Outcomes of the Surviving Sepsis Campaign in intensive care units in the USA and Europe: a prospective cohort study

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Summary

Background Mortality from severe sepsis and septic shock differs across continents, countries, and regions. We aimed to use data from the Surviving Sepsis Campaign (SSC) to compare models of care and outcomes for patients with severe sepsis and septic shock in the USA and Europe.

Methods The SSC was introduced into more than 200 sites in Europe and the USA. All patients identified with severe sepsis and septic shock in emergency departments or hospital wards and admitted to intensive care units (ICUs), and those with sepsis in ICUs were entered into the SSC database. Patients entered into the database from its launch in January, 2005, through January, 2010, in units with at least 20 patients and 3 months of enrolment of patients were included in this analysis. Patients included in the cohort were limited to those entered in the first 4 years at every site. We used random-effects logistic regression to estimate the hospital mortality odds ratio (OR) for Europe relative to the USA. We used random-effects linear regression to find the relation between lengths of stay in hospital and ICU and geographic region.

Findings 25 375 patients were included in the cohort. The USA included 107 sites with 18 766 (74%) patients, and Europe included 79 hospital sites with 6609 (26%) patients. In the USA, 12 218 (65·1%) were admitted to the ICU from the emergency department whereas in Europe, 3405 (51·5%) were admitted from the wards. The median stay on the hospital wards before ICU admission was longer in Europe than in the USA (1·0 *vs* 0·1 days, difference 0·9, 95% CI 0·8–0·9). Raw hospital mortality was higher in Europe than in the USA (41·1% *vs* 28·3%, difference 12·8, 95% CI 11·5–14·7). The median length of stay in ICU (7·8 *vs* 4·2 days, 3·6, 3·3–3·7) and hospital (22·8 *vs* 10·5 days, 12·3, 11·9–12·8) was longer in Europe than in the USA. Adjusted mortality in Europe was not significantly higher than that in the USA (32·3% *vs* 31·3%, 1·0, –1·7 to 3·7, p=0·468). Complete compliance with all applicable elements of the sepsis resuscitation bundle was higher in the USA than in Europe (21·6% *vs* 18·4%, 3·2, 2·2–4·4).

Interpretation The significant difference in unadjusted mortality and the fact that this difference disappears with severity adjustment raise important questions about the effect of the approach to critical care in Europe compared with that in the USA. The effect of ICU bed availability on outcomes in patients with severe sepsis and septic shock requires further investigation.

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Introduction

Mortality from severe sepsis and septic shock differs across continents, countries, and regions, with reported outcomes ranging between 22% and 76%.[1–8] This wide variation in mortality is probably due to several factors such as age, comorbid disease burden, regional health patterns, access to care, and various other unrecognised genomic influences.[9–14] Additionally, large differences exist in the delivery of health care between countries, which are exemplified by the differing numbers of beds in intensive care units (ICUs) referenced to either the population size or the number of beds in acute care hospitals.[15–23]

This wide global variation in ICU bed availability has given rise to several different care models for patients with severe sepsis. In countries with poor ICU bed availability, many patients with severe sepsis are admitted to the general wards initially, in which they are cared for until they either recover to discharge or worsen, necessitating transfer to ICU.[24] A major difference between the approaches to care in the USA and those in Europe is that the US model admits more patients directly to ICUs from emergency departments.[25] These different approaches to care for severe sepsis and septic shock allow for regional comparisons that might inform alternative treatment approaches for this susceptible population.

The Surviving Sepsis Campaign (SSC) is a global initiative launched at more than 200 sites internationally to measure and compare changes in adherence to sepsis quality indicators and to assess any association of compliance with in-hospital mortality. After the development of evidence-based guidelines,[26,27] the SSC steering committee partnered with the Institute for Healthcare Improvement to develop a quality improvement programme to extend the campaign guidelines to the bedside

management of patients with severe sepsis and those with septic shock.[28] In partnership with the Institute for Healthcare Improvement, key elements of the guidelines were identified and organised into so-called bundles of care.[29] A two-phase approach was established that included the generation of two sets of performance measures: the first to be accomplished within 6 h of presentation with severe sepsis (the resuscitation bundle) and a second set to be accomplished within 24 h (the management bundle).[25]

The aim of this study was to use the large database of the SCC to compare models of care and outcomes of compliance, mortality, and length of stay for patients with severe sepsis and septic shock in the USA and Europe.

