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Age-related incidence and outcomes of sepsis in California, 2008–2015

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Abstract

Purpose: Sepsis remains amongst the most common causes of death worldwide. It has been described as a disease of the elderly, but contemporary data on risk factors and mortality is lacking.

Materials and methods: Multi-center longitudinal cohort study using non-public, state of California data from January 1, 2008 to September 31, 2015. Patients with sepsis, severe sepsis, and septic shock were identified using ICD-9-CM diagnosis and procedure codes with age subgroups of 18–44, 45–64, 65–74, 75–84, and >85 years old. Descriptive statistics and a single direct logistic regression model were used to present data on incidence and mortality and to identify independent factors associated with mortality.

Results: Of 30,282,159 total inpatient encounters, 20,358,569 met inclusion criteria and 1,566,306 met sepsis criteria. Conditions associated with mortality included metastatic cancer, age, liver disease, residing in a care facility, and a gastrointestinal source of infection as well as

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Author contribution

GW, AM, CRT, AM, VR, VT, RH, and US conceptualized the manuscript. JB, RH, EC performed data curation, completed formal analysis and performed statistical analysis. All authors had a significant contribution to writing, review & editing of the initial and revised manuscript. GW takes responsibility for the manuscript as a whole.

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Declaration of Competing Interest

The remaining authors have no disclosures to report.

fungal infection. Mortality in the >85-year-old subgroup with septic shock was 45.7%, lower than previously reported.

Conclusion: Age remains an important sepsis risk factor, but other conditions correlated more closely with sepsis-associated death. Patients over 85 years of age suffering from septic shock may have a better chance of survival than previously thought.

Keywords

Sepsis; Septic shock; Geriatrics; Outcomes

1. Introduction

Sepsis, a life-threatening condition defined by a dysregulated host response to infection [1], remains one of the largest contributors to health loss worldwide [2]. Sepsis is associated with greater than 11 million deaths worldwide and accounts for a significant portion of global healthcare expenditures, with more than $24 billion dollars spent on sepsis-associated care in the United States alone in 2017. [2–6]. It is estimated that one third of patients who die in the hospital carry a diagnosis of sepsis [7,8]. Several studies have indicated that the incidence of sepsis is increasing [9], although a recent global study found the age standardized incidence to be declining [2].

Sepsis has been described as a disease of the elderly, with prior research showing over 60% of sepsis cases occurring in patients over the age of 65 [10]. In addition to the high incidence, sepsis-related mortality has been reported to be almost 80% in patients above 80 years of age admitted to the intensive care unit (ICU) [11,12]. While such studies have shown particularly poor outcomes in elderly patients, in the past few decades only few large epidemiologic studies on this topic that have been performed. Such information is particularly relevant given that the proportion of persons over the age of 65 worldwide has increased from 6% in 1990 to 9% in 2019, and is estimated to rise to 16% by 2050 [13].

Because the current incidence and outcome in this expanding population are not well-described, but may inform healthcare planning on an individual and systems level, we sought to quantify the incidence and outcomes related to sepsis across diverse age groups over an eight-year period, using a statewide database.

2. Methods

We performed a multi-center retrospective longitudinal cohort study of inpatient discharges from all non-military licensed acute care hospitals in the state of California between January 1, 2008 and September 31, 2015 (quarter 3), using non-public data from the Office of Statewide Health Planning and Development (OSHPD), which included overall California census data [14]. As ICD-10 codes were used after September 31st, 2015, data from the final quarter of 2015 (October 1st – December 31st) describing the number of Californians and admissions with sepsis was estimated based on the preceding 3 quarters. Patients who were less than 18 years of age, lacked a valid patient identifier, were admitted for non-acute care, or had a length of stay longer than 365 days were excluded. Sepsis visits were

identified and classified into sepsis, severe sepsis, and septic shock based on previously validated methodology, using up to 25 discharge diagnoses and 20 procedure codes (ICD-9) [7]. Patients' demographic, population, and dispositional data were also obtained from the OSHPD database. Chronic health information was procured from components of the Charlson Comorbidity Index (CCI), also abstracted from the OSHPD database. We use the term "sepsis syndrome" as a collective term to describe a patient with sepsis, severe sepsis, or septic shock throughout this manuscript.

