Staphylococcus aureus bloodstream infections: an important indicator for infection control. Chapter 2: Bloodstream infections – an abridged version

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Abstract

Staphylococcus aureus bloodstream (SAB) infections are common and serious causes of morbidity and mortality. They also cause considerable additional healthcare costs. In Australia, there are ~7000 SAB infection episodes per year and most of these are associated with healthcare procedures. In hospitals, data on all *S. aureus* bacteraemia episodes are relatively easy to collect. Collecting this data gives an accurate indication of the incidence of SAB infection in individual hospitals and whether they are healthcare-related infections (e.g. arising from intravenous catheter infections or surgical sites). These data also measure the relative proportion of methicillin-resistant *S. aureus* infections. When hospitals investigate the causes of individual healthcare-associated SAB infections, preventable factors will be identified. This should result in changes in clinical practice and protocols, while ongoing surveillance will allow an assessment of the efficacy of control measures. This will result in a decrease in the number of serious and life-threatening infections. This article is an abridged version of Chapter 2: 'Bloodstream infections' from the publication 'Reducing harm to patients from health care associated infection: the role of surveillance.' Cruickshank M, Ferguson J, editors. Sydney: Australian Commission on Safety and Quality in Health Care; 2008. The complete publication is available online at: www.safetyandquality.gov.au.

Introduction

Staphylococcus aureus bloodstream (SAB) infections cause a large proportion of serious healthcare-related infections. SAB infection has been reviewed in several publications,[1–11] including a recent and extensive chapter in a compilation of all healthcare-associated infections (HAIs) undertaken by the Australian Quality and Safety Commission.[12] This article summarises the main points from that chapter,[12] plus material from other sources.[3] In particular, it focuses on how SAB infection can be used as a tool in local and national quality improvement programs.

SAB infections are very common and are major causes of morbidity and mortality worldwide, leading to considerable additional healthcare costs.[1–12] In Australia there are ~7000 SAB infection episodes per year and most of these are associated with healthcare procedures.[1] Approximately half of all SAB infections have a hospital onset. The remainder are community onset. However, of these, about one-third of community-onset SAB infections are related to healthcare procedures.[1]

SAB infections are associated with a high mortality.[1–12] In the pre-antibiotic era, the associated death rate was 82%, and many cases occurred in young patients without underlying disease.[13] With methicillin-sensitive *S. aureus* (MSSA) the median mortality is now ~25%, and with methicillin-resistant *S. aureus* (MRSA) it is 35%.[14]

In Australia, the rate of SAB infection is 35 per 100 000 people per year.[1] This is a similar rate to England, where there were 19 244 episodes in 2003.[1,12,15] These rates are lower than estimated for the US in the only comparative study available (55/100 000 people per year).[1,15] The rate in Australia is higher than in Denmark[16,17] and Canada (19.7/100 000).[2]

In an Australian study, of the 3192 SAB infection episodes documented, 1571 (49%) had their onset in the community.[1] The median rate for SAB infection episodes was 1.48 per 1000 admissions (range 0.61–3.24), with a median rate for hospital-onset SAB infection of 0.7 per 1000, and a median rate for

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community onset of 0.8 per 1000 admissions. In a more recent study,[5] the Australian Group on Antimicrobial Resistance looked at the epidemiology and outcomes of SAB infection in 2005–2006 in mainly tertiary referral hospitals. A total of 1511 cases of SAB infection were documented, of which 66% occurred in males and 32% originated from vascular access devices. Bacteraemia had a community onset in 60% of cases, although half of these (31% of total) were healthcare associated. Overall, 57% of all episodes were healthcare associated. Mortality was measured at 7 days after blood culture collection and was 11.2%.

MRSA bloodstream infections

Increasing numbers of serious infections are caused by antibiotic-resistant strains. In the US, more than 10% of all bloodstream infections in hospitals are due to MRSA.[12] Patients with MRSA have worse outcomes than those infected with more sensitive strains. In the US, 75% of invasive MRSA infections were bloodstream infections and the rate of MRSA bloodstream infections was approximately 24 per 100 000 people per year.[18] In England in 2003, the MRSA bloodstream infection rate was 16 per 100 000 people per year.[1,8,19]

In Australia, the MRSA bloodstream infection rate is lower at 9.5 per 100 000 people per year.[1,12] In another population-based study, the incidence of healthcare-associated MRSA bloodstream infection varied from 0.6 to 13.3 per 100 000 population per year across different Australian States and Territories.[20] Western Australia, which has the most stringent MRSA control program, had the lowest rates.[20]

