Sepsis in the tropical Top End of Australia's Northern Territory: disease burden and impact on Indigenous Australians

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ABSTRACT

Objective: To describe the clinical and epidemiological features of sepsis and severe sepsis in the population of the tropical Top End of the Northern Territory of Australia and compare these with published estimates for temperate Australia, the United States and Europe.

Design, setting and participants: Prospective cohort study in the major hospital for tropical NT, a region where 27% of the population are Indigenous. We screened all adult (≥ 15 years) acute hospital admissions over a 12-month period (6 May 2007 – 5 May 2008) for sepsis by standard criteria, and collected standardised clinical data.

Main outcome measures: Population-based incidence of community-onset sepsis and severe sepsis requiring intensive care unit (ICU) admission; 28-day mortality rate and microbial epidemiology.

Results: There were 1191 hospital admissions for sepsis in 1090 patients, of which 604 (50.7%) were Indigenous people; the average age was 46.7 years. The age-adjusted annual population-based incidence of sepsis was 11.8 admissions per 1000 (mortality rate, 5.4%), but for Indigenous people it was 40.8 per 1000 (mortality rate, 5.7%). For severe sepsis requiring ICU admission, the incidence was 1.3 per 1000 per year (mortality rate, 21.5%), with an Indigenous rate of 4.7 per 1000 (mortality rate, 19.3%).

Conclusions: The incidence of sepsis in the tropical NT is substantially higher than that for temperate Australia, the United States and Europe, and these differences are mainly accounted for by the high rates of sepsis in Indigenous people. The findings support strategies to improve housing and access to health services, and reduce comorbidities, alcohol and tobacco use in Indigenous Australians. The burden of sepsis in indigenous populations worldwide requires further study to guide appropriate resourcing of health care and preventive strategies.

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Sepsis (an acute infection with a systemic response) and severe sepsis (sepsis resulting in organ dysfunction) are very costly and often fatal conditions,[1] and their incidence is increasing.[2] Severe sepsis has been estimated to cause as many deaths annually in the United States as acute myocardial infarction.[1] The epidemiology of sepsis has been well described in the US[1,2] and Europe,[3,4] but not in tropical regions or for indigenous populations. The one Australian study of sepsis epidemiology[5] did not include data from tropical areas of Australia or on Indigenous status. This study found that the population-based incidence of severe sepsis requiring admission to an intensive care unit (ICU) was 0.77 cases per 1000 per year,[5] which is comparable with figures reported from Europe and North America.[6]

The tropical Top End of the Northern Territory of Australia has a high proportion of Indigenous people, and the NT population has a high prevalence of infectious[7] and chronic diseases;[8] however, the epidemiology of sepsis in this population is unknown. Similar to many other indigenous peoples, Australia's Indigenous population has a lower life expectancy and a higher burden of chronic and infectious diseases than non-Indigenous Australians.[9]

Most large studies of sepsis epidemiology are retrospective database analyses based on discharge coding,[1,2,10] which is likely to significantly underestimate sepsis incidence.[11] Most prospective studies are limited to patients requiring ICU admission,[3,5] and are thus not representative of the true community burden of sepsis requiring hospitalisation. Patients with sepsis that requires hospital treatment, but not ICU admission, are common and have a high mortality rate,[1] but these patients are underrepresented in the medical literature.

In this prospective study, we describe the clinical and epidemiological features of sepsis and severe sepsis in tropical northern Australia, including the population-based incidence in Indigenous and non-Indigenous populations, the causative organisms and outcomes of treatment, and compare these with published estimates for populations in temperate Australia, the US and Europe.

