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MAJOR ARTICLE

A Major Reduction in Hospital-Onset *Staphylococcus aureus* Bacteremia in Australia—12 Years of Progress: An Observational Study

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Background. *Staphylococcus aureus* bacteremia (SAB) is a serious cause of morbidity and mortality. This longitudinal study describes significant reductions in hospital-onset SAB (HO-SAB) in Australian hospitals over the past 12 years.

Methods. An observational cohort study design was used. Prospective surveillance of HO-SAB in 132 hospitals in Australia was undertaken. Aggregated data from all patients who acquired HO-SAB was collected (defined as 1 or more blood cultures positive for *S. aureus* taken from a patient who had been admitted to hospital for >48 hours). The primary outcome was the incidence of HO-SAB, including both methicillin-resistant (MRSA) and methicillin-susceptible (MSSA) *S. aureus* strains.

Results. A total of 2733 HO-SAB cases were identified over the study period, giving an aggregate incidence of 0.90 per 10 000 patient-days (PDs) (95% confidence interval [CI], .86–.93). There was a 63% decrease in the annual incidence, from 1.72 per 10 000 PDs in 2002 (95% CI, 1.50–1.97) to 0.64 per 10 000 PDs (95% CI, .53–.76) in 2013. The mean reduction per year was 9.4% (95% CI, −8.1% to −10.7%). Significant reductions in both HO-MRSA (from 0.77 to 0.18 per 10 000 PDs) and HO-MSSA (from 1.71 to 0.64 per 10 000 PDs) bacteremia were observed.

Conclusions. There was a major and significant reduction in incidence of HO-SAB caused by both MRSA and MSSA in Australian hospitals since 2002. This reduction coincided with a range of infection prevention and control activities implemented during this time. It suggests that national and local efforts to reduce the burden of healthcare-associated infections have been very successful.

Keywords. bacteremia; bloodstream infection; healthcare-associated infections; infection control; *Staphylococcus aureus*.

In the past decade, efforts to decrease healthcare-associated infections (HAIs) have increased worldwide. More than a decade ago, the landmark report "To Err Is Human: Building a Safer Health System" had a major impact on focusing the attention of policy makers, the public, and healthcare workers (HCWs) on improving patient safety in healthcare facilities [1, 2]. In response, HCWs, hospitals, and health authorities across the world have increased efforts to keep people safe from potential harm associated with receiving healthcare [3, 4]. One infection of particular interest has been *Staphylococcus aureus* bacteremia (SAB). Worldwide, SAB is a serious cause of morbidity and mortality, with associated mortality rates of 20%–50% [5–7] and a significant associated economic burden [8].

HAI surveillance programs have been established in numerous countries to monitor and control the occurrence of HAIs. The prevention of infection requires a multifaceted approach [9], often making it difficult to determine the relative effect of each intervention. In

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the case of SAB, interventions to reduce its incidence include hand hygiene initiatives and improvements in the management of intravascular catheters [10–13]. Despite global concerns about serious HAIs such as SAB and the need to monitor the effect of interventions, international comparisons are limited. There are few longitudinal studies describing the incidence of SAB across a wide region [14]. The purpose of this longitudinal study is to describe significant reductions in hospital-onset SAB (HO-SAB) in Australian hospitals over the past 12 years.

METHODS

The study presents an analysis of prospective surveillance of laboratory-diagnosed HO-SAB cases according to agreed definitions [15]. The primary outcome was HO-SAB, which was defined as 1 or more blood cultures positive for *S. aureus,* taken from a patient who had been admitted to hospital for >48 hours. The term HO-SAB is defined as any case of SAB occurring >48 hours after admission. Only the first isolate per patient was counted, unless at least 14 days had passed without a positive blood culture, after which an additional episode was recorded. Surveillance data were collected and combined from 132 hospitals in 4 Australian states and territories, representing 24% of all Australian hospitals that reported having 1 or more patient-days in 2011–2012. Of the 132 hospitals, 110 are publicly funded; the reminder are privately funded. In Australia, approximately 68% of all hospital beds are publicly funded [16]. Data from all admissions to inpatient wards or units within acute public hospitals, including psychiatric, rehabilitation, and aged care admissions were included. For the period 1 January 2002–30 June 2013, HO-SAB surveillance and hospital bed-day data were provided by the Australian Capital Territory (ACT), South Australia (SA), Tasmania (TAS), and Western Australia (WA) HAI surveillance units. All jurisdictions involved in this study have a system where laboratory data can be directly extracted and used for validation of reported cases. Data from the states with larger populations (New South Wales, Victoria, and Queensland) were not available for the time period used for this study.

