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Comparison of the characteristics and clinical course of patients with bacteraemia due to *Burkholderia pseudomallei, Staphylococcus aureus* and *Escherichia coli in* tropical Australia

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ABSTRACT

Background: Burkholderia pseudomallei, Staphylococcus aureus and *Escherichia coli* are common causes of bacteraemia in the tropical Asia Pacific region. The 28-day mortality rate of *B. pseudomallei* bacteraemia in Thailand has been reported to be 66%, higher than the 28-day mortality rate of bacteraemia due to *S. aureus* (43%) and *E. coli* (19%) in that country. Individuals living in rural and remote locations in these Thai studies had an even poorer prognosis. The mortality rates of individuals with bacteraemia due to *B. pseudomallei, S. aureus* and *E. coli* in countries with well-resourced health systems like Australia have not been compared directly.

Methods: We examined all cases of bacteraemia due to *B. pseudomallei* (between 2016 and 2022) and *S. aureus* and *E. coli* (between 2016 and 2020) in the Far North Queensland region of tropical Australia. We compared the characteristics and clinical course of these patients. We also examined the contribution of age, gender, comorbidity, remote residence and First Nations Australian status to the patients' 30-day mortality.

Results: In total there were 177 (10.1%) episodes of bacteraemia due to *B. pseudomallei*, 601 (34.3%) due to *S. aureus* and 974 (55.6%) due to *E. coli.* Individuals with *B. pseudomallei* bacteraemia were younger than individuals with bacteraemia due to the other pathogens (median (interquartile range) age: 58 (47–67) versus 65 (49–77), $p < 0.0001$), they were less likely to live remotely (67/177 (37.9%) versus 730/1575 (46.4%), $p = 0.03$) and they did not have a greater rate of severe comorbidity (Charlson Comorbidity Index ≥ 5; 59/177 (33.3%) versus 624/1572 (39.7%), $p = 0.10$). There were 133/1752 (7.6%) who died within 30 days, which included 19/177 (10.7%) with *B. pseudomallei* bacteraemia, 62/601 (10.3%) with *S. aureus* bacteraemia and 52/974 (5.3%) with *E. coli* bacteraemia. In multivariate analysis that included all 5 pre-specified patient characteristics, the year of presentation and the 3 pathogens (with *E.coli* as the reference), *B. pseudomallei* bacteraemia (hazard ratio (HR) (95% confidence interval (CI): 2.52 (1.48–4.31), $p = 0.001$), *S. aureus* bacteraemia (HR (95% CI): 2.47 (1.69–3.59), $p < 0.0001$), severe comorbidity (HR (95% CI): 2.53 (1.66–3.85), $p < 0.0001$) and age (divided by 10) (HR (95% CI): 1.19 (1.06–1.34), $p = 0.001$) were independently associated with a higher 30-day mortality, while a rural/remote presentation (HR (95% CI): 0.53 (0.37–0.78), $p = 0.001$) was independently associated with a lower 30-day mortality. Among patients with *B. pseudomallei* bacteraemia, there was no association between any other of the pre-specified patient factors and 30-day mortality.

Conclusions: A well-resourced hub and spoke model of health care was able to minimise the 30-day mortality of individuals with *B. pseudomallei, S. aureus* and *E. coli* bacteraemia in this region of remote tropical Australia. However, *B. pseudomallei* bacteraemia had a higher 30-day mortality than bacteraemia due to *S. aureus* or *E. coli*, highlighting the lethal potential of the organism.

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1. Introduction

Melioidosis is an emerging, life-threatening tropical infectious disease caused by the environmental gram-negative bacterium *Burkholderia pseudomallei* (Meumann et al., 2023). Melioidosis is an opportunistic infection; up to 90 % of individuals who develop melioidosis have specific risk factors for the disease that include diabetes mellitus, chronic lung disease, chronic kidney disease, immunosuppression, malignancy, and hazardous alcohol use (Meumann et al., 2023). The clinical presentation of melioidosis is highly variable and almost any organ can be affected, but most patients have pneumonia and many are bacteraemic (Currie et al., 2021). Individuals with bacteraemic melioidosis are usually older, are more likely to have significant comorbidity and are more than twice as likely to die than individuals with melioidosis who are not bacteraemic (Prinsloo et al., 2023).

B. pseudomallei is hyperendemic in Southeast Asia and tropical Australia (Meumann et al., 2023). In Northern Thailand *B. pseudomallei* is the second most common cause of community acquired bacteraemia and has a very high mortality rate (Kanoksil et al., 2013, Somayaji et al., 2021). In a 2021 prospective observational study of patients admitted to a tertiary care hospital in Northeastern Thailand with community acquired bacteraemia between 2013 and 2017, the 28-day mortality of patients with *B. pseudomallei* was 66 % compared with a rate of 43 % and 19 % with *Staphylococcus aureus* and *Escherichia coli*, respectively. Over 90 % of the patients with *B. pseudomallei* bacteraemia in this resource-limited setting were transferred to the tertiary centre from smaller rural hospitals that were up to 200 km away (Somayaji et al., 2021). This contributed to the high mortality rates seen in this study as patients transferred from smaller, peripheral Thai hospitals with sepsis are more than twice as likely to die due to delays in the delivery of the best available medical care (Hantrakun et al., 2018).

Melioidosis is also a common cause of sepsis in Far North Queensland (FNQ), a region of 380,000km^2 in northeastern tropical Australia (Fig. 1) (Prinsloo et al., 2023). The annual incidence of melioidosis has more than quadrupled in the FNQ region in the last two decades and approximately 70 % of cases are bacteraemic (Prinsloo et al., 2023). Greater familiarity with melioidosis and access to advanced critical care support through the region's hub and spoke model of healthcare has resulted in a significant recent decline in the local case-fatality rate, however almost 10 % of people with culture-confirmed melioidosis in FNQ still die from their infection (Prideaux et al., 2025).

Urban expansion has resulted in a recent increase in the number of cases of melioidosis in Cairns, the main city in the region (Smith et al., 2021). However, the incidence of melioidosis is still higher in rural parts of the region, particularly in remote, socioeconomically disadvantaged Aboriginal and Torres Strait Islander communities (Stewart et al., 2017). The disadvantage experienced by many residents of these remote communities is associated with a greater burden of comorbidities, particularly diabetes, that increases the risk of developing melioidosis (Hanson et al., 2021, Prideaux et al., 2025). These comorbidities also increase the risk of infection with other pathogens and, as in Thailand, *S. aureus* and *E. coli* are among the most common causes of bacteraemia in both these remote communities and in the FNQ region more generally (Hanson et al., 2020, Basaglia et al., 2023).

This study examined individuals with bacteraemia due to *B. pseudomallei, S. aureus* and *E. coli* in the FNQ region of tropical Australia. The study aimed to compare the 30-day mortality rates of Australian patients with bacteraemia due to these three pathogens with the outcomes reported in the 2021 study from Thailand to gain insights into the impact of health system resourcing on the clinical outcomes of patients with blood stream infections (Somayaji et al., 2021). We were also interested to define the relative 30-day mortality rates of the three pathogens in Australia, to ascertain the impact of remote residence on patients' clinical course, and to determine if there were any additional clinical, demographic, or microbiological factors associated with patient death.