The proportion of SAB infection caused by MRSA varies in different European countries.[21] In 2002 in Denmark it was 1%, The Netherlands 1%, Austria 11%, Germany 19%, Spain 23%, France 33%, Italy 38%, Greece 44% and the UK 44%. In comparison, in Australia in 1999 to 2002, it was 26%[1] and in 2005/2006 it was 24%.[5]

In the UK, there has been mandatory measurement of all bloodstream infections caused by *S. aureus* (including MRSA) since 2001.[4] These surveillance data underpinned a multipronged effort to reduce healthcare-associated MRSA infection that included a root cause analysis of each episode.[21] Peak numbers of MRSA bloodstream infection have fallen by 40% from 2003 to 2007 (3955 to 2376 episodes, a rate in 2007 of 1.24 cases per 10 000 inpatient days).[4,12]

Australian data shows that MRSA caused 40% of hospital-onset SAB infection episodes and 12% of community-onset episodes.[1,12] The median rate of hospital-onset MRSA was 1.3 per 10 000 occupied bed days (OBDs) (range 0–3.9). This latter figure is similar to what is seen in the UK since 2007 after the reduction in MRSA numbers. The median rate for all SAB infections per 1000 OBDs was 4.3 per 10 000 OBDs (this includes all MRSA and MSSA infections). The median rate for all SAB infections (MRSA and MSSA) was 4.3 per 10 000 Occupied Bed Days (OBDs).

In the more recent Australian Group on Antimicrobial Resistance study[5] from Australia (2005–2006), of the 1511 SAB infection cases in 17 tertiary hospitals, MRSA was the pathogen in 24% of episodes. Of the MRSA episodes, 53% were of the typical multiresistant hospital type and 29% were of the community-associated type. Only about a quarter of these community-onset MRSA infections were caused by phenotypes of MRSA that were not multiresistant and thus more likely to be true community-acquired episodes of MRSA bacteraemia.[1,5,22]

Cost of SAB infections

In a Western Australia study, the average length of stay for patients with *S. aureus* bacteraemia was 26.5 days.[1] SAB infection episodes lead to considerable additional healthcare costs.[23]

A 3-month follow up of 70 consecutive patients in a prospective study at the Royal Adelaide Hospital during 1999–2000 determined the cost and outcomes of healthcare-associated SAB infection episodes.[12,24] The mortality rate at 90 days was 27% and in most cases (20%) SAB infection was the cause or a contributing factor. Complications occurred in 36% of patients, including multiple organ failure in nine patients and metastatic infection at other body sites in 11 patients. Complications occurred more often in those with MRSA.

The median excess length of stay was 13 days (AU$16 500). However, when the potential confounding effect of length of stay before infection was taken into account, the median difference in excess length of stay reduced to 11.5 days (AU$12 430) per case. From the perspective of the hospital budget, the shortfall in notional case-mix reimbursement for the 70 cases was A$730 000, or A$10 360 per case. However, this figure underestimates the true cost of infection, because the complex formula used for diagnosis related group (DRG)assignment and cost-weighting already includes some allowance for the development of complications of care.[12,24]

In 2006, there were 159 cases of healthcare-associated SAB infection reported to the South Australian HAI surveillance system and these SAB infections equated to about A$2 million in excess costs. It also equates to a loss of 32 lives and ~330 years of healthy life lost in South Australia annually. The opportunity cost was the loss of ~1400 patient days that could have been used to treat other patients if these infections had been prevented.[12,24]

Methods for surveillance of SAB infection

The traditional method for determining those episodes that were healthcare-associated (>48 h after admission to hospital)

substantially underestimates the number of episodes of bacteraemia that are healthcare associated.[1,12] In Australia, of 971 episodes of SAB infection where full data from three teaching hospitals were available, 64–75% of the total SAB infection episodes were healthcare associated.[1] However, only 46–61% of the episodes were acquired while the patient was an inpatient (i.e. >48 h in hospital). Thus, in these hospitals, about one-third of all healthcare-associated episodes were acquired by either outpatients or short-stay patients. These latter episodes are thus better defined as 'non-inpatient, health-care associated.' About two-thirds of all SAB infection episodes in Australia are associated with healthcare or medical procedures (i.e. all hospital-onset episodes and about one-third of community-onset episodes).