All contributing hospitals used the HO-SAB definition as described earlier and provided bed-day denominator data to the HAI surveillance units. There were minor variations in the denominator used to calculate rates. ACT and WA used occupied bed-days (OBDs) for the entire study period, whereas SA used OBDs from 2002 to June 2006, and subsequently used patient-days [16]. Similarly, TAS used OBDs from 2005 until June 2008, when patient days were subsequently used. The changes in denominators during the study period have negligible impact as the yearly variance between the 2 measures ("occupied" compared to "patient" days) is estimated to be <1% [17]. For convenience, we use the term patient-days (PDs) for the remainder of the paper.

Statistical Analysis

Statistical analysis was conducted using IBM Statistics version 20.0. The incidence of HO-SAB per 10 000 PDs was calculated as [HO-SAB cases / number of PDs × 10 000]; 95% confidence intervals (CIs) were calculated for Poisson distributed counts. Monthly, quarterly, and yearly incidence rates were obtained for HO-SAB. Monthly incidence of HO-SAB over the entire study period was tested using time-series analysis (regression analysis), to allow for autocorrelation between monthly measurements. Adjustment for seasonality was not undertaken.

To determine whether there was an issue of "dilution" of rates from the later inclusion of PDs from smaller hospitals with a much lower-risk patient population and very few episodes, further analysis was undertaken. First, when new hospitals contributed data, comparisons of the mean HO-SAB rate before and after the addition of new hospitals were undertaken using analysis of variance. Second, monthly aggregate incidence of HO-SAB from the original 15 contributing hospitals and from larger, more complex peer group hospitals (principal referral hospitals as defined by the Australian Institute of Health and Welfare) [18] was analyzed separately over the entire study period using time-series analysis.

Ethical Statement

This study was approved by the human research ethics committee at Avondale College of Higher Education (H0013060).

RESULTS

The number of hospitals contributing data to the state surveillance systems increased progressively from 15 in 2002 to 132 hospitals by 2011; this number was sustained until 2013. Of these 132 hospitals, 81 were from SA, 46 from WA, 4 from TAS, and 1 from ACT. A total of 2733 HO-SAB cases were identified over the study period, giving an aggregate incidence of 0.90 per 10 000 PDs (95% CI, .86–.93). There was a 63% decrease in the annual incidence, from 1.72 per 10 000 PDs in 2002 (95% CI, 1.50–1.97) to 0.64 per 10 000 PDs (95% CI, .53–.76) in 2013. Further descriptive HO-SAB data by year are presented in Table 1. Using time-series analysis (regression), there was a mean reduction in the incidence of HO-SAB over the entire study period of 9.4% per year (95% CI, −8.1% to −10.7%; Figure 1).

Over the study period, the annual incidence of methicillin-resistant *S. aureus* (MRSA) HO-SAB significantly reduced by 76% from 0.77 to 0.18 per 10 000 PDs ($P < .001$). The proportion of HO-SAB that was caused by MRSA reduced from 44.7% to 28.0%. Cases of HO-SAB caused by both MRSA and methicillin-susceptible *S. aureus* (MSSA) significantly reduced during the study period ($P < .001$) (Table 1 and Figure 2). Aggregated data at the jurisdictional level also indicated a

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Table 1. Yearly Incidence of Hospital-Onset *Staphylococcus aureus* Bacteremia

