Disparities in patient mortality following intensive care admission due to adult community-acquired sepsis in Aotearoa New Zealand, 2009–2019

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ABSTRACT

AIM: To characterise patient mortality risk following intensive care unit (ICU) admitted community-acquired sepsis (CAS) in Aotearoa New Zealand (Aotearoa), comparing in-hospital and post-discharge mortality and associated risk factors.

METHODS: We examined de-identified, linked ICU-admitted adult patient data from ICU sites in Aotearoa retrieved from the Australian and New Zealand Intensive Care Society's CORE adult patient database (ANZICS-CORE-APD) between 2009 and 2019. Patients were followed from ICU admission to death or 365 days post-hospital discharge alive, using descriptive, survival and regression analyses. The outcomes of interest were in-hospital mortality and post-discharge mortality during the first 365 days.

RESULTS: In-hospital mortality was 16.3%. Post-discharge mortality was 3.6% by 30 days after discharge, 9.1% by 180 days and 12.9% by 365 days. There was no significant difference in in-hospital mortality risk by ethnicity or New Zealand Index of Deprivation quintile of usual residence. By contrast, significant differences in post-discharge survival were observed by ethnicity, area deprivation quintile and presence of severe comorbidities, particularly for Māori usually resident in high-deprivation areas.

CONCLUSIONS: There was no evidence of associations between in-hospital mortality and ethnicity or socio-economic deprivation; however, these associations become marked post-discharge. Interventions should be implemented to support early identification and management of CAS and address health inequities following hospital discharge.

Sepsis, organ failure resulting from a dysfunctional response to infection,[1] is a common cause of ICU admission and in-hospital mortality in high-income countries. Due to improved sepsis screening, identification and treatment, in-hospital mortality due to sepsis is decreasing, although this is experienced differentially between patient populations.[2] Sepsis survival is associated with ongoing immune dysfunction, organ system impairment, hospital readmission and an increased risk of post-discharge mortality.[3–6] Disproportionately affecting older, immunocompromised, socio-economically and ethnically marginalised patient populations, sepsis-associated mortality is a substantial public health concern.

Aotearoa New Zealand has an ageing and multimorbid population, with significant health disparities existing between Māori, Pacific peoples and non-Māori, non-Pacific populations, and those living in areas with high socio-economic deprivation scores.[7,8] Exacerbated by the ongoing effects of colonisation, marginalisation and systemic violence, the life expectancy of Māori is substantially lower than that of non-Māori.[9,10] Patient populations of Māori ethnicity and those resident in areas with high socio-economic deprivation scores frequently have disparate rates of chronic disease, multimorbidity and hospitalisations compared to non-Māori populations and those resident in areas with the lowest socio-economic deprivation scores.[7,8] Increasing age, chronic comorbidities and multimorbidity are significant risk factors for sepsis-associated intensive care unit (ICU) admission and in-hospital mortality.[11]

Emerging research suggests ethnic and socio-economic deprivation disparities observed in chronic disease incidence may similarly translate into patient outcomes following sepsis-associated ICU admission in Aotearoa. A cohort study conducted over 5 years in the Waikato Region identified significant ethnic and age disparities in sepsis incidence and sepsis-associated mortality.[12] Similarly, a large, retrospectively designed, prospective cohort study characterising ethnic disparities in overall ICU admissions in

Aotearoa identified Māori as having an increased likelihood of ICU admission due to sepsis compared to non-Māori.[13]

There is a scarcity of research characterising adult ICU admission due to community-acquired sepsis (CAS) and the associated mortality risk, both in-hospital and following hospital discharge in Aotearoa. Therefore, we characterised patient outcomes following a CAS-associated ICU admission in Aotearoa between 2009 and 2019 by describing mortality and mortality risk associated with variables identifiable at hospital admission by admission status.