2.1 Data analysis

Demographic and baseline characteristics of our dataset are provided as patient encounters between 2008 and 2015 divided into the following groups: 18–44, 45–64, 65–74, 75–84, >85 years, and all ages. The incidence of sepsis by age group from 2008 to 2015 is provided per 1000 hospital admissions and overall California population (per 1000 adult population). In-hospital mortality rate (per 1000 admissions) and population mortality rate (per 10,000 adult Californians) are provided as a function of the above age groups. Admission and discharge locations are provided as aggregate data based on the same age groups. Descriptive statistics are used as indicated. Due to such a large sample size, all population comparisons were considered statistically significant, and are not presented with a *p*-value.

A single, direct logistic regression model was developed using visit as the unit of analysis to determine the independent association of each factor with hospital mortality. The selection of factors was based on clinical relevance and previously published research, given the available data from OSHPD. These factors included patient age in years (<65, ≥65), male gender, number of failed organs (0, 1, 2, ≥3), route of admission (skilled nursing facility (SNF) or intermediate care (IC)), primary and/or secondary diagnoses of myocardial infarction, congestive heart failure, dementia, liver disease, diabetes, renal disease and metastatic carcinoma, site of infection (respiratory, central nervous system, gastrointestinal, urinary, and skin/soft tissue), and cause of infection (gram-positive, gram-negative, other bacteria, fungi, multiple, or none of the above). All factors were entered into the model regardless of bivariate association with the outcome and were used as categorical variables, with the first category serving as the reference. Multi-co-linearity diagnostics were assessed for the model and co-linearity was not found to be a significant issue. Variance inflation factor (VIF) values for all variables were found to be acceptable, ranging from 1.0 to 2.2. Adjusted odds ratios and 95% confidence intervals are reported for each factor. An alpha level equal to 0.05 was used for interpretation of statistical significance for all statistical analyses. Missing data for all variables were minimal (<0.1%), and patient encounters with missing data were excluded. All statistical analyses were conducted using the IBM SPSS Statistics 26.0 software package (IBM Corp., Armonk, NY). This study was reviewed and approved by the Institutional Review Board of the University of California San Francisco.

3. Results

3.1. Baseline characteristics of study population

We identified a total of 30,282,159 recorded admissions to acute care facilities from January 1, 2008 to September 31, 2015 in the state of California. After applying exclusion criteria, we identified 20,358,569 patient encounters, of which 1,566,306 (7.6%) had a sepsis syndrome recorded during their admission. “Sepsis” was present in 25.9%, “severe sepsis” in 52.6%, and “septic shock” in 21.5% of these patients (Table 1). Diabetes (37.3%), renal disease (30.4%), and chronic pulmonary disease (27.8%) were the most prevalent underlying comorbidities.

3.2. Sepsis culture data and site of infection of study population

Gram-negative infections (27.4%) were more prevalent than gram-positive infections (20.0%). Fungi were identified in 3.0% of cases. However, 53.9% of all septic patients did not have a causative organism identified. The most common overall site of infection was the genitourinary tract (38.5%) followed by the respiratory system (31.1%) (Table 2).

3.3. Sepsis incidence over time

The overall incidence of a sepsis diagnosis increased from 5.42 cases per 1000 adult residents of California in 2008 to 9.2 cases per 1000 adult residents in 2015, a 69.0% increase over the 8-year study period (Fig. 1a). Although there was a rise in all categories of sepsis, the largest change in incidence occurred in patients with severe sepsis, which increased by 85.2% over our 8-year study period. The proportion of admitted patients with a sepsis syndrome increased from 55.6 per 1000 admitted patients in 2008 to 106.8 per 1000 in 2015, an increase of 92.2%. We also found that the incidence of severe sepsis showed the greatest increase in proportion to admitted patients, from 28.0 to 59.1 per 1000 admitted patients, an increase of 110.7%. (Fig. 1b).