Year	Hospitals	No. of PDs	Rate per 10 000 PDs		
			MSSA (95% CI) (No.)	MRSA (95% CI) (No.)	SAB (95% CI) (No.)
2002	15	1 208 009	0.95 (.79–1.14) (115)	0.77 (.62–.94) (93)	1.72 (1.50–1.97) (208)
2003	15	1 231 463	0.74 (.59–.91) (91)	0.60 (.47–.75) (74)	1.34 (1.14–1.56) (165)
2004	15	1 230 235	0.78 (.63–.95) (96)	0.46 (.34–.59) (56)	1.24 (1.05–1.45) (152)
2005	19	1 407 243	0.91 (.76–1.08) (128)	0.47 (.36–.60) (66)	1.38 (1.19–1.59) (194)
2006	19	1 620 486	0.79 (.66–.94) (128)	0.33 (.25–.43) (54)	1.12 (.97–1.30) (182)
2007	22	2 081 367	0.65 (.55–.77) (136)	0.29 (.22–.38) (61)	0.95 (.82–1.09) (197)
2008	65	3 566 709	0.71 (.63–.81) (254)	0.24 (.19–.29) (85)	0.95 (.85–1.06) (339)
2009	68	3 686 420	0.57 (.50–.65) (210)	0.21 (.17–.26) (78)	0.78 (.69–.88) (288)
2010	74	3 922 593	0.62 (.54–.70) (242)	0.18 (.14–.23) (71)	0.80 (.71–.89) (313)
2011	132	4 119 269	0.52 (.45–.60) (215)	0.23 (.18–.28) (93)	0.75 (.67–.84) (308)
2012	132	4 297 326	0.44 (.38–.50) (187)	0.16 (.12–.20) (68)	0.59 (.52–.67) (255)
2013[a]	132	2 072 993	0.46 (.37–.56) (95)	0.18 (.13–.25) (37)	0.64 (.53–.76) (132)
Total	. . .	30 444 113	0.62 (.60–.65) (1897)	0.28 (.26–.29) (836)	0.90 (.86–.93) (2733)

Abbreviations: CI, confidence interval; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *Staphylococcus aureus*; PD, patient-days; SAB, *Staphylococcus aureus* bacteremia.

[a] Till 30 June 2013.

reduction in both MSSA and MRSA HO-SAB, consistent with trends reported in Table 1 and Figure 1. These data are not specifically reported, as to do so would potentially identify individual hospitals.

During the study period, the number of hospitals contributing data increased from 15 to 132. When new hospitals contributed data, a significant decrease in the mean incidence of HO-SAB only occurred when the number of contributing hospitals increased from 16 to 19 in June 2005 ($P = .02$). There was no further significant change to the mean incidence of HO-SAB when additional hospitals contributed data.

To test the possibility that dilution of rates was occurring by the addition of lower-risk hospitals' data, analysis of data from the original 15 contributing hospitals was undertaken for the entire study period. In these 15 hospitals, there was a significant reduction in the incidence of HO-SAB of 6.5% (95% CI, −4.9% to −8.1%) per year, compared with 9.4% for the entire cohort of hospitals. When analysis was performed on data from the principal referral hospitals only [18], there was an annual mean

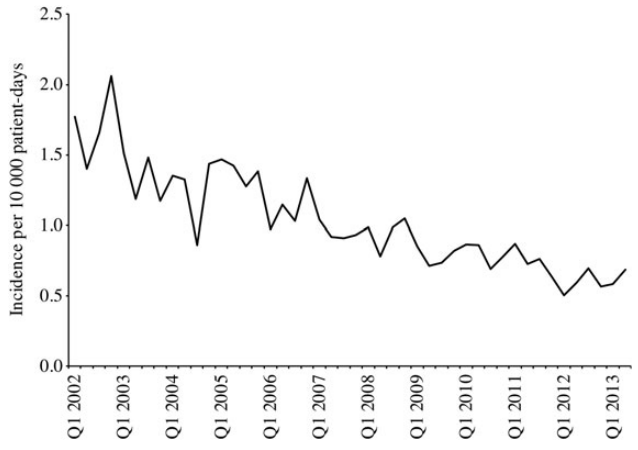


Figure 1. Quarterly incidence of hospital-onset *Staphylococcus aureus* bacteremia—all hospitals, 2002 to 30 June 2013.

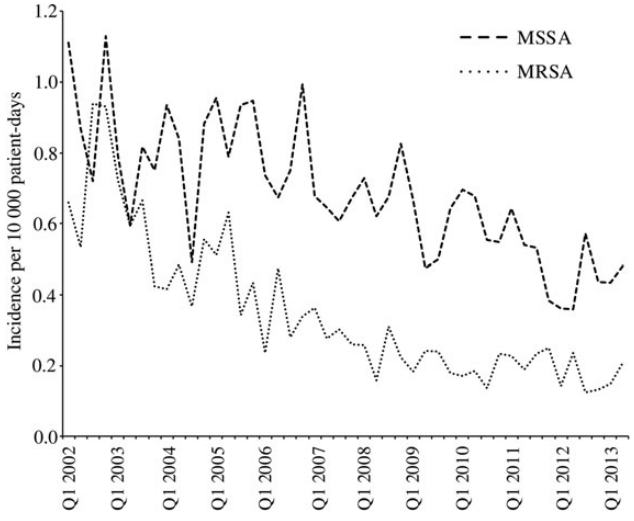


Figure 2. Quarterly incidence of hospital-onset methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-susceptible *Staphylococcus aureus* (MSSA) bacteremia—all hospitals, 2002 to 30 June 2013.

