The burden of invasive infections in critically ill Indigenous children in Australia

Justyna A Ostrowski[1,2], Graeme MacLaren[3,4,5], Janet Alexander[6], Penny Stewart[7], Sheena Gune[7], Joshua R Francis[8,9], Subodh Ganu[10], Marino Festa[11], Simon J Erickson[12], Lahn Straney[13], Luregn J Schlapbach[1,2,14]

The known Sepsis is one the main causes of death in children worldwide. Childhood mortality in high income countries is higher in indigenous populations, but the contribution of infections to excess mortality in this vulnerable group is unknown.

The new Intensive care unit admission rates for invasive infections were higher for Aboriginal and/or Torres Strait Islander children than for non-Indigenous Australians, particularly for staphylococcal infections, and the population-based ICU mortality attributable to infections was more than twice that of non-Indigenous children.

The implications Our results highlight an important area of health care inequity in a high income country that must be redressed.

Abstract

Objectives: To describe the incidence and mortality of invasive infections in Indigenous children admitted to paediatric and general intensive care units (ICUs) in Australia.

Design: Retrospective multi-centre cohort study of Australian and New Zealand Paediatric Intensive Care Registry data.

Participants: All children under 16 years of age admitted to an ICU in Australia, 1 January 2002 – 31 December 2013. Indigenous children were defined as those identified as Aboriginal and/or Torres Strait Islander in a mandatory admissions dataset.

Main outcomes: Population-based ICU mortality and admission rates.

Results: Invasive infections accounted for 23.0% of non-elective ICU admissions of Indigenous children (726 of 3150), resulting in an admission rate of 47.6 per 100 000 children per year. *Staphylococcus aureus* was the leading pathogen identified in children with sepsis/septic shock (incidence, 4.42 per 100 000 Indigenous children per year; 0.57 per 100 000 non-Indigenous children per year; incidence rate ratio 7.7; 95% CI, 5.8–10.1; *P* < 0.001). While crude and risk-adjusted ICU mortality related to invasive infections was not significantly different for Indigenous and non-Indigenous children (odds ratio, 0.75; 95% CI, 0.53–1.07; *P* = 0.12), the estimated population-based age-standardised mortality rate for invasive infections was significantly higher for Indigenous children (2.67 per 100 000 per year *v* 1.04 per 100 000 per year; crude incidence rate ratio, 2.65; 95% CI, 1.88–3.64; *P* < 0.001).

Conclusions: The ICU admission rate for severe infections was several times higher for Indigenous than for non-Indigenous children, particularly for *S. aureus* infections. While ICU case fatality rates were similar, the population-based mortality was more than twice as high for Indigenous children. Our study highlights an important area of inequality in health care for Indigenous children in a high income country that needs urgent attention.

Of the estimated 6.3 million deaths of children under 5 years of age worldwide in 2013, 51.8% were attributable to infectious diseases.[1,2] While most infection-related deaths occur in low income countries, infectious diseases also continue to cause significant mortality in high income countries.[3] We have recently reported that the incidence of severe infections in children that require admission to an intensive care unit (ICU) was increasing in Australia and New Zealand,[4] consistent with recent reports from the United States.[5] About 25% of deaths in paediatric ICUs are related to severe infections, and case fatality rates are as high as 17%.[4]

In countries such as Canada, the US, Australia and New Zealand, indigenous status is a risk factor for childhood mortality because of a complex interplay of factors, including remoteness and access to health care, socio-economic and educational resources.[6] In Australia, children of Aboriginal and Torres Strait Islander background are more than twice as likely to die during childhood than non-Indigenous Australian children.[6] Indigenous Australian children have a higher risk of contracting infectious diseases, including otitis media and pyoderma, as well as invasive infections, including bloodstream infections, pneumonia and bronchiectasis;[7-11] invasive infection rates are comparable with those in low and middle income countries. While the population-based incidence of sepsis, ICU admission, and mortality are reported to be significantly higher for Indigenous Australian adults,[9] analogous data for Indigenous children have not been published.

In this article we report on severe infections in Indigenous children in Australia, using the previously published Australian and New Zealand paediatric sepsis study dataset.[4] The aim of our study was to assess the epidemiology and mortality of severe infections in critically ill Indigenous Australian children, and to compare them with those for Australian children of non-Indigenous background.

