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ORIGINAL ARTICLE

Mortality after Severe Sepsis and Septic Shock in Swedish Intensive Care Units 2008-2016—A nationwide observational study

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Background: Recent studies have reported substantially decreased hospital mortality for sepsis, but data are scarcer on outcomes after hospital discharge. We studied mortality up to 1 year in Swedish intensive care unit (ICU) patients with and without sepsis.

Methods: Demographic and medical data for all registered adult general ICU patients admitted between 01-01-2008 and 30-09-2016 were retrieved from the Swedish Intensive Care Registry and linked with the National Patient Register for comorbidity data and the Cause of Death Register for death dates. The population was divided in two cohorts; (a) Patients with a diagnosis of severe sepsis or septic shock and (b) All other ICU patients. Crude yearly mortality was calculated, and logistic regression was used to analyse predictors of mortality.

Results: 28 886 sepsis and 221 941 nonsepsis ICU patients were identified. In the sepsis cohort, in 2008 unadjusted mortality was 32.6% at hospital discharge, 32.7% at 30 days, 39% at 90 days and 46.8% at 365 days. In 2016, mortality was 30.5% at hospital discharge, 31.9% at 30 days and 38% at 90 days. Mortality at 365 days was 45.3% in 2015. Corresponding nonsepsis mortality was 15.4%, 16.2%, 20% and 26% in 2008 and 15.6%, 17.1%, 20.7% and 26.7% in 2016/2015. No consistent decrease in odds of mortality was seen in the adjusted analysis.

Conclusions: Mortality in severe sepsis and septic shock is high, with more than one in three patients not surviving three months after ICU admission, and adjusted mortality has not decreased convincingly in Sweden 2008-2016.

Trial Registration: The study was registered prospectively, ClinicalTrials.gov ID: NCT03489447.

1 | INTRODUCTION

Sepsis is a syndrome with a variable presentation and severity. Although common definitions were designed to define a group of patients with a similar clinical condition, highly variable outcomes have been reported.[1-4] Accurate data on mortality are important for allocation of resources, benchmarking, evaluation of interventions and research.

Recent studies have reported continuously decreasing hospital mortality in patients with severe sepsis.[5-9] Particularly, Kaukonen et al revealed in a carefully performed binational study a substantial decrease

in hospital mortality in critically ill patients which kept pace with a similar decrease in nonsepsis patients.[5] While decreasing hospital mortality suggest improved care, the need for data on longer term outcomes were immediately voiced.[10] There are numerous publications with time-fixed long-term outcomes after sepsis and septic shock but there is a scarcity of studies that analyse longitudinal trends of these outcomes. Time-fixed mortality mitigates bias associated with hospital mortality, since outcome on discharge from hospital may be affected by mortality/morbidity trade-offs in ICU care and local discharge practices.[11] Verifying a mortality decrease sustained over time would increase understanding of how the epidemiology of severe sepsis has evolved.

Prior studies from the Swedish Intensive Care Registry (SIR) have demonstrated the feasibility to capture long-term outcomes with minimal loss to follow-up.[12,13] Hence, we set out to investigate whether mortality up to one year among critically ill patients with severe sepsis has changed from 2008 to 2016 and also to study the nonsepsis ICU population for comparison. Additionally, we wanted to investigate if patient demographics and comorbidity have changed over the same period, and whether these factors were associated with mortality.

Editorial Comment

This comprehensive, nationwide registry-based analysis revealed that survival of sepsis patients treated in Swedish intensive care units has not improved from 2008 to 2016. Further studies are needed to discern the reasons for this important finding.

2 | METHODS

2.1 | Ethics approval and consent

The study was approved by the local ethics committee, date of approval 20-01-2015, application no. 2015/519. Informed consent was waived as the data sources operate within the legal framework of Swedish Health Data Registries which allow use of anonymized data without informed consent, and personal identification numbers were blinded.

