



Original Article

Antimicrobial-resistant central line-associated bloodstream infections in adult intensive care units: findings from an Australian surveillance network, 2011–2022

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Abstract

Objective: We aimed to describe the incidence, pathogens, and antimicrobial susceptibility of central line-associated bloodstream infections (CLABSI) in adult intensive care units (ICU).

Design: State surveillance data from 2011 to 2022 were analyzed to identify patient and device days and CLABSI events. Pathogen data were analyzed to determine the most common organisms and patterns of antimicrobial resistance grouped into 3-year time epochs.

Setting: Adult ICU in Victoria, Australia.

Participants: Healthcare organizations participating in CLABSI state surveillance.

Results: 608 events were reported over 751,350 device days. Overall, CLABSI incidence was 0.81 per 1,000 central-line days, with a 49.3% rate reduction from 2011 to 2022 (1.39 to 0.70 per 1,000 central-line days). Overall device utilization ratio was 0.57, with a 15.4% reduction from 2011 to 2022 (0.67 vs 0.56). Of 690 pathogens, the most common by rank order were coagulase-negative Staphylococci (CNS), *Candida* species, *Staphylococcus aureus*, and *Enterococcus faecalis*. The proportion of CNS-causing events increased by 69.0% from 2011 to 2022; this trend was not observed for other organisms. For every increase in epoch, a 33% decrease in methicillin-resistant *S. aureus* (MRSA), 4% increase in vancomycin-resistant *Enterococcus faecium*, and 12% increase in ceftriaxone-resistant *Escherichia coli* pathogens were observed.

Conclusions: We demonstrate a decreasing incidence of CLABSI in Victorian adult ICU and an increasing burden of infections due to CNS. No significant time trend increases in antimicrobial-resistant organisms, including MRSA, vancomycin-resistant *E. faecium*, and ceftriaxone-resistant *E. coli* were observed. These findings are relevant for identifying priorities for CLABSI prevention in Victorian adult ICU.

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Background and aim

Central line-associated bloodstream infections (CLABSI) in intensive care units (ICU) are significant healthcare-associated infections (HAI), resulting in increased mortality, length of stay, and healthcare costs. Optimizing infection prevention and control and antimicrobial stewardship practices is essential to prevent HAI and the emergence of antimicrobial resistance. Over the last 2 decades, there have been extensive efforts to prevent CLABSI using multimodal care bundles^{1,2} and as part of hospital quality improvement initiatives.^{3,4}

Victoria is the second most populous Australian jurisdiction with a population of over 6.7 million. Hospitals have participated in a state surveillance program for HAI since 2002, coordinated by the Victorian Healthcare Associated Infection Coordinating Centre (VICNISS). Although resistant pathogens have been reported in hospital settings within this region,^{5,6} it is not clear if emergent pathogens have specifically contributed to CLABSI burden, and no recent evaluation of CLABSI pathogen antimicrobial susceptibility has been performed. A timely review of CLABSI pathogens is beneficial to identify future opportunities for CLABSI prevention.⁷

The aim of this study was to describe CLABSI incidence, pathogens responsible for infection, and antimicrobial susceptibility of pathogens reported between 2011 and 2022 in adult ICU in Victoria, Australia.

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Methods

Definitions

The VICNISS CLABSI surveillance module, as previously described,⁸ is based on methods employed by the Centers for Disease Control and Prevention's National Healthcare Safety Network.⁹ A CLABSI event is a primary bloodstream infection in a patient with a central venous catheter (CVC) in place for 2 or more consecutive days prior to the event and where pathogen and clinical criteria are met.

Data collection

Continuous surveillance is undertaken in hospitals by infection prevention and control staff trained in VICNISS data submission. CLABSI event data include hospital and ICU admission dates, patient demographics, clinical and laboratory criteria, organism, and antimicrobial susceptibilities. Denominator data include a number of ICU patients and those with a CVC in place; these are used to determine the device utilization ratio (DUR) and CLABSI rate per 1,000 CVC days.

Analysis

Data from 2011 to 2022 were analyzed for changes in rates, pathogens, and antimicrobial resistance. CVC surveillance data and patient demographics are summarized annually using the median and interquartile ranges for continuous data with categorical data described by frequencies and percentages. Yearly DUR values were calculated by dividing the number of CVC days by the number of patient days. Annual CLABSI rates, derived by dividing the total number of CLABSI events by the total number of CVC days, were calculated per 1,000 CVC days, with 95% Poisson exact confidence intervals. Mixed effects negative binomial regression was used to assess whether any time trend was present in the annual CLABSI rates. Robust standard errors were applied to account for misspecifications, and the hospital identifier was modeled as a random effect to adjust for intrahospital correlation. The total number of CVC days per period was fitted as the exposure.