2. Methods

This retrospective study was performed at Cairns Hospital, the 771-bed referral hospital for the FNQ region. Cairns Hospital serves an estimated resident population of 290,000, about 120,000 of whom live in rural and remote locations in the region. Approximately 17 % of the FNQ population identify as Aboriginal and Torres Strait Islander Australians (hereafter referred to, respectfully, as First Nations Australians) (Australian census 2021).

Cairns Hospital also has the referral laboratory for the public health system in FNQ. Potential participants were identified from the Queensland public health system's state-wide electronic laboratory database, AUSLAB. Any individual with a positive blood culture for *B. pseudomallei, S. aureus* and *E. coli* that was processed at the Cairns Hospital laboratory between January 1, 2016, and December 31, 2020 was eligible for inclusion in the study; patients with positive blood cultures for *B. pseudomallei* between January 1, 2021 and December 31, 2022 were also included in the study to ensure an adequate sample size for comparisons. Only patients with community acquired bacteraemia were eligible for the study and so patients with their first positive blood culture for *S. aureus* and *E. coli* >72 h after their admission to hospital

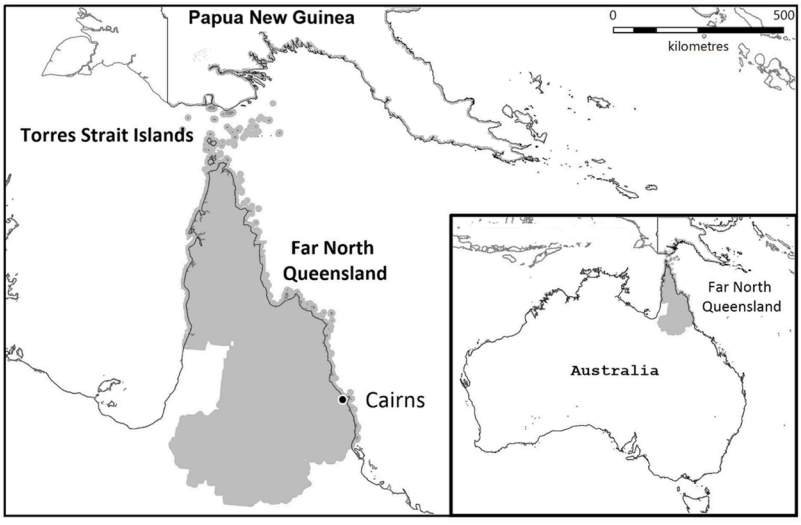

Fig. 1. Map of far north Queensland, tropical Australia.

were excluded – the same definition as the one used in the 2021 Thai comparator study – as these infections were more likely to have been hospital acquired (Somayaji et al., 2021). Episodes of bacteraemia with the same organism in the same individual within 90 days were also excluded.

The patients' medical records were reviewed to identify their demographic factors, their comorbidities and their clinical course. Individuals presenting for initial care to a health facility other than Cairns Hospital were said to have a rural or remote presentation. If these patients were – or were not – then referred to Cairns Hospital for escalation of care, this was recorded. All individuals receiving care in Queensland's public health system, are asked whether they identify as a First Nations Australian; the patient's reply was documented. Comorbidity was quantified using the Charlson Comorbidity Index with severe comorbidity defined as a Charlson Comorbidity Index ≥ 5 (Charlson et al., 1987). The study's primary endpoint was all cause, 30-day mortality.

2.1. Statistical analysis

Data were de-identified, entered into an electronic spreadsheet (Microsoft Excel) and analysed using statistical software (Stata version 18.0). Groups were compared using the Chi-squared test or the Wilcoxon rank sum test, as appropriate. Logistic regression was used to examine the demographic characteristics of the individuals with the different pathogens. Age, in years, was divided by 10 to facilitate comparison. Multivariate analysis was used to identify independent associations between these demographic characteristics and the presence of bacteraemia with the different pathogens using a backwards stepwise approach; variables were selected for consideration in the multivariate model if their p-value in univariate analysis was <0.10. Associations with 30-day mortality were determined using Cox regression. Five prespecified patient factors (gender, age, initial presentation to a rural or remote facility, identification as a First Nations Australian and severe comorbidity) as well as the year of presentation and the three pathogens (with *E. coli* as the reference) were considered. A multivariate model was developed using a backwards stepwise method to identify independent associations between these factors and 30-day mortality. In the analysis that examined independent predictors of death in individuals presenting to a rural or remote health centre, interhospital transfer was also added to the model to determine if this had any impact on survival. Changes over time in 30-day mortality were assessed using logistic regression.

2.2. Ethical approval

The study was approved by the Far North Queensland Human Research Ethics Committee (HREC/15/QCH/46-977 and EX/2021/QCH/76622-1536QA). As the data were retrospective and de-identified, the Committee waived the requirement for informed consent.

3. Results

There were 3379 records of bacteraemia with *B. pseudomallei, S. aureus* or *E. coli* identified in the FNQ region during the study period, 1485 (43.9 %) of these records were excluded as they occurred during a single clinical episode while 142 (4.2 %) were felt likely to represent a hospital-acquired *S. aureus* or *E. coli* bacteraemia. In total there were 1752 episodes of bacteraemia – which occurred in 1674 individuals – included in the analysis: 177 (10.1 %) due to *B. pseudomallei*, 601 (34.3 %) due to *S. aureus* and 974 (55.6 %) due to *E. coli* (Fig. 2, Supplementary Figure 1).

The median (interquartile range (IQR)) age of the individuals at the time of their presentation was 64 (48–76) years and 933/1752 (53.3 %) were male. Of the 1737 individuals with First Nations Australian status recorded, 530 (30.5 %) identified as a First Nations Australian. Of the 1749 individuals with sufficient data to calculate a Charlson Comorbidity Index, 683 (39.1 %) had severe comorbidity.

There were 797/1752 (45.5 %) who presented initially to a health facility in a rural or remote location. Patients presenting to a rural or