2.2 | Setting, participants and data

Data were retrieved from SIR on all adult general ICU patients (≥18 yrs.) admitted between 01-01-2008 and 30-09-2016. SIR covered 49/69 (71%) and 63/64 (99%) of general ICUs in Sweden during 2008 and 2016, respectively. All ICUs operated as closed units and the number of ICU beds in 2016 was 2-6 in 26 local hospitals, 6-12 in 24 county hospitals and 4-20 in 13 regional hospitals. The population was divided in two cohorts; 1, patients with severe sepsis/septic shock and 2, all other patients. In SIR, severe sepsis and septic shock were two of four key discharge diagnoses with a detailed guideline aimed to improve coding accuracy and reliability. The diagnoses were set according to the American College of Chest Physicians/Society of Critical Care Medicine (ACCP/SCCM) criteria, where severe sepsis was defined as sepsis with hypotension, hypoperfusion or organ dysfunction and septic shock as sepsis with fluid refractory hypotension.[14] The criteria remained unchanged during the study period, but in 2010 the initially used code A41.9 was broken up into R57.2 (septic shock) and R65.1 (systemic inflammatory response syndrome of infectious origin with organ dysfunction). Confirmation of the accuracy of the diagnoses was required at ICU discharge. Data on admitting unit, age, gender, surgical status, Simplified Acute Physiology Score (SAPS) 3, and occurrence of invasive ventilation or continuous renal replacement therapy (CRRT), were retrieved.[15] Data were linked at an individual level with the National Patient Register (NPR) of the Swedish board of Health and Welfare (Socialstyrelsen), adding ICD-10 discharge diagnoses from all hospital admissions between 01-01-2003 and 30-09-2016, and dates of death were retrieved by linkage with the Cause of Death Register (CDR), finally yielding a dataset with blinding of personal identification numbers. We had no direct access to the above mentioned registers during the creation of the study dataset. We limited the dataset to the first ICU admission during the period for any individual, and discharge diagnoses from hospital admissions during 5 years preceding this, which was considered a representative period.

Data on chronic comorbidity were used to calculate the Charlson Comorbidity Index (CCI).[16] Diagnoses were coded according to the Charlson-Deyo algorithm modified for ICD-10.[16,17]

2.3 | Statistical analysis

Demographic and clinical characteristics in 2008 and 2016 were compared with Student´s *t*-test or Mann-Whitney *U*-test, respectively, for parametric and nonparametric continuous variables, and proportions were compared with χ^2 test.

Crude mortality at 30 and 90 days for the whole population and specified subgroups was compared between 2008 and 2016. 365 day mortality was compared between 2008 and 2015 as we did not have complete 1 year follow-up for patients admitted in 2016. Changes were assessed with χ^2-test.

Yearly unadjusted mortality for all septic and nonseptic patients, respectively, at hospital discharge, 30 and 90 days was calculated for the entire period 2008 to 2016, and at 365 days for 2008-2015.

Relevant predictors of mortality, determined by expert opinion and previous experience and tested in univariable logistic regression, were entered in a multivariable logistic regression model, including year of admission as a categorical variable, with mortality at 30, 90 and 365 days as outcome.

2.4 | Missing data and bias

We excluded 3.3% of patients from the mortality analysis because they were foreign citizens, had concealed personal identity numbers

or incomplete death dates and so were lost to follow-up. A relatively high number of patients, 11.5% in the sepsis cohort and 24.1% in the nonsepsis cohort, did not have SAPS3 scores, principally due to a gradual introduction of the SAPS3 risk adjustment model 2008-2010. A smaller number of patients had missing data on surgical status. For these missing data, multiple imputation was carried out using the method of chained Equations[18] For each variable with missing values this method uses regression techniques on the other variables in the analysis set to estimate the conditional distribution of the missing values, from which values to impute are drawn.

Finally, we performed sensitivity analyses by studying adjusted mortality odds ratios only including patients from units reporting to SIR from the start of the study period, and by repeating analyses without imputation of missing data (complete case analysis).

Statistica® v. 13.3, Statsoft, Tulsa, OK, and R, v. 3.5.0, were used in the analyses.

3 | RESULTS

We identified 28 886 sepsis patients and 221 941 nonsepsis patients in the register. A flow chart describing the patient selection in the different analyses is presented in Figure 1.