	USA	Europe	p value*
Count	18766 (74·0%)	6609 (26·0%)	
Hospital mortality	5313 (28·3%)	2719 (41·1%)	<0·0001
Origin			<0·0001
Emergency department	12218 (65·1%)	2159 (32·7%)	
Ward	4763 (25·4%)	3405 (51·5%)	
ICU	1785 (9·5%)	1045 (15·8%)	
Hospital mortality if origin is emergency department	3008 (24·6%)	736 (34·1%)	<0·0001
Hospital mortality if origin is ward	1661 (34·9%)	1481 (43·5%)	<0·0001
Hospital mortality if origin is ICU	644 (36·1%)	502 (48·0%)	<0·0001
Median ICU length of stay (days)	4·2 (2·2–8·9)	7·8 (3·4–17·2)	<0·0001
Median hospital length of stay (days)	10·5 (5·8–18·9)	22·8 (11·1–43·3)	<0·0001
Median length of stay before ICU admission (days)	0·1 (0·0–0·6)	1·0 (0·2–6·0)	<0·0001
Median length of stay before ICU admission if origin is emergency department (days)	0·1 (0·0–0·2)	0·2 (0·0–0·4)	<0·0001
Median length of stay before ICU admission if origin is ward (days)	1·5 (0·4–5·6)	3·4 (0·8–10·4)	<0·0001
Median length of stay before ICU admission if origin is ICU (days)	0·3 (0·0–2·0)	1·3 (0·1–6·2)	<0·0001
Organ failure			
Cardiovascular	16407 (87·4%)	5769 (87·3%)	0·769
Pulmonary	3674 (19·6%)	3147 (47·6%)	<0·0001
Haematology	3879 (20·7%)	2218 (33·6%)	<0·0001
Hepatic	1586 (8·5%)	909 (13·8%)	<0·0001
Renal	6490 (34·6%)	3071 (46·5%)	<0·0001
Mechanical ventilation	7761 (41·4%)	4498 (68·1%)	<0·0001
Number of acute organ dysfunction			
1	9098 (48·5%)	1854 (28·1%)	<0·0001
2	6564 (35·0%)	2163 (32·7%)	0·0009
3	2461 (13·1%)	1628 (24·6%)	<0·0001
4	572 (3·0%)	748 (11·3%)	<0·0001
5	71 (0·4%)	216 (3·3%)	<0·0001
Cardiovascular			
No cardiovascular dysfunction	1865 (9·9%)	653 (9·9%)	0·893
Cardiovascular dysfunction no hypotension	4104 (21·9%)	808 (12·2%)	<0·0001
Lactate concentration >4 mmol/L only	1316 (7·0%)	193 (2·9%)	<0·0001
Vasopressors only	8356 (44·5%)	3782 (57·2%)	<0·0001
Lactate concentration >4 mmol/L and vasopressors	3125 (16·7%)	1173 (17·8%)	0·041
Nosocomial infection	3506 (18·7%)	2809 (42·5%)	<0·0001

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Methods

Study design and patients

Part of the SSC included the creation and maintenance of a database of select information on patients and institutions. The entry of patient details into this electronic database was voluntary and at the discretion of treating clinicians. This study is an analysis of this prospectively collected database.

We analysed data from patients entered into the SSC database from its launch in January, 2005, to January, 2010. The a priori data analysis plan limited inclusion to sites with at least 20 patients and at least 3 months of enrolment of patients. Patients included in the cohort were limited to those entered in the first 4 years at every site and included only data from Europe and the USA. All patients had to have had confirmed severe sepsis or septic shock according to the SSC diagnosis screening approach and have been treated within the ICU. We recorded the location from which the patients were first identified with severe sepsis or septic shock (emergency department, ward, or ICU). Hospitals in both Europe and the USA opted to enter patients in the SSC database and, as such, this was not a randomised study that compared Europe with the USA.

