Assessing the impact of a 'bundle of care' approach to *Staphylococcus aureus* bacteraemia in a tertiary hospital

Jared Green [a,*], Julia Howard [b], Avinesh Shankar [c], Richard Clinghan [b], Tessa Luff [c], Mark Birch [a,c], Alan Pithie [a,c], Anja Werno [b], Sarah Metcalf [a,c], Stephen Chambers [a,d]

[a] Department of Infectious Diseases, Christchurch Hospital, New Zealand
[b] Department of Microbiology, Canterbury Health Laboratories, Christchurch, New Zealand
[c] Department of General Medicine, Christchurch Hospital, New Zealand
[d] Department of Pathology, University of Otago, Christchurch, New Zealand

ARTICLE INFO

SUMMARY

Background: Staphylococcus aureus bacteraemia is associated with significant morbidity and mortality. There is evidence that standardised care bundle implementation may improve the rates of appropriate investigations and improve overall management. A *S. aureus* bacteraemia care bundle was introduced at Christchurch Hospital, New Zealand in early 2014. We assessed the impact of the intervention on the management and outcome of *S. aureus* bacteraemia.

Methods: A cohort study of cases of *S. aureus* bacteraemia was conducted following standardised care bundle introduction. Prospective enrolment of post-intervention patients occurred from 1st January 2014 to 30th June 2015, with retrospective review of pre-intervention cases from 1st January 2009 to 31st December 2013.

Results: In the pre-intervention period 447 patients had at least one episode of *S. aureus* bacteraemia compared to 151 patients in the post-intervention period. The two groups were similar by gender, ethnicity, and age. Significant increases in Infectious Diseases consultation rate (86.6% vs 94.8%; p=0.009), echocardiography (76.3% vs 96.3%; p<0.001), urine culture (74.0% vs 91.9%; p<0.001), follow up blood cultures (44.2% vs 83.0%; p<0.001), and at least 2 weeks of parenteral therapy (83.5% vs 92.9%; p=0.014) were observed after introduction of the bundle. There were no significant differences in rates 30-day mortality (18.6% vs. 20.5%; p=0.596), but there was a reduction in episodes of relapsed infection in the post-intervention cohort (7.4% vs 1.3%; p=0.004).

Conclusion: An integrated care bundle for the management of *S. aureus* bacteraemia resulted in increased use of quality of care indicators and infectious diseases review and improved patient outcome.

* Corresponding author: Address: Infectious Diseases and General Physician, Department of Medicine Waikato Hospital, Pembroke street, Private Bag 3200, Hamilton 3240, New Zealand. Tel.: +6421865335.
E-mail address: Jared.green@waikatodhb.health.nz (J. Green).

Staphylococcus aureus bacteraemia (SAB) is the most common hospital acquired and the second most common community acquired bloodstream infection in the world [1]. Australian data suggests that it accounts for 1.48 per 1000 hospital admissions at a cost of AUD $22,000 per episode [2]. The mortality rate was stated at 76–83% in the pre-antibiotic era [3]. It remains a cause of significant morbidity and death, with mortality rates ranging from 16-40% at 90 days [2–9]. This rate has remained remarkably stable over time [7].

New Zealand has among the highest rates of staphylococcal infection in the world. From 2000-2011, the averaged incident rate was 127 per 100,000 per year for all staphylococcal infections and 14 per 100,000 per year for staphylococcal sepsis [10]. Mäori and Pasifika peoples are 2–5 times more likely to suffer from staphylococcal infections than European/Päkeha New Zealanders [10,11]. Likewise, a disproportionate burden of morbidity from SAB is borne by Māori and Pasifika [5,7].This is also true for also indigenous Australians [7,12]. However, this does not appear to translate into excess mortality [5,7,12]. In previous New Zealand research, the relative risk of developing SAB was 1.8 for Maori and 4.0 for Pasifika but European/Päkeha ethnicity carried a relative risk for mortality at 30 days of 1.4 [5]. In another Australasian study, 30-day mortality was 22.2% for Europeans, 9.7% for Mäori, and 5.7% for Aboriginal and Torres Straight Island People [7].

Little is known about the molecular epidemiology of meticillin susceptible *S. aureus* (MSSA) in New Zealand, although a 2014 point prevalence survey noted that the CC1, CC188, CC5, and CC121 clones predominate [11]. The prevalence of meticillin resistant *S. aureus* (MRSA) in New Zealand is 8.9–10% [11,13]. Six MRSA clones accounted for 90.6% of all MRSA in a 2017 point-prevalence survey (AK3, Queensland clone MRSA, WR/AK1, EMRSA-15, USA300 MRSA, and WSPP MRSA) [14]. Panton-Valentine Leukocidin is expressed by 25.2% of both MRSA and MSSA in New Zealand [11].