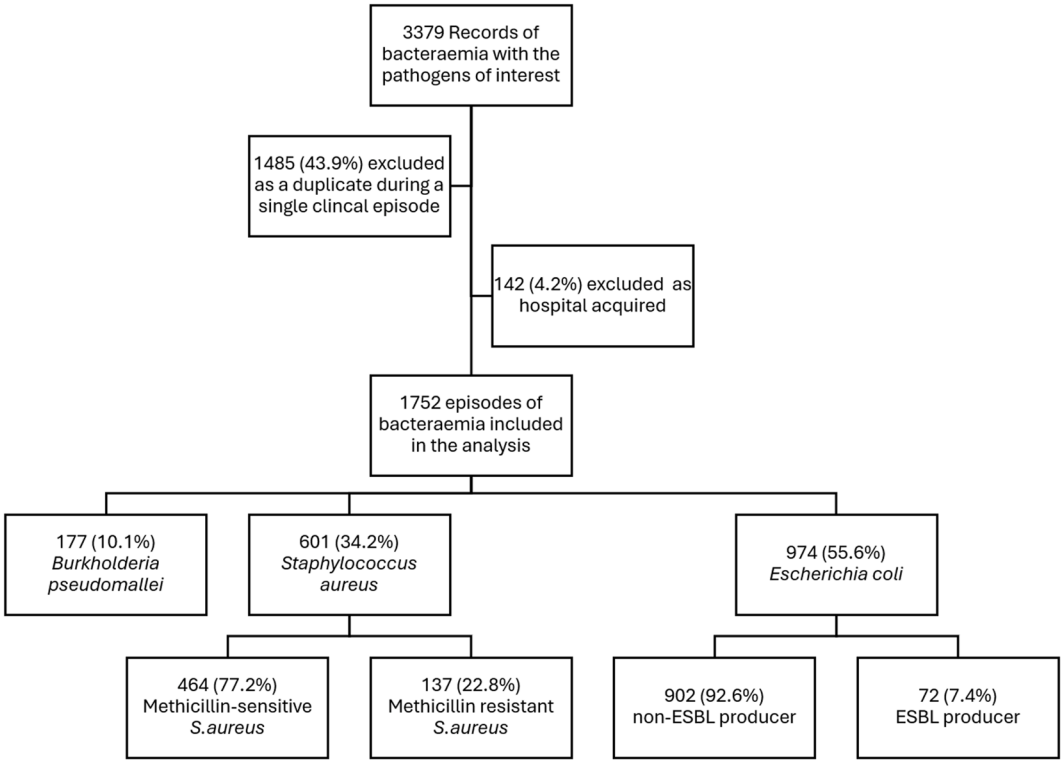

Fig. 2. The study cohort.
ESBL: extended-spectrum beta-lactamase.

remote facility were more likely to identify as a First Nations Australian than individuals presenting directly to Cairns Hospital but they were less likely to have severe comorbidity (Supplementary Table 1). There were 439/797 (55.1 %) who were transferred from the rural or remote facility to Cairns Hospital for escalation of their care. Patients presenting to a health facility in a rural or remote location with *B. pseudomallei* bacteraemia were more likely to be transferred to Cairns Hospital for ongoing care (64/67, 95.5 %) than patients with *S. aureus* (190/261, 72.8 %) or *E. coli* (185/469, 39.5 %) bacteraemia ($p < 0.0001$). Patients presenting to a rural or remote health facility who were transferred to Cairns Hospital were younger than patients who were not transferred (median (IQR) age 62 (45–72) versus 68 (51–80) years, $p < 0.0001$) and were less likely to have severe comorbidity (138/439 (31.4 %) versus 139/358 (38.8 %), $p = 0.03$). The characteristics of the patients with bacteraemia due to each of the three pathogens are presented in Table 1 and Supplementary Tables 2 & 3.

3.1. Outcomes

In the 1752 episodes of bacteraemia, there were 133 (7.6 %) deaths within 30 days; 37/133 (28 %) deaths occurred within 72 h of admission and 64/133 (48 %) occurred within the first 7 days. There was no change in 30-day mortality over the 2016–2020 period (OR) (95 % CI)): 1.05 (0.92–1.20), $p = 0.44$). The pathogen with the greatest 30-day mortality was *B. pseudomallei* (Fig. 3, Table 2).

In the 1752 episodes of bacteraemia there were 280 (16.0 %) admissions to ICU (Supplementary Figure 2); 58/177 (32.8 %) episodes of *B. pseudomallei* bacteraemia resulted in death or ICU admission compared with 168/601 (28.0 %) episodes of *S. aureus* bacteraemia ($p = 0.22$) (Supplementary Table 4).

The patient characteristic associated with the greatest 30-day mortality was severe comorbidity (Table 3). Increasing age was also associated with 30-day mortality across the cohort (HR (95 % CI: 1.29 (1.17–1.42), for every decade increase, $p < 0.0001$) (Fig. 4).

In multivariate analysis, that included all 5 pre-specified patient characteristics, the year of presentation and the 3 pathogens (with *E.coli* as the reference), *B. pseudomallei* bacteraemia (hazard ratio (HR) (95 % confidence interval (CI): 2.52 (1.48–4.31), $p = 0.001$), *S. aureus* bacteraemia (HR (95 % CI): 2.47 (1.69–3.59), $p < 0.0001$), severe comorbidity (HR (95 % CI): 2.53 (1.66–3.85), $p < 0.0001$) and age (divided by 10) (HR (95 % CI): 1.19 (1.06–1.34), $p = 0.001$) were independently associated with a higher 30-day mortality, while rural/remote presentation (HR (95 % CI): 0.53 (0.37–0.78), $p = 0.001$) was independently associated with a lower 30-day mortality.

The 30-day mortality of individuals with *B. pseudomallei, S. aureus* or *E. coli* bacteraemia who presented initially to a rural or remote facility is presented in Table 4 and Fig. 5. The demographic characteristics of the individuals who presented initially to a rural or remote facility and their association with 30-day mortality are presented in Supplementary Table 5 and Supplementary Figure 3. In multivariate analysis of the individuals that presented to a rural or remote facility that included all 5 pre-specified patient characteristics, the year of presentation, the 3 pathogens (with *E.coli* as the reference) and whether the patient was transferred to Cairns Hospital for escalation of care, *B. pseudomallei* bacteraemia (hazard ratio (HR) (95 % confidence interval (CI): 5.88 (2.15–16.14), $p = 0.001$) and *S. aureus* bacteraemia (HR (95 % CI): 2.88 (1.40–5.95), $p = 0.004$) were independently associated with a higher 30-day mortality, while transfer to Cairns Hospital (HR (95 % CI): 0.44 (0.22–0.90), $p = 0.02$) was independently associated with a lower 30-day mortality.

3.2. Patients with B. pseudomallei bacteraemia

Among patients with *B. pseudomallei* bacteraemia, there was no association between 30-day mortality and age, nor any other of the other pre-specified patient factors (Supplementary Figure 4 & Supplementary Table 6); 3/7 (42.9 %) individuals aged less than 20 years of age with *B. pseudomallei* bacteraemia died compared with 3/57 (5.3 %) individuals with *S. aureus* bacteraemia and 0/23 (0 %) individuals with *E. coli* bacteraemia aged less than 20 years ($p = 0.004$). There were only three individuals with *B. pseudomallei* bacteraemia who presented to a rural/remote facility who were not transferred to Cairns Hospital for escalation of care. In two individuals (one with widely metastatic cancer and one with decompensated Child Pugh C cirrhosis), a palliative course was pursued and both individuals died shortly afterwards. The third individual was an 86-year-old female receiving prednisone for polymyalgia rheumatica who had a Charlson Comorbidity Index of 7. She survived her admission to the rural facility but died 4 months later from

Table 1
Demographic and clinical characteristics of the patients with bacteraemia in Far North Queensland during the study period, stratified by the causative pathogen.