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reduction in the incidence of HO-SAB of 11.2% (95% CI, −9.2% to −13.2%). Therefore, it is unlikely that there was a significant "dilution" effect caused by progressive inclusion of many smaller hospitals to account for the observed results.

DISCUSSION

Our study reports a major, sustained, and significant reduction in HO-SAB in a large number of Australian hospitals since 2002. Although other studies have also documented a reduction in national incidence of HO-SAB [11, 19–23] they have mostly focused on MRSA. None have reported such a large reduction in both MSSA and MRSA HO bacteremia. Additionally, we report longitudinal data, a key strength of our study.

Comparisons of the incidence of HO-SAB between countries are difficult, given the variety of definitions for cases and denominator data. In England, "Trust Apportioned" cases (occurring after the third day of admission) of MRSA bacteremia have been collected since 2008. This has a close similarity to the HO-SAB definition used in our study. Their data suggest that a significant reduction in incidence of MRSA bacteremia occurred between 2008–2009 and 2012–2013, from an incidence of 0.43–0.12 cases per 10 000 bed-days ($P < .01$) [21]. This latter figure in England is lower than that reported in our study for 2013 (0.18 per 10 000 PDs). It is not possible to determine whether a reduction in MSSA bacteremia also occurred in England during the same period, as these data are not available.

In a Scottish study, the prevalence of HO-SAB in an inpatient population reported a 41% decrease between 2006 and 2010, from 0.73 to 0.50 cases per 1000 acute OBDs [19]. The incidence of HO-MRSA bacteremia fell from 0.16 to 0.03 per 1000 acute OBDs; however, unlike our study, the rates of HO-MSSA bacteremia remained unchanged. Their reported incidence of HO-MRSA bacteremia is higher than the incidence in the last year of our study (0.03 per 1000 acute OBDs vs 0.18 per 10 000 PDs), assuming the calculation of bed-days is similar. The authors suggested that the introduction of a universal MRSA admission screening program was associated with significant reductions in rates of MRSA bacteremia but made no discernible impact on burdens from MSSA bacteremia and that declines occurred almost exclusively in MRSA-related disease [19]. There is no national mandate regarding MRSA or MSSA patient screening in Australia. Consistent with other studies, the Scottish study found that upward pressure on MSSA rates was not observed, and that MRSA appears to add to, rather than displace, MSSA infection [20].

There are no national data from the United States on the incidence of HO-SAB; however, some studies provide insight into trends. A study undertaken by Kallen and colleagues examined invasive healthcare-associated MRSA infections in 9 metropolitan areas [24]. In patients with an invasive HO-MRSA infection, the proportion of these caused by HO-MRSA bloodstream infections decreased slightly from 87% to 84% between 2005 and 2008 ($P = .06$). A significant reduction in MRSA bacteremia related to a device was also identified in Veteran Affairs hospitals, after the introduction of MRSA prevention and control bundle [23].

In the largest study of SAB to date, the incidence of SAB was compared in 5 countries, incorporating nearly 20 000 episodes [25]. During the 9 years studied, several regions reported decreases in HO-MSSA, but only 2 regions observed a significant decrease in both HO-MSSA and HO-MRSA bacteremia (Copenhagen City and Sherbrooke). In a recent study from Victoria in Australia, data from 119 public and 4 private hospitals were analyzed for a 3-year period (2010–2012) [26]. Healthcare-associated SAB (ie, any case associated with receiving healthcare) infection rates decreased from 1.4 to 0.7 per 10 000 OBDs ($P < .001$), whereas healthcare-associated MRSA bacteremia decreased from 0.4 to 0.1 per 10 000 OBDs ($P < .001$).

