



Epidemiology of severe sepsis: 2008-2012



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ABSTRACT

Introduction: Severe sepsis continues to be a significant burden on society.

Methods: Using the *International Classification of Diseases, Ninth Revision, Clinical Modification* codes, we analyzed the Healthcare Cost and Utilization Project National Inpatient Sample in order to estimate epidemiologic trends of severe sepsis from the years 2008 to 2012. The 2010 US Census, which included 308 745 538 individuals, was used to calculate incidence per 100 000 persons.

Results: There were a total of 6067 789 discharges for severe sepsis. The annual incidence increased from 346/100 000 to 436/100 000 persons ($P < .05$). Individuals with 3 or greater organ system failures increased from 31.6% to 35.5% ($P < .05$), and they accounted for 57.2% to 66.7% of the total number of deaths. Overall mortality decreased from 22.2% to 17.3% ($P < .05$). Length of stay decreased from 9 to 7 days ($P < .05$). Those discharged to home with and without home-health increased (23%–27%; $P < .05$), but those discharged to skilled nursing facilities remained the same (35%).

Conclusions: The incidence of severe sepsis continues to increase, whereas mortality decreases. However, one third of patients (those with ≥ 3 organ system failures) account for two thirds of the total number of deaths. More people are discharged home, whereas stable numbers go to facilities.

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1. Introduction

Severe sepsis continues to be a significant burden on society, recently cited as being the leading cause of in-hospital death in the United States [1] and consuming almost half of intensive care unit resources [2]. It continues to have a persistent increase in incidence, and in-hospital mortality is currently estimated to be 20% to 45% [3]. Although there have been landmark changes in the way severe sepsis is understood [4], debate continues about the best way to treat it [4–12].

Within the realm of understanding the significance of severe sepsis on a broad level, a number of epidemiologic studies have been done using retrospective databases. These studies span a period of approximately 30 years (1979–2009) [1,2,13–17]. Throughout this period, specific trends have emerged. There has been an increasing incidence of severe sepsis and an increasing number of total deaths, but a decrease in overall in-hospital case mortality. Studies also report an increase in the number of organ systems (OSs) failing, supporting increased severity of illness. However, there has been a decrease in length of in-hospital stay, along with a decrease in the number of people discharged to home, coupled with an increase in the number of people discharged to

facilities, such as skilled nursing facilities (SNFs). As demographics have been analyzed, there has been an increase in the age at which severe sepsis occurs, as well as a slight predominance in male patients.

The goal of this study was to evaluate the epidemiologic trends of severe sepsis from the years 2008 to 2012 using the Healthcare Cost and Utilization Project National (Nationwide) Inpatient Sample (HCUP NIS) database. As Kumar and colleagues [15] note, it is important to understand the epidemiologic trends of sepsis, given its clinical significance, in order to make appropriate resource allocation decisions and judgments on the efficacy of the prevailing treatment paradigm.

2. Materials and methods

2.1. Data source

The NIS is the largest publicly available all-payer inpatient health care database in the United States. The NIS is part of the HCUP, sponsored by the Agency for Healthcare Research and Quality. The HCUP is a collection of health care databases that create a national-level resource of longitudinal hospital care data in the United States. At present, 44 states are included in the NIS, which contains data from more than 7 million hospital stays from about 1000 hospitals each year [18].

For each hospitalization, the NIS includes 1 primary diagnosis with up to 24 secondary diagnoses and 15 procedures for that stay. Insurance status is also included. Hospitals included in the database primarily

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include specialty hospitals, public hospitals, and academic medical centers. All of the hospitals are stratified by ownership, bed size, teaching status, urban/rural location, and US region. From this information, various epidemiologic data, such as health care access, charges, and outcomes, are able to be analyzed [19].

Prior to 2012, the NIS approximated a 20% sample of US hospitals. Beginning in 2012, the NIS became a 20% sample of discharges from all community hospitals in HCUP. This differs from the prior years' practice of sampling hospitals and determining discharge information from only those sampled hospitals; now all hospitals are included and a representative sample is taken from each facility [19].

To account for this change in method, the database has made available discharge trend weights for the years prior to 2012. These weights have been calculated in the same way as the weights used for 2012 so as to allow for consistency in analyzing trends including 2012 and prior years [19]. These adjustment weights were used for our analysis of the database.

All patient identifiers are removed from the HCUP NIS database, and thus no institutional review board approval was required to analyze these data.