Pathogen data from blood cultures, grouped into 3-year epochs (2011–2013, 2014–2016, 2017–2019, and 2020–2022) and described by frequencies and percentages, were analyzed to identify the most common organisms and antimicrobial resistance. Changes in pathogen incidence over time were evaluated using mixed effects Poisson regression with robust standard errors, the hospital identifier as a random effect, and the total number of CVC days per period fitted as the exposure. Mixed effects negative binomial regression was applied where overdispersion was present.

To assess changes in pathogen-specific antimicrobial resistance, Poisson regression was used where the total number of the specific pathogen per epoch formed the exposure. For *Staphylococcus aureus*, any reported resistance to methicillin, oxacillin, flucloxacillin, or cefoxitin was classified as methicillin-resistant *S. aureus* (MRSA). For *Enterococcus faecium* or *Enterococcus faecalis*, reported resistance to vancomycin was classified as vancomycin-resistant *E. faecium* or *E. faecalis*. For *Escherichia coli* and *Klebsiella pneumoniae*, reported resistance to ceftriaxone or ciprofloxacin and fluconazole for *Candida* spp. was classified as resistant to these agents. Susceptibility analysis of fungal isolates over time was not carried out as insufficient results were available in the study extract.

The effect size for each regression model was quantified as the incidence risk ratio. Linear and nonlinear models were compared

using the likelihood ratio test to determine the best fit for the observed data.

All statistical analyses were performed using STATA/SE 18.0 (StataCorp LP, College Station, TX, USA).¹⁰

Ethics

This study was approved by the human research ethics committee associated with the administration of the VICNISS program (RMH QA2022086).

Results

Between 2011 and 2022, 608 CLABSI events were reported over 751,350 CVC days from 47 participating facilities (Table 1). Of the 28 public and 19 private hospitals that participated, 22 (78.6%) and 15 (78.9%), respectively, reported at least 1 event. The median age of patients was 54.9 years (interquartile range: (24, 68)) with 65.8% males and with a median length of stay in ICU before CLABSI event of 8 days (Supplementary file 1).

CLABSI rates and DUR

Overall CLABSI incidence was 0.81 per 1,000 CVC days; a 49.3% rate reduction was observed from 2011 to 2022 (1.39 to 0.70 per 1,000 CVC days) (Figure 1). The largest reduction in CLABSI rates was observed in the period 2011–2014, after which a plateauing of incidence has been observed. For the period 2011–2022, the DUR decreased by 15.4% from 0.67 to 0.56, with the largest reduction observed from 2011 to 2013. Overall, the DUR was 0.57.

CLABSI pathogens

Overall, 690 pathogens consisting of 72 unique species were responsible for the 608 reported CLABSI events. Most events were monomicrobial (88.0%), with an increase in the proportion of gram-positive organisms causing CLABSI over time. By pathogen, the most common by rank order were coagulase-negative Staphylococci (CNS), *Candida* spp., *S. aureus*, *E. faecalis*, *E. faecium*, and *E. coli* (Table 2). The proportion of CNS-causing CLABSI events increased by 69.0% from 2011 to 2022, with the largest increase observed from time epoch 1 (2011–2013) to 2 (2014–2016). This trend was not observed for other organisms.

Antimicrobial resistance

The proportion of antimicrobial-resistant pathogens by time epoch is presented in Table 3.

Gram-positive organisms

For CLABSI events due to *S. aureus*, an approximate 33% decrease in methicillin resistance was observed for every increase in 1 time epoch. On the other hand, for events due to *E. faecium*, an approximate 4% increase in vancomycin resistance was observed for every increase in 1 time epoch. No analysis was possible for *E. faecalis* due to insufficient data.

Gram-negative organisms

For CLABSI events due to *E. coli*, an approximate 12% increase in ceftriaxone resistance was observed for every increase in 1 time epoch. For CLABSI events due to *K. pneumoniae*, no meaningful result was possible due to insufficient data. No carbapenem resistance was reported in gram-negative pathogens.

