016 to 2018 (Figure 31); and ST22-IV was the most common cause of hospital-onset disease in Victoria.

Figure 29: MRSA clones, percentage of all MRSA, Victoria, AGAR, 2013–2018



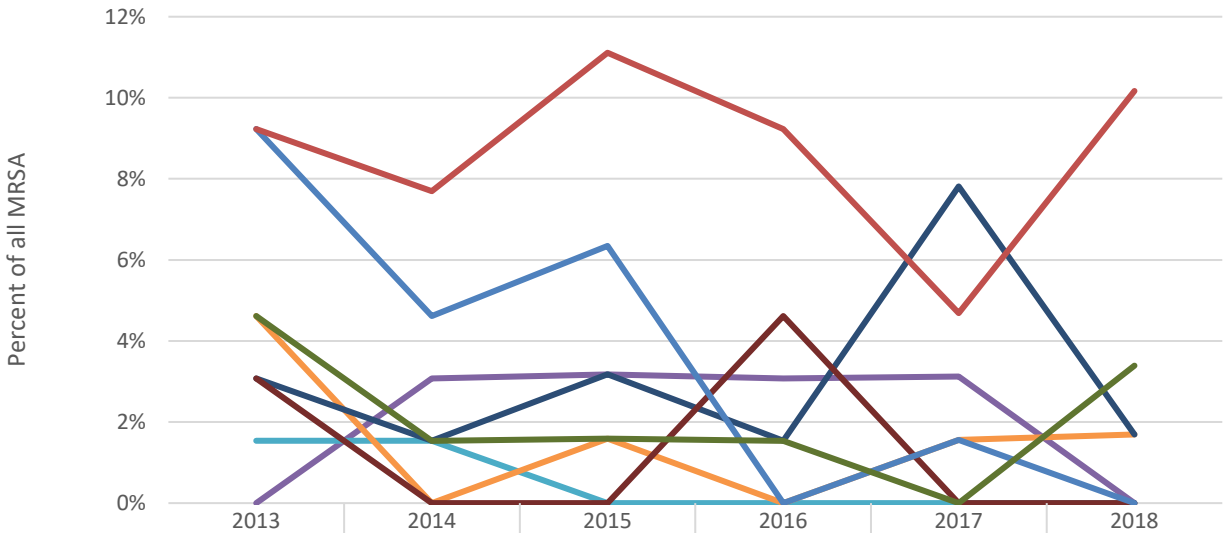
	2013 (n = 64)	2014 (n = 61)	2015 (n = 62)	2016 (n = 63)	2017 (n = 61)	2018 (n = 57)
ST22-IV	21.88%	29.51%	27.42%	25.40%	21.31%	26.32%
ST239-III	21.88%	13.11%	8.06%	4.76%	1.64%	1.75%
Other HA	4.69%	0.00%	0.00%	1.59%	0.00%	1.75%
Other CA	9.38%	14.75%	22.58%	17.46%	31.15%	31.58%
ST78-IV	1.56%	3.28%	0.00%	0.00%	1.64%	0.00%
ST5-IV	6.25%	3.28%	1.61%	9.52%	6.56%	5.26%
ST45-V	14.06%	13.11%	11.29%	11.11%	18.03%	12.28%
ST30-IV	4.69%	3.28%	4.84%	9.52%	1.64%	1.75%
ST1-IV	9.38%	9.84%	4.84%	4.76%	3.28%	8.77%
ST93-IV	6.25%	9.84%	19.35%	15.87%	14.75%	10.53%

Figure 30: Contribution of community-onset disease by major clones, percentage of all MRSA, Victoria, AGAR, 2013–2018



	2013 (n = 64)	2014 (n = 61)	2015 (n = 62)	2016 (n = 63)	2017 (n = 61)	2018 (n = 57)
ST93-IV	6%	6%	16%	12%	11%	10%
ST78-IV	0%	2%	0%	0%	2%	0%
ST5-IV	2%	3%	0%	9%	5%	3%
ST45-V	11%	11%	8%	9%	9%	10%
ST30-IV	2%	3%	5%	5%	2%	2%
ST239-III	12%	8%	2%	5%	0%	2%
ST22-IV	12%	20%	16%	15%	16%	15%
ST1-IV	5%	8%	3%	3%	3%	5%