Characteristics of the patients in 2008 and 2016 are presented in Table 1. There was a small increase in mean age for both sepsis patients, from 64.8 (16.6) to 66.3 (16.6) years (+1.5 years, 95% CI 0.6-2.5, $P = .002$) and nonsepsis patients, from 59.6 (19.6) to 61.1 (19.2) years (+1.5 years, 95% CI 0.4-2.6, $P < .001$), and a small increase in the prevalence and severity of chronic comorbidity in the sepsis cohort. Gender distribution was unchanged with more male patients in the cohorts. Non-surgical admissions accounted for a majority of the cases. The average SAPS3 score decreased slightly in the sepsis cohort from 68.9 (14.3) to 67.1 (14.2), (−1.8, 95% CI −2.6 to −1, $P < .001$), between 2008 and 2016. The number of patients receiving invasive ventilation and CRRT increased in both groups during the same period. Median ICU and hospital length of stay (LoS) decreased between 2008 and 2016.

In the sepsis cohort (Figure 2) between 2008 and 2016, the crude hospital mortality changed from 32.6% to 30.5% (−2.1%, 95% CI −4.7 to 0.5), 30 day mortality from 32.7% to 31.9% (−0.8%, 95% CI −3.4 to 1.8) and 90 day mortality from 39% to 38% (−1%, 95% CI −3.7 to 1.7) 365 day mortality changed between 2008 and 2015 from 46.8% to 45.3% (−1.5%, 95% CI −4.3 to 1.3). Corresponding figures in the nonsepsis cohort (Figure 3) were 15.4% to 15.6% (+0.2%, −1.8 to 2.2), 16.2% to 17.1% (+0.9%, −1.2 to 3), 20% to 20.7% (+0.7%, −1.5 to 3) and 26% to 26.7% (+0.7, −1.8 to 3.2).

Age, sex, SAPS3 score, CCI, hospital type (local, county, regional), invasive ventilation, CRRT and type of admission (medical, surgical), together with year of admission, were entered into a multivariable logistic regression model, calculating adjusted odds ratios for 30, 90 and 365 day mortality, presented in Tables 2 and 3.

Unadjusted mortality at 30 and 90 days for the sepsis and nonsepsis subgroups 2008 vs 2016 and 365 day mortality 2008 vs 2015 are presented in Figure S4 in the Supporting information. A decreased 365-day mortality was seen in sepsis patients without chronic comorbidity (CCI = 0), $P < .001$). 90- and 365-day mortality increased in medical and decreased in surgical patients without sepsis. ($P < .001$).

In the adjusted model, age, SAPS3 score and CCI were predictors of mortality at all time points, and CCI was an increasingly strong predictor with longer follow-up. Non-surgical admissions had higher odds of mortality than surgical admissions. Female patients had higher odds of mortality compared to males. Invasive ventilation and RRT was associated with increased odds of death. There was no consistent effect of year of admission on odds of mortality. These findings were stable in the sensitivity analyses including only units reporting to the registry from the start of the study period, and when performing the analysis without imputation of missing data