Table 1. Central venous catheters under surveillance and central line-associated bloodstream infections outcomes, 2011–2022

Year	Number of hospitals	Number of device days	Number of events	CLABSI rate (per 1,000 device days)		Number of patient days	DUR	Number of pathogens	Monomicrobial infection		Polymicrobial infection	
				95% Confidence interval					n	%	n	%
2011	26	59,151	82	1.39	[1.10, 1.72]	88,919	0.67	88	78	95.1	4	4.9
2012	26	58,507	54	0.92	[0.69, 1.20]	94,267	0.62	56	52	96.3	2	3.7
2013	26	55,425	51	0.92	[0.69, 1.21]	95,691	0.58	67	36	70.6	15	29.4
2014	31	59,262	58	0.98	[0.74, 1.27]	102,702	0.58	71	46	79.3	12	20.7
2015	32	62,837	39	0.62	[0.44, 0.85]	108,941	0.58	53	26	66.7	13	33.3
2016	34	64,915	39	0.60	[0.43, 0.82]	113,168	0.57	41	37	94.9	2	5.1
2017	35	60,913	45	0.74	[0.54, 0.99]	108,938	0.56	52	38	84.4	7	15.6
2018	37	63,764	49	0.77	[0.57, 1.02]	117,704	0.54	55	45	91.8	4	8.2
2019	44	74,181	56	0.75	[0.57, 0.98]	137,235	0.54	61	52	92.9	4	7.1
2020	45	56,399	48	0.85	[0.63, 1.13]	108,994	0.52	50	46	95.8	2	4.2
2021	45	66,275	38	0.57	[0.41, 0.79]	121,847	0.54	41	35	92.1	3	7.9
2022	45	69,721	49	0.70	[0.52, 0.93]	123,897	0.56	55	44	89.8	5	10.2
Total	47	751,350	608	0.81	[0.75, 0.88]	1,322,303	0.57	690	535	88.0	73	12.0

Note. CLABSI, central line-associated bloodstream infections; DUR, device utilization ratio.

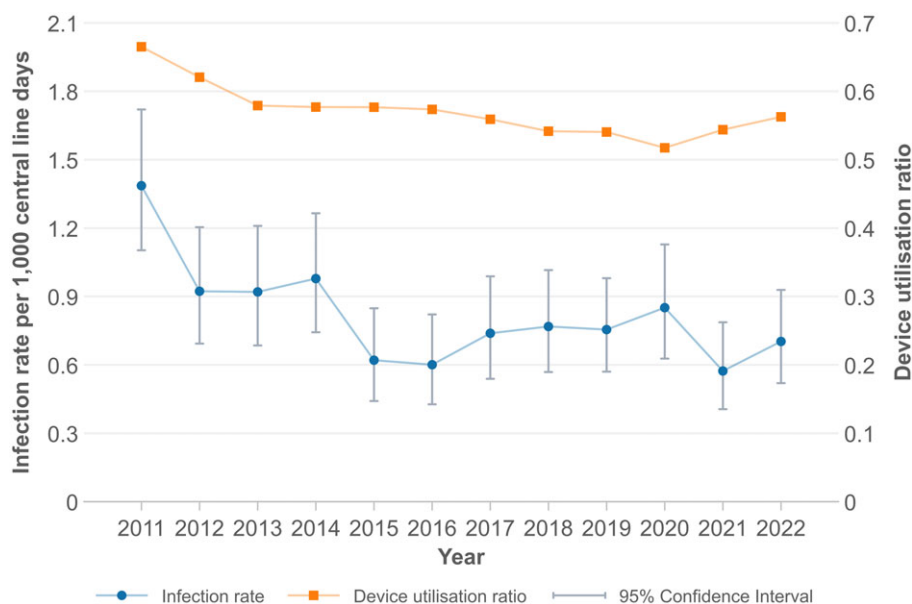
Table 2. Central line-associated bloodstream infection pathogens and time trends, 2011–2022