METHODS

Setting

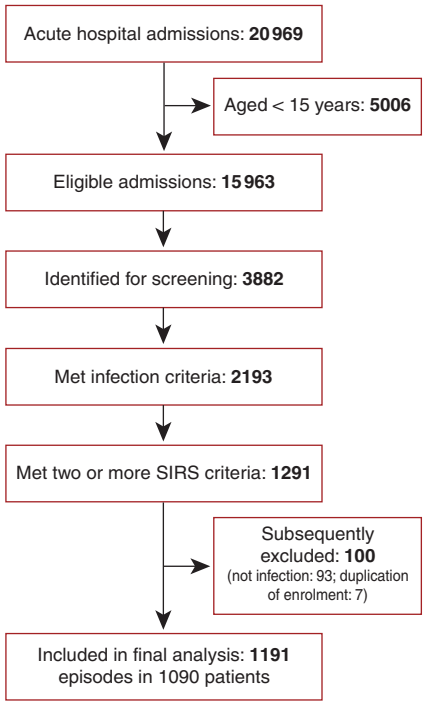
Royal Darwin Hospital (RDH) is a 350-bed teaching hospital in Darwin (latitude 12.5° S) in the tropical Top End of the NT. RDH is the only hospital for a population of 130 000 over an area of 115 000 km^2 (primary catchment area), and serves as a referral hospital (including for ICU admission) for a total population of 170 000 over an area of 500 000 km^2. Indigenous Australians comprise 27% of the catchment population, and 30.3% of the population live in "remote" or "very remote" areas.[12]

Recruitment and data collection

We undertook a prospective cohort study comprising every adult (≥ 15 years) acute admission to RDH for a 12-month period from 6 May 2007 to 5 May 2008. In this period, we evaluated daily every admission to RDH by admission diagnosis. All patients whose admission diagnosis could possibly represent an infection, or was missing, underwent screening for study inclusion: examination of the medical record, the observation chart, and pathology results; and, where necessary, discussion with the patient's treating clinician. In addition, daily screening rounds were conducted of the ICU and the emergency department. Finally, all positive results of blood cultures for the study period were examined, and those for episodes not already included in the study were evaluated. All data were collected by one of three trained study staff.

All patients who met predefined criteria for probable or definite infection (see Definitions), in addition to at least two criteria for the systemic inflammatory response syndrome (SIRS),[13] were enrolled in the study. SIRS criteria (see Definitions) were required to be present concurrently within a 24-hour period, within the first 48 hours of hospital admission. Patients' discharge summaries and pathology results were assessed at the time of hospital discharge, and those with a non-infectious cause of SIRS were subse-

1 Recruitment flowchart



SIRS = systemic inflammatory response syndrome.[13] ◆

2 Baseline characteristics of study subjects, by Indigenous status*

Characteristic	Total ($n = 1191$)	Indigenous ($n = 604$)	Non-Indigenous ($n = 587$)	P†
Mean age in years (SD)	46.7 (17.4)	43.2 (14.4)	50.2 (19.2)	< 0.001
Male	624 (52.4%)	261 (43.2%)	363 (61.8%)	< 0.001
Remote-dwelling‡	288 (24.2%)	251 (41.6%)	37 (6.3%)	< 0.001
Hazardous alcohol use§	339 (46.2%)	246 (62.0%)	93 (27.7%)	< 0.001
Current smoking¶	413 (52.1%)	266 (66.5%)	147 (37.4%)	< 0.001
Chronic renal disease**	140 (11.8%)	114 (18.9%)	26 (4.4%)	< 0.001
Chronic liver disease**	111 (9.3%)	80 (13.2%)	31 (5.3%)	< 0.001
Diabetes	285 (23.9%)	188 (31.1%)	97 (16.5%)	< 0.001
Chronic lung disease**	159 (13.4%)	98 (16.2%)	61 (10.4%)	0.001
Immunosuppression††	50 (4.2%)	13 (2.2%)	37 (6.3%)	0.001
Malignancy	58 (4.9%)	17 (2.8%)	41 (6.9%)	0.002