3.4. Incidence as a function of age

While patients 65 years and older represented only 15–17% of the population in California during 2008–2015, they comprised 60.4% of all admissions with sepsis syndromes (50% of sepsis, 64.6% of severe sepsis, and 62.7% of septic shock admissions). In 2015, patients greater than 84 years old were 30.6 times more likely to be hospitalized with a sepsis syndrome than patients 18–44 years old, and 8.5 times more likely than patients 45–64 years old. Though the youngest group (18–44 years) showed the lowest incidence of sepsis, this group showed the highest overall increase of 155.2% (from 17.8 cases in 2008 to 45.3 in 2015 per 1000 admissions), with the relative increases highest in sepsis (197.5%) and severe sepsis (145.3%) (Fig. 1b). Patients 18–44 years old also had a high prevalence of comorbidities, 62.7% had a CCI of at least of 1, and 24.7% had a CCI of 3 or greater. The lowest relative increase in the incidence of any type of sepsis syndrome (per population and per admission) was seen in patients 85 years and older (Fig. 1a and b).

3.5. Mortality associated with sepsis

Between 2008 and 2015, 15% percent of all patients with a sepsis syndrome did not survive to hospital discharge. Mortality related to sepsis was 2.0% for those with sepsis, 12.3% for those with severe sepsis, and 37.4% for those with septic shock over the study period. In 2008, the mortality rate for patients hospitalized with a sepsis syndrome was 19.9%; in 2015, the rate decreased to 11.8%. All age groups saw significantly reduced mortality from 2008 to 2015, with the largest percentage drop in patients in the 18–44 age group (a 58.7% decrease, Fig. 1d and Supplementary Table S1). Patients 65 years and older saw a decrease in mortality from 22.8% to 14.4%. After stratification into different categories of sepsis, we found that starting in 2009, no age group had a sepsis-related mortality rate greater than 50% (Supplementary Table S1).

The overall mortality rate with a sepsis-associated diagnosis was largely static from 2008 to 2015, ranging from 10.4 deaths per 10,000 adults in California (2012) to 10.8 deaths per 10,000 adults in California (2009) (Fig. 1c). Likewise, when the mortality rate in California was stratified by age, there was minimal change in the number of deaths per 10,000 adult California population between 2008 and 2015 within age groups (Fig. 1c). However, advanced age was significantly associated with higher rates of death per adult California population.

3.6. Factors associated with mortality

We performed a multivariate logistic regression of the overall study population to determine characteristics that conferred an increased likelihood for sepsis-related mortality. Factors associated with increased mortality included: 1) increasing presence of organ failure (OR 24.28 for ≥3 organs, 8.79 for 2 organs, 3.32 for 1 organ), 2) metastatic carcinoma (OR 3.04), 3) age above 65 years (OR 1.82), 4) infection caused by fungi (OR 1.63) or unknown cause of infection (culture-negative, OR 1.58), and 5) presence of liver disease (OR 1.57) (Table 3).

3.7. Admission route and discharge disposition

Most patients admitted with a sepsis syndrome came from home (77.9%), followed by skilled nursing facilities or intermediate care (11.4%), acute inpatient hospital care (5.9%), and residential care facilities (2.2%), indicating a trend that was mirrored in each sepsis subtype. With increasing age, the rate of admission from home decreased, from 88.8% in the youngest group to 68.9% in the oldest group, while admissions from skilled nursing facility or intermediate care increased from 3.1% to 18.5%, respectively (Fig. 2a and b). Overall, patients with admissions for any sepsis syndrome were discharged home (33.3%), to skilled nursing facility or intermediate care (25.9%), to home health services (15.9%), to acute care within the hospital (4.7%), or to residential care facilities (0.9%) while 15% died in the hospital and 1.3% left against medical advice. A similar distribution was observed in each of the sepsis subtypes. Increasing age dramatically affected disposition: the youngest group was discharged home in 61.0% of cases, compared to 16.3% of the patients >85 years old. Discharge to skilled nursing facility or intermediate care disposition occurred in 7.7% of patients in the 18–44 group and 37.3% of patients >85 years old (Fig. 2b). As the severity of sepsis increased, discharge to home also decreased: In the youngest group, discharge to

home decreased from 73.1% for those with sepsis to 37.3% for those with septic shock. In the oldest group, discharge to home decreased from 25.3% for those with sepsis to 6.7% for those with septic shock.