Materials and methods

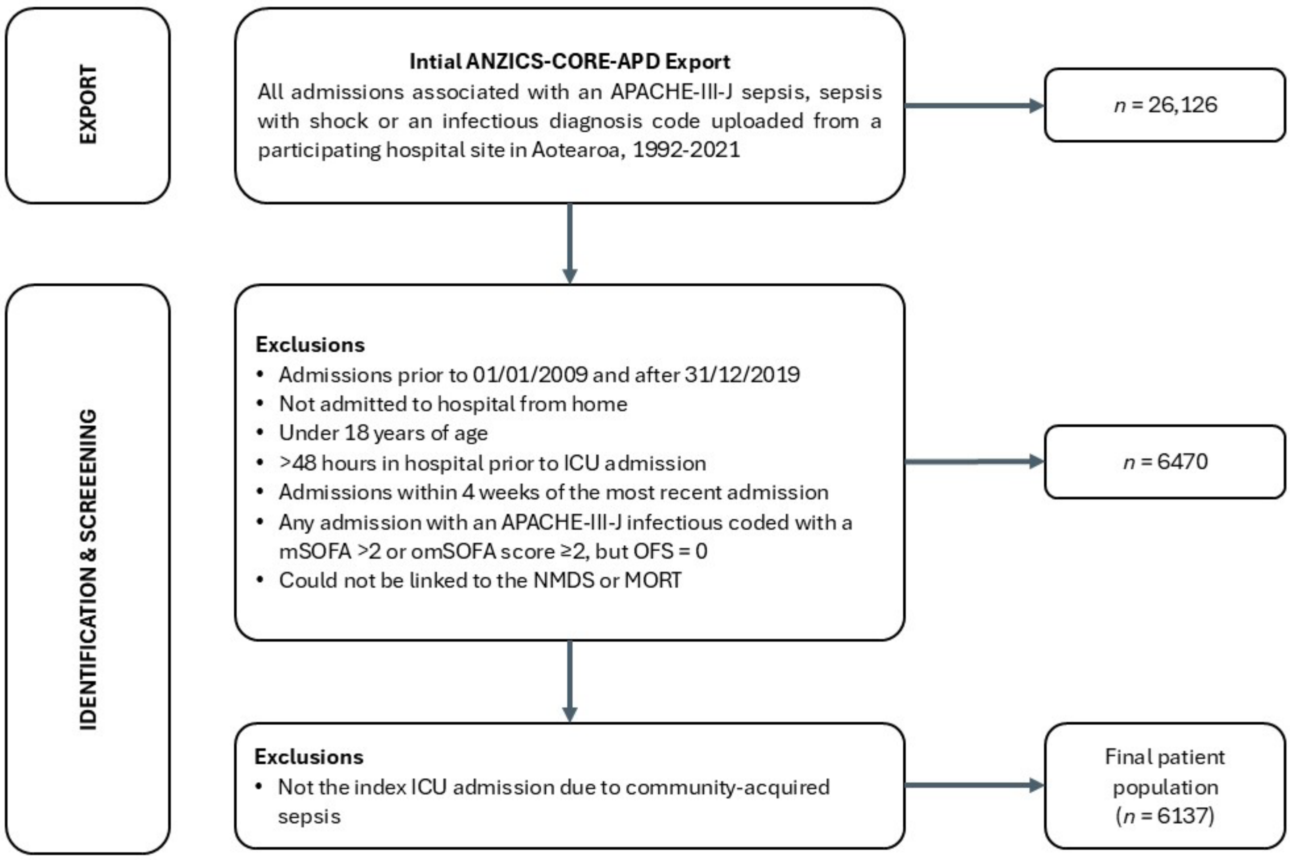
Study design and setting

We undertook a retrospective observational study using de-identified ICU admission data from hospital sites in Aotearoa between 2009 and 2019, retrieved from the Australian and New Zealand Intensive Care Society Centre for Outcome and Resource Evaluation Adult Patient Database (ANZICS-CORE-APD), deterministically linked to the National Minimum Dataset (NMDS) and the Mortality Collection (MORT) (Figure 1). Ethical approval for this study was obtained through the University of Otago Human Ethics Committee, reference ID HD20/075. Patient consent was not required as no patients were directly involved in the current study, and we used de-identified data. The ANZICS-CORE-APD is a binational, multicentre database with over 2 million ICU admissions, which has been previously described and contains admission data for most ICU sites in Aotearoa. The NMDS and MORT databases are collated and curated by Manatū Hauora (the New Zealand Ministry of Health) and contain hospital discharge codes and death data.

CAS definition and cohort identification

Sepsis was defined as explicit or implicit as per Sepsis-3.[1] Explicit sepsis was characterised by the presence of an APACHE-III-J sepsis or

Figure 1: Study population selection.



septic shock code (501, 502, 503 and 504). Implicit sepsis was characterised by the presence of an infectious APACHE-III-J code (Appendix Table 1), a modified sequential organ failure assessment (mSOFA) score >2 or an obstetrically modified SOFA[14] (omSOFA) score =2, and an organ failure score (OFS) ≥1. mSOFA and omSOFA scores were calculated based on clinical patient data (Appendix Table 2A and 2B), and OSF scores were attributed based on individual mSOFA or omSOFA organ system values. Cases with an mSOFA score of ≤2 or an omSOFA score of <2 were categorised as non-severe infections and excluded from the current study. Other exclusions included severe infection-associated admissions where an mSOFA or omSOFA score could not be calculated, admissions aged <18 years, hospital admission not from home, patients having spent >48 hours in-hospital before critical care admission and patients' subsequent events. Patients were followed from ICU admission until death or 365 days post-discharge alive. Hospital discharge was characterised as discharge from the hospital site in which the sepsis-associated ICU admission occurred.

Ethnicity and socio-economic deprivation classification

Ethnicity was defined using NMDS data and was grouped into prioritised ethnic groups: Māori, Pacific peoples, Asian and non-MPA (non-Māori, non-Pacific, non-Asian ethnicity). In 2018, this method of ethnic grouping divided the population of Aotearoa into Māori (16.5%), Pacific peoples (8.1%), Asian (15.1%) and non-MPA (European and Other; 72.9%).[15] Socio-economic status was categorised by the use of the New Zealand Index of Deprivation (NZDep),[16] a census-based small-area measure of socio-economic deprivation in Aotearoa. The NZDep is a previously validated measure of small-area socio-economic deprivation composed of eight variables (communication, income, employment, qualifications, home ownership, state support, living space and living conditions), and it is updated with each 5-year national census dataset.[16] Patients were categorised by the NZDep2018 quintile of their usual residence, NZDep Q1 (least deprived areas) to NZDep Q5 (most deprived areas).

Outcomes

The two outcomes of interest were CAS-associated in-hospital mortality and post-discharge mortality following a CAS-associated ICU-admission, censored at 365 days following discharge.

Outcome confounders

Variables evaluated in the current study included baseline population descriptors: age, sex, prioritised ethnicity, NZDep quintile, pre-existing severe comorbidities, severe multimorbidity defined using APACHE-III ("severe comorbidities") and prognostic factors identified through hospital discharge codes associated with the current sepsis-associated admission or previous hospitalisations, including substance use as identified by counselling for tobacco, hazardous alcohol use, obesity identified by counselling for obesity, hypertension, type-2 diabetes and blood or immune system deficiencies.

Statistical analyses

All statistical analyses were performed using STATA/SE 17.0 (StataCorp) and R 4.0 (R Statistical Foundation, Vienna, Austria). We calculated frequencies (*n*), percentages (%) and means (SD) as appropriate to characterise the cohort descriptively. Risk ratios (RR) and 95% confidence interval (CI) estimates for in-hospital mortality risk were computed using the quasi-Poisson distribution specification and robust variance estimation. Hazard ratios (HR) and CI estimates for post-discharge mortality were estimated using Cox proportional-hazard regression and the "survival" package 3.5.5 in R. Follow-up observations were censored if no death occurred within the pre-specified 365-day follow-up period from hospital discharge and the Efron approximation was applied to tied follow-up times. RR, HR and CI estimates were computed for univariable and multivariable models adjusted for 1) age and sex, and 2) age, sex, ethnicity, socio-economic deprivation and severe multimorbidity. A RR or HR >1.0 indicated an increased mortality risk for patients with that variable compared to patients without the variable. Kaplan–Meier curves were used to describe the survival probabilities over the follow-up period for the entire cohort, stratified by ethnicity. Cox proportional-hazard models fit post-discharge survival probabilities for the sepsis survivors identified as Māori and non-MPA, 60–79 years, usually resident in NZDep Q1 or NZDep Q5 areas, with no severe comorbidity, 1 severe comorbidity or ≥2 severe comorbidities. Two-sided tests were conducted with type I error set at 5%.

Results

From 1 January 2009–31 December 2019, 6,137 community-associated sepsis admissions were identified from 17 ICU sites across Aotearoa. The majority of the cohort was non-MPA (3,723/6,137, 60.7%), male (3,458/6,137, 56.3%), aged between 40 and 79 years (4,576/6,137, 74.6%) and usually resident in NZDep Q4 or NZDep Q5 areas (3,141/6,137, 51.2%). Most had no severe comorbidities (4,783/6,137, 77.9%). Table 1 shows prevalence differences in baseline demographics, pre-existing conditions, sepsis risk factors and clinical characteristics stratified by ethnicity.