Methods

We performed a multi-centre, retrospective national cohort study of Australian and New Zealand Paediatric Intensive Care (ANZPIC) Registry data (http://www.anzics.com.au/pages/CORE/ANZPICR-registry.aspx). The ANZPIC Registry is a state-funded mandatory registry that prospectively records data for paediatric admissions to all Australian and New Zealand paediatric and general ICUs, collected by trained ICU data collectors, with central data validation and auditing. Details of our study methods and use of registry data have been published

[1] Mater Research Institute, University of Queensland, Brisbane, QLD. [2] Lady Cilento Children's Hospital, Brisbane, QLD. [3] University of Melbourne, Melbourne, VIC. [4] Royal Children's Hospital, Melbourne, VIC. [5] National University Health System, Singapore, Singapore. [6] Australian and New Zealand Paediatric Intensive Care Registry (CORE), Brisbane, QLD. [7] Alice Springs Hospital, Alice Springs, NT. [8] Royal Darwin Hospital, Darwin, NT. [9] Menzies School of Health Research, Charles Darwin University, Darwin, NT. [10] Women's and Children's Hospital Adelaide, Adelaide, SA. [11] Children's Hospital at Westmead, Sydney, NSW. [12] Princess Margaret Hospital for Children, Perth, WA. [13] Monash University, Melbourne, VIC. [14] Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland. ✉ l.schlapbach@uq.edu.au ▪ doi: 10.5694/mja16.00595 ▪ See Editorial, p. 000 ▪ Online first 30/01/17

previously.[4] Only data from Australian units were included in the analysis reported in this article.

Our primary study group included Indigenous children less than 16 years of age who required non-elective admission to a paediatric or general ICU in Australia between 1 January 2002 and 31 December 2013. Indigenous status was defined by identification of the child as Aboriginal and/or Torres Strait Islander in the ANZPIC dataset. Non-Indigenous children under 16 years of age who required non-elective admission to an ICU in Australia during the same period served as a comparison group.

Infection groups were defined according to the diagnostic coding for each patient in the ANZPIC Registry, including the principal diagnosis, underlying diagnosis, and any of the associated diagnoses. "Invasive infection" included sepsis, septic shock, toxic shock, meningitis, pneumonia/pneumonitis, peritonitis, necrotising fasciitis, septic arthritis, osteomyelitis, endocarditis, tracheitis, and epiglottitis. We performed subgroup analyses of data for children with coded diagnoses of sepsis, septic shock or toxic shock. Sepsis and septic shock were defined according to the consensus definition.[12]

The primary outcome was ICU mortality. Severity of illness at ICU admission was assessed with the Paediatric Index of Mortality 2 (PIM2).[13] Secondary outcomes included duration of invasive and non-invasive ventilation, length of stay in the ICU, length of stay in hospital, hospital mortality, and blood culture results.

The following comorbidities and underlying disease groups were defined: premature birth (earlier than 37 weeks' gestation), congenital heart disease, chronic pulmonary disease, chronic renal disease, chronic neurological disease (encephalopathy, chronic central or peripheral nervous system disease), burns, and immunodeficiency or immunosuppression (with subgroups: haematological or solid organ tumour, status post-bone marrow transplantation, and solid organ transplant recipients).

Age-specific population data were obtained from the Australian Bureau of Statistics.[14] Age-standardised admission rates were calculated with reference to the 2013 Indigenous population.[15] Non-Indigenous admission rates were age-standardised with reference to 2013 non-Indigenous Australian population figures.[14]

Statistical analysis

Data are presented as numbers and percentages, or as means with standard deviations. Means for subgroups were compared in t tests. Admission rates were calculated for estimating population-based incidence and mortality rates. Rates were compared as incidence rate ratios, and proportions for Indigenous and non-Indigenous admissions were compared in exact binomial tests.

Analyses included every ICU admission. We compared differences between the first 6 years of the study (2002−2007: initiation of the "Surviving Sepsis Campaign", after publication of the sepsis consensus definition), and the second 6 years of the study (2008−2013: period following publication of the second edition of the "Surviving Sepsis" guidelines[16]). In addition, trends during the 12-year study period were assessed by linear regression. We used the PIM2 score to adjust for the severity of illness of children. For risk prediction models, we used a saturated logistic regression model, clustering on site. For multivariable models, all significant predictors from the univariable analyses were included. We used a backward stepwise elimination procedure to eliminate non-significant predictors ($P > 0.05$). The severity of illness for Indigenous and non-Indigenous children admitted to an ICU were compared in a Wilcoxon rank-sum test.