		Odds ratio [a]	p	Adjusted Odds ratio [b]	p
B. pseudomallei n = 177					
-Age (years)[c]	58 (47–67)	0.91 (0.85–0.97)	0.007	–	
-Male gender	129 (73 %)	2.58 (1.82–3.64)	<0.0001	3.04 (2.12–4.34)	<0.0001
-First Nations Australian	73 (41 %)	1.69 (1.23–2.33)	0.001	2.23 (1.60–3.11)	<0.0001
-Rural/remote presentation	67 (38 %)	0.71 (0.51–0.97)	0.03	0.66 (0.48–0.92)	0.01
-Severe comorbidity [d]	59 (33 %)	0.76 (0.55–1.05)	0.10	–	
S. aureus n = 601					
-Age (years) [c]	58 (43–71)	0.84 (0.80–0.88)	<0.0001	0.80 (0.76–0.85)	<0.0001
-Male gender	397 (66 %)	2.23 (1.82–2.74)	<0.0001	2.37 (1.91–2.94)	<0.0001
-First Nations Australian	171/594 (29 %) [e]	0.88 (0.71–1.10)	0.26	0.71 (0.56–0.91)	0.008
-Rural/remote presentation	261 (43 %)	0.88 (0.72–1.07)	0.21	–	
-Severe comorbidity [d]	202/598 (34 %) [f]	0.71 (0.58–0.87)	0.001	–	
E. coli n = 974					
-Age (years) [c]	68 (54–79)	1.22 (1.17–1.28)	<0.0001	1.30 (1.22–1.35)	<0.0001
-Male gender	407 (42 %)	0.34 (0.28–0.42)	<0.0001	0.29 (0.24–0.36)	<0.0001
-First Nations Australian	286/966 (30 %) [e]	0.91 (0.74–1.12)	0.36	–	
-Rural/remote presentation	469 (48 %)	1.27 (1.05–1.54)	0.01	1.34 (1.10–1.65)	0.004
-Severe comorbidity [d]	422 (43 %)	1.51 (1.24–1.83)	<0.0001	–	

Numbers presented as absolute number (%), except age presented as median (interquartile range).
[a] Odds ratio in univariate logistic regression.
[b] Odds ratio in multivariate logistic regression.
[c] In the univariate and multivariate logistic regression the age is divided by 10.
[d] Charlson Comorbidity Index ≥ 5.
[e] There were 15 individuals in whom First Nations Status was not recorded.
[f] There were 3 individuals in whom a Charlson Comorbidity Index could not be determined.

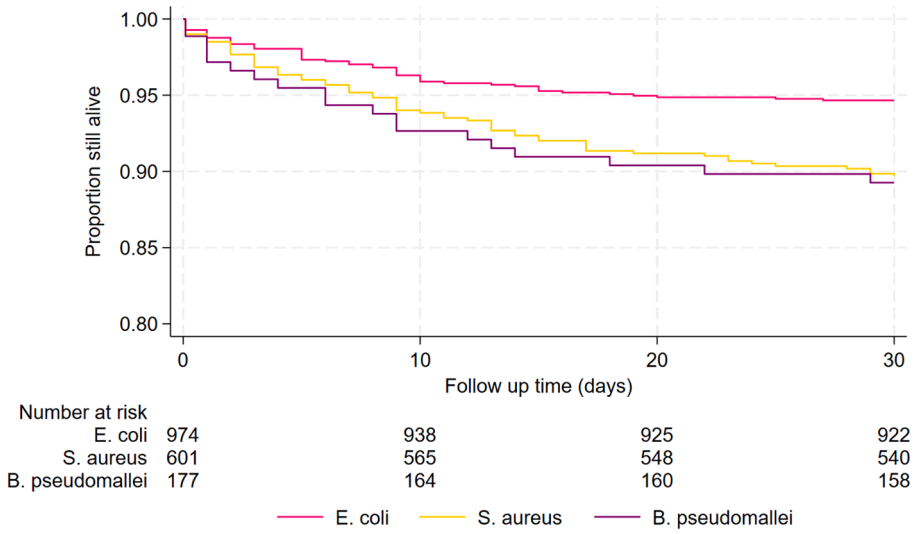

Fig. 3. Kaplan Meier survival curve demonstrating the 30-day mortality of the 1752 patients in the entire cohort stratified by causative pathogen.

Table 2
Hazard ratios for death within 30 days of presentation for *B. pseudomallei* and *S. aureus* bacteraemia, with *E. coli* bacteraemia as the reference.

Pathogen	n	30-day mortality n (%)	Hazard ratio (95 % CI)	p
B. pseudomallei	177	19 (10.7 %)	2.07 (1.22–3.49)	0.007
S. aureus	601	62 (10.3 %)	1.97 (1.36–2.85)	<0.0001
-*MSSA*	464	52 (11.2 %)	2.14 (1.46–3.14)	<0.0001
-*MRSA*	137	10 (7.3 %)	1.39 (0.71–2.73)	0.34
E. coli	974	52 (5.3 %)	Reference	–
-Non-ESBL producing	902	48 (5.3 %)	–	–
-ESBL producing	72	4 (5.6 %)	–	–

MSSA: methicillin-sensitive *S. aureus*; MRSA: methicillin-resistant *S. aureus*; ESBL: extended-spectrum beta-lactamase.

a cardioembolic stroke.

3.3. Patients with S. aureus bacteraemia

Among patients with *S. aureus* bacteraemia, severe comorbidity and increasing age were independently associated with a higher 30-day mortality, while male gender and rural/remote presentation were independently associated with a lower 30-day mortality (Supplementary Figure 5 and Supplementary Table 7). There was no difference in 30-day mortality between methicillin-resistant *S. aureus* (MRSA) and methicillin-sensitive *S. aureus* (MSSA) (HR (95 % CI): 0.64 (0.33–1.28), $p = 0.21$) (Supplementary Figure 6).

3.4. Patients with E.coli bacteraemia

Among patients with *E.coli* bacteraemia, male gender, severe comorbidity and increasing age were independently associated with a higher 30-day mortality, while rural/remote presentation was independently associated was a lower 30-day mortality (Supplementary Figure 7 and Supplementary Table 8). There was no difference in 30-day mortality between extended-spectrum beta-lactamase (ESBL) producing *E. coli* and non-ESBL producing *E. coli* HR (95 % CI): 1.05 (0.38–2.92), $p = 0.92$) (Supplementary Figure 8).

4. Discussion

The study highlights the success of the hub and spoke model of care in the management of life-threatening infection in this region of tropical

Table 3
Association between selected patient characteristics and 30-day mortality.