Choice of denominators and numerators when calculating SAB infection rates

One of the issues that arises when calculating rates for healthcare-associated SAB infection is what to include in the numerator and in the denominator when rates are calculated. We believe all healthcare-associated episodes should be included, that is all episodes that are hospital onset plus those from the community that are healthcare related (e.g. associated with an intravenous catheter). One option for the denominator and a relatively easy one to collect is to use OBDs (and preferably call them as they are in the US, 'patient days'). Day-only cases also need to be included, because these will also be represented in the episodes of SAB infection (e.g. with dialysis or intravenous therapy, which will often have been day-only cases). However, most definitions used to date, for example, from the UK, New Zealand and Australia, have excluded day-only patients from the denominators.

Using different denominator and numerators creates difficulties in making comparisons over time or between hospitals, States or countries. However, although the values of the rates will change when different values are used in the numerator and denominators, the trends in any graphs will often stay the same even when different values are used. Hence, the use of any particular denominator is probably of less importance than ensuring that there is consistency in what is used.

Figure 1 shows rates of healthcare-associated SAB infection that have occurred at the Canberra Hospital since 1998, calculated with different denominators.[12] The graphs in this figure all show the same trend with time. There was a peak in episodes in 2000 because the hospital had higher MRSA rates at that time; action was then taken and MRSA numbers decreased. Another rise in MRSA occurred in 2006.

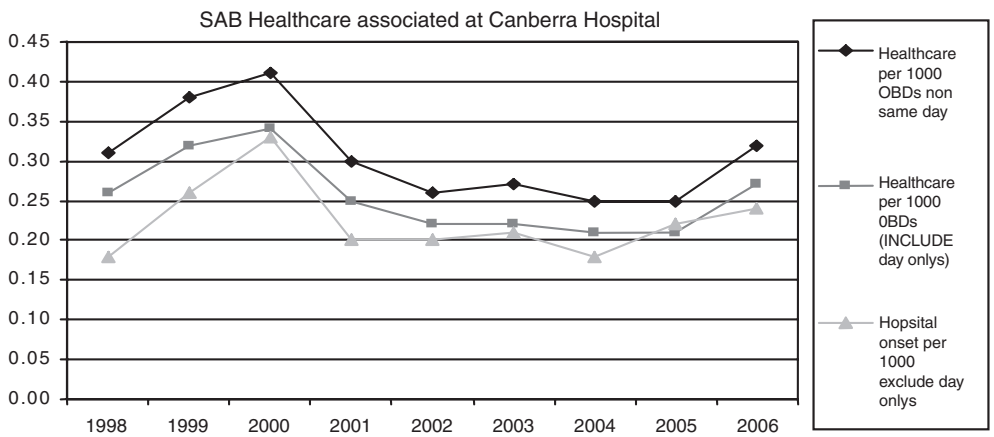
Current surveillance systems and results in Australia

South Australia, Western Australia and Queensland conduct Statewide surveillance of healthcare-associated SAB infection in their public hospitals and some private hospitals. NSW is planning to commence a program to do this in their public hospitals. Tasmania has made SAB infection a notifiable disease since 2008. Other local facilities and regions in other jurisdictions also conduct such surveillance.

In December 2008, the Australian Ministers endorsed a recommendation proposed by the Australian Commission on Safety and Quality on Health Care (ACSQHC) that all hospitals monitor and report rates of SAB infection through their relevant jurisdiction. Through ongoing discussion with the ACSCHC's Private Hospital Sector Committee, a reporting system for private hospitals will be devised to complement the public hospital data collection. In the same month, rates of SAB infection were included as an indicator for the National Healthcare agreements at the Council of Australian Governments.

A consensus definition for SAB infection was proposed by the ACSQHC HAI Surveillance Committee in November 2008. This

Figure 1. Effect of denominator on calculation of rate of healthcare-associated* Staphylococcus aureus *bloodstream infections at Canberra Hospital, 1998–2006.



definition was endorsed by the ACSQHC Inter-Jurisdictional and Private Sector Hospitals Committees in January 2009.

A dataset for jurisdictional submission of SAB infection to a national data collection was recommended by the ACSQHC HAI Surveillance Committee in February 2009 and endorsed by the Inter-Jurisdictional Committee in April 2009.

A national collection of SAB infection data using the consensus definition commenced in April 2009 as an outcome measure of hand hygiene compliance through the ACSQHC National Hand Hygiene Initiative conducted by Hand Hygiene Australia.