The global SSC improvement initiative was reviewed and approved by the Cooper University Hospital Institutional Review Board (Camden, NJ, USA) as meeting criteria for exempt status. Individual hospitals were encouraged to refer to these documents and submit to their local institutional review boards per local policy for documentation of exempt status or waiver of consent. The US Department of Health and Human Services' Office for Human Research Protections had previously clarified that quality improvement activities such as SSC often qualify for exemption and do not require individual informed consent.[30]

Outcomes

In the original report of the SSC data,[25] the primary outcome measure of this study was change in compliance with bundle targets over time. We chose this outcome measure to quantify the effect of the multifaceted intervention on clinical practice behaviour. We defined compliance as evidence that all bundle elements were achieved within the indicated timeframe (ie, 6 h for the resuscitation bundle and 24 h for the management bundle). Secondary outcome measures reported included hospital mortality, hospital length of stay, and ICU length of stay.

Statistical analysis

We compare clinical characteristics across Europe and the USA using either the Pearson χ^2 test for categorical variables or the Wilcoxon rank-sum test for continuous variables. We present categorical variables as counts and percentages and continuous variables as medians. We present patient characteristics as differences including the

95% CI instead of p values because of the large sample sizes. Differences are absolute values. We used random-effects logistic regression to estimate the hospital mortality odds ratio (OR) for Europe relative to the USA and random-effects linear regression to find the relation between lengths of stay in hospital and ICU and geographic region. Length of stay is right skewed and was natural-log transformed to meet normality conditions and stabilise the variance across groups. When the regression coefficients are back-transformed to length of stay, the exponentiated coefficient is interpreted as a multiplier of length of stay of Europe relative to the USA. This approach takes into account that patients who are nested within individual sites (hospitals) and thus uses the within-site and between-site variance to estimate the standard error used to test model coefficients. Since the study's goal was not to estimate the probability of hospital mortality, but rather to identify the role of geographic region on survival, we used a risk factor modelling approach to identify which covariates to add to the model. We included only covariates that acted either as a confounder or as an effect modifier. A confounder was identified when its addition changed the hazard ratio (HR) associated with the risk factor (geographic region) by more than 10% in either direction, without considering statistical significance. We deemed a covariate that had a significant (p value ≤0·05) interaction with geographic region to be an effect modifier. We used this same statistical approach to find the relation between length of stay and region. We ran all analyses using Stata 12.1 (Stata Corporation, College Station, TX, USA).

Role of the funding source

The sponsor of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

25 375 patients fulfilled the cohort description and were analysed from the database (table 1). The USA included 107 sites with 18 766 (74%) patients while Europe included 79 hospital sites with 6609 (26%) patients. The predominant cause of severe sepsis from either region was pneumonia. Most patients at time of ICU admission had multiple organ failure, tissue hypoperfusion (as evidenced by hypotension or hyperlactataemia), and required mechanical ventilation. The overall hospital mortality was 32% (8032 of 25 375 patients died).

More patients in the USA than in Europe were admitted to ICUs from emergency departments; in Europe more patients were admitted from general wards (table 1). The median stay on the hospital wards before ICU admission was longer in Europe (difference 0·9 days, 95% CI 0·8–0·9). The percentage of patients presenting with single-organ failure was significantly higher in the USA than in Europe. Patients in Europe had more multiple organ dysfunction than those in USA. Nosocomial infection was more common in Europe than in the USA (difference 23·8%, 22·5–25·1). More patients were treated with mechanical ventilation in Europe than in the USA (26·7%, 25·4–28·0). Raw hospital mortality was higher in Europe than in the USA (12·8%, 11·5–14·7) across all locations where sepsis was diagnosed. The