We used the 2006 Australian Bureau of Statistics Remoteness Structure to classify each patient's residential postcode as a major city, inner regional, outer regional, remote, or very remote Australia. Where postcodes contained different remoteness classifications, we assigned the classification applicable to the greater land area of the postcode.[17]

All analyses were conducted in Stata 12.1 (StataCorp). $P < 0.05$ was deemed statistically significant.

Ethics approval

The development of the research proposal was conducted in consultation with local Aboriginal Liaison officers and medical experts working with Aboriginal and Torres Strait Islander children in ICUs, and in accordance with national guidelines for ensuring cultural sensitivity. Approval was obtained from the Mater Health Services Aboriginal liaison officer. Ethics approval, including for waiver of informed consent, was obtained from the Mater Health Services Human Research Ethics Committee, Brisbane (reference, MHS HREC EC00332; HREC/13/MHS/153/AM02). The Registry was approved by the Human Research and Ethics Committee of the Royal Children's Hospital (Brisbane).

Results

Study population

During 1 January 2002 − 31 December 2013, 82 750 children were admitted to a paediatric or general ICU in Australia; 4864 (5.9%) were of Indigenous (Aboriginal and/or Torres Strait Islander) background. Data for the 3150 Indigenous children who were non-electively admitted (65% of Indigenous patients) were included in our study. The proportion of children admitted to an ICU who were Indigenous Australians increased slightly but significantly over the study period, from 4.9% in 2002 to 6.3% of admissions in 2013 (0.13% per year; 95% confidence interval [CI], 0.01−0.17%; $P = 0.037$).

Invasive infections accounted for 23.0% of non-elective admissions of Indigenous children to ICUs (726 of 3150), compared with 17.3% for non-Indigenous children (8002 of 46 238; $P < 0.001$); 9.6% of Indigenous patients (303 of 3150) presented with severe sepsis or septic shock. The median age of Indigenous children at admission with invasive infections was 1.7 years (interquartile range [IQR], 0.4−6.7; range, 0−16 years), and 405 (55.8%) were boys. Overall, 39.7% of Indigenous patients with invasive infections had a major comorbidity. Detailed demographic and clinical data for patients with or without sepsis/septic shock are included in Box 1.

Admission rates

The estimated population-based age-standardised ICU admission rate for Indigenous children for all invasive infections was 47.6 per 100 000 children per year, rising from 30.7 in 2002 to 72.0 per 100 000 in 2013; the mean annual increase in this rate was 2.61 per 100 000 children per year (95% CI, 1.20−4.02; $P = 0.002$). The population-based admission rate for sepsis/septic shock was estimated to be 19.8 per 100 000 children per year, rising from 14.3 in 2002 to 34.8 per 100 000 in 2013; the mean annual increase in this rate was 1.45 per 100 000 children per year (95% CI, 0.62−2.28; $P = 0.003$; Box 2, Appendix 1).

The estimated population-based admission rate of non-Indigenous patients for all invasive infections was 15.9 per 100 000 children per year (annual increase, 0.67 per 100 000 children per year; 95% CI, 0.42−0.90; $P < 0.001$). The population-based admission rate for

1 Baseline characteristics and severity of disease at admission for Indigenous children admitted to an intensive care unit (ICU) with an invasive infection