SAB is characterised by its propensity to relapse. Apparent reinfections or metastatic complications within 90 days of cessation of therapy are usually found to be due to the same strain [15,16]. Multiple factors have been found to improve the management of SAB and its outcomes. Most prominently among these are bedside Infectious Diseases (ID) consultation and the use of β-lactam therapy to treat meticillin-susceptible isolates [6,8,17–21]. Conversely, the absence of formal Infectious Diseases consultation and parenteral treatment durations shorter than ten days have been found to place patients at risk of adverse outcomes [22–24]. Similarly, there are multiple patient factors that are suggestive of complicated *S. aureus* bacteraemia such as the presence of embolic stigmata on cutaneous examination, persistence of fever while on appropriate management, and persistence of bacteraemia at 48–96 hours while on appropriate antimicrobial therapy [3,25].

Development of integrated "bundles of care" with multiple evidence-based interventions has been found to have protective effects in the management of SAB [1,4,17]. Following the publication of a bundle of care study from Spain, a similar SAB management protocol was developed for use at Christchurch Hospital [4].

Christchurch Hospital is the main acute hospital operated by Canterbury District Health Board, which provides acute care to a population of 567,870 and is the tertiary referral centre for the upper South Island of New Zealand [26]. Christchurch Hospital co-locates with Christchurch Women's Hospital in a campus of 833 beds [27]. Specialties offered include haematology and stem cell transplantation, renal transplantation, cardiothoracic surgery, neurosurgery, obstetrics and gynaecology, and plastic surgery.

Methods

A case of SAB was defined as a patient for whom at least one blood culture isolate identified as *S. aureus*. The SAB bundle of care was designed with reference to the bundle study published by López-Cortés et al. [4]. A document was developed for educational purposes, providing a brief introduction, references, and details on the structured intervention. This document was placed in the clinical notes of each patient assessed by the Infectious Diseases Registrar in addition to the standard Infectious Diseases review documentation. In addition to automatic, non-discretionary ID review of cases of SAB, the bundle mandated echocardiography (transthoracic [TTE] in the first instance, transoesophageal [TOE] as required), early use of beta-lactam therapy (flucloxacillin or cefazolin), dosing advice and provided information on MRSA risk factors. Separate instructions were made regarding the importance of commencing appropriate therapy for MRSA (acknowledging the mortality benefit associated with appropriate initial therapy) [28]. Rates of invasive MRSA infection have been low in our setting, as such empiric MRSA treatment was not considered necessary for most patients, without specific risk factors. The protocol advised the collection of blood cultures 48–72 hours following the initiation of therapy. In addition, urine culture and microscopy were suggested as further surrogate measures of complicated bacteraemia, as has been noted elsewhere [7]. The need for prompt source control of foci of infection was emphasised, including the removal of infected vascular access devices. A minimum treatment duration of 14 days was mandated, consistent with published guidelines [8,29,30]. The SAB bundle was developed by JKG (with input from SCLM and STC) in December 2013, and formally implemented in January 2014.

The department of Infectious Diseases introduced a policy of automatic, non-discretionary review of patients with invasive isolates of *S. aureus* in mid-2013, late in the pre-intervention period but did not have a formalised departmental SAB guideline prior to the development of the bundle. Direct notification of results was made to the Infectious Diseases registrar by the Microbiology registrar or Clinical Microbiologist; resulting in bedside review.

A before and after study methodology was applied to assess the performance of the *S. aureus* bacteraemia bundle. De-identified data including patient demographics, diagnosis, antimicrobial susceptibility pattern, comorbidities, treatment outcome, and length of treatment were prospectively collated in a Microsoft Excel™ (Microsoft Corporation; Redmond, Washington, USA) database maintained by the Infectious Diseases registrars for all cases of *S. aureus* bacteraemia diagnosed between 1st January 2014 and 30th June 2015. The comparator dataset was retrospectively drawn from cases of *S. aureus* bacteraemia identified from 1st January 2009 to 31st December 2013. These were identified by interrogation of Canterbury Health Laboratories' Delphic LIS™ platform (Sysmex corporation, Kobe, Japan). A Charlson comorbidity index was calculated for each patient for the relevant admission [31]. Cases of SAB were recorded as community-acquired, health-care-associated, or hospital-acquired as per the criteria outlined by Friedman et al. [32]. Diagnoses of deep foci of infection were confirmed by radiological or microbiological investigation as appropriate. All cases of endocarditis were diagnosed using the modified Duke criteria [33].