	USA	Europe	p value*
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Infection site			
Pneumonia	8589 (45·8%)	2986 (45·2%)	0·409
Urinary tract	5744 (30·6%)	570 (8·6%)	<0·0001
Abdominal	3589 (19·2%)	2105 (31·9%)	<0·0001
Meningitis	204 (1·1%)	157 (2·4%)	<0·0001
Skin	1369 (7·3%)	272 (4·1%)	<0·0001
Bone	302 (1·6%)	75 (1·1%)	0·006
Wound	1119 (6·0%)	159 (2·4%)	<0·0001
Catheter	928 (4·9%)	174 (2·6%)	<0·0001
Endocarditis	196 (1·0%)	95 (1·4%)	0·010
Device	264 (1·4%)	60 (0·9%)	0·002
Other infection	2850 (15·2%)	498 (7·5%)	<0·0001

Data are number of patients (%) or median (IQR). ICU=intensive care unit. *p value is based on either Pearson's χ^2 test for categorical variables or Wilcoxon rank-sum test for continuous variables.

Table 1: **Descriptive statistics by region**

	USA (N=18 766)	Europe (N=6609)	p value
Compliance with all applicable elements of sepsis resuscitation bundle	21·6%	18·4%	<0·0001
Serum lactate obtained within 6 h of presentation	70·1%	71·9%	0·005
Blood cultures obtained before broad-spectrum antibiotic administration	83·7%	64·7%	<0·0001
Broad-spectrum antibiotic given within 3 h of admission to emergency department or 1 h of non-emergency department admission	70·8%	63·9%	<0·0001
For hypotension or lactate concentration >4 mmol/L, 20 mg/kg crystalloid fluid bolus delivered followed by vasopressors if needed to maintain MAP ≥65 mm Hg	70·0%	72·6%	0·0001
For septic shock or lactate >4 mmol/L, CVP ≥8 mm Hg achieved within 6 h of presentation	25·7%	45·2%	<0·0001
For septic shock or lactate >4 mmol/L, $ScvO_2$ 70% (or SvO_2 65%) achieved within 6 h of presentation	17·1%	25·8%	<0·0001
Compliance with all applicable elements of sepsis management bundle	19·8%	28·2%	<0·0001
Low dose steroids given in accordance with standardised ICU policy within 24 h of presentation	59·6%	71·0%	<0·0001
Drotrecogin alfa given in accordance with standardised ICU policy within 24 h of presentation	39·8%	64·2%	<0·0001
Glucose control maintained >lower limit of normal with median <150 mg/dL (8·3 mmol/L) 6–24 h after presentation	53·5%	56·8%	<0·0001
Median inspiratory plateau pressure <30 cm H_2O over first 24 h after presentation	84·7%	85·1%	0·516

MAP=mean arterial pressure. CVP=central venous pressure. $ScvO_2$=central venous oxygen saturation. SvO_2=mixed venous oxygen saturation. ICU=intensive care unit.

Table 2: **Compliance with sepsis care measures**

	Emergency department	Ward	ICU	Total hospital mortality
USA	3008/12 212	1661/4763	664/1785	5313/18 766
Europe	766/2159	1481/3405	502/1045	2719/6609
OR unadjusted	1·65 (1·42–1·91); p<0·0001	1·51 (1·30–1·71); p<0·0001	1·61 (1·32–1·96); p<0·0001	1·80 (1·58–2·06); p<0·001
OR adjusted*	1·05 (0·89–1·23); p=0·597	1·00 (0·86–1·18); p=0·965	1·19 (0·96–1·47); p=0·106	1·05 (0·92–1·21); p=0·467

OR=odds ratio. ICU=intensive care unit. *Adjusted for admission source (emergency department, ward, or ICU), pulmonary infection (yes or no), mechanical ventilation (yes or no), pulmonary organ failure (yes or no), interaction between pulmonary organ failure and mechanical ventilation, cardiovascular organ failure (yes or no), haematological organ failure (yes or no), hepatic organ failure (yes or no), renal organ failure (yes or no), time in hospital before ICU admission, site quarter, and shock set (no cardiovascular disease, cardiovascular disease without hypotension, lactate concentration >4 mmol/L only, vasopressors only, or lactate concentration >4 mmol/L plus vasopressors).