	Invasive infection without sepsis/septic shock	Invasive infection with sepsis/septic shock
Number of children	423	303
Age of child		
Median (IQR), years	1.6 (0.4−5.5)	1.9 (0.4−8.5)
Neonates (< 28 days old)	8 (1.9%)	19 (6.3%)
Infants (28−364 days old)	162 (38.3%)	95 (31.4%)
1−4 years old	138 (32.6%)	88 (29.0%)
5−9 years old	59 (14.0%)	43 (14.2%)
10−15 years old	56 (13.2%)	58 (19.1%)
Sex		
Boys	235 (55.6%)	170 (56.1%)
Admission category		
Direct paediatric ICU admission*	284 (67.1%)	219 (72.3%)
Inter-hospital transport	180 (42.6%)	140 (46.2%)
Risk category		
Any comorbidity	148 (35.0%)	140 (46.2%)
Immunodeficiency or immunosuppression†		
Oncology‡	6 (1.4%)	19 (6.3%)
Bone marrow transplantation	4 (0.9%)	2 (0.6%)
Transplantation‡	0	1 (0.3%)
Chronic neurological disease	42 (9.9%)	18 (5.9%)
Chronic respiratory disease	38 (9.0%)	14 (4.6%)
Congenital heart disease	13 (3.1%)	17 (5.6%)
Premature birth	27 (6.4%)	30 (9.9%)
Burns	6 (1.4%)	10 (3.3%)
Chronic renal failure	4 (0.9%)	1 (0.3%)
Severity		
Mean ICU length of stay (SD), days	5.2 (9.6)	6.8 (8.3)
Mechanical ventilation in the first hour	222 (52.5%)	161 (53.1%)
Intubation and ventilation	256 (60.5%)	215 (71.0%)
Mean PIM2 score (range)	5.0% (0.2−95.6%)	8.4% (0.2−99.5%)
Extracorporeal membrane oxygenation	1 (0.2%)	7 (2.3%)
Acute respiratory distress syndrome	7 (1.7%)	14 (4.6%)
Renal replacement therapy	4 (0.9%)	11 (3.6%)

PIM2 = Paediatric Index of Mortality 2 (mean probability of death). * Other admissions were to mixed ICUs. † Including primary immunodeficiency and secondary immunodeficiency (oncology, bone marrow transplantation, other transplantation, other immunosuppression). ‡ Excluding bone marrow transplantation. ◆

12.3%), peritonitis (22 of 726, 3.0%), and osteomyelitis (16 of 726, 2.2%). The main pathogens identified in critically ill Indigenous children admitted with sepsis/septic shock were *Staphylococcus aureus* (22% of patients) and *Neisseria meningitidis* (11%; Box 3). A bacterial aetiology was identified in 54% of patients and a viral co-infection was reported in 11% of cases. No pathogen was recorded for 38% of episodes of sepsis/septic shock. The proportion of patients diagnosed with *N. meningitidis* infection decreased from 16% in 2002−2007 to 8% of those with sepsis/septic shock during 2008−2013 ($P = 0.044$), but no substantial changes in the frequency of infection with other pathogens were observed.

The estimated population-based *S. aureus* sepsis admission rate was 4.42 per 100 000 children per year for Indigenous children and 0.57 per 100 000 children per year for non-Indigenous children (rate ratio, 7.7; 95% CI, 5.8−10.1; $P < 0.001$).
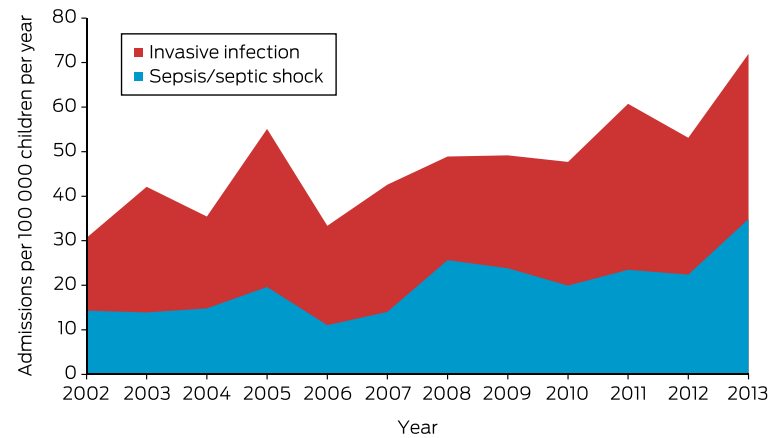
Outcomes

The mean ICU and hospital lengths of stay for Indigenous children with an invasive infection were 5.8 and 26.9 days respectively. The crude ICU mortality for all invasive infections in Indigenous children was 5.6% (41 of 726), and 8.3% among those with sepsis/septic shock (25 of 303); the rates for non-Indigenous children were 6.5% and 10.2% respectively (data not shown). The predicted risk of death for non-Indigenous children (PIM2 score) was significantly lower in 2008−2013 than in 2002−2007, but there was no clinically or statistically significant decline in scores for Indigenous children (Appendix 2). After adjusting for PIM2 score in logistic regression, there was no significant difference in mortality between Indigenous and non-Indigenous children (odds ratio, 0.75; 95% CI, 0.53−1.07; $P = 0.12$). Invasive infections were involved in 29.3% of deaths of Indigenous children with a non-elective ICU admission. We estimated a population-based age-standardised ICU mortality rate for invasive infections in Indigenous children of 2.67 per 100 000 children per year, compared with 1.04 per 100 000 children per year for non-Indigenous children (rate ratio, 2.65; 95% CI, 1.88−3.64; $P < 0.001$).