* Data are number (%) unless stated otherwise. † *P* values compare Indigenous with non-Indigenous subjects. ‡ Remote-dwelling was defined according to the Accessibility / Remoteness Index of Australia.[18] § Hazardous alcohol use was defined as ethanol ingestion of > 40 g/day for a man or > 20 g/day for a woman.[19] The denominator for hazardous alcohol use was 733 (Indigenous, 397; non-Indigenous, 336) due to missing data. ¶ The denominator for current smoking was 793 (Indigenous, 400; non-Indigenous, 393) due to missing data. ** Definitions for chronic renal, liver and lung disease are those used in the revised Charlson Comorbidity Index.[20] †† Immunosuppression was defined as HIV infection with CD4 counts of < 200 *or* use of any of the following medications within the past 3 months: prednisolone > 0.5 mg/kg per day (or the equivalent) for more than 14 days; immunosuppressive drugs used for bone marrow or solid organ transplantation or cancer chemotherapy. ◆

quently excluded. A subset of 184 patients from this cohort who had pneumonia have been previously reported as part of an evaluation of pneumonia scoring systems.[14]

Definitions

Acute admission was defined as any admission to the acute hospital, excluding day procedures and attendance for routine haemodialysis. More than one admission for sepsis could be counted for the same patient, but readmission within 14 days of discharge was not counted as a separate episode.

Criteria for probable or definite infection were those used in the PROWESS (Recombinant Human Activated Protein C Worldwide Evaluation in Severe Sepsis) study;[15] ie, proven infection, or suspected infection, as evidenced by one or more of the following: (i) white cells in a normally sterile body fluid; (ii) perforated viscus; (iii) radiographic evidence of pneumonia in association with the production of purulent sputum; (iv) a syndrome associated with a high risk of infection (eg, ascending cholangitis); and (v) a visible site of infection (eg, cellulitis, abscess).

Criteria for SIRS were two or more of the following: (i) body temperature ⩾ 38° C or ⩽ 36° C; (ii) heart rate ⩾ 90 beats/min; (iii) respiratory rate ⩾ 20 breaths/min or a $PaCO_2$ ⩽ 32 mmHg or the use of mechanical ventilation; and (iv) a white blood cell count ⩾ 12×10^9/L or ⩽ 4×10^9/L or > 10% band forms.

Severe sepsis was defined as sepsis plus at least one sepsis-related organ dysfunction within the first 48 hours after admission, as defined in the PROWESS study.[15]

Data management and statistical analysis

After hand-checking of all case record forms, and data entry (Epidata 3.1, EpiData Foreningen, Odense, Denmark), 10% of entries were checked for errors, with a resulting error rate of < 0.1% of fields. Denominators for population-based incidence calculations were taken from the Australian Bureau of Statistics (ABS) estimated population figures for June 2007.[16] Sepsis incidence was only calculated for patients whose current residence was within the primary catchment area of RDH; the incidence of severe sepsis requiring ICU admission was calculated using the primary catchment area for the ICU, a significantly larger area. Age-adjusted rates were calculated by the direct method, against the 2001 Standard Australian Population.[17] Comparator studies of sepsis epidemiology were included if they used a similar methodology and reported comparable data to those reported in our study.

Factors associated with mortality and readmission for sepsis were assessed using logistic regression models with backwards stepwise selection. All single variables with a Wald *P* value of ⩽ 0.10 were included in the initial model. Patients with active orders limiting life-sustaining treatment were excluded from the mortality risk-factor analysis.

Indigenous population estimates were taken from ABS data from the 2006 census.[12] Confidence intervals for age-adjusted rates were calculated using the Poisson distribution; *P* values of < 0.05 were considered significant. All statistical calculations were performed using Stata v10 (StataCorp, College Station, Tex, USA).

Ethics approval

Our study was approved by the Human Research Ethics Committee of the NT Department of Health and the Menzies School of Health Research.

RESULTS

Recruitment and baseline characteristics

There were 1191 hospital admissions for community-onset sepsis in 1090 patients

over the 12-month period (Box 1): patients' mean age was 46.7 years, 52.4% were male, and 50.7% were Indigenous. The Indigenous population differed substantially from the non-Indigenous population in demographic characteristics, comorbidities, and alcohol and tobacco use (Box 2).