Figure 31: Contribution of hospital-onset disease by major clones, percentage of all MRSA, Victoria, AGAR, 2013–2018,

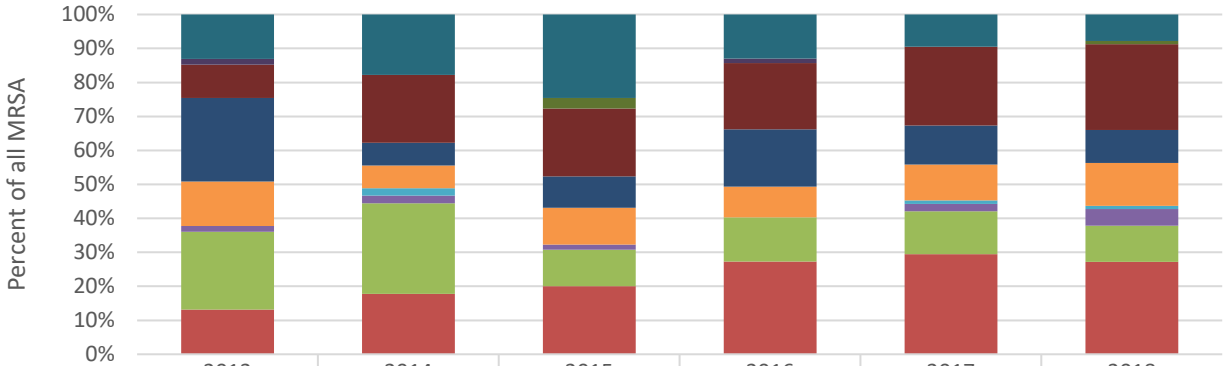


	2013	2014	2015	2016	2017	2018
ST93-IV	0%	3%	3%	3%	3%	0%
ST78-IV	2%	2%	0%	0%	0%	0%
ST5-IV	5%	0%	2%	0%	2%	2%
ST45-V	3%	2%	3%	2%	8%	2%
ST30-IV	3%	0%	0%	5%	0%	0%
ST239-III	9%	5%	6%	0%	2%	0%
ST22-IV	9%	8%	11%	9%	5%	10%
ST1-IV	5%	2%	2%	2%	0%	3%

Western Australia

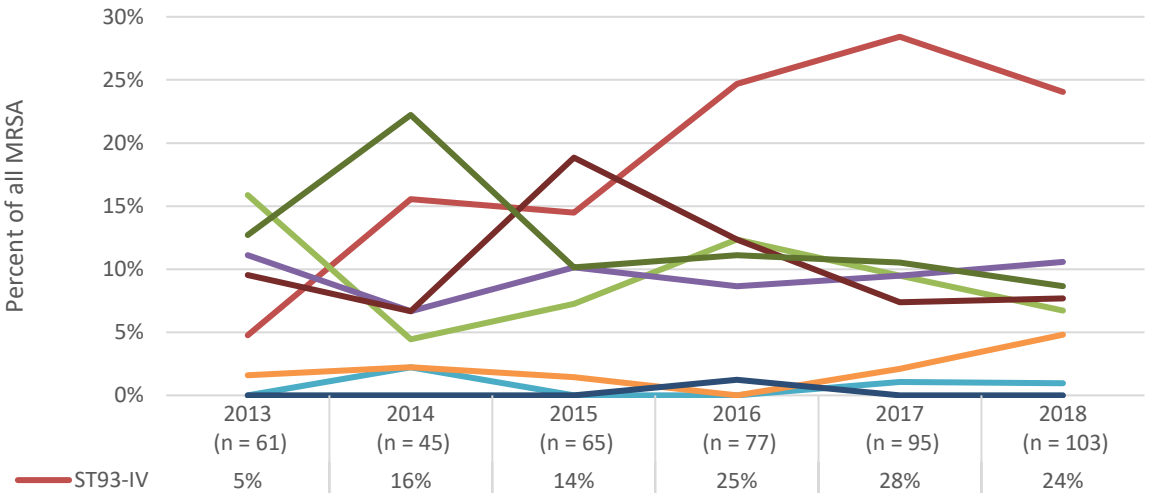
From 2013 to 2018, the majority of MRSA disease in Western Australia was attributable to community-onset (92%) disease, with community-associated clones predominating (86%). Total cases of MRSA rose appreciably from 2014 to 2018 (Figure 32). Community-onset ST93-IV disease, as described previously, caused almost one in four episodes (24%) of all MRSA in Western Australia in 2018, rising from 5% in 2013 (Figure 33). From 2013 to 2018, ST78-IV, ST1-IV and ST22-IV all decreased as causes of hospital-onset MRSA episodes. In contrast to other states and territories, from 2013 to 2018 ST239-III did not cause any significant amount of hospital-onset disease in Western Australia due to local active screening processes (Figure 34).