South Australia

Seven major South Australian public hospitals have contributed bloodstream infection data to the South Australian Department of Health since 1997.[12] Surveillance for bloodstream infection was expanded in 2002 and the number of contributors increased to 14 metropolitan hospitals (including both private and public). Until 2002, the definitions used for this surveillance included only hospital-onset episodes (i.e. occurred >48 h after admission). From 2002 onwards, the national definitions developed by the Australian Infection Control Association were adopted, which thus included non-inpatient healthcare-associated episodes.[25]

Figures 2 and 3 show the trend in SAB infection for the two time periods. Figure 2 clearly illustrates the rise and then fall of MRSA as a percentage of all healthcare-associated *S. aureus* blood isolates over a 10-year period. Data for this chart include hospital-onset episodes only.

Figure 3 presents the data as rates, using overnight OBDs as the denominator (i.e. excluding day-only patients). The numerator includes all healthcare-associated episodes, both inpatient and non-inpatient.

Overall, in South Australia since 2002, in the 14 hospitals undertaking healthcare-associated SAB infection surveillance, the aggregate rate per 10 000 OBDs has fallen from 2.1 to 1.43, a fall of more than 30%. In the type 1 hospitals (tertiary referral), the rate has fallen more substantially from 3.10 to 1.86 per 10 000 OBDs, a fall of more than 40%.

The aggregate rate of SAB infection in 2006 for these 14 hospitals was 1.43 per 10 000 OBDs (range 0–2.35). Using separations as a denominator, the aggregate rate is 0.79 per 1000 separations (range 0–1.58).

The decline in rates of SAB infection episodes in South Australian hospitals over the past 5 years was associated with multiple interventions within the major metropolitan hospitals, including:

- the widespread introduction of alcohol-based hand hygiene from 2002;
- the establishment of a State-wide link nurse program in 2003, following its successful operation in two of the larger metropolitan hospitals;
- regular feedback of surveillance data on MRSA, bloodstream infection and antibiotic usage to contributors;
- the development of an intensive MRSA screening and control program in one of the largest hospitals.

The Canberra Hospital

Data from 1998 to 2006 is available from an ongoing surveillance program at the Canberra Hospital, a 500-bed tertiary referral hospital.[12] The study prospectively followed all episodes of

Figure 2. **Staphylococcus aureus** *bloodstream infections for seven major South Australian metropolitan hospitals.*

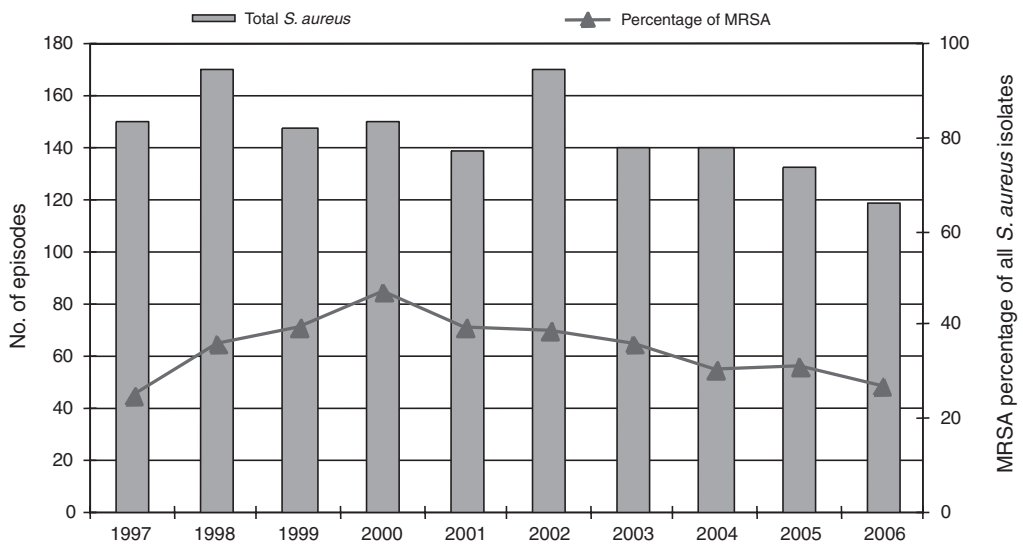
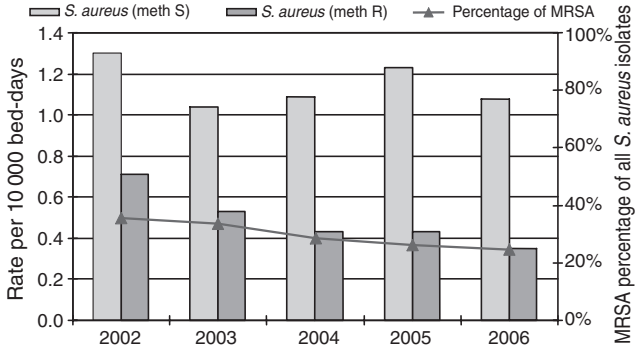