Sepsis incidence

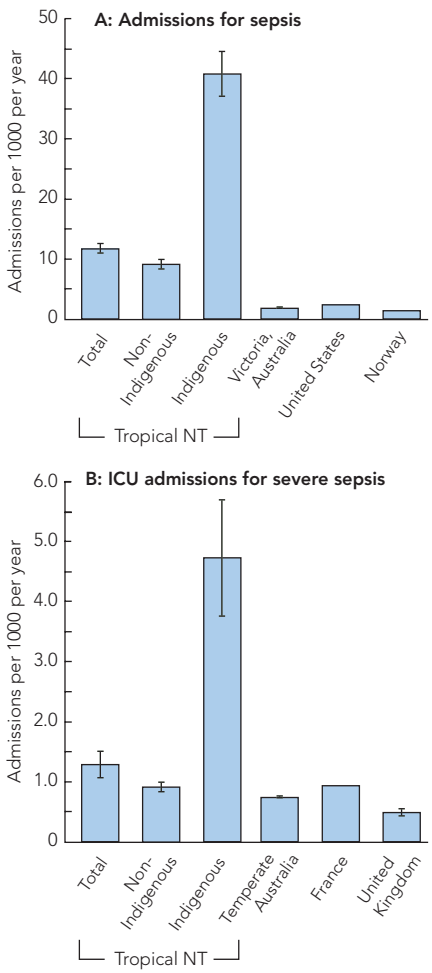
The overall population-based, age-adjusted incidence (95% CI) of sepsis was 11.8 (11.0–12.5) admissions per 1000 population per year compared with 40.8 (37.1–44.5) in Indigenous people (Box 3, A). The rates for severe sepsis requiring admission to the ICU were 1.3 (1.1–1.5) admissions per 1000 population per year overall and 4.7 (3.8–5.7) for Indigenous people (Box 3, B).

There were a total of 15 963 adult acute hospital admissions during the study period, of which the 1191 admissions with sepsis comprised 7.5%. There were 835 ICU admissions during the same period, of which community-onset sepsis accounted for 190 (22.8%) and community-onset severe sepsis for 150 (18.0%).

Details of infection

A causative organism was identified in 541 episodes of sepsis (45.4%); *Staphylococcus aureus* was the most common causative organism and *Escherichia coli* was the most common blood isolate (Box 4). Overall, the most common focus of infection was skin and soft tissue (32.8%) and, among those

3 Population-based incidence of sepsis requiring hospital admission (A) and severe sepsis requiring ICU admission (B) in the tropical Top End of the Northern Territory compared with other regions*



ICU = intensive care unit. * Data are age-adjusted number of incident cases per 1000 population per year. Vertical lines at the top of each bar represent 95% CIs, where available. Data sources: Victoria, Australia;[21] United States;[2] Norway;[10] temperate Australia;[5] France;[22] United Kingdom.[4] ◆