There are several potential explanations for the reduction in HO-SAB described in our study. Australian states and territories have had a long history of implementing statewide infection prevention and control initiatives. At a national level, the work undertaken by the Australian Commission on Safety and Quality in Health Care (an independent statutory authority) in the area of HAI prevention is notable [27]. The Commission has led several major HAI prevention initiatives that were additional to those from state and local hospital initiatives. These initiatives included the development of national surveillance programs for HAIs, national evidence-based guidelines, training and support for improved clinician capacity in infection prevention and control, development of a national hand hygiene initiative, and new accreditation standards. Hospitals who contributed data to this study were involved in these national initiatives, in addition to local and jurisdictional HAI prevention initiatives. The reduction in SAB observed in this study is unique, given the reduction in both MSSA and MRSA HO-SAB. We believe a major factor was that national, jurisdictional, and local interventions did not just focus on MRSA, but on all cases of healthcare-associated SAB and an overall effort to reduce all HAIs [10, 12, 26–28].

Regardless of how the data in our study are analyzed, a significant downward trend in the incidence of HO-SAB, including MRSA and MSSA, is seen (Figure 3). To determine whether the observed reduction in HO-SAB was simply offset by increased healthcare delivery in the community and a subsequent increase in non-inpatient healthcare-associated SAB, we examined 2 further pieces of data. First, we explored hospital activity data and found there was only a 0.7% reduction in the average number of hospital beds per 1000 population in Australia between 2007–2008 and 2011–2012 [29]. We also identified a 2.7% increase in overnight admissions in Australian hospitals

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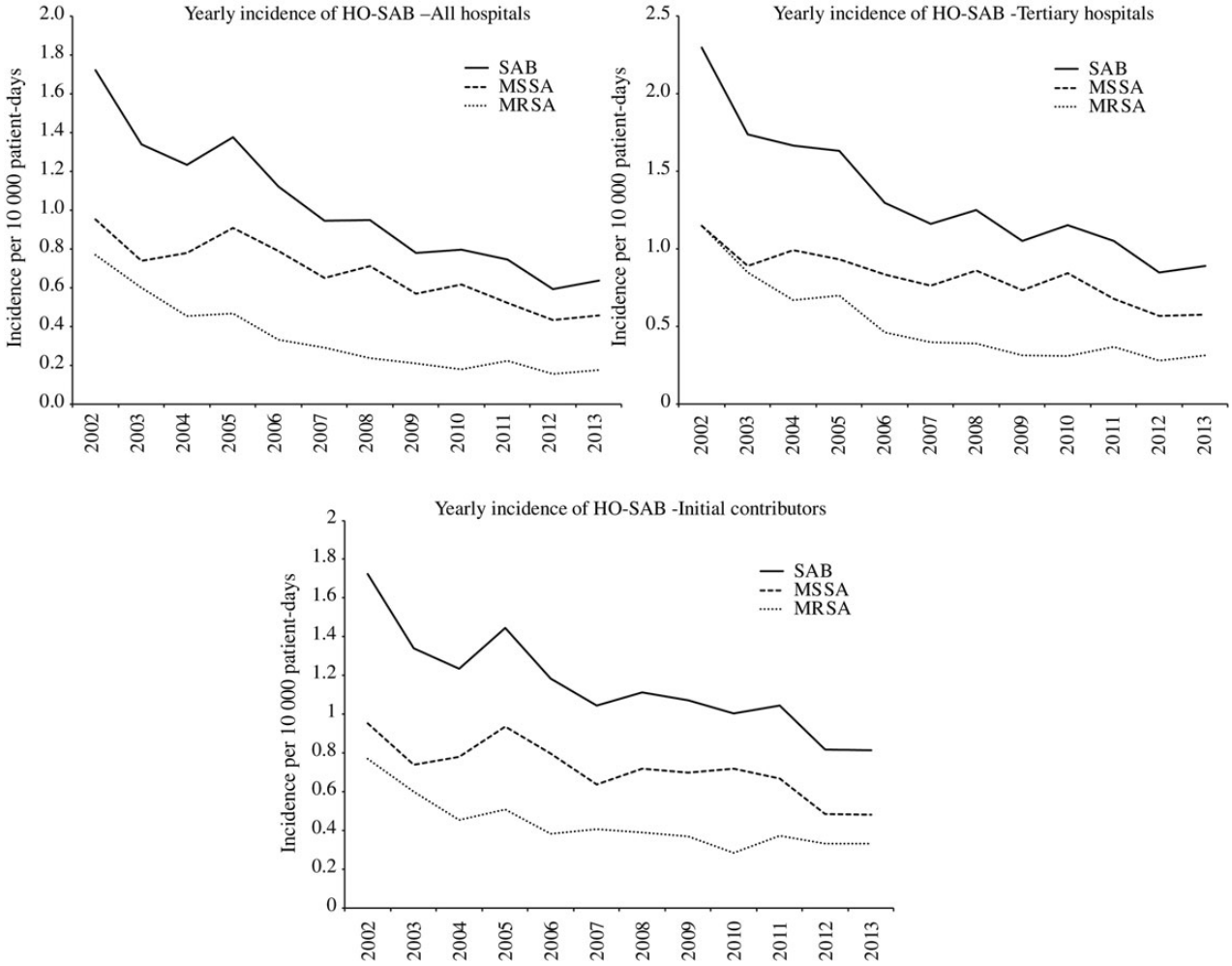