Univariate logistic regression models (Box 4, Appendix 3) identified that a comorbidity (in particular, immunosuppression or chronic neurological disease) and severity markers (including need for mechanical ventilation, extracorporeal membrane oxygenation, and renal replacement) were significant predictors of mortality of Indigenous children with invasive infections. In multivariate analyses, immunosuppression, chronic neurological disease, and need for mechanical ventilation or renal replacement remained significantly associated with mortality; the strongest effect size was associated with the need for mechanical ventilation. Similar findings were made for children with sepsis, except that congenital heart disease, rather than immunosuppression or neurological disease, was a significant predictor of mortality in both uni- and multivariate analyses.

sepsis/septic shock was estimated to be 6.8 per 100 000 children per year (annual increase, 0.15 per 100 000 children per year; 95% CI, 0.05−0.26; $P = 0.009$).

Infection focus and pathogens

The most frequent invasive infectious conditions in Indigenous patients were pneumonia (394 of 726, 54.3%), meningitis (89 of 726,

Discussion

This is the largest study to have examined life-threatening infections in Indigenous Australian children, exploring an important area of

2 Age-standardised admission rate of Indigenous children to intensive care units for all invasive infections

causing significant excess childhood mortality. In contrast to previous studies that focused on mild to moderate infections, our study examined severe, life-threatening infections. During 2002–2013, the ICU admission rate for invasive infections was three times as high for Indigenous as for non-Indigenous children (47.6 v 15.9 per 100 000 children per year); the estimated population-based ICU mortality attributable to invasive infections was more than double that for non-Indigenous children.

Our findings parallel reports of disproportionate infectious disease burdens in other indigenous populations.[6,8,18-20] High rates of infectious diseases, including ear and respiratory tract infections, have consistently been reported for Canadian First Nations, Inuit and Métis peoples, Native Americans, Alaskan and Hawaiian Natives, and New Zealand Pacific and Māori peoples. Children in these populations experience poorer overall health outcomes than non-indigenous children, including higher infant and childhood mortality.[6] Risk factors that contribute to the high incidence of infectious diseases among indigenous children include lower socio-economic status, overcrowding, poor access to sanitation, clean water and health facilities, and differences in hygiene and health-seeking behaviour.[21]

health inequity in a high income country. Our population-based study of more than 3000 Indigenous children admitted to ICUs found a disproportionately high burden of disease associated with invasive infections in Aboriginal and Torres Strait Islander children,

3 Identified pathogens in Indigenous children admitted to an intensive care unit with sepsis or septic shock

	Year of admission			
	2002–2007	2008–2013	P*	2002–2013
Number of patients	108	195		303
Bacterial				
Staphylococcus aureus (methicillin-sensitive or -resistant)	21 (19%)	46 (24%)	0.40	67 (22%)
Neisseria meningitidis	17 (16%)	16 (8%)	0.044	33 (11%)
Streptococcus pneumoniae	2 (2%)	9 (5%)	0.22	11 (4%)
Coagulase-negative *Staphylococcus*	0	2 (1%)	0.29	2 (1%)
Group A *Streptococcus, Streptococcus viridans*	6 (6%)	11 (6%)	0.98	17 (6%)
Group B *Streptococcus*	0	1 (1%)	0.46	1 (< 1%)
Escherichia coli	4 (4%)	4 (2%)	0.39	8 (3%)
Pseudomonas aeruginosa	4 (4%)	4 (2%)	0.39	8 (3%)
Klebsiella spp.	1 (1%)	6 (3%)	0.23	7 (2%)
Haemophilus influenzae type B	2 (2%)	0	0.057	2 (1%)
Other bacteria	8 (7%)	25 (13%)	0.15	33 (11%)
Any bacteria	**56 (52%)**	**108 (55%)**	**0.55**	**164 (54%)**
Fungal				
Candida, Aspergillus spp., other fungus	5 (5%)	13 (7%)	0.47	18 (6%)
Viral co-infection				
Influenza	2 (2%)	2 (1%)	0.55	4 (1%)
Parainfluenza	0	2 (1%)	0.29	2 (1%)
Respiratory syncytial virus	2 (2%)	7 (4%)	0.39	9 (3%)
Adenovirus	1 (1%)	7 (4%)	0.17	8 (3%)
Cytomegalovirus, Epstein–Barr, herpes simplex, varicella zoster viruses	1 (1%)	5 (3%)	0.33	6 (2%)
Enterovirus	0	2 (1%)	0.29	2 (1%)
Other viruses	1 (1%)	3 (2%)	0.66	4 (1%)
Any viral co-infection	**7 (6%)**	**26 (13%)**	**0.067**	**33 (11%)**
No bacterial, fungal or viral organism identified	**47 (44%)**	**67 (34%)**	**0.12**	**114 (38%)**