Figure 3. Rates of methicillin-sensitive and methicillin-resistant **Staphylococcus aureus** *bloodstream infections for 14 South Australian hospitals.*



SAB infection that were hospital-onset, plus all non-inpatient healthcare-associated episodes as well as community-onset episodes. When rates were calculated using the denominator of OBDs (excluding day-only patients), the SAB infection rates varied from 0.25 to 0.41 per 1000 bed days. Figure 1 shows the variations that occurred from year to year.

Over the 9-year study period there were 615 SAB infection episodes, of which 124 were caused by MRSA (20.1%). The number of SAB infection episodes varied from 55 to 79 per year. Of these, those that were community-onset varied from 14 to 40 episodes, non-inpatient healthcare associated from 4 to 18 episodes, and inpatient healthcare-associated episodes varied from 21 to 45 episodes per year. In 2005, there were 67 SAB infection episodes, of which 33 were inpatient healthcare-associated episodes and three were non-inpatient healthcare-associated episodes. The rate of healthcare-associated SAB infection was 0.72 per 1000 separations (or 1.7 per 1000 separations if day-only cases are excluded).

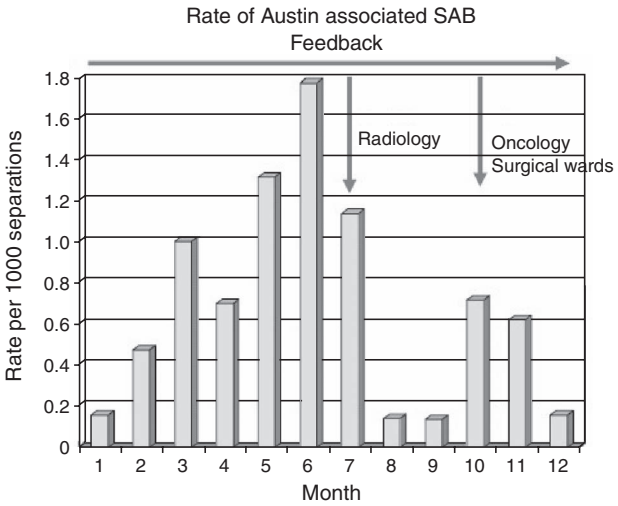
The Austin Hospital

SAB infection data has been collected at the Austin hospital in Melbourne.[12,26] Austin-associated SAB infection episodes refer to all inpatient episodes plus all healthcare-associated community-onset episodes. There were a total of 240 SAB infection episodes in 27 months, with 131 of them being Austin episodes (96 inpatient and 35 non-inpatient) and 109 being community-associated episodes. The overall rate of Austin-associated SAB infection was 0.7 per 1000 separations. However, in the first 9 months it was 1.1 per 1000 separations, and during the 18-month period after the *S. aureus* bacteraemia surveillance program was introduced, it dropped to 0.51 per 1000 separations, a reduction in rate of 55% (see Figure 4).

Australia New Zealand Co-operative on Outcomes in Staphylococcal Sepsis

A prospective trans-Tasman study of SAB infection outcomes commenced in 2007.[27] Data are entered by 27 hospital laboratory services over an internet interface. From June 2007, to May 2008

Figure 4. Rate of Austin-associated **Staphylococcus aureus** *bloodstream infections.*



1994 entered cases had completed 30-day follow up. Where an infection source was known 1840 episodes in 657 a device was a cause with CVC being the most common. MRSA causesd 450 episodes (24%) and of these 123 were community MRSA.

A total of 10.1% of SAB infection cases were caused by penicillin-susceptible strains. Infections associated with indwelling devices were the most commonly recorded clinical association (27%). The 7-day all-cause mortality was 10.8% and the 30-day mortality was 20.6%. Mortality was similar for community-onset and hospital-onset infections.