Figure 32: MRSA clones, percentage of all MRSA, Western Australia, AGAR, 2013–2018,



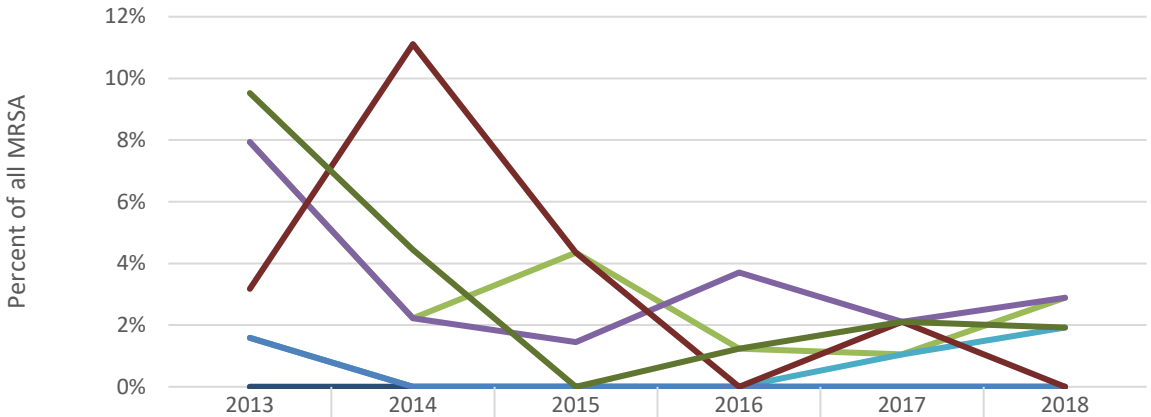
	2013 (n = 61)	2014 (n = 45)	2015 (n = 65)	2016 (n = 77)	2017 (n = 95)	2018 (n = 103)
ST22-IV	13%	18%	25%	13%	9%	8%
ST239-III	2%	0%	0%	1%	0%	0%
Other HA	0%	0%	3%	0%	0%	1%
Other CA	10%	20%	20%	19%	23%	25%
ST78-IV	25%	7%	9%	17%	12%	10%
ST5-IV	13%	7%	11%	9%	11%	13%
ST45-V	0%	2%	0%	0%	1%	1%
ST30-IV	2%	2%	2%	0%	2%	5%
ST1-IV	23%	27%	11%	13%	13%	11%
ST93-IV	13%	18%	20%	27%	29%	27%

Figure 33: Contribution of community-onset disease by major clones, percentage of all MRSA, Western Australia, AGAR, 2013–2018