Patients were included in the study if they were 18 years of age or above. Patients were excluded if they were lost to follow-up. The main outcome variables of the before and after study were the adherence to the quality of care indicators of Infectious Diseases review, follow up blood cultures, echocardiography, beta lactam therapy (where appropriate), urine culture and a 14-day minimum parenteral course. A β-lactam was defined as any β-lactam antimicrobial with appropriate anti-staphylococcal activity. Appropriate use of a β-lactam was defined as greater than 50% of the total parenteral treatment duration. Secondary outcome measures were all cause mortality at 7, 14, and 30 days; and relapsed infection (either bacteraemia or confirmed deep-site infection due to *S. aureus*) in the 90 days following the cessation of planned antimicrobial therapy. The first episode of bacteraemia for each patient was included for analysis.

Identification of isolates of *S. aureus* either employed phenotypic techniques, automated identification with BD Phoenix™ (Becton, Dickinson, and Company; Franklin Lakes, New Jersey, USA), or Matrix Assisted Laser De-ionisation Time of Flight (MALDI-TOF. Bruker Corporation; Billerica, Massachusetts, USA). Antimicrobial susceptibility testing was performed using either disk-based methodology or automated microdilution (BD Phoenix™). Screening for meticillin resistance was done using cefoxitin disks and employed standard protocols. Clinical Laboratory and Standards Institute (CLSI) standards for antimicrobial susceptibility testing were employed by the laboratory until 2012, with European Committee on Antimicrobial Susceptibility Testing (EUCAST) standards being employed subsequently.

The study group engaged in consultation with the Canterbury District Health Board's Te Komiti o Whakarite, and ethical approval for the study was subsequently given by the University of Otago/Canterbury District Health Board Ethics Committee (reference 15222).

Statistical analysis

Categorical variables were reported as proportions with the total number in each study group as the denominator.

Table I
Demographics

	Pre-intervention	Post-intervention	P value
Total	447	151	
Age*	64.7 (±17.8)	63.8 (±18.8)	0.588
Female**	168 (37.6)	57 (37.8)	0.971
Ethnicity**			
European/Pākeha	363 (81.2)	124 (82.1)	0.803
Māori	38 (8.5)	13 (8.6)	0.967
Pacific Island	18 (4.0)	3 (2.0)	0.312
Asian	5 (1.1)	0 (0.0)	0.337
Middle East/Latin American/ African	2 (0.4)	0 (0.0)	1.000
Other	16 (3.6)	11 (7.3)	0.058
S. aureus* typ*			
Penicillin susceptible	73 (16.3)	8 (5.3)	0.001
Methicillin resistant	2 (0.4)	6 (4.0)	0.004
Acquisition**			
Community acquired	186 (41.6)	82 (54.3)	0.007
Healthcare associated	163 (36.5)	41 (27.2)	0.047
Hospital acquired	98 (21.9)	28 (18.5)	0.378

Key: *mean (standard deviation).
** total (percentage).

Continuous variables were reported as means and standard deviations for normally distributed variables and medians and ranges for non-normally distributed data. Univariate analysis was performed using Fisher's exact test or Pearson X^2 test where appropriate for categorical variables, and the Independent samples t-test for continuous variables. All p-values calculated were 2-tailed, and p-values <0.05 were considered significant. Statistical analysis was performed using SPSS™ v25.0 (IBM, Chicago, Illinois, USA).

Results

During the study period there were 598 adult cases: 447 in the pre-intervention period (2009−13) and 151 in the bundle period (2014−15). Six cases were lost to follow up in the pre-intervention cohort and one in the bundle cohort. The demographics of the two groups were equivalent for age (mean 64.7 years vs 63.8; p=0.588), ethnicity, and gender (Table I). The bundle cohort had a higher proportion of community acquired SAB (41.6% vs 54.3%; p=0.007) but proportions of hospital acquired SAB were similar (21.9% vs 18.5%; p=0.378). There was no significant difference between the mean Charlson comorbidity indices of the two groups (3.92 vs 4.15; p=0.451) (Table II).

There was a higher incidence of penicillin-susceptible *S. aureus* in the pre-intervention cohort. In contrast, there was a significant difference in incidence of MRSA bacteraemia between the pre- and post-intervention groups (2/447 vs 6/151 [0.4% vs 4.0%]; p=0.004) (Table II).