4. Discussion

In this study, we evaluated a large administrative database including 1,566,306 septic patient hospitalizations in California between 2008 and 2015. Our major findings are that: 1) sepsis remains a disease disproportionately affecting the elderly; 2) while the overall incidence of sepsis rose during our study period, sepsis-related mortality fell; and 3) the overall mortality rate within age groups in California associated with sepsis remained constant. In-hospital mortality was associated with age but also with comorbidities, such as advanced cancer and liver disease. As expected, overall organ failure as a marker of disease severity was significantly associated with death. As compared to gram-positive infections, fungal infections were associated with higher mortality rates, as were culture-negative infections. Importantly, despite age being a risk factor for death, the mortality of patients with septic shock who were over 85 years of age was much lower than previously reported [12] and the percentage of all septic people over 85 discharged to home was above 20%.

Sepsis remains an international problem and is responsible for approximately 20% of deaths worldwide [2]. While low-income countries are disproportionately affected, recent data suggest that survival is increasing across the globe. Additionally, the United Nations has estimated that persons >65 years old will nearly double in the next 30 years. Thus, care of septic patients older than 65 is an important international subject. Data from Taiwan found a decrease in mortality in elderly patients, and in particular, a 22% decrease in patients older than 85 years old from 2002to 2012 [21]. However, it is uncertain if our data apply to countries with healthcare systems, resources, and income levels distinct from the United States. Future investigations that inform care of elderly patients are indicated to help healthcare providers better treat for such patients and provide appropriate prognostic information to patients and families.

We identified a significant increase in the incidence of sepsis in relation to the general California population and in patients admitted to an acute care facility in California. An aging population in California may explain some of this trend given the higher incidence of sepsis in the elderly. Higher rates of comorbidity, greater reliance on healthcare services, awareness of sepsis, and changes in administrative coding practices may also contribute to our findings showing an increase in sepsis incidence [7,15,16]. The possibility of “upcoding” simple infections to sepsis in order to maximize reimbursement, which has been previously reported, cannot be excluded [17].

Interestingly, the age group with the largest relative increase in sepsis diagnoses over time was the younger age group (age 18–44 years). While speculative, this somewhat unexpected observation could be explained by heightened awareness of possible sepsis, even in the younger population [9,10]. However, it is of note that this age group had a significant number of various comorbid conditions: 62.7% had CCI ≥ 1 and 24.7% had CCI ≥ 3. Additional work is merited to further investigate this unexpected finding.

Sepsis-related mortality decreased over the reporting period. This has been noted in other epidemiologic studies evaluating sepsis, as well as randomized controlled trials over the past few decades [18–20]. The sepsis mortality rate per California population, however, remained constant and is likely explained by the increased rate of diagnosis of sepsis in this population. This finding argues that an increase in the identification of sepsis, potentially those with more subtle signs of infection, less ill patients, or aggressive administrative coding, may be responsible for the improved hospital mortality rate by inflating the denominator. Despite the increasing incidence in the younger population, age remains an important factor when considering the overall likelihood of death from sepsis. Patients older than 85 years were 30.6 times more likely to develop sepsis than patients within the ages of 18 and 44, a finding that is consistent with that of a recently-published large epidemiologic study [21]. When considering the prognosis in the elderly septic patient, it is noteworthy that that mortality associated with septic shock in patients over the age of 85 was less than 50% in our study, contrasting prior studies that demonstrated greater than 80% mortality in patients older than 80 years [5]. Whether this decrease in mortality represents more modern care or an increased rate of diagnosis in non-fatal cases remains uncertain [8].

When assessing other predisposing conditions associated with sepsis mortality, we found that a history of metastatic carcinoma and liver disease had the most significant mortality association. Our data indicate that, in contrast to a prior study [10], a history of metastatic carcinoma had a higher association with death, as compared to age. Advanced cancer has been identified as a major cause contributing to death in patients with sepsis despite optimal care [22,23]. The increased survival of cancer patients in the past few decades due to advances in therapy may have contributed to our findings [24].