	2013 (n = 61)	2014 (n = 45)	2015 (n = 65)	2016 (n = 77)	2017 (n = 95)	2018 (n = 103)
ST93-IV	5%	16%	14%	25%	28%	24%
ST78-IV	16%	4%	7%	12%	9%	7%
ST5-IV	11%	7%	10%	9%	9%	11%
ST45-V	0%	2%	0%	0%	1%	1%
ST30-IV	2%	2%	1%	0%	2%	5%
ST239-III	0%	0%	0%	1%	0%	0%
ST22-IV	10%	7%	19%	12%	7%	8%
ST1-IV	13%	22%	10%	11%	11%	9%

Figure 34: Contribution of hospital-onset disease by major clones, percentage of all MRSA, Western Australia, AGAR, 2013–2018



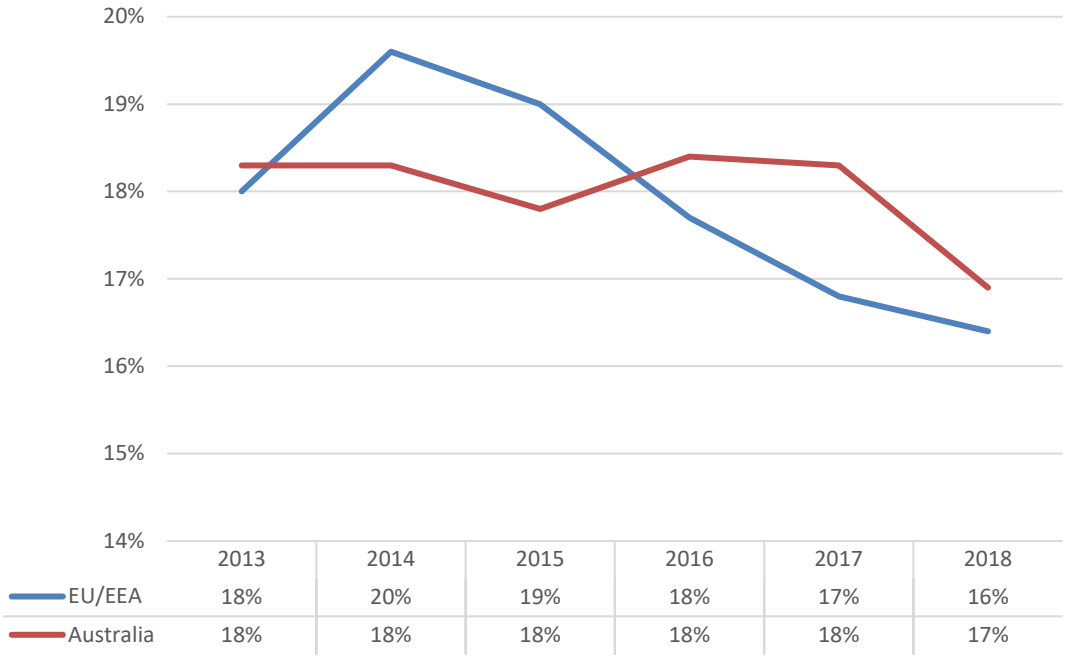
	2013	2014	2015	2016	2017	2018
ST93-IV	8%	2%	4%	1%	1%	3%
ST78-IV	8%	2%	1%	4%	2%	3%
ST5-IV	2%	0%	0%	0%	1%	2%
ST45-V	0%	0%	0%	0%	0%	0%
ST30-IV	0%	0%	0%	0%	0%	0%
ST239-III	2%	0%	0%	0%	0%	0%
ST22-IV	3%	11%	4%	0%	2%	0%
ST1-IV	10%	4%	0%	1%	2%	2%

EU/EEA = European Union and European Economic Area

International comparisons

The AURA Surveillance System compares Australian rates of methicillin resistance to European countries participating in the EARS-Net program.[45] In 2017, the proportion of methicillin resistance reported in Australia was above the European Union and European Economic Area (EU/EEA) mean percentage (18.4% versus 16.9%). Trends from 2013 to 2108 are shown in Figure 35. It is important to note that there are varying proportions of HA- and CA-MRSA in countries that contribute EARS-Net data, similar to the variation between Australian states and territories.[79] Although the EARS-Net data does not include place of onset, in 2014, 33.4% of all MRSA was community-onset.[80]

Figure 35: Methicillin resistance in *Staphylococcus aureus* in Australia and European countries, 2013–2018



	2013	2014	2015	2016	2017	2018
EU/EEA	18%	20%	19%	18%	17%	16%
Australia	18%	18%	18%	18%	18%	17%

Commentary

Analyses of AGAR MRSA bacteraemia data between 2013 and 2018 identified has important national and state and territory trends, which should inform local therapeutic, quality improvement and infection prevention and control initiatives.