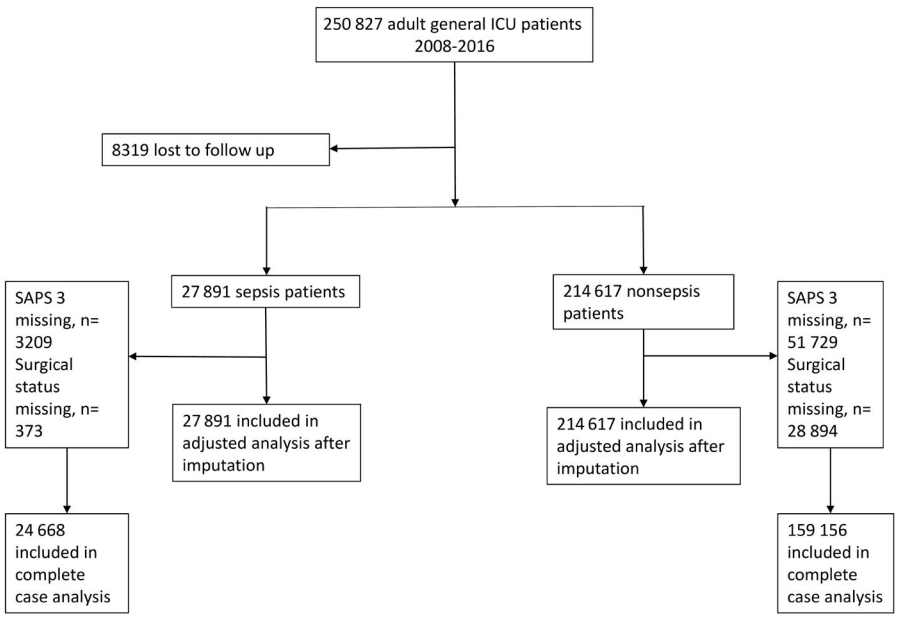

FIGURE 1 Flow diagram of patients included in the analyses

TABLE 1 Characteristics of the sepsis and nonsepsis populations

Year	2008	2008	2016	2016	2016 vs 2008[a]	2016 vs 2008[a]
Diagnosis	**Sepsis**	**Nonsepsis**	**Sepsis**	**Nonsepsis**	**Sepsis**	**Nonsepsis**
Age (mean, SD)	64.8 (16.6)	59.6 (19.6)	66.3 (16.6)	61.1 (19.2)	1.5 (0.6- 2.5), *P* = .002	1.5 (0.4-2.6), *P* < .001
Age n (%)						
18-50 years	349 (16.5)	5615 (29.5)	436 (15.6)	4360 (26.3)	−0.9 (−3 to 1.2), *P* = .37	−3.2 (−5.7 to −0.6), *P* < .001
51-60 years	305 (14.4)	2655 (14)	306 (10.9)	2163 (13)	−3.5 (−5.4 to −1.6), *P* < .001	−1 (−2.9 to −0.9), *P* = .01
61-70 years	556 (26.3)	4160 (21.9)	736 (26.3)	3690 (22.2)	0 (−2.5 to 2.5), *P* = .98	0.3 (−2 to 2.6), *P* = .4
71-80 years	577 (27.3)	3999 (21)	831 (29.7)	4069 (24.5)	2.4 (−0.1 to 4.9), *P* = .07	3.5 (1.1-5.9), *P* < .001
80+ years	326 (15.4)	2609 (13.7)	492 (17.6)	2325 (14)	2.2 (0.1-4.3), *P* = .046	0.3 (−1.7 to 2.2), *P* = .4
Gender, n (%)						
Female	871 (41.2)	7965 (41.8)	1190 (42.5)	6976 (42)	1.3 (−1.5 to 4), *P* = .37	0.2 (−2.6 to 3), *P* = .72
Male	1242 (58.8)	11 073 (58.2)	1611 (57.5)	9628 (58)	−1.3(−4.1 to 1.5), *P* = .37	−0.2 (−3 to 2.6), *P* = .72
Type of Admission, n (%)						
Medical	1790 (84.7)	14 194(80.3)	2371 (84.7)	12 485 (81.1)	0 (−2 to 2), *P* = .95	0.8 (−1.4 to 3), *P* = .055
Surgical	323 (15.3)	3486 (19.7)	430 (15.3)	2906 (18.9)	0 (−2 to 2), *P* = .95	−0.8 (−3 to 1.4), *P* = .055
SAPS3 score (mean, SD)	68.9 (14.3)	52.6 (15.4)	67.1 (14.2)	53 (15.6)	−1.8 (−2.6 to −1), *P* < .001	0.4(−0.48 to 1.3), *P* = .062
CCI (median, IQR)	2 (0-3)	1 (0-2)	2 (1-4)	1 (0-2)	0, *P* = .05[b]	0, *P* < .001[c]
CHF, n (%)	421 (19.9)	2574 (13.5)	647 (23.1)	2456 (14.8)	3 (0.9-5.5), *P* = .008	1.3 (−0.6 to 3.3), *P* < .001
CPD, n (%)	306 (14.5)	2293 (12)	485 (17.3)	2354 (14.2)	2.8 (0.7-4.9), *P* = .007	2.2 (0.3-4.1), *P* < .001
CLD, n (%)	149 (7.1)	906 (4.8)	216 (7.7)	848 (5.1)	0.6 (−0.9 to 2), *P* = 0. 38	0.3 (−0.9 to 1.5), *P* = .13
CRD, n (%)	200 (9.5)	847 (4.5)	345 (12.3)	975 (5.9)	2.8 (1-4.5), *P* = .002	1.4 (0.15-2.6), *P* < .001
Malignancy, n (%)	488 (23.1)	2407 (12.6)	644 (23)	2293 (13.8)[b]	−0.1 (−2.5 to 2.3), *P* = .9	1.2 (−0.7-3.1), *P* = .001
Diabetes, n (%)	454 (21.5)	3486 (18.3)	710 (25.4)[b]	3131 (18.9)	3.9 (1.5-6.3), *P* = .002	0.6 (−1.5 to 2.8), *P* = .19
ICU LoS (median, IQR)	3 (1-7)	1 (1-2)	2 (1-5)	1 (1-2)	−1, *P* < .001	0, *P* < .001[c]
Hospital LoS (median, IQR)	13 (6-25)	7 (3-14)	10 (5-20)	6 (3-13)	−3, *P* < .001	−1, *P* < .001
Invasive ventilation, n (%)	814 (38.5)	3824 (20.1)	1189 (42.5)	5327 (32.1)	4 (1.2-6.8), *P* = .006	12 (9.6-14.4), *P* < .001
CRRT, n (%)	283 (13.4)	313 (1.6)	449 (16)	490 (3)	2.6 (0.6-4.6), *P* = .01	1.4 (0.6-2.2), *P* < .001