A total of 1,663 deaths were observed after ICU admission, of which 60.2% occurred in-hospital (1,002/1,663) and 39.7% in the 365-day post-discharge follow-up (661/1,663). Table 2 reports patient mortality by admission status. Most patients surviving to hospital discharge were discharged home (4,216 /5,135, 82.1%) or to other healthcare facilities (600/5,135, 11.2%). Overall, mortality risk following CAS-associated ICU admission was 27.1%; in-hospital it was 16.3% (1,002/6,137), and in the 5,135 hospital survivors post-discharge it was (cumulatively) 3.6% by 30 days after discharge, 9.1% by 180 days and 12.9% by 1 year. Substantial differences in case fatality risk per 100 CAS ICU admissions were observed between patient populations, both in the hospital and during the follow-up period (Table 2). Post-discharge survival analyses showed marked differences in sepsis survival by ethnicity (Figure 2): survival was particularly low for Māori usually resident in NZDep Q5 areas with severe multimorbidity (Figure 3).

We identified mortality risk associated with variables observable at or within the first 48 hours of ICU admission, RRs for in-hospital mortality risk and HRs for post-discharge mortality risk (Table 2). Variables significantly associated with an increased mortality risk while in-hospital included older age, severe multimorbidity, previously identified hypertension and hazardous alcohol use, and the presence of septic shock or acute renal failure. Male sex was independently associated with a decrease of in-hospital mortality risk (Figure 4). There was no evidence that ethnicity and usual residence in NZDep Q5 areas were associated with an increased risk of in-hospital mortality (Figure 4). Comparatively, in the follow-up period, discharged patients of Māori ethnicity and those usually resident in NZDep Q5 areas had an increased mortality risk compared with non-MPA and those usually resident in NZDep Q1 areas (Figure 4). Pacific and Asian ethnicity was associated with a decreased mortality risk in the post-discharge period. Other variables independently associated with an increased mortality risk included older age, severe multimorbidity, residing in NZDep Q5 areas, previously identified hypertension and blood/immune deficiencies and acute renal failure. There was no evidence type 2 diabetes and tobacco use, although highly prevalent in the study population, were associated with in-hospital or post-discharge mortality.

Discussion

This current study is one of the few to compare mortality risk in a well-characterised population of ICU-admitted CAS and septic shock patients during their inpatient and post-discharge periods. In this study of more than 6,000 adult CAS-associated ICU admissions, we observed an in-hospital mortality rate of 16.0%. Among in-hospital survivors followed for up to 365 days, there was an additional post-discharge mortality rate of 12.9%, with a disproportionate mortality distribution over age, ethnic groups and NZDep score quintiles by admission status. Additionally, we identified a significantly inequitable spread of mortality risk among patient sub-populations, particularly after hospital discharge. The marked disparities identified in our analysis suggest the need to identify and implement interventions to reduce health inequities for patients after hospital discharge as a key part of improving outcomes for ICU-admitted CAS patients.

The in-hospital mortality found in our study is similar to the findings from previous studies in high-income countries.[2,12,17] Our results were also broadly in line with the findings of a recent meta-analysis. Fleischmann et al. (2016) estimated in-hospital severe sepsis mortality rate between 2003 and 2015 to be 18–33%, dependent on the sepsis definition followed.[2] Globally, few studies characterising post-discharge sepsis-associated mortality specifically differentiate between hospital-acquired sepsis and CAS. Consequently, post-discharge mortality at 365 days for all sepsis admissions varies markedly, up to 45% in recent studies, depending on the country and patient population.[18–23] In Aotearoa, only one study characterised sepsis-related deaths in the post-discharge period, identifying a mortality risk of 37.7% at 365 days; however, the results of the current study could not be directly compared as it measured death

Table 1: Demographic characteristics, pre-existing conditions, sepsis risk factors and clinical severity by ethnicity.

Variables	Total cohort[a] (n=6,137)	Ethnicity[a]				p-value[b]
		Māori (n=1,467)	Pacific (n=656)	Asian (n=291)	Non-MPA (n=3,723)	
Sex						
Male	3,458 (56.3)	782 (53.3)	344 (52.4)	146 (50.2)	2,186 (58.7)	<0.001
Female	2,679 (43.7)	685 (46.7)	312 (47.6)	145 (49.8)	1,537 (41.3)	
Age						
Age, years	60.5 (±17.0)	54.8 (±16.0)	53.3 (±16.5)	54.1 (±17.6)	64.5 (±16.3)	<0.001
Age group						
<40 years	868 (14.1)	284 (19.4)	160 (24.4)	74 (25.4)	350 (9.4)	<0.001
40–59 years	1,803 (29.4)	567 (38.7)	240 (36.6)	90 (30.9)	906 (24.3)	
60–79 years	2,773 (45.2)	565 (38.5)	234 (35.7)	112 (38.5)	1,862 (50.0)	
≥80 years	693 (11.3)	51 (3.5)	22 (3.4)	15 (5.2)	605 (16.3)	
Socio-economic deprivation						
NZDep Q1 (lowest)	792 (12.9)	78 (5.3)	26 (4.0)	49 (16.8)	639 (17.2)	<0.001
NZDep Q2	1,012 (16.5)	136 (9.3)	48 (7.3)	59 (20.3)	769 (20.7)	
NZDep Q3	1,146 (18.7)	200 (13.6)	69 (10.5)	61 (21.0)	816 (21.9)	
NZDep Q4	1,576 (25.7)	383 (26.1)	153 (23.3)	74 (25.4)	966 (25.9)	
NZDep Q5 (highest)	1,565 (25.5)	670 (45.7)	358 (54.6)	43 (14.8)	494 (13.3)	

Table 1 (continued): Demographic characteristics, pre-existing conditions, sepsis risk factors and clinical severity by ethnicity.