Patient characteristic	n	30-day mortality n (%)	Hazard ratio (95 % CI)	p
All patients	**1752**	**133 (7.6 %)**	–	–
Gender				
Male gender	933	81 (8.7 %)	1.38 (0.98–1.96)	0.07
Female gender	819	52 (6.4 %)		
First Nations Australian status [a]				
First Nations Australian	530	24 (4.5 %)	0.50 (0.32–0.78)	0.002
Non-First Nations Australian	1207	112 (8.9 %)		
Presentation site				
Rural/remote presentation [b]	797	39 (4.9 %)	0.48 (0.33–0.70)	<0.0001
Urban presentation	955	94 (9.8 %)		
Comorbidity				
Severe comorbidity [c]	683	90 (13.2 %)	3.41 (2.37–4.90)	<0.0001
No severe comorbidity	1066	43 (4.0 %)		
Escalation of care [d]				
Interhospital transfer	439	18 (4.1 %)	0.70 (0.37–1.31)	0.26
No interhospital transfer	358	21 (5.9 %)		

[a] There were 15 individuals in whom First Nations Status was not recorded.
[b] Individuals presenting for initial care to a health facility other than Cairns Hospital.
[c] Charlson Comorbidity Index ≥5. There were 3 individuals in whom a Charlson Comorbidity Index could not be determined.
[d] Only includes the 797 individuals who presented to a rural/remote health centre.

Australia. The 30-day mortality of individuals with *B. pseudomallei* bacteraemia in this cohort was over six times lower than that seen in individuals with *B. pseudomallei* bacteraemia in Northern Thailand between 2013 and 2017 (Somayaji et al., 2021). Meanwhile the 30-day mortality of individuals with *S. aureus* and *E. coli* bacteraemia was almost four times lower than was seen in that Thai cohort. Indeed, the overall 30-day mortality of 7.6 % in bacteraemic individuals in this cohort compares favourably with the 30-day mortality rates in individuals with bacteraemia in other high-income settings (Holm et al., 2021, Melzer and Welch, 2013, Laurier et al., 2024). These outcomes were possible despite the fact that the FNQ region covers an area of approximately 380,000km^2 with some individuals living over 900 km away from the nearest referral hospital.

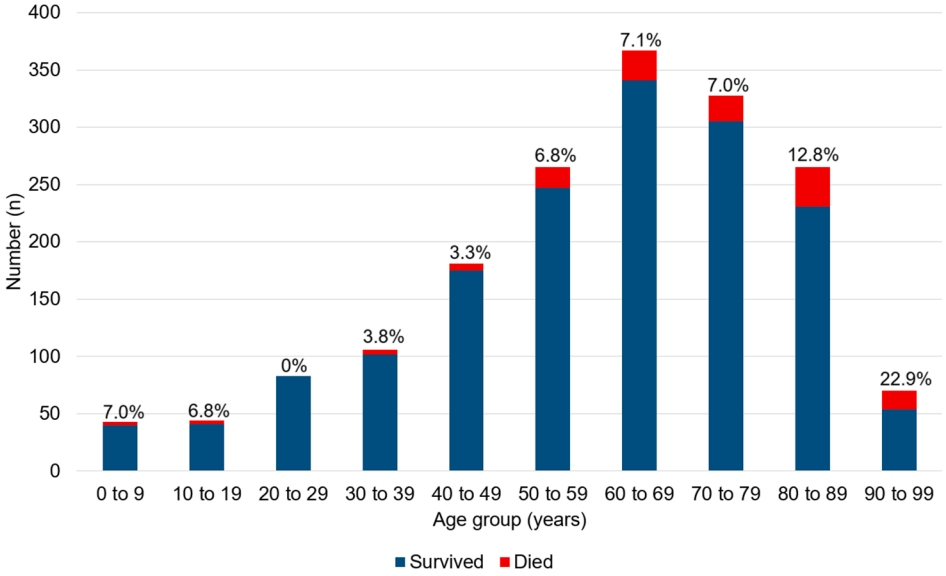

Fig. 4. Association between age and 30-day mortality of the 1752 episodes of *B. pseudomallei, S. aureus* and *E. coli* bacteraemia.

Table 4
Hazard ratios for death within 30 days of presentation at a rural or remote health facility for *B. pseudomallei* and *S. aureus* bacteraemia, with *E. coli* bacteraemia as the reference.

Pathogen	n	30-day mortality n (%)	Hazard ratio (95 % CI)	p
B. pseudomallei	67	7 (10.5 %)	3.44 (1.40–8.44)	0.007
S. aureus	261	17 (6.5 %)	2.05 (1.03–4.11)	0.04
-*MSSA*	199	15 (7.5 %)	2.39 (1.17–4.89)	0.02
-*MRSA*	62	2 (3.2 %)	1.00 (0.23–4.38)	1.0
E. coli	469	15 (3.2 %)	Reference	–
-Non-ESBL producing	449	15 (3.3 %)	–	–
-ESBL producing	20	0	–	–

MSSA: methicillin-sensitive *S. aureus*; MRSA: methicillin-resistant *S. aureus*; ESBL: extended-spectrum beta-lactamase.

These encouraging findings are likely to be explained by the prompt access to guideline-concordant sepsis care in Australia's well-resourced universal health system. There have been major recent advances in critical care knowledge which have resulted in significant improvement in the outcomes of patients with sepsis (Evans et al., 2021, Kaukonen et al., 2014). However, the care of patients with life-threatening bacteraemia in FNQ has been further enhanced by national efforts to increase the awareness of sepsis, by the promulgation of locally relevant electronic guidelines for the management of sepsis (particularly optimal empirical antibiotic therapy) and by access to centrally coordinated aeromedical retrieval services that expedite patient transfer to referral centres where they are able to access sophisticated imaging and receive advanced multidisciplinary critical care support (Sepsis Australia 2025, Franklin et al., 2021, Sepsis resources for health professionals, 2025, Salaveria et al., 2021, Boyle et al., 2024, Pownell et al., 2025).

A Thai study of community acquired infection and sepsis identified that patients transferred from other hospitals to referral centres were twice as likely to die from their infection due to delays in patients having access to optimal care (Hantrakun et al., 2018). In contrast, in our series,

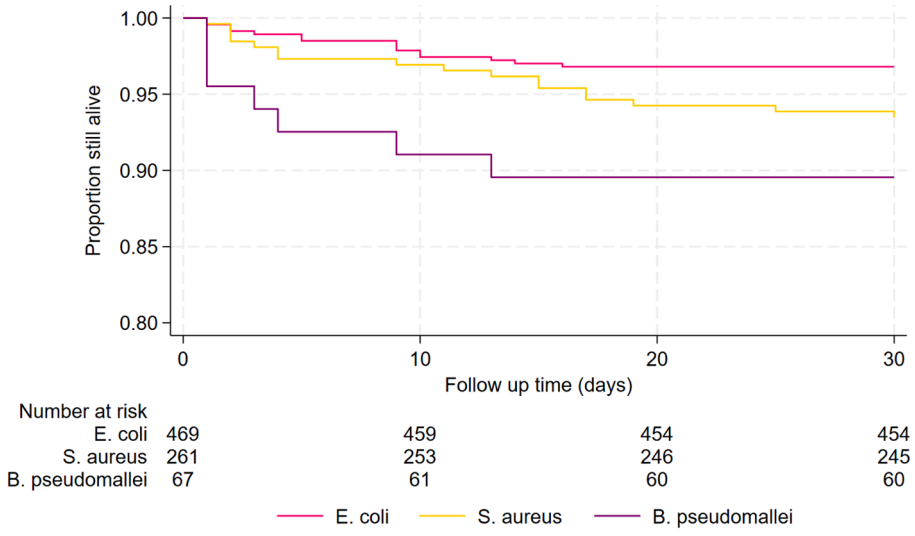

Fig. 5. Kaplan Meier survival curve demonstrating the 30-day mortality of the 797 patients who initially presented to a rural or remote health facility, stratified by causative pathogen.