Pathogens by rank order [^]	Overall		Time epoch										IRR [95% CI]	P value
	2011–22		2011–13		2014–16		2017–19		2020–22					
	n	%	n	%	n	%	n	%	n	%				
<i>Staphylococcus coagulase-negative</i>	166	24.1	28	13.3	40	24.2	57	33.9	41	28.1	1.05 [0.85, 1.29]	0.654		
<i>Staphylococcus epidermidis</i>	103	14.9	11	5.2	18	10.9	44	26.2	30	20.5	1.25 [0.91, 1.70]	0.163		
<i>Candida</i> spp.*	97	14.1	35	16.6	23	13.9	18	10.7	21	14.4	0.80 [0.67, 0.94]	0.008		
<i>Candida albicans</i>	41	5.9	18	8.5	8	4.8	5	3.0	10	6.8	0.74 [0.54, 1.00]	0.054		
<i>Staphylococcus aureus</i>	78	11.3	21	10.0	23	13.9	15	8.9	19	13.0	0.91 [0.73, 1.13]	0.385		
<i>Enterococcus faecalis</i>	66	9.6	25	11.8	21	12.7	8	4.8	12	8.2	0.71 [0.55, 0.93]	0.012		
<i>Enterococcus faecium</i>	64	9.3	23	10.9	12	7.3	16	9.5	13	8.9	0.83 [0.58, 1.18]	0.298		
<i>Escherichia coli</i>	35	5.1	11	5.2	10	6.1	5	3.0	9	6.2	0.87 [0.68, 1.10]	0.233		
<i>Serratia marcescens</i>	18	2.6	11	5.2	1	0.6	1	0.6	5	3.4	0.63 [0.43, 0.92]	0.016		
<i>Klebsiella pneumoniae</i>	18	2.6	1	0.5	6	3.6	9	5.4	2	1.4	1.12 [0.83, 1.53]	0.463		
<i>Enterobacter cloacae</i>	14	2.0	11	5.2	0	0.0	0	0.0	3	2.1	0.59 [0.25, 1.38]	0.226		
<i>Pseudomonas aeruginosa</i>	11	1.6	4	1.9	2	1.2	4	2.4	1	0.7	0.74 [0.57, 0.96]	0.026		

Note. IRR, incidence risk ratio.

[^]Denominator is the total number of pathogens by time epoch.

*No *Candida auris* reported.

**Figure 1.** Central line-associated bloodstream infection rates and device utilization ratio, 2011–2022.

Discussion

This study provides the most comprehensive report of CLABSI burden and pathogen susceptibility in Australia to date, with an analysis of time trends over the last decade. The data set is representative of adult ICU in Victoria, which comprises approximately 20% of ICU beds in Australia.¹¹ This report provides new insights into previously reported data from 2009 to 2013.⁸ We demonstrate a decreasing incidence of CLABSI in adult ICU settings, which plateaued in 2015. Although overall incidence has decreased, the burden of infections due to CNS has proportionally increased. Notably, we did not identify any significant time trend increases in antimicrobial-resistant

organisms, including MRSA, vancomycin-resistant *E. faecium*, and extended-spectrum beta-lactamase (ESBL)-producing *Enterobacteriales*. These findings are relevant for identifying priorities and suitable approaches to CLABSI prevention in Victorian adult ICU.

The trend we observed of decreasing central-line infections in adult ICU is consistent with trends reported internationally.^{7,12} This observed reduction in CLABSI rates corresponded to the introduction of CLABSI surveillance in Victorian hospitals in 2002,⁸ the inclusion of CLABSI as a key performance indicator for Victorian hospitals in 2008,¹³ and the promotion and implementation of bundles of care for prevention by local hospital-level

Table 3. Antimicrobial susceptibility for top-ranked pathogens responsible for central line-associated bloodstream infections, Victorian adult intensive care unit patients, 2011–2022