Variables	Total cohort[a] (n=6,137)	Ethnicity[a]				p-value[b]
		Māori (n=1,467)	Pacific (n=656)	Asian (n=291)	Non-MPA (n=3,723)	
Severe comorbidities						
Cardiovascular	349 (5.7)	136 (9.3)	38 (5.8)	7 (2.4)	168 (4.5)	<0.001
Hepatic	96 (1.6)	25 (1.7)	12 (1.8)	4 (1.4)	55 (1.5)	0.865
Immune[c]	474 (7.7)	96 (6.5)	36 (5.5)	17 (5.8)	325 (8.7)	0.010
Renal	329 (5.4)	138 (9.4)	63 (9.6)	14 (4.8)	138 (3.7)	<0.001
Respiratory	360 (5.9)	143 (9.7)	44 (6.7)	4 (1.4)	169 (4.5)	<0.001
Severe multimorbidity						
None	4,783 (77.9)	1,038 (70.8)	500 (76.2)	248 (85.2)	2,997 (80.5)	<0.001
1 severe comorbidity	1,140 (18.6)	343 (23.4)	121 (18.4)	40 (13.7)	636 (17.1)	
≥2 severe comorbidities	214 (3.5)	86 (5.9)	35 (5.3)	3 (1.0)	90 (2.4)	
Sepsis prognostic factors[d]						
Diabetes, type 2[e]	1,541 (25.1)	496 (33.8)	282 (43.0)	81 (27.8)	682 (18.3)	<0.001
Hypertension	1,215 (19.8)	303 (20.7)	142 (21.6)	40 (13.7)	730 (19.6)	0.009
Obesity[e]	398 (6.5)	172 (11.7)	84 (12.8)	4 (1.4)	138 (3.7)	<0.001
Hazardous alcohol use	295 (4.8)	118 (8.0)	26 (4.0)	5 (1.7)	146 (3.9)	<0.001
Tobacco use	3,199 (52.1)	987 (67.3)	290 (44.2)	71 (24.4)	1,851 (49.7)	<0.001

Table 1 (continued): Demographic characteristics, pre-existing conditions, sepsis risk factors and clinical severity by ethnicity.

Variables	Total cohort[a] (n=6,137)	Ethnicity[a]				p-value[b]
		Māori	Pacific	Asian	Non-MPA	
		(n=1,467)	(n=656)	(n=291)	(n=3,723)	
Blood/immune deficiencies	1,067 (17.4)	289 (19.7)	111 (16.9)	38 (13.1)	629 (16.9)	0.019
Clinical severity						
Septic shock	2,164 (35.3)	536 (36.5)	249 (38.0)	109 (37.5)	1,270 (34.1)	0.116
Invasive ventilation	1,597 (26.0)	340 (23.2)	172 (26.2)	85 (29.2)	1,000 (26.9)	0.024
Acute renal failure	955 (15.6)	233 (15.9)	119 (18.1)	36 (12.4)	567 (15.2)	0.107
ANZROD score	0.06 [0.02,0.19]	0.05 [0.02,0.16]	0.05 [0.02,0.16]	0.04 [0.02,0.16]	0.07 [0.03,0.21]	0.489
ICU LOS, days	2.0 [1.0,3.9]	2.0 [1.0,3.8]	1.8 [0.9,3.3]	1.8 [1.0,3.5]	2.1 [1.1,4.1]	0.512
Hospital LOS, days	7.2 [4.1,13.5]	7.0 [4.1,13.0]	7.4 [4.0,13.7]	7.3 [4.5,13.1]	7.2 [4.1,13.8]	0.319

[a]n (%), mean (±SD) or median [interquartile range].
[b]Pearson's Chi-squared test with Yates' continuity correction or Kruskal–Wallis >2 sample test.
[c]Includes cancer and human immunodeficiency virus (HIV).
[d]Unless otherwise identified, sepsis development risk factors were identified through previous hospital admission ICD-10-AM codes.
[e]Current hospital admission.
Non-MPA = non-Māori, non-Pacific, non-Asian; ANZROD = Australian and New Zealand Risk of Death; ICU = intensive care unit; LOS = length of stay.

Table 2: In-hospital and post-discharge mortality by admission status.

Variable	Mortality outcomes by admission status							
	In-hospital				Post-discharge			
	Deaths[a] (n=1,002)	CFR[b]	Unadjusted RR[c] (95% CI)	Adjusted RR[c] (95% CI)	Deaths[a] (n=661)	CFR[b]	Unadjusted HR[d] (95% CI)	Adjusted HR[d] (95% CI)
Sex								
Female	447 (44.6)	16.7	ref	ref	247 (37.4)	11.1	ref	ref
Male	555 (55.4)	16.0	1.0 (0.9–1.1)	-	414 (62.6)	14.3	1.3 (1.12–1.53)	-
Ethnicity								
Non-MPA	672 (67.1)	18.0	ref	ref	412 (62.3)	13.5	ref	ref
Māori	199 (19.9)	13.6	0.8 (0.6–0.9)	0.9 (0.8–1.1)	189 (28.6)	14.9	1.1 (0.93–1.31)	1.5 (1.25–1.79)
Pacific	89 (8.9)	13.6	0.8 (0.6–0.9)	1.0 (0.8–1.2)	47 (7.1)	8.3	0.6 (0.44–0.80)	0.8 (0.61–1.13)
Asian	42 (4.2)	14.4	0.8 (0.6–1.1)	1.0 (0.8–1.4)	13 (2.0)	5.2	0.4 (0.21–0.64)	0.5 (0.29–0.87)
Age								
≤39 years	41 (4.1)	4.7	ref	ref	28 (4.2)	3.4	ref	-
40–59 years	208 (20.8)	11.5	2.4 (1.8–3.4)	-	159 (24.1)	10.0	3.0 (2.04–4.56)	-
60–79 years	553 (55.2)	19.9	4.2 (3.1–5.7)	-	347 (52.5)	15.6	4.9 (3.36–7.25)	-
≥80 years	200 (20.0)	28.9	6.1 (4.4–8.4)	-	127 (19.2)	25.8	8.6 (5.73–12.99)	-
Socio-economic deprivation								
NZDep Q1 (least)	131 (13.1)	16.5	ref	ref	76 (11.5)	11.5	ref	ref
NZDep Q2	172 (17.2)	17.0	1.0 (0.8–1.3)	1.1 (0.9–1.3)	96 (14.5)	11.4	1.0 (0.7–1.3)	1.0 (0.8–1.4)

Table 2 (continued): In-hospital and post-discharge mortality by admission status.