individuals presenting to a rural or remote site with *B. pseudomallei, S. aureus* or *E. coli* bacteraemia were, in multivariate analysis, almost twice as likely to survive as individuals presenting directly to the referral centre. The 30-day mortality of individuals who presented initially to a rural or remote facility of less than 5 % echoes similarly low case-fatality rates of patients in remote FNQ presenting with other life-threatening infections including *Streptococcus pyogenes* bacteraemia, leptospirosis and rickettsial diseases (Nguyen et al., 2025, Stratton et al., 2025, Gavey et al., 2025). Almost 45 % of the patients in the current study who presented initially to a rural or remote facility were not transferred to Cairns Hospital for escalation of care suggesting that healthcare workers at rural or remote facilities are able to recognise the high-risk patient proficiently while also enabling lower risk patients – and older patients with greater comorbidity in whom transfer would be inappropriate or futile – to stay closer to home and family, while simultaneously reducing costs for the health system.

B. pseudomallei was the least common of the three pathogens examined in the cohort, but it had the highest 30-day mortality. This is despite the fact that individuals with melioidosis were younger than the individuals with the other pathogens and that a lower proportion of individuals with melioidosis had severe comorbidity. Individuals with melioidosis were also more likely to be transferred to Cairns Hospital for escalation of care than the individuals with the other pathogens. The relatively high mortality of individuals with *B. pseudomallei* bacteraemia identified in our cohort echoes the study in Northeastern Thailand which compared the clinical course of individuals with bacteraemia due to *B. pseudomallei, S. aureus* and *E. coli* and which identified that the case-fatality rate of individuals with *B. pseudomallei* bacteraemia was one-and-a-half that of individuals with *S. aureus* bacteraemia and over three times the rate that seen in individuals with *E. coli* bacteraemia (Somayaji et al., 2021).

An array of virulence factors allows *B. pseudomallei* to adhere to, invade and multiply within host cells while resisting immune clearance and they can have a significant impact on the clinical phenotype and clinical course of individuals with melioidosis (Meumann et al., 2023, Sarovich et al., 2014, Gora et al., 2022). It is likely that these virulence factors contributed to our finding that individuals with *B. pseudomallei* bacteraemia in our cohort had a 30-day mortality that was almost twice that of the individuals with *E. coli* bacteraemia. The presence of these virulence factors may also contribute to the relatively high case-fatality rate seen in younger individuals aged in our cohort. Older age is an independent predictor of mortality in large series of patients with melioidosis, however, it was notable that over 40 % of the individuals with *B. pseudomallei* bacteraemia aged less than 20 in our cohort died within 30 days (Currie et al., 2021, Smith et al., 2017).

The incidence of melioidosis in FNQ is higher in individuals with a remote residence, greater comorbidity and in those identifying as a First Nations Australian and we had hypothesised that these three factors would also have an impact on survival (Prinsloo et al., 2023, Stewart et al., 2017). However, it was notable that among individuals with *B. pseudomallei* bacteraemia there was no association between any of these factors and 30-day mortality. The continuing gap in health outcomes between First Nations and non-First Nations Australians remains stubbornly persistent (Commonwealth Closing the Gap 2024 Annual Report and 2025 Implementation Plan, 2025). This is at least partly related to the social determinants of health, higher rates of comorbidity and the challenges of delivering optimal, culturally appropriate medical care to remote settings (Determinants of health for first nations people: australian institute of health and welfare, 2024). However, while First Nations Australians were over-represented amongst the individuals with *B. pseudomallei* bacteraemia (and, indeed, *S. aureus* and *E. coli* bacteraemia) a lower proportion of First Nations Australians than non-First Nations Australians with melioidosis died from their infection.

The relatively high survival rate in the patients with *B. pseudomallei* bacteraemia in this cohort may be partly explained by the fact that over 98 % of them were managed in Cairns Hospital where a recent increase in the incidence of the disease has resulted in greater familiarity with the infection and a decline in the case fatality rate (Prinsloo et al., 2023). The hospital is also able to provide access to sophisticated imaging (including positron emission tomography-computed tomography and magnetic resonance imaging) which help define unexpected foci of infection, specialist surgical support that ensures optimal source control and a specialist infectious diseases service that ensures patients receive the optimal dose and duration of antibiotic therapy (Boyle et al., 2024, Dadwal et al., 2024, Kozlowska et al., 2018). These therapeutic strategies, of course, are also equally applicable to individuals with *S. aureus* and *E. coli* bacteraemia.

It was notable that the relative incidence of *S. aureus* and *E. coli* bacteraemia in this Australian cohort was far higher than in the Thai comparator study (Somayaji et al., 2021). This is likely to reflect differences in population demographics, the prevalence of comorbidities and the access to diagnostic support. The high proportion of community acquired *S. aureus* isolates in the FNQ region that were methicillin-resistant has been noted previously (Guthridge et al., 2019). It was encouraging to see that there was no difference in the 30-day mortality between individuals with a MRSA and a MSSA bacteraemia. Indeed, the 30-day mortality of 7.3 % among individuals with MRSA bacteraemia in the cohort is lower than contemporary studies from other well-resourced settings, speaking to prompt consideration of the possibility of MRSA infection and its appropriate therapy (Bai et al., 2022, Biggs et al., 2023, Guthridge et al., 2021). There was also no difference in 30-day mortality between individuals with *E. coli* bacteraemia with isolates that did – and did not – produce an ESBL. This may be at least partly explained by the recommendation in local guidelines to include meropenem in the empirical regimen of individuals with sepsis (Sepsis resources for health professionals, 2025). The inclusion of meropenem in these guidelines is primarily to cover the possibility of melioidosis, but it also has the additional benefit of covering local ESBL-producing *E. coli* infections.

Although the study's demographic, microbiological and outcome data are robust, as a scientific enterprise it has many limitations. Its retrospective nature is likely to have resulted in underreporting of some comorbidities which would tend to underestimate the burden of severe comorbidity in the cohort. The clinical presentation of the patients was not included in the analysis which is important because the clinical phenotype of individuals with bacteraemia can vary significantly (Dolby et al., 2022). It would be helpful to know the source of the bacteraemia and the illness severity when the patient presented for care. The clinical management of the patients was also not examined in any detail; in particular, we were unable to access information about the antibiotic regimen that the patients received, and the time that elapsed prior to the administration of appropriate therapy (if, indeed, they received it at all). This is important as Thai authors have suggested that patients receiving empirical antibiotics with activity against the aetiologic organism prior to – or during – transfer was associated with survival (Somayaji et al., 2021). We have reported the 30-day mortality rates, but it is likely that in many of the cases attending clinicians pursued a less aggressive approach, without escalation of care. This is evidenced by the lower rate of interhospital transfer of older individuals with greater comorbidity who initially presented to a rural or remote health facility. It is important to highlight that although we compare the 30-day mortality rates of patients in the well-resourced Australian and resource-limited Thai setting, Australia and Thailand clearly have quite different populations and the countries have very different health systems. Blood cultures are commonly collected in individuals presenting with evidence of infection in Australia, while in Thailand there is less access to microbiological support and blood cultures are more likely to be performed in the most seriously ill patients in referral centres (Deen et al., 2012, Rhodes et al., 2019). The Thai patients may therefore represent a more critically ill population. It is also important to highlight that the Thai cohort was managed between the years of 2013 and 2017 and there have been significant advances in critical care management since that time (Evans

et al., 2021). The study was performed in FNQ, a unique region of tropical Australia, which may limit the generalisability of these findings to other jurisdictions. However, a high index of suspicion for sepsis, prompt antibiotic therapy and, if appropriate, early referral for escalation of care are almost certainly likely to be equally relevant in these locations (Evans et al., 2021).