* 2002–2007 v 2008–2013. ◆

4 Summary of uni- and multivariate models for mortality associated with invasive infections in Indigenous (Aboriginal and Torres Strait Islander) children requiring intensive care unit (ICU) admission*

A. All invasive infections

	Patients	Deaths	Univariable analysis		Multivariable analysis	
			Odds ratio	P	Odds ratio	P
Total invasive infection cases	726	41 (5.6%)				
Remoteness: No significant differences						
Age†						
5–9 years old	102 (14.1%)	11 (27%)	2.70 (1.13–6.45)	0.025		
Risk category						
Immunodeficiency or immunosuppression	33 (4.6%)	6 (15%)	4.18 (1.62–10.8)	0.003	4.94 (1.59–15.4)	0.006
Oncology‡	25 (3.4%)	2 (4.9%)	1.48 (0.34–6.49)	0.61		
Bone marrow transplantation	6 (0.8%)	2 (4.9%)	8.73 (1.55–49.1)	0.014		
Solid organ transplant‡	1 (0.1%)	0	—			
Chronic neurological condition	60 (8.3%)	7 (17%)	2.46 (1.04–5.80)	0.041	2.58 (1.05–6.33)	0.039
Any comorbidity	288 (39.7%)	25 (61%)	2.51 (1.31–4.78)	0.005	—	
ICU size: No significant differences						
Admission category: No significant differences						
Time period						
2002–2007	295 (40.6%)	14 (34%)	Reference			
2008–2013	431 (59.4%)	27 (66%)	1.34 (0.69–2.60)	0.38		
Severity						
Intubation and mechanical ventilation	471 (64.9%)	40 (98%)	23.6 (3.22–172)	0.002	21.5 (2.88–160)	0.003
Extracorporeal membrane oxygenation	8 (1.1%)	3 (7.3%)	10.7 (2.47–46.6)	0.002	2.81 (0.45–17.4)	0.27
Acute respiratory distress syndrome	21 (2.9%)	4 (9.8%)	4.25 (1.36–13.3)	0.013	1.37 (0.34–5.49)	0.66
Renal replacement therapy	15 (2.1%)	6 (15%)	12.9 (4.34–38.2)	< 0.001	5.32 (1.45–19.5)	0.012

B. Children admitted with sepsis or septic shock

	Patients	Deaths	Univariable analysis		Multivariable analysis	
			Odds ratio	P	Odds ratio	P
Total non-elective sepsis and septic shock cases	303	25 (8.3%)				
Remoteness: No significant differences						
Age: No significant differences						
Risk category						
Congenital heart disease	17 (5.6%)	4 (16%)	3.88 (1.16–13.0)	0.027	4.39 (1.23–15.64)	0.023
ICU size: No significant differences						
Admission category: No significant differences						
Time period						
2002–2007	108 (35.6%)	6 (24%)	Reference			
2008–2013	195 (64.4%)	19 (76%)	1.84 (0.71–4.74)	0.21		
Severity						
Intubation and mechanical ventilation	215 (71.0%)	24 (96%)	10.9 (1.46–82.1)	0.020	8.04 (1.05–61.6)	0.045
Extracorporeal membrane oxygenation	7 (2.3%)	3 (12%)	9.34 (1.97–44.4)	0.005	1.97 (0.31–12.6)	0.48
Acute respiratory distress syndrome	14 (4.6%)	3 (12%)	3.31 (0.86–12.8)	0.082	1.73 (0.37–8.18)	0.49
Renal replacement therapy	11 (3.6%)	5 (20%)	11.3 (3.18–40.4)	< 0.001	6.77 (1.52–30.0)	0.012