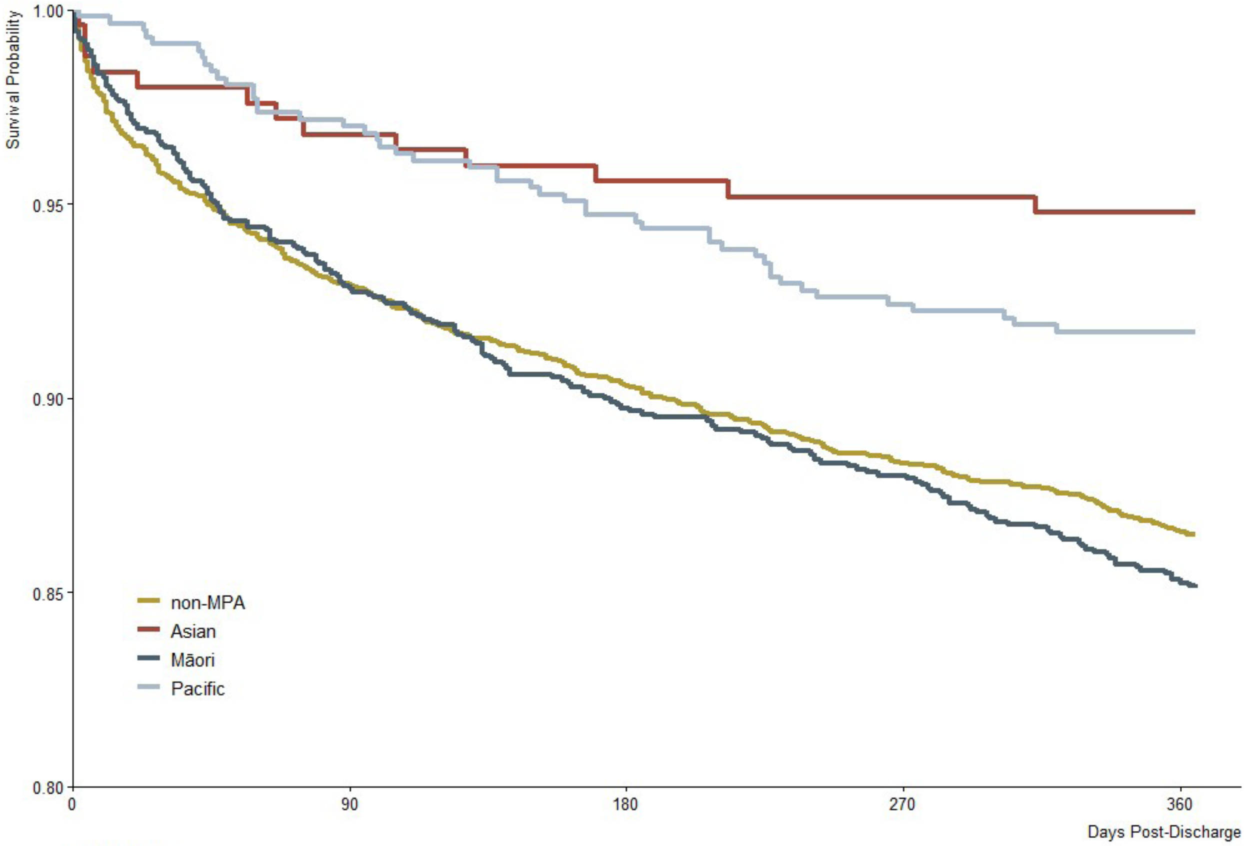
Variable	Mortality outcomes by admission status							
	In-hospital				Post-discharge			
	Deaths[a] (n=1,002)	CFR[b]	Unadjusted RR[c] (95% CI)	Adjusted RR[c] (95% CI)	Deaths[a] (n=661)	CFR[b]	Unadjusted HR[d] (95% CI)	Adjusted HR[d] (95% CI)
NZDep Q3	177 (17.7)	15.4	0.9 (0.8–1.1)	1.0 (0.8–1.2)	122 (18.5)	12.6	1.1 (0.8–1.5)	1.1 (0.9–1.5)
NZDep Q4	276 (27.5)	17.5	1.1 (0.9–1.3)	1.1 (0.9–1.4)	180 (27.2)	13.8	1.2 (0.9–1.6)	1.3 (1.0–1.7)
NZDep Q5 (most)	235 (23.5)	15.0	0.9 (0.7–1.1)	1.1 (0.9–1.3)	185 (28.0)	13.9	1.2 (0.9–1.6)	1.5 (1.2–2.0)
Severe comorbidities								
Respiratory	111 (11.1)	30.8	2.0 (1.7–2.4)	1.9 (1.6–2.2)	54 (8.2)	21.7	1.8 (1.4–2.4)	1.7 (1.3–2.2)
Cardiovascular	108 (10.8)	30.9	2.0 (1.7–2.4)	1.7 (1.4–2.0)	63 (9.5)	26.1	2.3 (1.8–3.0)	1.9 (1.4–2.4)
Hepatic	33 (3.3)	34.4	2.1 (1.6–2.8)	2.2 (1.7–2.9)	18 (2.7)	28.6	2.5 (1.6–4.0)	2.6 (1.6–4.1)
Renal	59 (5.9)	17.9	1.1 (0.9–1.4)	1.2 (0.9–1.5)	78 (11.8)	28.9	2.6 (2.1–3.3)	2.7 (2.2–3.5)
Immune	107 (10.7)	22.6	1.4 (1.2–1.7)	1.4 (1.2–1.6)	128 (19.4)	34.9	3.5 (2.9–4.3)	3.3 (2.7–4.0)
Number of severe comorbidities								
None	665 (66.4)	13.9	ref	ref	380 (57.5)	9.2	ref	ref
1	268 (26.7)	23.5	1.7 (1.5–1.9)	1.6 (1.4–1.9)	230 (34.8)	26.4	3.1 (2.7–3.7)	2.9 (2.5–3.5)
≥2	69 (6.9)	32.2	2.3 (1.9–2.9)	2.1 (1.7–2.6)	51 (7.7)	35.2	4.4 (3.3–5.8)	3.9 (2.9–5.2)
Sepsis prognostic factors								
Diabetes, type 2	278 (27.7)	18.0	1.1 (1.0–1.3)	1.0 (0.9–1.2)	197 (29.8)	27.2	1.3 (1.1–1.6)	1.2 (1.1–1.5)
Hypertension	260 (25.9)	21.4	1.4 (1.3–1.6)	1.2 (1.1–1.4)	183 (27.7)	24.7	1.8 (1.5–2.1)	1.4 (1.2–1.7)

Table 2 (continued): In-hospital and post-discharge mortality by admission status.