Abbreviations: CCI, Charlson Comorbidity Index; CHF, chronic heart failure; CLD, chronic liver disease; CPD, chronic pulmonary disease; CRD, chronic renal disease; CRRT, continuous renal replacement therapy; SAPS, Simplified Acute Physiology Score.

[a]Difference (95% CI).

[b]Increase.

[c]Decrease.

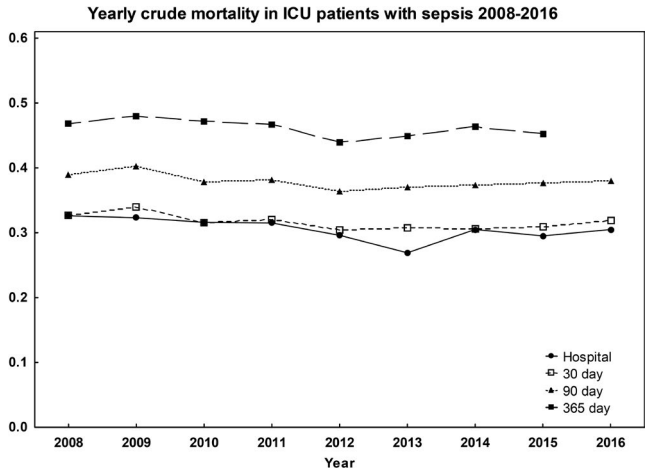

FIGURE 2 Crude mortality at hospital discharge, 30- 90- and 365 days for ICU patients with severe sepsis or septic shock

(complete case analysis). Results from the sensitivity analyses are available in Tables S3-S8 in the Supporting Information.

4 | DISCUSSION

The principal finding in this nationwide observational study of ICU patients with sepsis was that we found no substantial and consistent change in crude or risk factor adjusted mortality up to one year between 2008 and 2016. The results are in contrast with recent large observational studies that have demonstrated a substantial decrease in the mortality of severe sepsis in the 21st century. Notably, Kaukonen et al in a study of severe sepsis and septic shock patients in Australia and New Zealand presented a decrease in crude in-hospital mortality from 35% in 2002 to 18.4% in 2012, which was nearly linear over the study period.[5] A risk adjusted model also demonstrated a consistent annual decrease in the odds ratio for hospital mortality. The patients in this study had a lower average estimated mortality than our patients, but half of them received mechanical ventilation.

Kumar et al, with data from a large US inpatient database, found decreased crude in-hospital mortality rates for severe sepsis from 39.6% in 2000 to 27.3% in 2007 with an adjusted odds ratio 2007 vs 2000 of 0.46 (95% CI 0.44-0.49).[6] During the same time, the estimated incidence increased from 143/100 000 to 343/100 000. An increased fraction of survivors were discharged to long-term care facilities at the end of the study period.