The mean number of identified foci of invasive staphylococcal infection was similar in both groups (1.23±0.52 vs 1.22± 0.48; p=0.876). Deep foci of infection were present in 66.2% (296/447) of patients in the pre-intervention cohort and 68.9% (104/151) of the bundle cohort (p=0.549). The pre-intervention cohort included significantly more patients with a cutaneous focus of infection, but there were no other

Table II
Comorbidities

	Pre-Intervention	Post-Intervention	P value
Charlson Comorbidity Index*	3.92 (±3.28)	4.15 (±3.18)	0.45
Comorbidities**			
Diabetes Mellitus (DM) without complications	21 (4.7)	8 (5.3)	0.767
DM with complications	61 (13.6)	26 (17.2)	0.282
COPD	20 (4.5)	3 (2.0)	0.223
Solid organ malignancy (without metastases)	33 (7.4)	16 (10.6)	0.213
Solid organ malignancy (with metastases)	26 (5.8)	9 (5.6)	0.948
Lymphoma	10 (2.2)	2 (1.3)	0.738
Chronic liver disease (mild)	10 (2.2)	0 (0.0)	0.073
Chronic liver disease (moderate to severe)	13 (2.9)	7 (4.6)	0.307
Connective tissue disease	8 (1.8)	3 (2.0)	1.000
Cerebrovascular disease	33 (7.4)	7 (4.6)	0.243
Peripheral vascular disease	37 (8.3)	8 (5.3)	0.230
Congestive cardiac failure	56 (12.5)	19 (12.6)	0.986
Myocardial infarction	32 (7.2)	11 (7.3)	0.959
Chronic kidney disease (≥ stage 2)	60 (13.4)	28 (18.5)	0.125
Leukaemia	11 (2.5)	2 (1.3)	0.533

Key: * mean (standard deviation).
** total (percentage).

Table III
Diagnoses

	Pre-intervention	Post-intervention	P-value
Mean Number of Infectious Foci*	1.23 (0.53)	1.22 (0.48)	0.876
Diagnoses**,§			
Skin/soft tissue	51 (11.4)	5 (3.3)	0.002
Deep abscess	55 (12.3)	11 (7.3)	0.089
Osteo-articular	107 (23.9)	40 (26.5)	0.529
Endocarditis	41 (9.2)	13 (8.6)	0.835
Pneumonia/empyema	44 (9.8)	23 (15.2)	0.070
Urinary tract	27 (6.0)	13 (8.6)	0.275
Primary bacteraemia	81 (18.1)	25 (16.6)	0.663
Vascular access devices	81 (18.1)	32 (21.2)	0.405
Prosthetic valve/cardiac device	12 (2.7)	5 (3.3)	0.777
Orthopaedic prosthesis	31 (6.9)	12 (7.9)	0.677
Other	18 (4.0)	5 (3.3)	0.810

Key.
*mean (standard deviation).
** Each site of infection considered separately, i.e. percentages add to >100%.
§ Total (percentage).

significant differences between the two groups with respect to site of infection (Table III).

There was no significant difference in the rates of mortality at 7, 14, and 30 days among patients studied (Table III). There was a lower rate of relapsed infection of 1.3% in the bundle cohort, compared to 7.4% in the pre-intervention cohort (p=0.004) (Table IV). Of those who relapsed in the pre-intervention cohort, the 30-day mortality for the subsequent episode of bacteraemia was 15.2% (5/33) and one patient had three episodes of relapse and subsequently recovered. Both patients in the bundle cohort who relapsed recovered without further relapse of SAB.

There was a marked increase in the performance of all the diagnostic quality of care indicators, including Infectious Diseases consultation, echocardiography, urinalysis and repeat blood cultures in patients who survived to seven days following diagnosis (Table IV). While there was a trend towards increased use of transoesophageal echocardiography (TOE) in the bundle cohort, this did not reach statistical significance. In addition, there was a significant increase in the number of patients who received a minimum parenteral treatment duration of 14 days (83.5% vs 92.9%; p=0.014) as well as significant increase in the proportion of patients who had source control of drainable foci or removal of affected lines in the first 72 hours (85.2% vs 94.7%; p=0.040). There was no difference between the two groups in the proportion of patients who received β-lactam therapy for MSSA infection (Table IV).

Discussion

In this single-centre, tertiary hospital study, an integrated care bundle for the management of *S. aureus* bacteraemia was followed by a marked increase in the performance of most quality of care indicators. It did not make a significant impact on the proportion of patients who received beta-lactam based therapy, but this reflects the high utilisation of adequately prescribed antimicrobials in the pre-intervention cohort. While the rate of relapse in the pre-intervention group was low by reported standards [16,18,34], the bundle was associated with a reduction in the percentage who relapsed. This is consistent with the positive effects of Infectious Diseases review and the selected quality of care interventions which have also been demonstrated elsewhere [4,8]. Mortality rates were consistent with other studies performed in Australasia [2,5,7,12].