2.2. Study population

We searched the NIS database to identify patients older than 18 years discharged with a diagnosis of severe sepsis. The period was 2008 to 2012, the latest available data. *Severe sepsis* was defined as a set of *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* codes for septicemia, bacteremia, or fungemia plus additional codes for organ dysfunction, or the *ICD-9-CM* code for systemic inflammatory response syndrome due to infectious process with organ dysfunction (ie, severe sepsis), as described by previous studies [3,15] (Supplementary Table 1). The NIS database was used to determine overall incidence, percentage as a function of sex, admitting age in years, comorbidities, number of organ failures and mortality related to number of organ failures, overall inpatient mortality rate, the use of mechanical ventilation, length of stay (LOS), total charge, and discharge disposition. The HCUP NIS database lacks complete records concerning race, so this demographic variable was not examined.

2.3. Statistical analysis

All statistical analyses were done using IBM SPSS Statistics for Windows, Version 21 (IBM Corp, Armonk, NY). Continuous data (eg, age, LOS and total charge) were presented in terms of median and were compared by nonparametric testing. Categorical data, such as sex, race, comorbidities, and mortality, were presented in terms of ratio or incidence rate and were compared by χ^2 test or Fisher exact test. To calculate overall incidence, we used the weighted data provided by the NIS to determine national estimates, then combined it with the 2010 US Census in order to report it as incidence per 100,000 persons. We considered a *P* value less than .05 to be statistically significant. Multivariate analysis was used to determine independent effects of certain variables on the mortality rate between the years 2008 and 2012.

3. Results

3.1. Incidence and demographics

There were a total of 6067789 discharges for severe sepsis from 2008 to 2012, and the 2010 US census included 308745538 individuals. Over the study period, the annual incidence of discharges after severe sepsis increased from 346/100,000 to 436/100,000 individuals (Table 1). Each year had a statistically significant increase (*P* < .05). Male predominance had a slight but significant increase (*P* < .05), going from 50.3% to 51.1%. There was no significant change in the median age at admission (Table 2).

Table 1
Incidence, mortality, and total hospital charge of severe sepsis

	Incidence of severe sepsis per 100,000 people	Severe sepsis mortality rate (%)	Total charge	<i>P</i> *
2008	346	22.2	\$55,544.00	<.05
2009	366	20.4	\$56,869.00	<.05
2010	391	19.2	\$57,692.00	<.05
2011	425	18.1	\$57,987.00	<.05
2012	436	17.3	\$57,749.00	<.05

* *P* < .05 for annual changes within each category.

3.2. Comorbidities

All comorbidities examined showed an overall increase in frequency from 2008 to 2012 (*P* < .05), although changes from year to year were variable. Hypertension and fluid and electrolyte disorders had the largest increases (Table 2).

3.3. Organ system failure

With respect to OS injury and failure, 31.6% of individuals in 2008 were documented to have 3 or more OS failures. This number had a small but significant increase to 35.5% in 2012 (*P* < .05). Overall changes from 2008 to 2012 in all systems were significant (*P* < .05), with decreases only in respiratory and hematologic and increases in the remaining categories. Respiratory, cardiovascular, renal, and

Table 2
Characteristics of patients with severe sepsis 2008 vs 2012

Patient characteristics	2008	2012
Incidence*		
Per 100,000 individuals	346	436
Sex		
Male	50.3%	51.1%
Female	49.7%	48.9%
Age (y)	69	68
Comorbidities		
Congestive heart failure*	19.5%	23.7%
Chronic pulmonary disease*	19.7%	25.9%
Diabetes without chronic complications*	18.0%	25.0%
Renal failure*	23.9%	29.3%
Liver disease*	4.3%	6.4%
Obesity*	5.6%	12.9%
Hypertension*	42.4%	57.4%
Fluid and electrolyte disorders*	52.3%	62.4%
Organ failure		
% with ≥ 3 OSs*	31.6%	35.5%
Respiratory*	44.8%	43.6%
Cardiovascular*	41.3%	43.3%
Renal*	53.4%	56.5%
Hepatic*	4.3%	5.0%
Hematologic*	39.2%	37.7%
Metabolic*	15.8%	20.3%
Neurologic*	12.0%	18.3%
Mechanical ventilation		
Frequency*	28.6%	25.1%
Mortality		
Overall*	22.2%	17.3%
≥ 3 OS failures*	32.9%–63.0%	24%–59.1%
% of total deaths with ≥ 3 OS failures*	57.2%	66.7%
LOS* (d), median	9	7
Charge**		
US dollars, median	55,544	57,749
Discharge disposition ^{a-c}		
Discharged to home or self care ^a	23.0%	26.8%
Home health care ^b	14.7%	15.8%
Transfer to SNF, intermediate care facility, etc ^c	34.9%	35.2%

^a Overall a slight increase, but not every year is statistically different from the others.

^b Statistical increases for the first 4 years (*P* < .05).

^c No statistical differences between the years, except 2011.

* *P* < .05 for overall change from 2008 to 2012.

** *P* < .05 overall, but unable to tell yearly statistical significance.

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