Between 2013 and 2018, the proportion of *S. aureus* bacteraemias caused by MRSA remained relatively stable at between 17% and 18%. However, there were variations in trends for MRSA bacteraemia by place of onset which need to be considered, with the emergence of community-acquired (CA) MRSA as the dominant clonal group causing MRSA bacteraemia. Community-onset (CO) MRSA bacteraemia increased and hospital-onset (HO) MRSA bacteraemia decreased during this period. There were similar trends in the proportions of CA MRSA and hospital-acquired (HA) MRSA clones, with increases in CA-MRSA and decreases in HA-MRSA clones. This is because of increases in CA-MRSA as a cause of HO-MRSA bacteraemia during this time.

One reason for the changing proportion of HA-MRSA bacteraemia is a rapid decline in the prevalence of the ST239-III. This may be due to a decline in the virulence of this clone, as measured *in vitro* and *in vivo*.[13] Whilst there was also a reduction in the healthcare-associated clone ST22-IV as a cause of MRSA disease, the reductions were far less than for ST239-III, the other dominant healthcare-associated clone. Reductions in hospital-onset and healthcare-associated MRSA are likely attributable to concerted efforts in hospitals to control of *S. aureus* bacteraemia, such as improvements in the management of invasive devices, national reporting of *S. aureus* bacteraemia and the National Hand Hygiene Initiative.[36] However, as ST22-IV has reduced by smaller amount, it is possible that additional infection prevention and control processes may be needed for control of this clone.

Approximately 60% (data not shown) of all ST22-IV disease is community onset, varying by state and territory (50–80%). It has been hypothesised that the persistence of ST22-IV in hospital- and community-onset disease is due to increased rates of colonisation in residential aged care. [44] A recent survey undertaken by the National Centre for Antimicrobial Stewardship in residential aged-care facilities, supported by the Australian Commission on Safety and Quality in Health Care, identified high rates of inappropriate antimicrobial use[68], which could act as a driver for colonisation and subsequent infection. Overseas healthcare workers who may work in this setting may also be a contributing factor to the prevalence of these clones.

In 2018, ST93-IV, a community-associated clone, was the dominant MRSA clone across Australia, with disproportionate burden in the northern areas of Australia. Overall it caused 22% of all MRSA bacteraemias in Australia, and 1 in 4 community-onset infections. It has been proposed that the success of this clone can, in part, be attributed to PVL, which is analogous to the great success of the USA300 clone in the United States. However, if this were the case, then the Southwest Pacific clone, which also possesses this toxin and preceded the emergence of the Queensland clone, might have been expected to become more prominent earlier.

Notwithstanding the dominance of ST-93-IV, there is large variation in the burden of clones that cause community-onset disease, with consistencies in particular geographic regions. In northern Australia, ST93-IV predominates in Queensland, Western Australia and the Northern Territory. In contrast, the healthcare-associated clone, ST22-IV, is dominant in community-onset disease in most other states and territories. The exception is South Australia, where both clones fluctuated as the most common cause of community-onset disease from 2013 to 2018.

Other community-associated clones caused between 3% and 9% of all MRSA disease from 2013 to 2018. ST5-IV, ST45-V and ST1-IV each caused between 8% and 9% of all MRSA bloodstream infections; this varied by state and territory. Of these, ST1-IV seems to be decreasing, primarily as a result of decreases in northern Australia and South Australia. The other community-associated clones stabilised at 9% overall. Unknown community reservoirs may be a factor in relation to these clones; further research is required to investigate the issue.