4 Causative organisms in patients with sepsis and an identified pathogen*

Causative organism	Overall (*n* = 541)	Blood culture positive (*n* = 193)	Community-acquired (*n* = 404)	Health care-associated indicators† (*n* = 137)
Staphylococcus aureus	136 (25.1%)	33 (17.1%)	99 (24.5%)	37 (27.0%)
MSSA	106 (19.6%)	28 (14.5%)	77 (19.1%)	29 (21.2%)
nmMRSA	28 (5.2%)	4 (2.1%)	22 (5.4%)	6 (4.4%)
mMRSA	2 (0.4%)	1 (0.5%)	0	2 (1.5%)
Escherichia coli	96 (17.7%)	56 (29.0%)	74 (18.3%)	22 (16.1%)
Group A streptococci	48 (8.9%)	12 (6.2%)	35 (8.7%)	13 (9.5%)
Mixed group A streptococci and *S. aureus*‡	29 (5.4%)	—	28 (6.9%)§	1 (0.7%)§
Streptococcus pneumoniae	27 (5.0%)	18 (9.3%)	23 (5.7%)	4 (2.9%)
Pseudomonas spp	19 (3.5%)	2 (1.0%)	10 (2.5%)¶	9 (6.6%)¶
Mixed anaerobes	19 (3.5%)	1 (0.5%)	16 (4.0%)	3 (2.2%)
Burkholderia pseudomallei	17 (3.1%)	10 (5.2%)	13 (3.2%)	4 (2.9%)
Other β-haemolytic streptococci	14 (2.6%)	9 (4.7%)	8 (2.0%)	6 (4.4%)
Haemophilus spp	13 (2.4%)	2 (1.0%)	11 (2.7%)	2 (1.5%)
Acinetobacter spp	11 (2.0%)	7 (3.6%)	9 (2.2%)	2 (1.5%)
Klebsiella spp	10 (1.8%)	5 (2.6%)	9 (2.2%)	1 (0.7%)
Viridans group streptococci	7 (1.3%)	7 (3.6%)	3 (0.7%)	4 (2.9%)
Neisseria gonorrhoeae	7 (1.3%)	2 (1.0%)	6 (1.5%)	1 (0.7%)
Proteus spp	7 (1.3%)	2 (1.0%)	3 (0.7%)	4 (2.9%)
Influenza virus	6 (1.1%)	—	6 (1.5%)	0
Nocardia spp	5 (0.9%)	1 (0.5%)	4 (1.0%)	1 (0.7%)
Milleri group streptococci	5 (0.9%)	2 (1.0%)	4 (1.0%)	1 (0.7%)
Shigella spp	5 (0.9%)	—	4 (1.0%)	1 (0.7%)
Other**	60 (11.1%)	24 (12.4%)	39 (9.7%)	21 (15.3%)
Gram-positive bacterium	285 (52.7%)	90 (46.6%)	212 (52.5%)	73 (53.3%)
Gram-negative bacterium	236 (43.6%)	101 (52.3%)	176 (43.6%)	60 (43.8%)

MSSA = methicillin-susceptible *S. aureus*. mMRSA = multiresistant methicillin-resistant. *S. aureus*. nmMRSA = non-multiresistant methicillin-resistant *S. aureus*. * An organism was considered to be the primary causative organism if it was a pathogen consistent with the clinical presentation, isolated from an appropriate specimen collected within the period from 24 hours before to 48 hours after presentation to hospital. Non-sterile site isolates were only included if they were cultured from deep pus specimens or from purulent sputum, with a predominant growth of an organism seen on Gram stain. For each episode, the single most important causative organism was selected based on the clinical presentation. † Health care-associated indicators included haemodialysis, recent chemotherapy, hospital admission within the previous 90 days, and living in a residential care facility.[23] ‡ If group A streptococci and *S. aureus* were both isolated from pus specimens, a decision on the principal causative organism was not made, and both were included. § $P = 0.005$ and ¶ $P = 0.02$, comparing community-acquired with health care-associated infections; *P* values for all other organisms were non-significant. ** "Other" includes *Enterococcus* spp, *Enterobacter* spp, *Neisseria meningitidis*, *Candida* spp, *Bacteroides* spp, Dengue virus, *Plasmodium falciparum* and *Ehrlichia chaffeensis*. ◆

with severe sepsis, pneumonia was most common (44.8%).

Predictors of mortality

Severity and outcome measures in patients with severe and non-severe sepsis, including hospital- and 28-day mortality rates, are compared in Box 5. Mortality rates were low by Australian and international standards, with 28-day mortality rates for sepsis, severe sepsis and severe sepsis requiring ICU admission of 5.4%, 17.1% and 21.5%, respectively; the corresponding mortality rates in the Indigenous subgroup were 5.7%, 15.9% and 19.3%. There was no significant difference in mortality rates between remote-dwelling (6.7%) and urban-dwelling (5.0%) patients.