Variable	Mortality outcomes by admission status							
	In-hospital				Post-discharge			
	Deaths[a] (n=1,002)	CFR[b]	Unadjusted RR[c] (95% CI)	Adjusted RR[c] (95% CI)	Deaths[a] (n=661)	CFR[b]	Unadjusted HR[d] (95% CI)	Adjusted HR[d] (95% CI)
Immune suppressed	83 (8.3)	20.6	1.3 (1.1–1.6)	1.2 (1.0–1.5)	68 (10.3)	21.3	1.8 (1.4–2.3)	1.7 (1.3–2.2)
Obesity	64 (6.4)	16.1	1.0 (0.8–1.2)	1.0 (0.9–1.5)	43 (6.5)	12.9	1.0 (0.7–1.4)	1.2 (0.9–1.7)
Tobacco use	490 (48.9)	15.3	0.9 (0.8–1.0)	0.9 (0.8–1.0)	371 (56.1)	13.7	1.2 (1.0–1.4)	1.1 (1.0–1.3)
Hazardous alcohol use	62 (6.2)	21.0	1.3 (1.0–1.6)	1.5 (1.2–1.9)	26 (3.9)	11.2	0.9 (0.6–1.3)	1.0 (0.7–1.5)
Blood/immune deficiencies	209 (20.9)	19.6	1.3 (1.1–1.4)	1.1 (1.0–1.3)	158 (23.9)	18.4	1.6 (1.4–1.9)	1.5 (1.2–1.8)
Clinical severity								
Septic shock	425 (42.4)	19.6	1.4 (1.2–1.5)	1.3 (1.2–1.5)	217 (32.8)	12.5	1.0 (0.8–1.1)	0.9 (0.8–1.1)
Mechanical ventilation	464 (46.3)	29.1	2.4 (2.2–2.7)	2.7 (2.4–3.0)	98 (14.8)	8.6	0.6 (0.5–0.8)	0.7 (0.6–0.9)
Acute renal failure	361 (36.0)	37.8	3.1 (2.8–3.4)	2.8 (2.5–3.1)	106 (16.0)	17.8	1.5 (1.2–1.9)	1.4 (1.2–1.7)

Patient outcomes are presented by admission status, in-hospital and post-discharge as [a]number of deaths (%), [b]case fatality risk per 100 community-acquired sepsis intensive care unit admissions, and mortality risk ([c]RR = risk ratio; [d]HR = hazard ratio, unadjusted and adjusted for sex and age).
CFR = case fatality rate; CI = confidence interval.

Figure 2: Kaplan–Meier survival plot indicating the probability of patient survival by ethnicity from hospital discharge to 365 days post-discharge.



No. at Risk

	0	90	180	270	360
non-MPA	3051	2836	2757	2695	2642
Asian	249	241	238	237	236
Māori	1268	1178	1138	1116	1082
Pacific	567	550	537	524	520

Cumulative Deaths

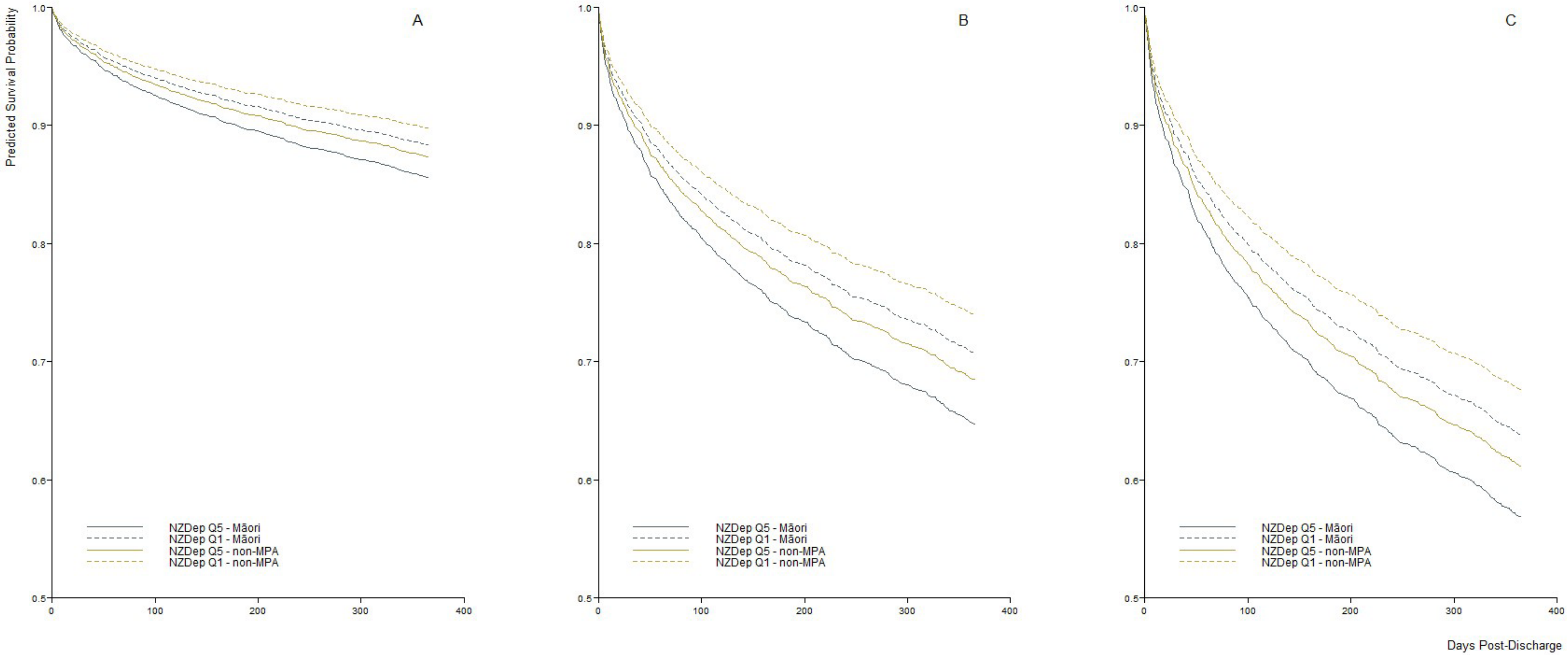
	0	90	180	270	360
non-MPA	0	216	295	356	410
Asian	0	8	11	12	13
Māori	0	91	130	152	187
Pacific	0	17	30	43	47

Kaplan–Meier curve for short-term survival following an index community-acquired sepsis intensive care unit admission by ethnicity. Survival analysis was censored at 365 days.

in the year from admission instead of specifically following discharge.[12] Our 365-day post-discharge mortality risk of 12.9% is lower than previous estimations from France and the United States,[21,24] potentially due to excluding hospital-acquired sepsis admissions.