Increases in CA-MRSA are important for hospital-based control of MRSA. When the patient's own skin flora includes MRSA, it is more likely that an episode of *S. aureus* bacteraemia, when it occurs in hospital, will be due to MRSA but attributed to a CA-MRSA clone.[81] Because of this, future improvement in prevention and control of hospital-onset MRSA will be dependent on community-associated clone dynamics, including active control strategies to reduce CA-MRSA carriage in the community.

In the One Health context, surveillance of livestock-associated clones is important in addressing antimicrobial resistance. To date, the livestock-associated clone ST398 has not been detected in AGAR surveys, despite its increasing importance in Australian pig herds.[76] This clone emerged in Europe in 2003, initially associated with pigs and pig farmers, and subsequently in other livestock.[73] In 2013, it was detected in a nasal swab from an Australian pig veterinarian[74], and subsequently detected at very low levels in pig herds across Australia.[75] A distinctive clone often carried by equine veterinarians in Australia, (WA-20 – ST612-IV)[78], has been found once in the 2013 survey; it caused a community-onset bloodstream infection.

There are several therapeutic implications of the changing spectrum of MRSA disease. As CA-MRSA increases in the community, the empiric treatment of skin and soft tissue infections with first-line agents becomes less reliable. Also, resistance patterns for MRSA disease as a group are changing; clindamycin has become unreliable as an empiric choice.[48] Microbiological sampling and confirmatory antimicrobial susceptibility testing are becoming increasingly important in some settings, both to identify whether MRSA is present and to confirm optimal oral therapeutic choices. Research also suggests that some clones (ST22-IV) have shown elevated minimum inhibitory concentrations to chlorhexidine.[40] Although the clinical significance of this is uncertain, this may have future implications for antiseptic choice in certain situations.[48]

Despite the diversity of clones by state and territory over time, the clear message in this longitudinal analysis is that it can no longer be assumed that MRSA clones are specific to either community or hospital environments; this is also the case internationally.[82] Whilst historically community- versus healthcare-associated clones were more distinctly associated with either community-onset or hospital-onset disease respectively, this is no longer a good surrogate definition to infer likely clonal type. This highlights the importance of AGAR genomic surveys to inform optimal prevention, control and treatment strategies.

There is no doubt that MRSA types and clones will continue to evolve in Australia. SCC*mec* is transmitted between strains of *S. aureus*, and probably between all staphylococcal species, including the many species of coagulase-negative staphylococci that colonise humans.[83] Each clone varies in its ability to spread and become a problem, and each likely requires specific measures for control. Both hospital- and community-based solutions may be required. Possible considerations include changes in surveillance, infection prevention and control including decolonisation, antimicrobial stewardship and antiseptic use practices.[84-87] Regardless of the causes of clonal success, MRSA disease in Australia will continue at high levels unless control of emerging and dominant clones, such as ST93-IV and ST22-IV, can be achieved.

Further research that could inform effective prevention and control strategies includes: clarification of clonal reservoirs; reasons for increasing hospital-onset disease, despite improvements in invasive device management; hand hygiene; antimicrobial stewardship; and environmental cleaning strategies. Analyses to identify the point at which hospital-based strategies alone are unlikely to control increases in hospital-onset disease due to CA-MRSA clones in Australia may be useful. Comparisons of interventions implemented by the states and territories from 2013 to 2018, which have led to reductions in MRSA disease, may also be useful.

Whilst trend analyses are important for system-based monitoring and strategy development, it is always important to remember that each case represents a person with severe clinical disease. These AGAR data, together with other analyses, suggest that the burden of MRSA invasive disease may disproportionately impact Australian indigenous communities and aged care residents. Prevention and control of MRSA in diverse community settings is a priority to address this situation and a focus for the states and territories.[88, 89]

This data is clearly showing that clonal variation cannot be explained by antimicrobial phenotypic or community- versus hospital-onset disease classifications alone. The MRSA clones will continue to evolve and inform opportunities for exploring opportunities for prevention and control of MRSA in Australia.

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