On multivariate analysis, the strongest independent predictors of 28-day mortality rate were: older age, living in residential care, the number of SIRS criteria met during the first 48 hours of hospitalisation, and a serum albumin level on admission of < 35 g/L (Box 6). The crude and age-adjusted population-based sepsis mortality rates were 44.57 deaths per 100 000 per year and 80.33 deaths per 100 000 per year, respectively.

Hospital admissions for severe sepsis

Of 272 admissions for severe sepsis, 122 (44.9%) were not admitted to the ICU. Of these 122, 110 (90.2%) had none of the following factors that might modify the probability of ICU admission: active orders limiting life-sustaining treatment, metastatic cancer, or residence in a nursing home. Median (interquartile range [IQR]) APACHE II (Acute Physiology and Chronic Health Evaluation) scores and 28-day mortality rates for patients with severe sepsis admitted only to the ward were 11 (9–13) and 10.7% compared with 20 (18–22) and 21.5% for those admitted to the ICU.

Readmissions for sepsis

Of the 1090 individuals in the cohort, 81 were readmitted for sepsis, at least once, more than 14 days after hospital discharge but within the 1-year study period. Of the 101 readmission episodes, only 9 (9.0%) had the same causative organism identified. The risk of mortality at 1 year of follow-up was not significantly different in those experiencing at least one readmission (17.2%) and those who were not readmitted (12.7%). The only independent risk factors for readmission after the first episode were: end-stage renal failure (odds ratio [95% CI] 2.91 [1.35–6.23]), chronic liver disease (2.73 [1.44–5.21]) and being Indigenous (1.82 [1.11–2.99]).

5 Severity and outcome of sepsis and severe sepsis episodes*

Severity/outcome measure	Total (*n* = 1191)	Severe sepsis† (*n* = 272)	Non-severe sepsis (*n* = 919)	*P*‡
Met two SIRS criteria§	438 (36.8%)	55 (20.2%)	383 (41.7%)	< 0.001
Met three or more SIRS criteria§	753 (63.2%)	217 (79.8%)	536 (58.3%)	< 0.001
Required ICU admission	190 (16.0%)	150 (55.1%)	40 (4.4%)	< 0.001
APACHE II score (median, IQR)	8 (4–13)	16 (9–22)	6 (3–10)	< 0.001
SOFA score (median, IQR)	1 (0–3)	4 (2–7)	1 (0–2)	< 0.001
Hospital length of stay in days (median, IQR)	5 (3–11)	8 (4–18)	4 (3–9)	< 0.001
ICU length of stay in days (median, IQR)	4 (2–8)	4 (2–9)	3 (1.5–6)	0.19
Hospital mortality¶	55 (5.0%)	42 (17.1%)	13 (1.5%)	< 0.001
28-day mortality**	56 (5.4%)	39 (17.1%)	17 (2.1%)	< 0.001

SIRS = systemic inflammatory response syndrome. ICU = intensive care unit. APACHE = Acute Physiology and Chronic Health Evaluation. IQR = interquartile range. SOFA = sequential organ failure assessment.
* Data are number (%) unless stated otherwise. † Severe sepsis was defined as sepsis with consequent organ dysfunction within the first 48 hours of hospital admission. ‡ *P* values compare severe sepsis with non-severe sepsis. § Criteria as defined by Bone et al[13] (see Definitions). ¶ Denominator was 1090 (number of individual patients [245 with severe sepsis; 845 with non-severe sepsis]), rather than 1191 (number of admissions). ** As reliable follow-up after hospital discharge was only available for Northern Territory residents, the denominator was 1028 patients (228 with severe sepsis; 800 with non-severe sepsis). ◆