The lower-than-expected mortality in patients over 85 years of age, and the importance of pre-existing factors such as metastatic cancer and liver disease, as well as disease-related organ failure, provide crucial prognostic information. While prior data suggested that a diagnosis of septic shock in patients over 80 years was a terminal condition in itself, our findings indicate that the presence of organ failure or metastatic cancer influence outcome to a much greater extent than age. The importance of additional inquiries into the optimal care of the elderly septic patient is emphasized by our findings that suggest that the aggressiveness of interventions performed is only partially determined by a patient's advanced age.

The majority of patients with sepsis syndromes are still admitted from and discharged to home, but this number decreases precipitously in older age groups in our study, which is consistent with prior reports [25]. Conversely, admissions from and discharges to nursing home and intermediate care facilities increase substantially with age. Taken together, these data suggest that an increasing number of patients diagnosed with sepsis are no longer able to maintain healthy lives outside of the institutional setting, which may be an important factor when discussing prognosis with patients and families. While our data do not speak to the quality of life after discharge from the acute care hospital, they do suggest that health systems should focus attention on postacute care facilities as part of sepsis management strategies across an extended continuum of care in the institutional context.

5. Limitations

As data were accessed from a statewide database, notable limitations include a small proportion of invalid patient identifiers, the absence of federal health care facilities, and lack of other important patient and visit characteristics, including urgency, access to primary care, and cost. The Centers for Disease Control and Prevention recently have advocated for the use of clinically-based definitions of sepsis; our definition of sepsis, severe sepsis, and septic shock was based on administrative data based on physician coding, which is most likely clinically-based but could be informed by other methods of diagnosis as well [7]. As ICD-10 codes were used after September 31st, 2015, the incidence of sepsis was estimated for the final quarter of 2015. We acknowledge that data from ICD-10 codes may change some of the results with newer data. Additionally, since we examined mortality in hospitalized patients in California only, our data may not have captured patients who expired at home or in another state. We acknowledge our results are from a specific region of the United States and may not apply to other countries or settings, which may have different availability of resources, practice patterns, or access to healthcare.

6. Conclusion

While age and comorbidities were associated with an increased risk for developing sepsis, pre-existing conditions other than age had higher odds ratios for sepsis-associated death. Patients over the age of 85 with septic shock may have a better chance of survival and higher rates of discharge to home than previously believed.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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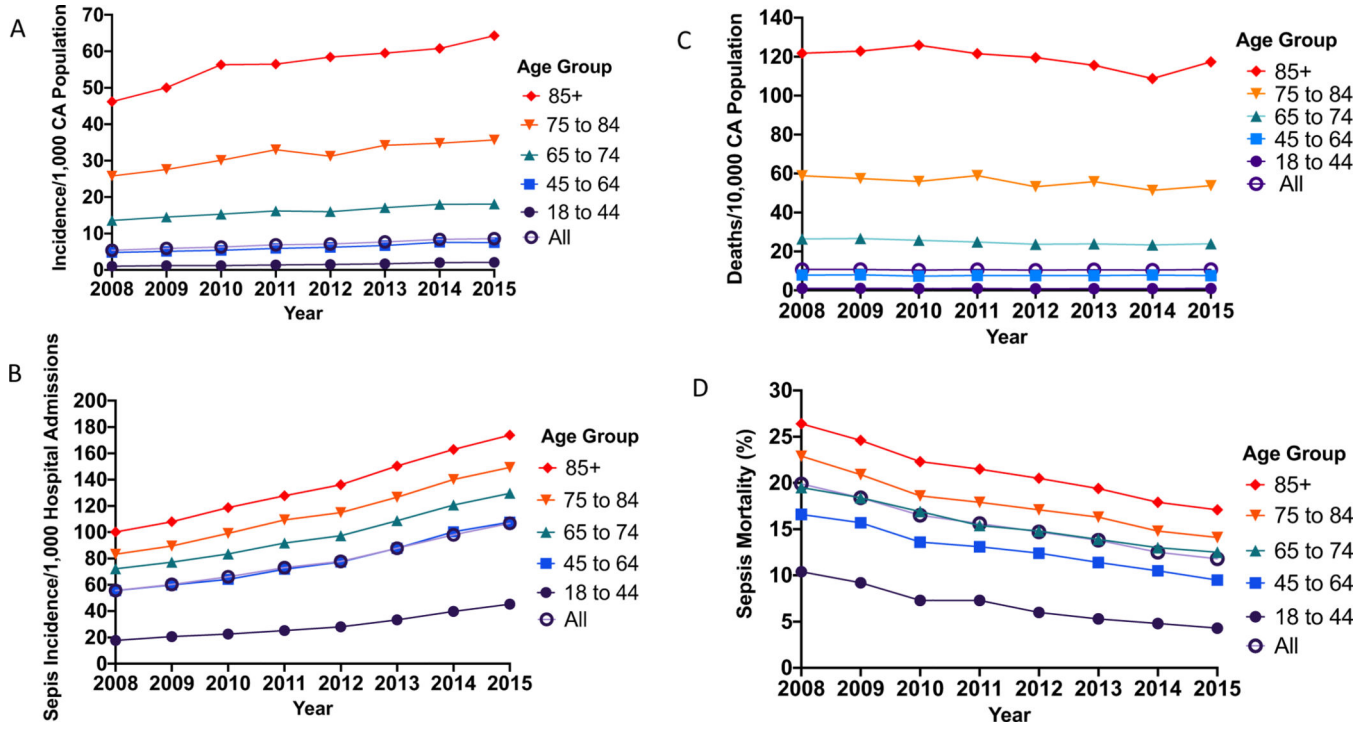