New Zealand

A system to measure healthcare-associated SAB infections per 1000 inpatient bed days (OBDs or patient days) has recently commenced across all regions of New Zealand. Figure 5 displays recently published rates.[28]

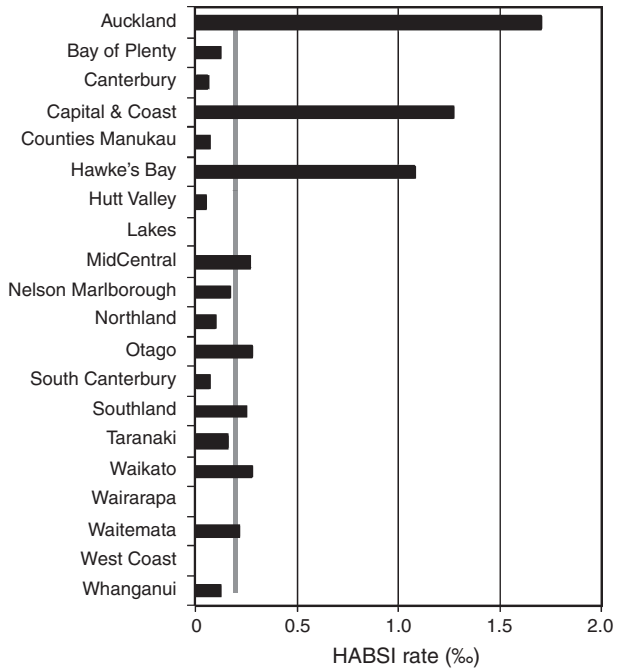
Proposal for collection of data in all hospitals[3]

(1) That all hospitals collect data on each episode of SAB infection. This can be then be expressed as the number of episodes per 1000 separations and per 10 000 OBDs.
(2) Data will be further divided into MRSA *v.* MSSA.
(3) SAB infection episodes will also be grouped into one of three categories: 'healthcare associated, inpatient', 'healthcare associated, non-inpatient' and 'community onset' according to nationally agreed definitions.

Proposal for using this data to prevent further infections

Each episode will be investigated and regarded as a 'signal event'. For those that are healthcare related, possible causes for

Figure 5. Hospital-acquired* Staphylococcus aureus *bloodstream infections, New Zealand (April–June 2007). The grey line denotes the nationwide rate for HA SA-BSI Auckland District Health Board has reported a rate against the number of patients rather than the number of bed days.



that episode will be identified by the infection control service of the hospital, so that predisposing factors can be monitored over time and compared between hospitals. Measures to improve compliance with appropriate clinical practices and/or changes in protocols should then be introduced to prevent future episodes.

Conclusions

SAB infections are common and serious and about two-thirds are related to healthcare procedures. They cause high levels of morbidity and mortality, and incur considerable healthcare costs. They are, however, often preventable.

The role of surveillance is an important tool to reduce healthcare-associated infections. The purpose of collecting, analysing and then acting on reliable surveillance data is to improve quality and patient safety within a service, facility or jurisdiction. Effective surveillance systems provide the impetus for change and make it possible to evaluate the effectiveness of interventions. To significantly reduce SAB infection and other HAIs, a multifaceted approach is required. This approach can be grouped into specific strategies at healthcare facility, jurisdictional and national levels.

A recommended hospital dataset has been proposed and endorsed by Australian States and Territories, and private hospitals, to provide timely and reliable feedback for clinicians to effectively manage HAIs. Local datasets can also inform local prevention strategies and improvement strategies.

At the State/Territory level, collated and analysed surveillance information can: inform policy, resource allocation and programs; be returned to hospitals for benchmarking and comparison; be used as the basis for liaison between health services and infectious disease experts to develop State-based priority programs to reduce HAI; and monitor State trends related to HAI.

When surveillance information is collated and analysed at a national level, it can: inform policy, resource allocation and programs; be returned to jurisdictions for benchmarking and comparison; be used as the basis for liaison between jurisdictions, health services and infectious disease experts to develop state and national-based priority programs to reduce HAI; and monitor national trends related to HAI.

The collection of this indicator will also assist in identifying healthcare-related factors associated with SAB infection, thereby allowing for interventions to be put in place. By measuring the incidence and looking into each case we can reduce subsequent HAIs.

Conflicts of interest

None declared.

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