Table 3: **Hospital mortality odds ratio by region for admission source measured random-effects logistic regression**

	USA			Europe		
	Emergency department	Ward	ICU	Emergency department	Ward	ICU
Survivors						
Hospital	9·7 (6·0–15·9)	16·6 (9·9–28·7)	18·0 (10·5–30·3)	18·6 (11·1–34·5)	32·9 (18·2–57·2)	38·2 (20·9–63·0)
ICU	3·6 (2·0–7·0)	5·0 (2·8–10·1)	8·4 (4·1–16·9)	6·6 (3·4–12·9)	7·7 (3·8–16·0)	15·2 (6·6–30·9)
Pre-ICU	0·1 (0·0–0·2)	1·2 (0·3–4·3)	0·2 (0·0–1·4)	0·2 (0·0–0·4)	2·7 (0·6–8·6)	1·1 (0·1–5·0)
Dead patients						
Hospital	5·2 (2·0–11·6)	11·3 (5·2–21·8)	13·0 (6·6–22·9)	7·9 (2·4–20·8)	19·0 (8·9–34·5)	22·3 (11·0–42·8)
ICU	3·9 (1·6–8·6)	4·8 (1·9–10·5)	8·9 (4·0–17·2)	5·0 (1·7–14·4)	7·4 (2·7–16·7)	13·7 (6·2–27·9)
Pre-ICU	0·1 (0·0–0·2)	2·5 (0·6–7·8)	0·5 (0·1–3·7)	0·2 (0·0–0·5)	4·4 (1·1–12·3)	1·8 (0·2–9·2)

Medians are shown with IQRs. ICU=intensive-care unit. Lengths of stay are shown in days.

Table 4: **Comparison of median length of stay by region, sepsis origin, and survival status**

	European LOS multiplier relative to the USA (95% CI)	p value
Unadjusted hospital LOS	1·96 (1·79–2·15)	<0·0001
Adjusted* hospital LOS	1·50 (1·42–1·58)	<0·0001
Unadjusted ICU LOS	1·66 (1·50–1·82)	<0·0001
Adjusted* ICU LOS	1·29 (1·20–1·40)	<0·0001

LOS=length of stay. ICU=intensive care unit. LOS was right skewed and was thus natural log transformed to meet normality conditions and stabilise the variance across groups. When the regression coefficients were back-transformed to length of stay, the exponentiated coefficient was interpreted as a multiplier of LOS of Europe relative to the USA. *Adjusted for survival status (alive at hospital discharge, died in the ICU, died in hospital post ICU discharge), admission source (emergency department, ward, or ICU), pulmonary infection (yes or no), mechanical ventilation (yes or no), pulmonary organ failure (yes or no), interaction between pulmonary organ failure and mechanical ventilation, cardiovascular organ failure (yes or no), haematological organ failure (yes or no), hepatic organ failure (yes or no), renal organ failure (yes or no), time in hospital before ICU admission, site quarter, and shock set (no cardiovascular disease, cardiovascular disease without hypotension, lactate concentration >4 mmol/L only, vasopressors only, or lactate concentration >4 mmol/L plus vasopressors).

Table 5: **Length of stay multiplier by region using random-effects linear regression**

See Online for appendix

median lengths of stay were longer in Europe than in the USA in ICU (difference 3·6 days, 3·3–3·7) and in hospital (12·3 days, 11·9–12·8).

Rates of compliance with the sepsis care measures differed significantly between regions (table 2). Complete compliance with all applicable elements of the sepsis resuscitation bundle was higher in the USA than in Europe (difference 3·2%, 95% CI 2·2–4·4) whereas compliance with four of six individual components of the resuscitation bundle was higher in Europe. Complete compliance with all applicable elements of sepsis management bundle was higher in Europe than in the USA (8·4%, 7·2–9·7).