Fig. 1.

(a) Incidence of sepsis per 1000 adult California population by year, stratified by age group. (b) Incidence of sepsis per 1000 adult hospital admissions by year, stratified by age group. (c) Deaths associated with sepsis per 10,000 adult California population by year, stratified by age group. (d) Mortality rate of septic patients by year, stratified by age group.

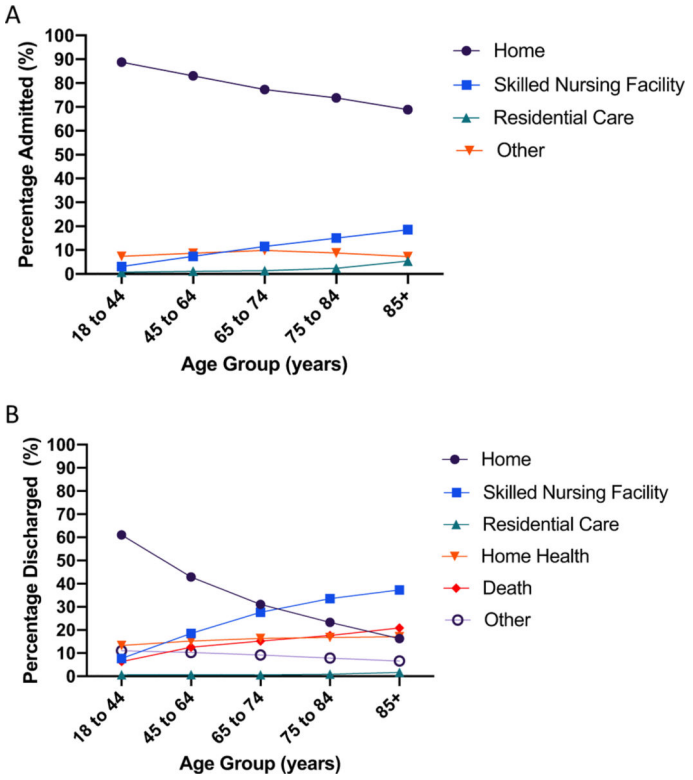

Fig. 2.

(a) Admission source for patients hospitalized with a diagnosis of sepsis, stratified by age group. (b) Discharge location for patients hospitalized with a diagnosis of sepsis, stratified by age group.

Table 1

Baseline characteristics of patients hospitalized with a sepsis diagnosis by age group and overall.