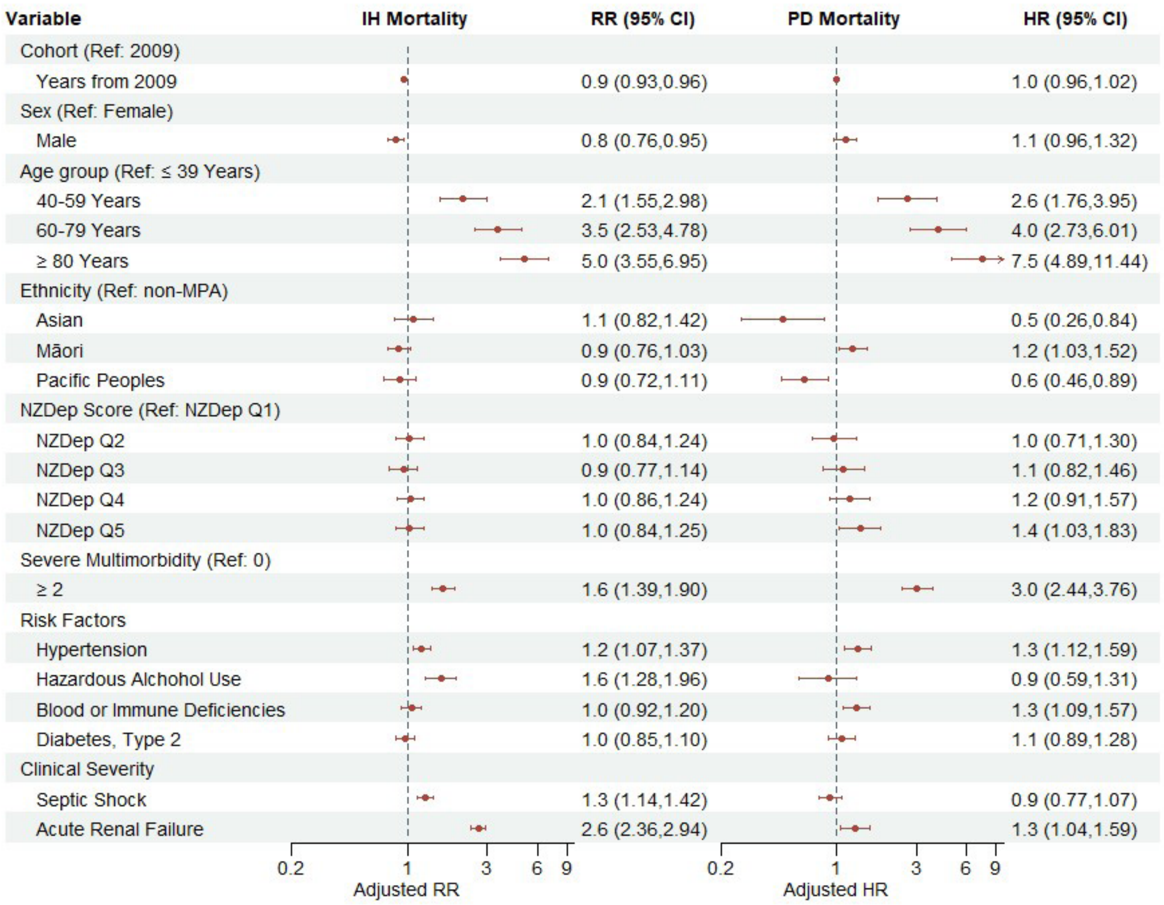
Similar to previous studies, we identified increasing age, hazardous alcohol use, blood or immune deficiencies, severe comorbidities and severe multimorbidity as strongly associated with in-hospital mortality.[25–27] We found no association between ethnicity or NZDep quintile and in-hospital mortality, consistent with studies conducted in Australia and the United Kingdom characterising sepsis mortality, where ethnicity and socio-economic deprivation were not associated with in-hospital mortality.[28,29] Our findings were also consistent with studies characterising overall ICU mortality by ethnicity in Aotearoa. A single-centre study conducted in Waikato over 15 years found no evidence of association between in-hospital mortality and ethnicity.[30] Similarly, a multicentre study characterising ICU patient outcomes for all patient populations admitted to 17 ANZICS-APD contributing sites in Aotearoa over 9 years found no evidence of associations between ethnicity and

Figure 3: Cox proportional-hazards plots indicating predicted average patient survival after an index intensive care unit admission due to community-acquired sepsis by ethnicity, NZDep quintile and severe comorbidity from hospital discharge to 365 days post-discharge.



Cox proportional-hazard models were used to predict the post-discharge survival of the average patient (male, 60–79 years) and to compare survival hazards among ethnic and socio-economic populations based on the degree of severe multimorbidity. Other covariates were set at mode levels (the most frequently occurring observations). The severity of severe multimorbidity was categorised as A: no severe comorbidities, B: one severe comorbidity and C: more than two severe comorbidities.

Figure 4: Association between patient characteristics (demographics, pre-existing conditions and risk factors) identifiable at or within 48 hours of intensive care unit (ICU) admission and in-hospital (IH) and post-discharge (PD) mortality.



Multivariable analysis of variables identifiable at ICU admission associated with IH and PD mortality. IH mortality risk is presented as rate ratio with 95% confidence interval; post-discharge mortality risk is presented as hazard ratio with 95% confidence interval. Both models are adjusted for year, sex, age, ethnicity, socio-economic deprivation and severe multimorbidity.

in-hospital mortality.[13]

We identified a significant risk of post-discharge mortality among patient populations with increasing age, chronic disease and severe multimorbidity, consistent with previous findings. Globally, significant post-discharge sepsis-associated mortality disparities are observable between patient populations, particularly populations with increasing age and/or those experiencing severe comorbidities and multimorbidity.[31,32] We also observed a similar level of severe comorbidity and multimorbidity in older patients living in areas of low socio-economic deprivation and younger patients living in areas of high socio-economic deprivation. Early onset of multimorbidity is strongly associated with socio-economic deprivation.[7,33] In Aotearoa, marginalised peoples—particularly patient populations of Māori ethnicity and those resident in high NZDep score areas—are disproportionately affected by chronic disease.[8,34] Patient populations of Māori ethnicity are significantly more likely to experience chronic comorbidities, and are more likely be resident in areas with high NZDep scores than non-Māori. This pattern may explain the increased risk of post-discharge mortality associated with patient populations of Māori ethnicity we observed and the decrease in post-discharge survival for Māori patient populations living in NZDep Q5 areas compared to non-MPA populations living in NZDep Q5 areas.

Our findings raise important public health concerns for patient populations usually resident in NZDep Q5 areas who develop CAS and survive to hospital discharge in Aotearoa. We found substantial evidence that the prevalence of CAS requiring ICU admission in Aotearoa was not equitably spread across patient populations, particularly observable within those usually resident in NZDep Q5 areas. Secondly, although in-hospital mortality risk was equivalent, we observed clear post-discharge mortality risk disparities at 365 days following hospital discharge between patient populations, specifically those with severe comorbidities and/or severe multimorbidity residing in NZDep Q5 areas, particularly for those of Māori ethnicity. Our results strongly demonstrate that both ethnicity and socio-economic deprivation are associated with an increased mortality risk for hospital survivors. In addition, due to the constraints of the linked ANZICS-CORE-APD data and focussing only on ICU-admitted CAS events, our results may have under-estimated the strength of mortality risk associated with demographic, pre-existing conditions and clinical variables. Interventions that modify the major social determinants of health, such as socio-economic deprivation, could potentially decrease the incidence of CAS requiring ICU admission in Aotearoa. More specifically, interventions to reduce diabetes and improve tobacco smoking cessation may reduce the incidence of ICU-admitted CAS in Aotearoa. A more detailed study is needed of morbidities following an ICU-admitted sepsis event and post-discharge sepsis-associated mortality to identify interventions to reduce these significant post-discharge mortality risk disparities.