The rate of relapse of SAB in our setting is among the lowest rates of relapse reported, even in the pre-intervention period [4,7,16]. Even so, the use of a structured intervention may have conferred further benefit. Beyond ensuring an adequate therapeutic duration, which is the single factor most likely to result in relapse, a SAB bundle likely acts as an attention to detail tool, ensuring that the disparate parts of SAB management are brought together in a timely and consistent fashion. Where bundles of care have been introduced for the management of SAB, they have generally been found to increase the uptake of investigations such as echocardiography and repeat blood cultures [4,6]. While bundles of care consistently increase the rate of usage of beta-lactam therapy for the management of methicillin susceptible SAB, other outcome measures are less consistent. In certain settings, such as that reported by Lopez-Cortes et al. [4] the introduction of a SAB bundle may reduce mortality, whereas in other settings, benefits have been limited to the performance of key clinical investigations mentioned above, or a relapse prevention benefit [4,6]. This may reflect the baseline conditions of the healthcare systems or hospital in which a SAB bundle is introduced rather than inherent flaws in the management approach. The lack of mortality benefit shown in this study may reflect

Table IV
Outcome measures

	Pre-Intervention	Post-Intervention	
Total	**N = 447**	**N = 151**	
Early Mortality/Palliation*	38 (8.5%)	13 (8.6%)	0.967
7 Day Mortality	51 (11.4)	16 (10.6)	0.784
14 Day Mortality	60 (13.4)	22 (14.6)	0.723
30 Day Mortality	83 (18.6)	31 (20.5)	0.596
Relapsed infection	33 (7.4)	2 (1.3)	0.004
Diagnostic Key Performance Indicators*	**N = 396**	**N = 135**	
ID consultation	343 (86.6)	128 (94.8)	0.009
Any Echocardiogram	302 (76.3)	130 (96.3)	<0.001
TOE	45 (11.4)	24 (17.8)	0.056
Urine culture	293 (74.0)	124 (91.9)	<0.001
Repeat Blood Culture	175 (44.2)	112 (83.0)	<0.001
Treatment Key Performance Indicators (KPI) §	**N = 387**	**N = 129**	
≥14 days parenteral therapy	323 (83.5)	119 (92.9)	0.014
B-lactam for MSSA††	371 (96.7)	119 (96.7)	1.000
All KPI	92 (23.8)	95 (73.6)	<0.001
Source control of drainable foci <72hrs*	**N = 216**	**N = 75**	
	184 (85.2)	71 (94.7)	0.040
Mean days parenteral Rx †	27.3 (±17.9)	23.8 (±13.6)	0.048

Key.
* Total (percentage).
** Assessed among survivors at day 7.
MRSA excluded from denominator.
§ Assessed among survivors at day 14.
† Mean (standard deviation).

the high rates of Infectious Diseases review, utilisation of beta-lactam therapy, early source control and effective therapeutic durations even in the baseline cohort, comparing favourably to the post-intervention data reported by López Cortés et al. [4].

Our study reports one of the highest rates of TTE performed in studies of SAB, but also one of the lower rates of TOE. The rates of endocarditis reported in our study were 9.2% and 8.6% respectively in the pre- and post-intervention groups (p=0.835). These rates are consistent with those found in other studies of SAB, including those with much higher published rates of TOE [35—39]. Despite the low rate of utilisation of TOE, the rates of endocarditis diagnosis in this study are consistent with those reported in other case series [9,35—38]. Some authors suggest forgoing TOE if repeat blood cultures are negative and no additional deep foci of infection are identified [38]. There can be little dispute that TOE is the superior echocardiographic modality for confirming diagnoses of endocarditis [37]. However, TTE is an effective risk stratification tool in SAB when used in conjunction with follow-up blood cultures, appropriate radiological investigation, and Infectious Diseases specialty guidance. Other authors have reported that TTE may miss 10—16% of diagnoses of endocarditis [7,36]. Using these figures, a blanket TOE policy may have potentiated the

diagnoses of 1—2 further cases of endocarditis in our study. The impact of this on likely therapeutic duration of patients may have been negligible given that mean durations of therapy in both cohorts were similar to those recommended by the European Cardiological Society and Australian therapeutic guidelines group for *S. aureus* endocarditis [40,41]. Furthermore, studies in Europe have suggested that short course therapy of 14 days of an isoxazolyl penicillin, such as oxacillin, with or without gentamicin may be sufficient for the treatment of right sided endocarditis in selected patients [42,43]. Despite our low rate of TOE usage, we think that TOE should be performed if a diagnosis of endocarditis is considered highly likely or SAB occurs in the setting of prosthetic heart valves or intracardiac devices, or for surgical assessment and planning in confirmed cases of infective endocarditis.