The unadjusted results suggest that the odds of hospital mortality were between 51% and 65% higher in Europe than in the USA (p<0·0001; table 3). This unadjusted result parallels the higher mortality noted in the patients in Europe compared with those in the USA. We entered all the adjustment variables into the model as confounders and not as effect modifiers on the basis of the statistical analysis. After adjusting for sepsis origin, pulmonary infection, cardiovascular organ failure, pulmonary organ failure, haematological organ failure, hepatic organ failure, renal organ failure, length of stay before ICU admission, mechanical ventilation, resuscitation performance, and management performance, the odds of mortality were between 5% and 19% higher in Europe than in the USA; however, these results were no longer significantly different from an OR of 1·0. A sensitivity analysis confirmed these results by use of propensity score matching 1716 patients in Europe with 1716 patients in the USA. The ORs and p values were similar to the adjusted analysis on the entire study population. Further details of this sensitivity analysis can be found in the appendix.

Length of stay in hospital, in ICU, and before ICU was greater in Europe than in the USA (table 4). In the ICU, the unadjusted length of stay in Europe was 1·66 times longer than the USA, whereas the adjusted length of stay was 1·29 times longer (both p values <0·0001; table 5). The unadjusted hospital length of stay was 1·96 times longer in Europe than in the USA, whereas the adjusted hospital length of stay was 1·50 times longer (both p values <0·0001; table 5).

Discussion

Unadjusted ICU mortality differed significantly between the USA and Europe: patients admitted to the ICU with severe sepsis and septic shock in Europe were more severely ill than those in the USA, as evidenced by increased numbers of organ failure and a greater need for mechanical ventilation, and a longer length of stay in

hospital in Europe than in the USA. Our results showed a clear mortality difference between the two regions. The higher unadjusted mortality OR in Europe disappeared with severity adjustment.

Although there are many descriptive studies in the literature about the difference in models of ICU care delivery between the USA and Europe, very few, if any, studies exist that directly compare outcomes in sepsis between Europe and the USA (panel). The present study is the first to directly compare outcomes between these regions in patients with severe sepsis and septic shock identified in the emergency department, general wards, and in the ICU.

The results of this study are intriguing and raise questions that, unfortunately, cannot be answered by the current database, but which should lead to further studies in the specialty. Perhaps the most significant difference between the two regions is the origin of patients before ICU admission. In the USA, close to two-thirds of patients were admitted to the ICU directly from the emergency department, whereas in Europe, most patients were admitted to ICUs from wards.

This study has several limitations. Hospitals in both Europe and the USA self-selected to enter patients in the SSC database. Therefore, this study was not a randomised study that compared Europe to the USA and the results might not be representative of either region. Perhaps the most important limitation of this study is that only patients admitted to the ICU were entered into the database. Hence the SSC database could not track the percentage of patients with severe sepsis who were admitted to the wards and discharged without ICU care—either because they improved without needing ICU admission or because they died on the ward. Therefore, the true mortality rate for patients admitted to wards with severe sepsis in both regions is not available. This limitation might account for the mortality difference between the two regions, since patients with severe sepsis admitted to the wards in Europe who do well and are ultimately discharged are not recorded. The true number of patients who did well on the wards as opposed to those who perhaps were inadequately resuscitated on the wards and, therefore deteriorated, is unknown.

Given the higher number of ICU beds per head in the USA than in Europe,[18] more patients with severe sepsis of lower acuity could possibly be admitted to the ICU. This limitation might account for the higher severity of illness noted in patients admitted to ICUs in Europe and also explain why, with severity adjustment, the OR for mortality did not differ significantly between the two regions. The alternative hypothesis is that, because of the more limited availability of ICU beds in Europe, patients with severe sepsis are triaged to wards, where they might receive less resuscitation and monitoring than in an ICU, leading to deterioration, and are then transferred into the ICU with a higher severity of illness and worse prognosis than if they had been initially admitted to the ICU. This hypothesis would also account for the higher acuity and mortality of patients admitted with severe sepsis into the ICU in Europe. The median length of stay on the wards before admission to ICU is only 2 days longer in Europe than in the USA (3·5 *vs* 1·4 days), which makes it more likely that the episode of sepsis associated with ICU admission is the same as that leading to initial admission to the wards in both Europe and the USA.