Strengths and limitations

Our study has several strengths. It was based on a large cohort of patient data from 17 ANZICS-CORE-APD contributing hospital sites across Aotearoa linked to the NMDS and MC for over 10 years. The linkage allowed us to follow patients post-discharge and compare in-hospital and post-discharge mortality. Linkage also allowed for a more in-depth characterisation of the ANZICS-CORE-APD patient cohort, particularly ethnicity, socio-economic deprivation and previously identified risk factors.

There are several limitations to our study. First, our results may not be generalisable to the wider population as the study was limited to patients admitted for intensive care in an ANZICS-CORE-APD contributing hospital site whose data could be linked to the NMDS and MC, and it is likely the true burden of treated and untreated CAS in Aotearoa is under-estimated. Second, the ANZICS-CORE-APD was designed to be a benchmarking database for quality improvement rather than an epidemiological database. As such, the ANZICS-CORE-APD does not collect data that we would find relevant to epidemiological studies characterising sepsis, such as differentiating between the site of infection for patients with complicated sepsis beyond describing sites as than genitourinary or other. Similarly, the ANZICS-CORE-APD has only recently started to collect data about patients' frailty before admission and does not currently collect data on health and quality of life before admission or on patient discharge, which would have improved the characterisation of the current cohort.

Conclusions

In Aotearoa, mortality following CAS-associated ICU admission remains high while in hospital and following discharge. The strong association between mortality risk, ICU-admitted CAS and the social determinants of health only becomes evident in the post-discharge period. This finding supports the need to identify and implement interventions to prevent sepsis, for early intervention to limit the necessity for ICU admission and to identify ways to address outcome disparities between patient populations following hospital discharge.

COMPETING INTERESTS

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Appendix

Appendix Table 1: APACHE-III-J diagnosis and sub-diagnosis sepsis or infectious disease codes identified in the current study population.

Diagnosis code group	APACHE-III diagnosis code	APACHE-III diagnosis sub-code*
Cardiovascular	109 – Other cardiovascular disease	109.06 – Endocarditis
Respiratory	210 – Parasitic pneumonia	210.02 – Pneumonia, parasitic (e.g., pneumocystis pneumonia)
	212 – Bacterial pneumonia	212.01 – Pneumonia, bacterial
		212.02 – Pneumonia, other
	213 – Viral pneumonia	213.01 – Pneumonia, viral
	1301 – Respiratory infection	1301.01 – Infection/abscess, other surgery for
Sepsis	501 – Sepsis, other than urinary	501.01 – Sepsis, cutaneous/soft tissue
		501.02 – Sepsis, gastrointestinal
		501.03 – Sepsis, gynaecologic
		501.04 – Sepsis, other
		501.05 – Sepsis, pulmonary
		501.06 – Sepsis, unknown
	502 – Sepsis of urinary tract origin	502.01 – Sepsis, renal/UTI (including bladder)
	503 – Sepsis with shock, other than urinary	503.01 – Sepsis with shock, not urinary tract
	504 – Sepsis of urinary tract origin with shock	504.01 – Sepsis with shock, urinary tract
Neurological	404 – Neurologic infection	404.01 – Abscess, neurologic
		404.02 – Encephalitis
		404.03 – Meningitis
	1506 – Other neurologic disease	1506.01 – Abscess/Infection-cranial, surgery for
Gastrointestinal	313 – Other GI inflammatory disease	313.01 – Cholangitis
		313.03 – GI abscess/cyst
		313.05 – Peritonitis
	1406 – Cholecystitis/cholangitis	1406.01 – Cholecystectomy/cholangitis, surgery for (gallbladder removal)

Appendix Table 1 (continued): APACHE-III-J diagnosis and sub-diagnosis sepsis or infectious disease codes identified in the current study population.

	1409 – Fistula/abscess surgery	1409.01 – Fistula/abscess, surgery for (not inflammatory bowel disease)
	1412 – Peritonitis	1412.01 – Peritonitis, surgery for
Renal/genitourinary	901 – Renal disorders	901.04 – Renal infection/abscess
Skin & soft tissue	1102 – Cellulitis/soft tissue infection	1102.01 – Cellulitis & localised soft tissue infections
	1904 – Cellulitis/soft tissue infection	1904.01 Cellulitis and localised soft tissue infections, surgery for

*Not all patients in the current study had an APACHE-III-J sub-diagnosis code, but all had an APACHE-III-J diagnosis code.
UTI = urinary tract infection; GI = gastrointestinal.

Appendix Table 2A: Modified sequential organ failure assessment (mSOFA) scoring.

Clinical variable	Score: 0	Score: 1	Score: 2	Score: 3	Score: 4
PaO2/FIO2	≥400mmHg	<400mmHg	<300mmHg	<200mmHg with respiratory support	<100mmHg with respiratory support
Platelets	≥150×109/L	<150×109/L	<100×109/L	<50×109/L	<20×109/L
Bilirubin	<20mmol/L	20–32mmol/L	33–101mmol/L	102–204mmol/L	>204mmol/L
Cardiovascular	MAP ≥70mmHg	MAP <70mmHg	-	-	Any use of inotropes
Glasgow Coma Scale score	15 points	13–14 points	10–12 points	6–9 points	<6 points
Creatinine	<110mmol/L	110–170mmol/L	171–299mmol/L	300–400mmol/L	>440mmol/L
Urine output	-	-	-	<500mL/day	<200mL/day

Appendix Table 2B: Obstetric modified sequential organ failure assessment (omSOFA) scoring.

Clinical variable	Score: 0	Score: 1	Score: 2
PaO2/FIO2	≥400mmHg	300–400mmHg	<300mmHg
Platelets	≥150×109/L	100–150×109/L	<100×109/L
Bilirubin	<20mmol/L	20–32mmol/L	>32mmol/L
Cardiovascular	MAP ≥70mmHg	MAP <70mmHg	Use of intropes
Glasgow Coma Scale score	Alert	Rousable by voice	Rousable by pain
Creatinine	<90mmol/L	90–120mmol/L	>120mmol/L
Urine output	-	-	-

PaO2/FIO2 = ratio of arterial oxygen partial pressure to fractional inspired oxygen; MAP = mean arterial pressure.