Differences in mortality between studies may be attributed to several factors, of which ICU admission criteria and variations in case mix are probably important. Uncomplicated infections requiring hospitalization but not ICU admission have low mortality, while the mean crude in-hospital mortality for septic shock was reported to be 46% on average in a meta-analysis of 44 studies of septic shock.[19,20]Although several longitudinal studies report late mortality for large sepsis cohorts, most included patients were not ICU patients and mortality rates at time points corresponding to our study were much lower, suggesting that illness severity was lower than in our cohort.[21,22] Sepsis mortality comparable to our results were found in two studies on mostly elderly, non-ICU patients with presumably more co-morbidities in comparison to our septic study cohort.[23,24] This is in line with the finding in this and other studies that, apart from the acute illness requiring intensive care, co-morbidity is an important determinant of longer term mortality.[25] In this context, the decreasing mortality in the subgroup of sepsis patients without chronic comorbidity found in our data could suggest that any improvements in care may have a greater impact in this group. In a recently reported follow-up of a randomized controlled trial (RCT) 6-month mortality was 32% which is lower than the 90-day mortality in our unselected sepsis cohort, a result probably explained by differences in patient selection driven by the inclusion criteria of the RCT.[26] Interestingly, the mortality of the Scandinavian patients in this multicentre trial was higher than that of the patients from Australia and New Zealand.

In contrast with the trend reported in epidemiological studies, our data did not demonstrate a substantially reduced mortality between 2008 and 2016.[5,6,27-29] The reasons for this are not clear. Hypothetically, there might be a difference between the fixed time mortality assessed in our study, and hospital mortality. However, the hospital mortality in our study was similar to mortality at 30 days and did not decrease significantly during the study period. Early mortality contributed substantially to total mortality, with 10.1% mortality on the first day and 19.9% in the first week after ICU admission in the sepsis cohort.

In a recently published study comparing ICU populations identified by sepsis 2 and sepsis 3 criteria, a decreasing hospital mortality was seen in sepsis without shock, but not in septic shock identified by the sepsis 3 criteria. These findings suggest that the frequency and severity of circulatory dysfunction in the case mix could have a considerable impact on the trend in mortality. [8]

Recent data suggest that increased recognition and coding of less severe cases might confound trends in mortality, creating the impression of a decrease.[30] A reported combined trend of increasing incidence and decreasing mortality might support such a hypothesis.[6]

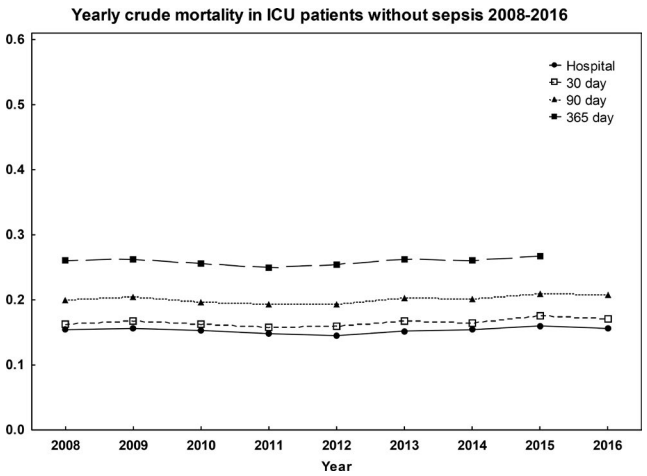

FIGURE 3 Crude mortality at hospital discharge, 30- 90- and 365 days for ICU patients without severe sepsis or septic shock

Of note, however, is that our data, reflecting the Swedish ICU population where sepsis is identified with ICD-10 codes registered by ICU physicians, do not show a decreasing mortality. An alternative explanation could be that Swedish health care has not improved as well as that in other countries for sepsis patients. Yet over a wide range of diagnoses, quality of Swedish health care is comparable to other Western countries.[31]

Our reported ICU LoS is shorter than in some other epidemiologic studies, but this parameter is highly variable between different cohorts according to recent sepsis studies, and not necessarily associated with outcome.[5,6,32-36] Furthermore, short ICU stays seem to be a characteristic of Nordic countries, as shown by a joint analysis of intensive care in Sweden, Finland and Norway, and probably reflect a small number of ICU beds per capita.[33,37] Mortality in Swedish ICUs is low and the short ICU LoS will increase demand for a high level of post-ICU care as the outcome will be greatly influenced by this.[33]

In some studies patients have been defined as septic or not at ICU admission or within the first 24 hours while in this study any sepsis occurring during the ICU episode was included.[5] This could potentially affect the case mix of the studies. However, regardless of the time of diagnosis, sepsis is a heterogeneous condition and the underlying comorbidity will vary. Also, the short average ICU LoS in this study implies that many patients are diagnosed within a short time frame.