Differences between sepsis in Indigenous and non-Indigenous patients

In Indigenous compared with non-Indigenous patients, the focus of infection was more likely to be pneumonia (38.3% v 23.3%; $P < 0.001$) or skin and soft tissue infection (36.0% v 29.5%; $P = 0.02$) and less likely to be intra-abdominal infection (6.8% v 14.3%; $P < 0.001$). There was no significant difference in the causative organisms between Indigenous and non-Indigenous patients. Indigenous patients were more likely to have severe sepsis (27.8% v 18.1%; $P < 0.001$) and to require ICU admission (20.1% v 11.9%; $P < 0.001$) than non-Indigenous patients. However, there was no significant difference in 28-day mortality rates between Indigenous and non-Indigenous patients, either for sepsis (5.7% Indigenous v 5.2% non-Indigenous) or severe sepsis (15.9% Indigenous v 18.9% non-Indigenous). Predictors of 28-day mortality rates were not significantly different in Indigenous compared with non-Indigenous patients.

DISCUSSION

In this first description of the epidemiology of sepsis in the tropical Top End of the NT, we have found that the incidence of sepsis is fivefold higher than that in temperate Australia, the US and Europe. Most of this difference is accounted for by the extremely high incidence in Indigenous Australians. Furthermore, sepsis accounted for a substantially higher proportion of hospital and ICU admissions than has been reported elsewhere.

Compared with temperate areas of Australia,[5] and the United Kingdom[4] and France,[22] the Top End has a significantly higher population-based incidence of severe sepsis requiring ICU admission, but this difference was entirely accounted for by the extremely high incidence in Indigenous people (Box 3, B). The rates of sepsis were about six times higher in our study than those reported from Victoria, a temperate region of Australia,[21] and the US[2] (Box 3, A), and much of this difference also derives from the rates in Indigenous people.

Patients in tropical NT with severe sepsis requiring admission to the ICU were younger than comparable patients in temperate Australia and had a lower 28-day mortality rate despite similar APACHE II and SOFA (sequential organ failure assessment) scores. Among those with severe sepsis, the two most common causative organisms (*S. aureus* and *E. coli*) were the same as those found in studies in temperate Australia,[5] Canada[25] and Europe,[3] but there were significantly more gram-negative bacteria and fewer fungi among the causative organisms found in our study than in each of the other studies.

It is unclear why the incidence of sepsis is fourfold higher in Indigenous than non-Indig-

enous people. The design of our study did not allow us to determine community-based risk factors for sepsis; however, Indigenous people in our study had an excess of multiple comorbidities, which have been previously shown to increase the risk of sepsis or severe infections. These include diabetes, excessive alcohol use, chronic liver disease and end-stage renal disease. Other factors that are likely to contribute to the high burden of sepsis in Indigenous people include poor housing with a lack of health hardware (eg, water and sewerage)[26] and overcrowding.[27]

There are no previous published studies describing the population-based epidemiology of sepsis in predominantly indigenous populations. However, high rates of infectious morbidity have been reported in indigenous populations in North America, Australia and New Zealand.[9] The high rate of sepsis found in our study may reflect the high incidence of infections in Indigenous people rather than a tendency to develop sepsis in response to infection, but this hypothesis remains to be tested.

In our study, the relatively low mortality rate in patients admitted to the ICU for severe sepsis (21.5%) is consistent with mortality rates previously reported in patients with severe sepsis from RDH ICU (21%–25%),[28,29] and is lower than the predicted mortality rate based on this cohort's median APACHE II score (25.6%). This may be explained by the younger population in tropical NT compared with temperate Australia and elsewhere; if so, similar APACHE II scores, despite younger age, imply either more severe physiological disturbance or more comorbidities in our study population compared with other populations.

There are several potential limitations of our study. We did not include patients with sepsis who did not require hospital admission, making it likely that we have underestimated the true incidence of sepsis. Our population may not be representative of those in other tropical areas, and it is unclear whether our results can be generalised to these areas. The strengths of our study include its prospective design, the capturing of an entire cycle of seasons over a year, and the inclusion of all patients hospitalised for sepsis rather than only patients admitted to the ICU.