The number of ICU beds available can vary significantly between European countries and between Europe and the USA. Within Europe, Germany has ten times the number of ICU beds per head compared with England. Both Germany and Belgium have more ICU beds per head than does the USA (24·6 in Germany, 21·9 in Belgium, and 20·0 in the USA) and Canada (13·5 beds per 100 000 population).[9] Cultural differences might also influence both the allocation and delivery of care. Cultural perspectives of how and if ICU resources should be used regarding end-of-life care could determine to whom ICU resources are provided, for what period of time resources are provided, and the influence of medical staff and families on decisions to withdraw life-sustaining therapies in the terminally ill.

Our study raises important questions. Is the higher mortality rate in Europe than in USA due to the lower number of ICU beds available in Europe, which exposed the higher percentage of patients being admitted to the ICU from the wards to less than optimum resuscitation? Or is the use of ICU resources—admission of patients who might be more appropriately cared for on the wards—excessive in the USA? Further studies are needed to elucidate more precisely the effect of these models on outcomes of sepsis.

In conclusion, patients admitted to the ICU with severe sepsis and septic shock in Europe were more severely ill

***Panel:* Research in context**

Systematic review

We searched PubMed with the search terms "sepsis outcomes international" and "comparison between sepsis outcomes." Although we found many descriptive studies about the difference in models of intensive care unit (ICU) care delivery between the USA and Europe, we found no studies that directly compared outcomes in sepsis between Europe and the USA. From that search we identified a few observational studies[31] that compared the outcomes of patients with severe sepsis and septic shock across countries. One of these, the PROGRESS study,[24] was a registry of patient with sepsis in several countries. We found several studies[14-20] that compared the use of ICU resource between the USA and the UK, but these studies did not report outcomes specific to patients with sepsis.

Interpretation

The present study is the first to directly compare outcomes, between Europe and the USA, in patients with severe sepsis and septic shock identified in the emergency department, general wards, and in ICUs. The significant difference in unadjusted mortality and the fact that this difference disappears with severity adjustment raise important questions about the effect of the approach to critical care in Europe compared with that in the USA. The effect of ICU bed availability on outcomes in patients with severe sepsis and septic shock requires further investigation.

than those in the USA and had a 10% higher unadjusted mortality rate. This difference disappeared after adjustment for severity of illness and organ dysfunction. Patients admitted to ICUs with severe sepsis in Europe were also more frequently admitted from hospital wards, whereas those in the USA were more likely to be admitted directly to ICUs. This study raises questions about the effect of the different models of ICU resourcing and use.

Contributors

MML was involved in the study design, data collection, data interpretation, and writing and final review of the report. J-LV participated in data interpretation and writing of the report. ST participated in the study design, collection of data, and data analysis, and designed and built the Surviving Sepsis Campaign database, which was responsible for the bulk of the international data collection effort. RPD, AA, and RB participated in the study design, data collection, data interpretation, and writing of the report. TO participated in the literature search and data interpretation and contributed to the original intellectual content, reviewing, and revising. AR participated in the data analysis and the interpretation, drafting, and critique of the report. GSP and SL participated in the data analysis, data interpretation, creation of figures, and writing of the report.

Conflicts of interest

AR was reimbursed for steering committee work by Eli Lilly and by Orion Pharmaceuticals; he has been a member of the advisory board of LiDCO and Biomereux; and he has received lecture fees from LiDCO and Edwards Lifesciences. RB's department and institution have received payment for research support and honoraria payments from Eli Lilly and Philips Medical Systems. All other authors declare that they have no conflicts of interest.

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