In many epidemiological studies, the outcome measure is hospital mortality, which can be influenced by discharge practices. Our

TABLE 2 Adjusted odds ratios for 30-, 90- and 365-day mortality in the sepsis population

Variable	OR (95% CI) 30 day mortality	OR (95% CI) 90 day mortality	OR (95% CI) 365 day mortality
SAPS3[a]	1.06 (1.06-1.06)	1.06 (1.05-1.06)	1.05 (1.05-1.06)
CCI[a]	1.10 (1.09-1.12)	1.16 (1.15-1.18)	1.25 (1.23-1.27)
Age 50-59 years[b]	1.23 (1.07-1.4)	1.22 (1.08 −1.38)	1.34 (1.19-1.52)
Age 60-69 years[b]	1.5 (1.35-1.7)	1.56 (1.41-1.74)	1.68 (1.51-1.87)
Age 70-79 years[b]	1.83 (1.63-2.05)	1.98 (1.78-2.2)	2.23 (2.06-2.51)
Age 80+ years[b]	3.22 (2.85-3.64)	3.52 (3.14-3.95)	3.87 (3.44-4.35)
Medical admission[c]	1.38 (1.27-1.51)	1.35 (1.24-1.46)	1.28 (1.17-1.39)
Local hospital[d]	1 (0.92-1.09)	0.97 (0.89-1.05)	0.95 (0.87-1.03)
County hospital[d]	1.10 (1.04-1.19)	1.04 (0.97-1.11)	1 (0.93-1.07)
Invasive ventilation	1.83 (1.71-1.95)	1.84 (1.73-1.96)	1.52 (1.42-1.62)
CRRT	1.08 (0.99-1.17)	1.2 (1.1-1.3)	1.11 (1.01-1.21)
Female sex[e]	1.22 (1.15-1.3)	1.18 (1.12-1.25)	1.05 (1.04-1.17)
Admission year 2009[f]	0.98 (0.85-1.13)	0.98 (0.85-1.13)	0.96 (0.94-1.11)
Admission year 2010[f]	0.89 (0.78-1.03)	0.89 (0.79-1.02)	0.97 (0.85-1.11)
Admission year 2011[f]	0.96 (0.84-1.09)	0.93 (0.82-1.06)	0.95 (0.84-1.08)
Admission year 2012[f]	0.87 (0.76-0.99)	0.85 (0.75-0.96)	0.83 (0.73-0.94)
Admission year 2013[f]	0.86 (0.76-0.98)	0.85 (0.75-0.97)	0.85 (0.74-0.96)
Admission year 2014[f]	0.88 (0.77-1)	0.89 (0.78-1.01)	0.92 (0.81-1.05)
Admission year 2015[f]	0.89 (0.79-1.02)	0.9 (0.79-1.02)	0.87 (0.77-0.98)
Admission year 2016[f]	0.94 (0.82-1.08)	0.91 (0.8-1.04)	—

Abbreviations: CCI, Charlson Comorbidity Index; CRRT, Continuous Renal Replacement Therapy; SAPS, Simplified Acute Physiology Score.

[a]One point increase.

[b]Reference 18-49 years.

[c]Reference surgical admission.

[d]Reference regional hospital.

[e]Reference male.

[f]Reference year 2008.

data allow longer term follow-up of the admitted patients. An additional strength is the nation-wide data, since a majority of general ICU patients with sepsis diagnoses in Sweden during the period was included. Also, apart from ICU related data, we could link chronic health status to outcome data.

A limitation of the study, as of similar studies, is that it is dependent on coding practices. ICUs reporting to SIR typically have access to software-integrated guidelines on how to assign ICD-10 codes. The designation by SIR of severe sepsis as one of a few key diagnoses aimed to diminish the number of missing cases and coding errors. While ICD-10 coding definitions and use may vary across countries and health care systems, the purpose of the three codes used on discharge from ICU was solely to facilitate follow-up of sepsis as defined in Methods. Another limitation is that the coverage of SIR increased during the study period. However, key findings were unchanged in a sensitivity analysis with only units reporting from the start of the period. Finally, we used imputation to account for a significant number of missing data on relevant parameters. The results remained when we performed an identical analysis using complete cases only, indicating that the key findings were robust.