Organism	Antimicrobial	Sensitivity	Overall		Time epoch					IRR [95% CI]	P value			
			2011–22		2011–13		2014–16		2017–19				2020–22	
<i>S. aureus</i>	Methicillin	Resistant	19	24.4	10	47.6	3	13.0	3	20.0	3	15.8	0.67 [0.43, 1.05]	0.079
		Sensitive	55	70.5	8	38.1	19	82.6	12	80.0	16	84.2	–	–
		Not reported	4	5.1	3	14.3	1	4.3	0	0	0	0	–	–
<i>Candida</i> spp.	Fluconazole	Resistant	6	6.2	0	0	0	0	4	22.2	2	9.5	2.38 [1.02, 5.54]	0.045
		S-DD	4	4.1	0	0	0	0	2	11.1	2	9.5	–	–
		Sensitive	19	19.6	0	0	0	0	7	38.9	12	57.1	–	–
		Not reported	68	70.1	35	100	23	100	5	27.8	5	23.8	–	–
<i>E. faecalis</i>	Vancomycin	Resistant	3	4.5	3	12.0	0	0	0	0	0	0	–	–
		Sensitive	52	78.8	13	52.0	20	95.2	8	100	11	91.7	–	–
		Not reported	11	16.7	9	36.0	1	4.8	0	0	1	8.3	–	–
<i>E. faecium</i>	Vancomycin	Resistant	40	62.5	12	52.2	10	83.3	10	62.5	8	61.5	1.04 [0.80, 1.36]	0.771
		Sensitive	18	28.1	6	26.1	2	16.7	5	31.3	5	38.5	–	–
		Not reported	6	9.4	5	21.7	0	0	1	6.3	0	0	–	–
<i>E. coli</i>	Ceftriaxone	Resistant	6	17.1	2	18.2	1	10.0	1	20.0	2	22.2	1.12 [0.57, 2.20]	0.743
		Sensitive	22	62.9	6	54.5	9	90.0	1	20.0	6	66.7	–	–
		Not reported	7	20.0	3	27.3	0	0	3	60.0	1	11.1	–	–
	Ciprofloxacin	Resistant	9	25.7	3	27.3	1	10.0	2	40.0	3	33.3	1.17 [0.67, 2.02]	0.587
		Sensitive	23	65.7	7	63.6	9	90.0	3	60.0	4	44.4	–	–
<i>K. pneumoniae</i>	Ceftriaxone	Resistant	2	11.1	0	0	0	0	2	22.2	0	0	1.88 [0.26, 13.40]	0.529
		Sensitive	13	72.2	1	100	6	100	5	55.6	1	50.0	–	–
		Not reported	3	16.7	0	0	0	0	2	22.2	1	50.0	–	–
	Ciprofloxacin	Resistant	2	11.1	0	0	0	0	2	22.2	0	0	1.88 [0.26, 13.40]	0.529
		Sensitive	15	83.3	1	100	5	83.3	7	77.8	2	100	–	–
		Not reported	1	5.6	0	0	1	16.7	0	0	0	0	–	–

Note. IRR, incidence risk ratio; *S. aureus*, *Staphylococcus aureus*; S-DD, susceptible-dose dependent; *E. faecalis*, *Enterococcus faecalis*; *E. faecium*, *Enterococcus faecium*; *E. coli*, *Escherichia coli*; *K. pneumoniae*, *Klebsiella pneumoniae*.

initiatives and release of guidelines on management of central lines by Australia New Zealand Intensive Care Society in 2012.^{14,15} Reported rates are much lower than other countries with less developed programs of surveillance and infection prevention.^{16,17}

Other studies have reported changes in patterns of pathogens in non-Australian ICU over time. US ICU participating in Centers for Disease Control and Prevention's National Healthcare Safety Network surveillance reported a significant reduction in *S. aureus* incidence rates from 2006 to 2010¹⁸ and a significant reduction in CNS and *S. aureus* with an increase in *Candida* spp./yeast CLABSIs in adult ICU from 2011 to 2017.⁵ In US adult ICU in 2017, the most frequently reported pathogens were *Candida* spp./yeast (25.1%), followed by *Enterococcus* spp. (16.9%), CNS (13.8%), and *S. aureus* (9.1%).¹⁹ We previously reported significant reductions in *Enterococcus* spp., *S. aureus*, and CNS in the VICNISS adult ICU cohort from 2009 to 2013, with the most frequently identified pathogens being *Enterococcus* spp. (26.3%), *Candida* spp. (15.4%), *S. aureus* (13.3%), and CNS (10.4%).⁸

From 2011 to 2022, we observed a reduction in the total number of pathogens in adult ICU corresponding to a decrease in CLABSI rates. However, we report significant increases in the proportion of CNS with over 1 in 5 CLABSI events attributed to CNS pathogens since 2014. These events were identified using internationally accepted surveillance criteria specifically developed to distinguish CLABSI events from potential contaminants (ie, requirement for 2 or more positive blood cultures to confirm infection). The contribution of CNS pathogens to CLABSI events is comparable to, or higher than, those reported by others using comparable surveillance methodology (the United States 14%, Scotland 19%, Belgium 19%).^{7,20} Potentially contributing factors include lapses in infection prevention measures such as hand hygiene, aseptic technique, and transmission-based precautions, which are amenable to targeted interventions.