Our study noted an increase in the incidence of MRSA bacteraemia during the study period. While there is currently no national surveillance of SAB in New Zealand to reference this against, point prevalence rates of MRSA were noted to increase from 10.2 per 100,000 to 20.4 per 100,000 from 2009-2015 in nationwide surveys [14]. These rates were markedly higher in Mäori and Pasifika (38.5 per 100,000 and 76.2 per 100,000 respectively) populations. In a related 2014 point-prevalence survey, 8.9% of *S. aureus* isolates in New Zealand were meticillin resistant [11], although results for the Southern region, which includes Canterbury District Health Board, noted a lower prevalence of 5.1% [11].

Among the strengths of this study are the high level of coordination between the Microbiology laboratory and Infectious Diseases department, potentiating the strategy of expectant review. The single-centre nature of the study may be considered a weakness, but in the relatively remote setting of the Canterbury region, a single, large, acute hospital setting with centralised laboratory processing enabled easier standardisation of the management of complex conditions such as SAB. Other strengths include the use of evidence-based care indicators and structured nature which would make this intervention replicable in similar settings. This study will have the inherent limitations of before and after study designs and non-assessed variables may have had impact on the results.

In conclusion, our results add further support to the growing body of evidence that a structured care bundle improves the management of SAB by increasing the utilisation of key investigations as well as increasing the proportion of patients who receive adequate courses of therapy. In addition, it may provide additional benefit in terms of relapse prevention.

Credit author statement

Assessing the impact of a 'bundle of care' approach to *Staphylococcus aureus* bacteraemia in a tertiary hospital.

Jared K Green: conceptualisation, formal analysis, investigation, data curation, writing draft, writing: reviewing and editing, projection administration.

Julia Howard: investigation, writing draft writing: reviewing and editing.

Avinesh Shankar: investigation, data curation.

Richard Clinghan: investigation.

Tessa Luff: investigation.

Mark Birch: supervision.

Alan Pithie: supervision.

References

[1] Liu C. A Quality of Care Bundle for Treatment of *Staphylococcus aureus* Bacteremia: Ready for Prime Time? Clinic Infect Dis 2013;57(9):1234−6. https://doi.org/10.1093/cid/cit502.

[2] Collignon P, Nimmo GR, Gottlieb T, Gosbell IB. *Staphylococcus aureus* bacteraemia, Australia. Emerg Infect Dis 2005;11(4):554−61.

[3] Van Hal SJ, Jensen SO, Vaska VL, Espedido BA, Patersen DL, Gosebell IB. Predictors of Mortality in *Staphylococcus aureus* bacteraemia. Clin Microbiol Rev 2012;25(2):362−86. https://doi.org/10.1128/CMR05022-11.

[4] López Cortés LE, Dolores del Toro M, Gálvez Acebal J, Bereciarrtua Bastarrica E, Carmen Fariñas M, Sanz Franco M, et al. Impact of an Evidence Based Bundle Intervention in the Quality-of-Care Management and Outcome of *Staphylococcus aureus* Bacteremia. Clinic Infect Dis 2013;57(9):1225−33. https://doi.org/10.1093/cid/cit499.

[5] Hill PC, Birch M, Chambers S, Drinkovic D, Ellis-Pegler RB, Everts R, et al. Prospective study of 424 cases of *Staphylococcus aureus* bacteraemia: determination of factors affecting incidence and mortality. Intern Med J 2001;31:97−103.

[6] Nguyen CT, Gandhi T, Chenoweth C, Lassiter J, Dela Pena J, Eschenauer G, et al. Impact of an antimicrobial stewardship-led intervention for *Staphylococcus aureus* bacteraemia: a quasi-experimental study. J Antimicrob Chemother 2015;70:3390−6. https://doi.org/10.1093/jac/dkv256.

[7] Turnidge JD, Kotsanas D, Munckhof W, Roberts S, Bennett CM, Nimmo GR, et al. *Staphylococcus aureus* bacteraemia: a major cause of mortality in Australia and New Zealand. Med J Aust 2009;191:368−73.

[8] Bai AD, Showler A, Burry L, Steinberg M, Ricciuto DR, Fernandes T, et al. Impact of Infectious disease consultation on quality of care, mortality, and length of stay in *Staphylococcus aureus* bacteremia: results from a multi-center cohort study. Clinic Infect Dis 2015;60(10):1451−61. https://doi.org/10.1093/cid/civ120.

[9] Robinson JO, Pozzi-Langhi S, Phillips M, Pearson JC, Christiansen KJ, Coombs GW, et al. Formal infectious diseases consultation is associated with decreased mortality in *Staphylococcus aureus* bacteraemia. Eur J Clin Microbiol Infect Dis 2012;31:2421−8.

[10] Williamson DA, Zhang J, Ritchie SR, Roberts SA, Fraser JD, Baker MG. *Staphylococcus aureus* Infections in New Zealand, 2000-2011. Emerg Infect Dis 2014;20(7):1156−61. https://doi.org/10.3201/eid2007.131923.