The results of this study raise questions that warrant further investigation. As the mortality in the studied population does not appear to have changed significantly over recent years, it is important to seek explanations and study the primary causes of death in these patients, as this could allow better follow-up and possibly preventive interventions. Furthermore, a comparison between

TABLE 3 Adjusted odds ratios for 30- 90- and 365-day mortality in the nonsepsis population

Variable	OR (95% CI) 30 day mortality	OR (95% CI) 90 day mortality	OR (95% CI) 365 day mortality
SAPS3[a]	1.09 (1.09-1.09)	1.08 (1.08-1.08)	1.07 (1.07-1.08)
CCI[a]	1.10 (1.10-1.11)	1.16 (1.15-1.17)	1.25 (1.24-1.25)
Age 50-59 years[b]	1.53 (1.43-1.63)	1.58 (1.49-1.67)	1.63 (1.54-1.72)
Age 60-69 years[b]	1.65 (1.56-1.74)	1.78 (1.69-1.87)	1.81 (1.73-2.09)
Age 70-79 years[b]	1.87 (1.77-1.98)	2.09 (1.99-2.2)	2.14 (2.04-2.25)
Age 80+ years[b]	3.07 (2.9-3.25)	3.41 (3.23-3.6)	3.78 (3.59-3.98)
Medical admission[c]	1.71 (1.64-1.78)	1.56 (1.5-1.62)	1.38 (1.33-1.43)
Local hospital[d]	1.42 (1.36-1.48)	1.44 (1.39-1.5)	1.45 (1.4-1.5)
County hospital[d]	1.51 (1.46-1.56)	1. 5 (1.45-1.55)	1.51 (1.47-1.56)
Invasive ventilation	1.42 (1.38-1.48)	1.3 (1.26-1.45)	1.09 (1.06-1.13)
CRRT	1.22 (1.13-1.31)	1.4 (1.31-1.51)	1.34 (1.25-1.44)
Female sex[e]	1.08 (1.05-1.11)	1.08 (1.05-1.11)	1.06 (1.03-1.09)
Admission year 2009[f]	1.02 (0.95-1.09)	1.02 (0.95-1.08)	1 (0.94-1.06)
Admission year 2010[f]	0.97 (0.9-1.03)	0.96 (0.9-1.02)	0.96 (0.91-1.01)
Admission year 2011[f]	0.96 (0.9-1.02)	0.96 (0.9-1.02)	0.97 (0.92-1.02)
Admission year 2012[f]	0.92 (0.86-0.98)	0.89 (0.84-0.95)	0.93 (0.88-0.98)
Admission year 2013[f]	0.91 (0.85-0.98)	0.91 (0.85-0.97)	0.93(0.97-0.98)
Admission year 2014[f]	0.91 (0.85-0.97)	0.91 (0.85-0.96)	0.93 (0.88-0.99)
Admission year 2015[f]	0.98 (0.92-1.05)	0.95(0.9-1.01)	0.96 (0.91-1.01)
Admission year 2016[f]	0.93 (0.87-1)	0.92 (0.86-0.98)	—

Abbreviations: CCI, Charlson Comorbidity Index; CRRT, Continuous Renal Replacement Therapy; SAPS, Simplified Acute Physiology Score.

[a]One point increase.

[b]Reference 18-49 years.

[c]Reference surgical admission.

[d]Reference regional hospital.

[e]Reference male.

[f]Reference year 2008.

sepsis populations in different health care systems might provide clues to the reasons for the observed differences between recent studies, and facilitate more generalizable benchmarking.

5 | CONCLUSIONS

In the Swedish ICU population with severe sepsis and septic shock, as in the nonsepsis ICU population, we did not see a major decrease in mortality over recent years.

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CONFLICT OF INTERESTS

Dr Walther was chairman and member of the board of the Swedish Intensive Care Registry from 2001 to 2012. Dr Agvald Öhman was a board member from 2007 to 2012, and chairman from 2012 to 2018, for the Swedish Intensive Care Registry.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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