Figure 3. Yearly incidence of hospital-onset *Staphylococcus aureus* bacteremia (HO-SAB), 2002 to 30 June 2013. Abbreviations: MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *Staphylococcus aureus*; SAB, *Staphylococcus aureus* bacteremia.

over the same period [29]. Second, we examined non-inpatient healthcare-associated SAB data for the 4 last years of our study period in all jurisdictions. We found no evidence of an increase in non-inpatient SAB during this time. Consequently, we are confident that the decrease in HO-SAB observed in our study was not offset by increases in non-inpatient SAB or changes in the at risk population.

Our study is unique because we identified a significant decrease in both MRSA and MSSA HO-SAB over the course of the study and are unaware of any nation reporting similar findings in a longitudinal manner. Of the limited Australian population-based studies available, data suggest that the overall incidence of SAB (including HO and community-onset cases) has not significantly increased or decreased in 2 regions within Australia [25, 30]. Put simply, in Australia, reductions in HO-SAB have not been driven by an overall reduction in the incidence of SAB or reductions in either HO-MRSA or HO-MSSA bacteremia individually, a point of distinction from other notable studies [5, 11, 19].

A strength of this study is the application of a consistently applied internationally recognized definition for HO-SAB, and that data were captured for an extended period (12 years). However, a limitation of using this definition is that not all cases of healthcare-associated SAB will be captured. For example, cases of SAB occurring within 48 hours of hospitalization but associated with prior healthcare interventions such as intravascular devices or surgery will not be included [31]. Previous studies suggest that using a time frame of 48 hours postadmission will fail to identify approximately 30% of cases [26, 30]. It was not possible to obtain longitudinal data using a more comprehensive healthcare-associated SAB definition, as this approach did not commence in all states in Australia until 2010. Further limitations of our study included our inability to collect data on comorbidities, strain typing, and

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treatment data, which may have been helpful to explain observed differences in incidence over long time periods.

All jurisdictions involved in this study have had a history of making data publicly available on SAB, and the data presented in our study are consistent with and significantly builds on previously published work [12, 25, 30]. We report an incidence of HO-SAB in 2002 of 1.73 per 10 000 PDs. If this rate remained constant during the entire study period, 5274 cases of SAB would have potentially occurred in the contributing jurisdictions. This suggests that there were about 2500 fewer cases of HO-SAB across the study period from the participating hospitals. As a result, assuming a mortality of 21%, ≥500 lives were saved over the study period, as a result of the reduction in HO-SAB incidence [7].

We commend those responsible for infection prevention and control initiatives at a local, jurisdictional, and national level. The Australian experience showing reductions in both MSSA and MRSA HO-SAB highlights the need to tackle HAIs in a multifaceted manner, with a strong national focus, supported by local interventions. Policy makers should not focus prevention strategies on one organism or infection, and researchers should, where possible, consider the value of examining multiple HAI outcomes to evaluate infection prevention initiatives.

Notes

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Author contributions. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication. B. G. M. and P. C. were involved at every stage from the literature search, planning, and design of the study, data collection, data analysis, data interpretation, and writing. R. M., I. W., and A. W. were involved data collection, data interpretation, and writing. B. G. M. and P. C. are the guarantors. All authors had full access to the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis. All authors were involved in the drafting the work or revising it critically for important intellectual content and final approval of the version to be published.

Potential conflicts of interest. All authors: No potential conflicts of interest.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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