[11] Heffernan H, Bakker S, Woodhouse R, Dyet K, Williamson D. Demographics, antimicrobial susceptibility and molecular epidemiology of *Staphylococcus aureus* in New Zealand. Wellington, New Zealand: Institute of Environmental Science and Research; 2014. https://surv.esr.cri.nz/PDF_surveillance/Antimicrobial/Staph/2014Saureussurveyreport.pdf.

[12] Hewagama S, Spelman T, Einsiedel LJ. *Staphylococcus aureus* bacteraemia at Alice Springs Hospital. Intern Med J 2011:505−12. https://doi.org/10.1111/j.1445-5994.2011.02449.x.

[13] Williamson DA, Coombs GW, Nimmo GR. *Staphylococcus aureus* "'Down Under": contemporary epidemiology of *S. aureus* in Australia, New Zealand, and the South West Pacific. Clin Microbiol Infect 2014;20:597−604.

[14] Heffernan H, Bakker S. 2017 Survey of methicillin-resistant *Staphylococcus aureus* (MRSA). Wellington, New Zealand: Institute of Environmental Science of Research; 2017. https://surv.esr.cri.nz/PDF_surveillance/Antimicrobial/MRSA/MRSA_2017.pdf.

[15] Fowler VG, Kong LK, Corey R, Gottlieb GS, McClelland RS, Sexton DJ, et al. Recurrent *Staphylococcus aureus* bactereamia: pulsed-field gel electrophoresis findings in 29 patients. J Infect Dis 1999;179:1157−61.

[16] Chang FY, Peacock JE, Musher DM, Triblett P, MacDonald BB, Mylotte JM, et al. *Staphylococcus aureus* bacteremia: recurrence and the impact of antibiotic treatment in a prospective multi-centre study. Medicine 2003;82(5):322−32. https://doi.org/10.1097/01.md.0000091184.93222.09.

[17] Jenkins TC, Price CS, Sabel AL, Mehler PS, Burman WJ. Impact of Routine Infectious Diseases Service Consultation on the Evaluation, Management, and Outcomes of *Staphylococcus aureus* Bacteremia. Clinic Infect Dis 2008;46:1000−8. https://doi.org/10.1086/529190.

[18] Martin L, Tova Harris M, Brooks A, Main C, Mertz D. Management and Outcomes in Patients with *Staphylococcus aureus* Bacteremia after implementation of mandatory infectious diseases consult: a before and after study. BMC Infect Dis 2015;15(568). https://doi.org/10.1186/s12879-015-1296-y.

[19] Chan KE, Warren HS, Thadhani RI, Steele DJR, Hymes JL, Maddux FW, et al. Prevalence and Outcomes of Antimicrobial Treatment for *Staphylococcus aureus* Bacteremia in Outpatients with ESRD. J Am Soc Nephrol 2012;23:1551−9. https://doi.org/10.1681/ASN.2012010050.

[20] Turner RB, Valcarlos E, Won R, Change E, Schwartz J. Impact of infectious diseases consultation on outcomes of patients with *Staphylococcus aureus* bacteremia in a community health system. Antimicrob Agents Chemother 2016;60:5682−7. https://doi.org/10.1128/AAC.00439-16.

[21] Nagao M, Iinuma Y, Matsumara Y, Shirano M, Matsushima A, Takakura S, et al. Closer cooperation between infectious diseases physicians and attending physicians can result in better management and outcomes for patients with *Staphylococcus aureus* bacteraemia. Clin Microbiol Infect 2010;16:1783−8. https://doi.org/10.1111/j.1469-0691.2010.03156.x.

[22] Dutta A. Neglected guidelines of *Staphylococus aureus* bacteremia. SMH annual meeting; 2015. Abstract 77, http://www.shmabstracts.com/abstract/neglected-guidelines-of-staphylococcus-aureus-bacteremia/ [07-Jan-17 3:18:06 PM].

[23] Choong YP, Moon SM, Bang KM, Park HJ, Park SY, Kim MN, et al. Treatment Duration for Uncomplicated *Staphylococcus aureus* bacteremia to prevent relapse: Analysis of a Prospective Observational Cohort Study. Antimicrob Agents Chemother 2013;57(3):1150−6.

[24] Forsblom E, Ruotsaleinen E, Ollgren J, Järvinen A. Telephone consultation cannot replace bedside infectious consultation in the management of *Staphylococcus aureus* bacteremia. Clinic Infect Dis 2013;56(4):527−35. https://doi.org/10.1093/cid/cis889.