Acknowledging these limitations, the study demonstrates that the hub and spoke model of care in Australia's well-resourced health system can minimise the 30-day mortality of patients with *B. pseudomallei, S. aureus* and *E. coli* bacteraemia. Future prospective studies might examine detailed aspects of individual patient management to determine which therapeutic interventions are responsible for these encouraging outcomes and how they may be delivered in a cost-effective manner. The possibly counterintuitive finding that patients presenting to rural and remote health facilities have better outcomes is a consistent observation in the FNQ region (Nguyen et al., 2025, Stratton et al., 2025, Gavey et al., 2025). Future prospective studies might explore whether this is explained by lower rates of complex comorbidity, differences in health seeking behaviour, or better access to care in rural and remote FNQ. These studies might also examine barriers to individuals presenting directly to Cairns Hospital for care, so that they may be overcome.

5. Conclusions

A hub and spoke model of care is able to minimise the 30-day mortality of individuals with *B. pseudomallei, S. aureus* and *E. coli* bacteraemia in this region of remote, tropical Australia. Across the cohort, severe comorbidity and older age were associated with poorer survival but First Nations Australian status and remote residence were not. Even in Australia's well-resourced universal health system over 10 % of individuals with *B. pseudomallei* bacteraemia died within 30 days – the highest 30-day mortality rate of these three pathogens – emphasising the organism's lethal potential.

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CRediT authorship contribution statement

Kelly Baker: Writing – review & editing, Writing – original draft, Methodology, Investigation, Data curation. **Alistair Lau:** Writing – review & editing, Data curation. **Arish Soogrim:** Writing – review & editing, Data curation. **Tej Shukla:** Writing – review & editing, Data curation. **Jasraaj Singh:** Writing – review & editing, Data curation. **Felix Torrance:** Writing – review & editing, Data curation. **John Maclean:** Writing – review & editing, Data curation. **Simon Smith:** Writing – review & editing, Investigation, Data curation. **Josh Hanson:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.actatropica.2025.107851.

Data availability

Data will be made available on request.

References

Australian census: Australian Bureau of Statistics. Canberra.; [Available from: https://www.abs.gov.au/census , 2021, Accessed 27 October 2024.

Bai, A.D., Lo, C.K.L., Komorowski, A.S., Suresh, M., Guo, K., Garg, A., et al., 2022. Staphylococcus aureus bacteraemia mortality: a systematic review and meta-analysis. Clinic. Microbiol. Infect 28 (8), 1076–1084.

Basaglia, A., Kang, K., Wilcox, R., Lau, A., McKenna, K., Smith, S., et al., 2023. The aetiology and incidence of infective endocarditis in people living with rheumatic heart disease in tropical Australia. Eur. J. Clin. Microbiol. Infect. Dis 42 (9), 1115–1123.

Biggs, H., Jackson, K.A., Nadle, J., Petit, S., Ray, S.M., Dumyati, G., et al., 2023. 2456. Methicillin-Resistant Staphylococcus aureus Bacteremia 30-Day Mortality During 2020 Compared to 2016-2019: assessing the Impact of COVID-19. Open Forum. Infect. Dis 10 (Supplement_2).

Boyle, R., Withey, G., Smith, S., Hanson, J., 2024. Mycotic aneurysms due to Burkholderia pseudomallei in Far North Queensland, tropical Australia: a case series and review of the literature. Acta. Trop 260, 107480.

Charlson, M.E., Pompei, P., Ales, K.L., MacKenzie, C.R., 1987. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J. Chronic. Dis 40 (5), 373–383.

Commonwealth Closing the Gap 2024 Annual Report and 2025 Implementation Plan, 2025. National Indigenous Australians Agency (NIAA, Canberra.

Currie, B.J., Mayo, M., Ward, L.M., Kaestli, M., Meumann, E.M., Webb, J.R., et al., 2021. The Darwin Prospective Melioidosis Study: a 30-year prospective, observational investigation. Lancet Infect. Dis 21 (12), 1737–1746.

Dadwal, P., Bonner, B., Fraser, D., Loveridge, J., Withey, G., Puri, A., et al., 2024. Bone and joint infections due to melioidosis; diagnostic and management strategies to optimise outcomes. PLoS Negl. Trop. Dis 18 (7), e0012317.

Deen, J., von Seidlein, L., Andersen, F., Elle, N., White, N.J., Lubell, Y., 2012. Community-acquired bacterial bloodstream infections in developing countries in south and southeast Asia: a systematic review. Lancet Infect. Dis 12 (6), 480–487.

Determinants of health for first nations people: australian institute of health and welfare 2024 Australian GovernmentCanberra [Available from https://www.aihw.gov.au/reports/australias-health/social-determinants-and-indigenous-health Accessed 17 September 2024.

Dolby, H.W., Clifford, S.A., Laurenson, I.F., Fowler, V.G., Russell, C.D., 2022. Heterogeneity in Staphylococcus aureus Bacteraemia Clinical Trials Complicates Interpretation of Findings. J. Infect. Dis 226 (4), 723–728.

Evans, L., Rhodes, A., Alhazzani, W., Antonelli, M., Coopersmith, C.M., French, C., et al., 2021. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. Intens. Care. Med 47 (11), 1181–1247.

Franklin, R.C., King, J.C., Aitken, P.J., Elcock, M.S., Lawton, L., Robertson, A., et al., 2021. Aeromedical retrievals in Queensland: a five-year review. Emerg. Med. Australas 33 (1), 34–44.

Gavey, R., Stewart, A.G.A., Bagshaw, R., Smith, S., Vincent, S., Hanson, J., 2025. Respiratory manifestations of rickettsial disease in tropical Australia; Clinical course and implications for patient management. Acta. Trop 266, 107631.

Gora, H., Hasan, T., Smith, S., Wilson, I., Mayo, M., Woerle, C., et al., 2022. Melioidosis of the central nervous system; impact of the bimABm allele on patient presentation and outcome. Clin. Infect. Dis.

Guthridge, I., Smith, S., Horne, P., Hanson, J., 2019. Increasing prevalence of methicillin-resistant Staphylococcus aureus in remote Australian communities: implications for patients and clinicians. Pathology 51 (4), 428–431.