We cannot exclude the possibility that the higher incidence of sepsis in the Top End of the NT compared with incidence estimates from elsewhere reflects methodological differences. The comparator studies for sepsis incidence were all retrospective and based on discharge coding,[2,10,21] a study design that is likely to substantially underestimate the true incidence of sepsis.[11] This may explain why we found high rates of sepsis, but not of severe sepsis requiring ICU admission, in non-Indigenous people. The comparator study for severe sepsis requiring ICU admission in temperate Australia was prospective,[5] and used very similar inclusion criteria and definitions, suggesting that the observed difference in incidence in the two studies is a true phenomenon. This emphasises that the primary finding of our study is the high rate of sepsis in Indigenous people, rather than in residents of the tropical NT in general.

6 Risk factors for 28-day mortality on univariate and multivariate analysis,* grouped according to the PIRO system

Risk factor	Univariate analysis† Odds ratios (95% CI)§	Multivariate analysis‡ Odds ratios (95% CI)§
Predisposing factors		
Age ⩾ 45 years¶	2.7 (1.4–5.3)	2.3 (1.1–4.7)
Age ⩾ 65 years¶	6.1 (3.1–12.1)	5.6 (2.7–11.6)
Female sex	0.6 (0.4–0.9)	—
Residential care	5.7 (2.2–14.0)	5.7 (1.7–18.0)
Chronic lung disease	3.5 (2.1–6.1)	—
Chronic renal disease**	2.5 (1.4–4.6)	2.1 (1.0–4.4)
Infection characteristics		
Skin or soft tissue focus††	0.12 (0.04–0.34)	0.30 (0.10–0.88)
Pneumonia	3.0 (1.8–4.9)	—
Bacteraemia	2.9 (1.7–5.0)	—
Response to infection		
Met three SIRS criteria‡‡	5.70 (2.18–14.85)	4.1 (1.4–12.0)
Met four SIRS criteria‡‡	11.4 (4.4–30.0)	5.2 (1.8–15.0)
Albumin < 35 g/L§§	6.6 (3.8–11.0)	4.9 (2.3–10.0)
Bilirubin	1.01 (1.01–1.02)	—
Acute confusion	5.9 (2.9–12.3)	1.3 (1.1–1.6)
Platelet count	0.996 (0.994–0.999)	—
Mean arterial pressure	0.966 (0.944–0.988)	—
Oxygen saturation	0.859 (0.787–0.936)	—
Organ dysfunction		
Septic shock	7.1 (4.3–11.8)	2.3 (1.1–4.5)
Acute renal failure	6.9 (3.3–14.0)	3.7 (1.6–8.6)
Acute respiratory failure	4.2 (2.2–8.1)	2.7 (1.3–5.7)
Acidosis	4.3 (2.2–8.4)	—

PIRO = predisposition, infection characteristics, response to infection, organ dysfunction.[24]
SIRS = systemic inflammatory response syndrome.
* Data were analysed by logistic regression analysis with backward stepwise elimination. † Only significant variables are shown. ‡ Only variables remaining in the final model are shown. § Odds ratios are given to one or two significant figures except for continuous dependent variables, where three significant figures are used. ¶ Comparator = age ⩽ 44 years. ** Defined as usual serum creatinine level > 150 μmol/L, or receiving chronic haemodialysis or peritoneal dialysis. †† Compared with all other foci of infection. ‡‡ Met SIRS criteria[13] within a 24-hour period in the first 48 hours of hospital admission (comparator: two SIRS criteria). §§ Lowest serum albumin concentration within first 24 hours of hospitalisation (comparator: albumin level ⩾ 35 g/L). ◆

In conclusion, the incidence of sepsis in the tropical Top End of the NT is substantially higher than that in temperate Australia and other countries, and this difference is largely explained by higher rates in Indigenous people. Efforts at decreasing this burden should focus on improving housing and access to health services, and addressing comorbidities, and alcohol and tobacco use. Prospective studies are needed in indigenous populations globally to define the burden of sepsis and to inform appropriate resourcing of health services and community-based treatment and prevention strategies.

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COMPETING INTERESTS

None identified.

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