[25] Fowler VG, Olsen MK, Corey R, Woods CW, Cabell CH, Reller B, et al. Clinical Identifiers of Complicated *Staphylococcus aureus* Bacteremia. Arch Intern Med 2003;63:2066—72.

[26] Ministry of Health (New Zealand) Manatū Hauora. Wellington, New Zealand. http://www.https://www.health.govt.nz/new-zealand-health-system/my-dhb/canterbury-dhb.

[27] Ministry of Health (New Zealand) Manatū Hauora. Wellington, New Zealand. http://www.health.govt.nz/your-health/certified-providers/public-hospital/christchurch-hospital.

[28] Paul M, Kariv G, Goldberg E, Raskin M, Shaked H, Hazzan R, et al. Importance of appropriate antibiotic therapy for methicillin-resistant *Staphylococcus aureus* bacteraemia. J Antimicrob Chemother 2010;65:2658—65. https://doi.org/10.1093/jac/dkq373.

[29] Liu C, Bayer A, Cosgrove SE, Daum RS, Fridkin SK, Gorwitz RJ, et al. Clinical Practice Guidelines for the Infectious Diseases Society of America for the Treatment of Methicillin Resistant *Staphylococcus aureus* Infections in Adults and Children: Executive Summary. Clinic Infect Dis 2011;52(3):285—92. https://doi.org/10.1093/cid/cir034.

[30] Turnidge J, Grayson ML. Optimum Treatment of Staphylococcal Infections. Drugs 1993;45(3):353—6.

[31] Charlson ME, Pompei P, Ales KL, Mackenzie CR. new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373—83.

[32] Friedman ND, Kaye KS, Stout JE, McGarry SA, Trivette SL, Briggs JP, et al. Healthcare associated bloodstream infections in adults: a reason to change the accepted definition of community-acquired infections. Ann Intern Med 2002;137:791—7.

[33] Li JS, Sexton DJ, Mick N, Nettles R, Fowler VG, Ryan T, et al. Proposed Modifications to the Duke Criteria for the Diagnosis of Infective Endocarditis. Clinic Infect Dis 2000;30(4):633—8. https://doi.org/10.1086/313753.

[34] Valentin T, Ruzica-Rosalia L, Hoenigl M, Zollner-Schwetz I, Krause R. Survival of Patients with *Staphylococcus aureus* Bacteremia. Clinic Infect Dis 2014;58:599—600.

[35] Holden E, Bashir A, Das I, Morton H, Steadman CD, Nightengale P, et al. *Staphylococcus aureus* bacteraemia in a UK tertiary referral centre: a 'transoesophageal echocardiogram for all' policy. J Antimicrob Chemother 2014;69:1960—5. https://doi.org/10.1093/jac/dku082.

[36] Joseph JP, Meddows TR, Webster DP, Newton JD, Myerson SG, Prendergast D, et al. Prioritizing echocardiography in *Staphylococcus aureus* bacteraemia. J Antimicrob Chemother 2013;68:444—9. https://doi.org/10.1093/jac/dks408.

[37] Young H, Knepper BC, Price CS, Heard S, Jenkins TC. Clinical Reasoning of Infectious Diseases Physicians Behind the Use or Non-Use of Transesophageal Echocardiography in *Staphylococcus aureus* bacteremia. Open Forum Infect Dis 2016 Sept 21:1—3. https://doi.org/10.1093/ofid/ofw204.

[38] Van Hal SJ, Kelly MJ, Aronis C, Cranney GB, Jones PD. The role of transthoracic echocardiography in excluding left sided infective endocarditis in *Staphylococcus aureus* bacteraemia. J Infect 2005;51:218—21. https://doi.org/10.1016/j.inf.2005.01.011.

[39] Moise PA, Sakoulas G. *Staphylococcus aureus* bacteraemia management: where do we stand and where are we going? Evid Based Med 2015;20(4):126. https://doi.org/10.1136/ebmed-2014-110122.

[40] The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC). 2015 ESC Guidelines for the management of infective endocarditis. European Heart Journal 2015;36:3075—123. https://doi.org/10.1093/eurheartj/ehv319.

[41] Therapeutic Guidelines Limited. eTG complete. Melbourne, Victoria, Australia. 2017. www.tg.org.au.

[42] Chambers HF, Miller RT, Newman MD. Right-sided *Staphylococcus aureus* endocarditis in intravenous drug abusers: two-week combination therapy. Ann Intern Med 1988;109:619—24.

[43] Ribera E, Gomez-Jimenez J, Cortes E, del Valle O, Planes A, Gonzalez-Alujas T, et al. Effectiveness of Cloxacillin with and without gentamicin in short-term therapy for right sided *Staphylococcus aureus* Endocarditis. Ann Intern Med 1996;125(12):969—74.