ICU = intensive care unit. * Full results of the analyses are included in Appendix 3. † Reference: infants (28–364 days old); ‡ Excluding bone marrow transplantation. ◆

These key social and economic factors, recognised as major causes of poor health in low income countries, must also receive attention in high income countries if we are to improve national and global health outcomes for disadvantaged groups.[22]

Remoteness and difficulties in access to health care may also significantly increase the incidence of invasive infections in indigenous children that require treatment in ICUs, as delays in initiating appropriate treatment allow disease progression.[23]

This is consistent with our finding that Indigenous Australian children admitted to ICUs with invasive infections had higher median illness severity scores (PIM2) than non-Indigenous children during 2008−2013. This finding also suggests that a lower admission threshold for Indigenous children is unlikely to have contributed to their higher admission rate in our study. Further investigations in which outcomes are stratified according to the length of time to medical care may clarify the impact of remoteness on outcomes for children with infectious diseases.

The incidence of pneumococcal, group A streptococcal, and meningococcal disease in Indigenous Australian children has been reported to be 2−10 times that for non-Indigenous children residing in the same geographical area, despite 7-valent pneumococcal and meningococcal C vaccinations.[20,24,25] We measured a significant decrease in meningococcal sepsis among Indigenous children that coincided with the introduction of the conjugate meningococcal vaccine. While expanding targeted vaccination may lead to further reductions in bacterial sepsis rates, vaccine-based interventions are unlikely to be available soon for *S. aureus*, identified in 40% of Indigenous patients from whom bacteria were isolated in our study. In the overall Australian and New Zealand paediatric sepsis ICU study,[4] only 10% of sepsis cases were attributable to *S. aureus*, comparable with other cohorts.[26] Prospective studies that assess the continuing impact of vaccinations on severe infection rates among Indigenous children in Australia are needed to further define this important area of public health.

Very high rates of invasive staphylococcal infection have been reported in adult and paediatric Indigenous populations in Australia.[11] Excess rates of *S. aureus* infection have also been documented among Māori, Pacific Islanders and Samoans in New Zealand, Canadian Aboriginals, Alaskan Natives, Pacific Islanders in Hawaii, and Native Americans. Miles and colleagues[27] found that 81% of patients admitted to paediatric ICUs in New Zealand for invasive *S. aureus* infections were Pacific Island and Māori children, although these ethnic groups comprise only 22% of the population. It is possible that genetic susceptibility may contribute to differences in biological susceptibility to sepsis,[21] but further research is needed to clarify this question.

A number of limitations of our study need to be considered. It was based on a prospective paediatric ICU registry that does not capture infectious disease outcomes for newborns in neonatal nurseries or for children who die before they can be admitted to an ICU. The ANZPIC Registry captures 92−94% of paediatric patients admitted to ICUs in Australia, and the number of general ICUs contributing data to the registry increased during the study period. Admissions to general ICUs represented 17.1% of non-elective admissions recorded by this registry during 2008−2013, and 9.4% of admissions during 2002−2007. We therefore cannot exclude the possibility that we underestimated the true population-based incidence of severe infections.

Our primary outcome measure was ICU mortality. We did not detect major changes over time in mortality for Indigenous children admitted to ICUs with severe infections, but our study was not powered for subgroup mortality analyses. It is noteworthy that using mortality as an endpoint does not capture the impact of ICU admission on quality of life and health after discharge; clinically significant short and long term effects in former paediatric ICU patients have been documented.[27,28] Finally, Indigenous children in Australia live in diverse environments, ranging from cities to remote Indigenous communities. Our study did not stratify outcomes according to these potentially important differences, nor did we have access to data on socioeconomic status.

Conclusion

Children of Aboriginal and Torres Strait Islander background were three times more likely to be admitted to an ICU for severe infections than non-Indigenous children during 2002−2013, and the population-based mortality attributable to infections in Indigenous children was more than twice that for non-Indigenous children. Our study highlights an important area of inequality in health care for Indigenous children that requires urgent attention. Further research is needed to define risk factors and to develop and assess appropriately targeted interventions.

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