Guthridge, I., Smith, S., Law, M., Binotto, E., Hanson, J., 2021. Efficacy and Safety of Intravenous Lincosamide Therapy in Methicillin-Resistant Staphylococcus aureus Bacteremia. Antimicrob Agent. Chemother 65 (9), e0034321.

Hanson, J., Smith, S., Brooks, J., Groch, T., Sivalingam, S., Curnow, V., et al., 2020. The applicability of commonly used predictive scoring systems in Indigenous Australians with sepsis: an observational study. PLoS One 15 (7), e0236339.

Hanson, J., Smith, S., Stewart, J., Horne, P., Ramsamy, N., 2021. Melioidosis-a disease of socioeconomic disadvantage. PLoS. Negl. Trop. Dis 15 (6), e0009544.

Hantrakun, V., Somayaji, R., Teparrukkul, P., Boonsri, C., Rudd, K., Day, N.P.J., et al., 2018. Clinical epidemiology and outcomes of community acquired infection and sepsis among hospitalized patients in a resource limited setting in Northeast Thailand: a prospective observational study (Ubon-sepsis). PLoS. One 13 (9), e0204509.

Holm, M.K.A., Jansaker, F., Gradel, K.O., Nielsen, R.T., Ostergaard Andersen, C., Jarlov, J.O., et al., 2021. Decrease in All-Cause 30-Day Mortality after Bacteraemia over a 15-Year Period: a Population-Based Cohort Study in Denmark in 2000-2014. Int. J. Environ. Res. Public. Health 18 (11).

Kanoksil, M., Jatapai, A., Peacock, S.J., Limmathurotsakul, D., 2013. Epidemiology, microbiology and mortality associated with community-acquired bacteremia in northeast Thailand: a multicenter surveillance study. PLoS. One 8 (1), e54714.

Kaukonen, K.M., Bailey, M., Suzuki, S., Pilcher, D., Bellomo, R., 2014. Mortality related to severe sepsis and septic shock among critically ill patients in Australia and New Zealand, 2000-2012. JAMA 311 (13), 1308–1316.
Kozlowska, J., Smith, S., Roberts, J., Pridgeon, S., Hanson, J., 2018. Prostatic Abscess due to Burkholderia pseudomallei: facilitating Diagnosis to Optimize Management. Am. J. Trop. Med. Hyg 98 (1), 227–230.
Laurier, N., Karellis, A., Xue, X., Afilalo, M., Weiss, K., 2024. Strategies to reduce 28-day mortality in adult patients with bacteremia in the emergency department. BMC Infect. Dis 24 (1), 1384.
Melzer, M., Welch, C., 2013. Thirty-day mortality in UK patients with community-onset and hospital-acquired meticillin-susceptible Staphylococcus aureus bacteraemia. J. Hosp. Infect 84 (2), 143–150.
Meumann, E.M., Limmathurotsakul, D., Dunachie, S.J., Wiersinga, W.J., Currie, B.J., 2023. Burkholderia pseudomallei and melioidosis. Nat. Rev. Microbiol.
Nguyen, A.D.K., Han, W.M., Smith, S., Hanson, J., 2025. Prognostic factors in patients hospitalised with group A Streptococcus bacteraemia in tropical Australia. Acta. Trop 269, 107746.
Pownell, C., Marsden, B.E., Lam, W., Smith, S., Hanson, J., 2025. Prosthetic valve infective endocarditis due to Burkholderia pseudomallei: a case report and review of the literature. Acta. Trop 261, 107492.
Prideaux, L., Stratton, H., Sandeman, M., Smith, S., Hanson, J., 2025. The Association Between Statin Therapy and the Subsequent Clinical Course of Patients With Melioidosis. J. Trop. Med 2025, 8838580.
Prideaux, L., Sandeman, M., Stratton, H., Kelleher, A.D., Smith, S., Hanson, J., 2025. Melioidosis in people living with diabetes; clinical presentation, clinical course and implications for patient management. Acta. Trop 263, 107559.
Prinsloo, C., Smith, S., Law, M., Hanson, J., 2023. The Epidemiological, Clinical, and Microbiological Features of Patients with Burkholderia pseudomallei Bacteraemia-Implications for Clinical Management. Trop. Med. Infect. Dis 8 (11).
Rhodes, J., Jorakate, P., Makprasert, S., Sangwichian, O., Kaewpan, A., Akarachotpong, T., et al., 2019. Population-based Bloodstream Infection Surveillance in Rural Thailand, 2007-2014, 19. BMC Public Health, p. 521.
Salaveria, K., Smith, S., Liu, Y.H., Bagshaw, R., Ott, M., Stewart, A., et al., 2021. The Applicability of Commonly Used Severity of Illness Scores to Tropical Infections in Australia. Am. J. Trop. Med. Hyg 106 (1), 257–267.
Sarovich, D.S., Price, E.P., Webb, J.R., Ward, L.M., Voutsinos, M.Y., Tuanyok, A., et al., 2014. Variable virulence factors in Burkholderia pseudomallei (melioidosis) associated with human disease. PLoS One 9 (3), e91682.
Sepsis Australia: The George Institute, Sydney; 2025 [Available from: https://www.australiansepsisnetwork.net.au/ Accessed 27 October 2024.
Sepsis resources for health professionals: Queensland Health, Brisbane; 2025 [Available from: https://www.health.qld.gov.au/clinical-practice/guidelines-procedures/clinical-resources/sepsis-resources-for-health-professionals Accessed 15 June 2025.
Smith, S., Stewart, J.D., Tacon, C., Archer, N., Hanson, J., 2017. Children with melioidosis in Far North Queensland are commonly bacteraemic and have a high case fatality rate. Commun. Dis. Intell. Q. Rep 41 (4), E318–Ee21.
Smith, S., Horne, P., Rubenach, S., Gair, R., Stewart, J., Fairhead, L., et al., 2021. Increased Incidence of Melioidosis in Far North Queensland, Queensland, Australia, 1998-2019. Emerg. Infect. Dis 27 (12), 3119–3123.
Somayaji, R., Hantrakun, V., Teparrukkul, P., Wongsuvan, G., Rudd, K.E., Day, N.P.J., et al., 2021. Comparative clinical characteristics and outcomes of patients with community acquired bacteremia caused by Escherichia coli, Burkholderia pseudomallei and Staphylococcus aureus: a prospective observational study (Ubon-sepsis). PLoS. Negl. Trop. Dis 15 (9), e0009704.
Stewart, J.D., Smith, S., Binotto, E., McBride, W.J., Currie, B.J., Hanson, J., 2017. The epidemiology and clinical features of melioidosis in Far North Queensland: implications for patient management. PLoS. Negl. Trop. Dis 11 (3).
Stratton, H., Rosengren, P., Kinneally, T., Prideaux, L., Smith, S., Hanson, J., 2025. Presentation and Clinical Course of Leptospirosis in a Referral Hospital in Far North Queensland, Tropical Australia. Pathogens 14 (7).