We have not observed increasing rates of antimicrobial-resistant MRSA or *E. coli*; however, we report persistently high rates of vancomycin-resistant *E. faecium* in the Victorian ICU. The

proportion of vancomycin-resistant *E. faecium* isolated from our CLABSI cohort between 2017 and 2022 (61.5%–62.5%) is much higher than national data in 2020–2021 (12.5%–15.2%) but similar to data from their Victorian laboratories (61.6%–64.2%), where two-thirds are *vanB* type²¹. The proportion of *E. coli* resistance to ceftriaxone isolated from our CLABSI cohort between 2017 and 2022 (20.0%–22.2%) is higher than that reported in the Victorian cohort from national surveillance data in 2020–2021 (13.0%–17.0%)²¹. The proportion of MRSA isolated from our CLABSI cohort between 2017 and 2022 (15.8%–20.0%) is similar to that reported in the Victorian cohort from national surveillance data in 2020–2021 (approximately 12%–15%)²¹. Our reports of higher rates of resistance in *E. faecium* and *E. coli* than national surveillance reporting reflect different patient cohorts; although our data are derived from clinical infections attributed to healthcare intervention, national surveillance data are derived from sentinel pathology services around Australia and include hospital or community isolates and clinical or surveillance isolates. As community MRSA rates in Victoria are similar to hospitals, although ESBL *E. coli* and VRE rates are more common in hospitals, the differences in patient population are likely to partially account for our higher rates of resistance compared with national surveillance.

Our findings support the use of targeted approaches to further reduce CLABSI rates in Victorian ICU. CLABSI prevention approaches have involved the use of multimodal intervention bundles focused on CVC insertion and maintenance practices.^{4,14} Not all bundles incorporate equivalent components, and these may need to be reviewed to determine if they are effective and optimal for addressing current-era pathogens and antimicrobial resistance. The risk of CLABSI caused by skin organisms such as CNS and *S. aureus* can potentially be mitigated by improvements in hand hygiene, aseptic technique, and chlorhexidine bathing. CLABSI caused by *Enterobacteriales* may warrant novel approaches to active surveillance and isolation policies, environmental cleaning, and antimicrobial stewardship to further mitigate risk. The use of antiseptic or antimicrobial-impregnated devices is currently recommended as an additional strategy reserved for adult ICU settings with high CLABSI rates.¹ New interventions introduced into ICU settings to reduce the risk of HAI require careful consideration of their potential impact on environmental antimicrobial resistance against individual patient benefit. An example of this would be selective decontamination of the digestive tract in the treatment of critically ill patients. A meta-analysis²² showed that selective decontamination of the digestive tract with intravenous antibiotics reduced the risk for in-hospital mortality, ventilator-associated pneumonia, and ICU-acquired bacteremia.

Our evaluation of antimicrobial resistance in CLABSI pathogens can be used to assist local CLABSI treatment approaches. International guidelines support the use of empirical vancomycin for suspected device-related bloodstream infections, which is underpinned by our data where vancomycin would adequately cover many gram-positive organisms including MRSA and CNS but not VRE. We propose that the use of antibiotic agent/s to empirically cover antimicrobial-resistant organisms such as VRE and ESBL *Enterobacteriales* should be based on local antimicrobial susceptibility data. Our findings highlight the need for healthcare facilities in our region to review local epidemiology and antibiotic susceptibility of infections to support appropriate prescribing practices.

A limitation of our study is the use of phenotypic antimicrobial resistance reports, rather than genotyping, to define antimicrobial-

resistant pathogens responsible for CLABSI. Furthermore, we were not able to report on resistance trends in intrinsically sensitive *Candida* spp. such as *C. albicans*, due to missing data on fluconazole susceptibility. Although the evaluation of the relationship between CVC insertion and maintenance practices and infection burden was beyond the scope of the current study, we acknowledge this as a priority for future research to identify the impact of clinical practice on infection burden and pathogens.

Optimal infection prevention and control practices and implementing antimicrobial stewardship are essential measures to prevent HAI and the emergence of antimicrobial resistance in ICU. Further understanding of the burden and incidence of CLABSI, and changes in pathogen and resistance patterns, contributes to inform targets for future CLABSI prevention approaches. Although CLABSI rates in our region have continued to decline over recent years, the proportion attributable to CNS has increased, and novel approaches are required to specifically reduce risks for CNS infection.

Supplementary material. The supplementary material for this article can be found at <https://doi.org/10.1017/ice.2024.132>.

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