	18 to 44 (*n* = 170,516)	45 to 64 (*n* = 449,994)	65 to 74 (*n* = 314,405)	75 to 84 (*n* = 347,303)	≥ 85 (*n* = 284,088)	Overall (*n* = 1,566,306)
	%, (n)	%, (n)	%, (n)	%, (n)	%, (n)	%, (n)
Sex						
Male	49.4 (84308)	54.7 (246147)	52.8 (166006)	49.5 (171915)	41.8 (118749)	50.2 (786286)
Female	50.5 (86185)	45.3 (203847)	47.2 (148399)	50.5 (175388)	58.2 (165339)	49.8 (780020)
Sepsis Severity						
Sepsis	44.5 (75880)	28.2 (126898)	22.7 (71370)	21 (72934)	20.6 (58522)	25.9 (405673)
Severe Sepsis	40.9 (69741)	49.4 (222297)	53.8 (169150)	56.3 (195532)	59 (1667612)	52.6 (823877)
Septic Shock	14.7 (25066)	22.3 (100349)	23.6 (74200)	22.7 (78838)	20.3 (57670)	21.5 (336756)
Co-morbidities						
Myocardial Infarction	2 (3410)	7.5 (33750)	12 (37729)	13.8 (47928)	14 (39772)	10.4 (162896)
Congestive Heart Failure	7.5 (12789)	17.8 (80099)	26.8 (84261)	32.6 (113221)	36.9 (104828)	25.2 (394709)
Dementia	0.8 (1364)	1.5 (6750)	4.5 (14148)	10.3 (35772)	15 (42613)	6.4 (100244)
Chronic Pulmonary Disease	14 (23872)	24.5 (110249)	32.8 (103125)	33.1 (114957)	29.4 (83522)	27.8 (435433)
Liver Disease	11.3 (19268)	18.4 (82799)	10.9 (34270)	6.4 (22227)	3.6 (10227)	10.5 (164462)
Diabetes	20.1 (342745)	39.8 (179098)	45.5 (143054)	41.2 (143089)	29.6 (84090)	37.3 (584232)
Renal Disease	14.5 (24725)	25.7 (115648)	33.4 (105011)	36.7 (127460)	36.6 (103976)	30.4 (476157)
Site of Infection	8.9 (15176)	15.4 (69299)	18.4 (57851)	14.7 (51054)	9 (25568)	14 (219283)
AIDS/HIV	2.9 (4945)	1.8 (8100)	0.3 (943)	0.1 (347)	0 (0)	0.9 (14097)
Charlson Comorbidity Index						
0	37.3 (63602)	15.4 (69299)	9.8 (30812)	9.5 (32994)	12.3 (34943)	14.8 (231813)
1	19.3 (32910)	18 (80999)	15.4 (48418)	15.8 (54874)	18.4 (52272)	17.2 (269405)
2	18.8 (32057)	18.7 (84149)	17.8 (55964)	18.2 (63209)	19.7 (55965)	18.6 (291333)
3 or more	24.7 (42117)	47.9 (215547)	57 (179,211	56.5 (196226)	49.5 (140624)	49.4 (773755)

Table 2

Source of infection and culture result of patients hospitalized with sepsis diagnosis by age group and overall.

	18 to 44 (n = 170,516) %, (n)	45 to 64 (n = 449,994) %, (n)	65 to 74 (n = 314,405) %, (n)	75 to 84 (n = 347,303) %, (n)	≥ 85 (n = 284,088) %, (n)	OVERALL (n = 1,566,306) %, (n)
Cause of Sepsis						
Gram positive	23.8 (40501)	23.9 (60566)	19.3 (60556)	17.3 (60251)	15.2 (43148)	20 (311845)
Gram negative	23.5 (39996)	25.1 (113150)	28.1 (103901)	29.9 (103901)	29.4 (83639)	27.6 (428962)
Anaerobes	0.9 (1596)	1.0 (4621)	1.0 (3225)	1.1 (3662)	0.9 (2690)	1.0 (15794)
Other Bacteria	3.0 (5126)	2.7 (12163)	2.2 (7019)	2.1 (7266)	1.9 (5354)	2.3 (36928)
Fungi	4.1 (6946)	3.6 (16203)	3.2 (9976)	2.5 (8792)	1.8 (5058)	2.9 (46975)
None of the above	52.9 (90250)	51.9 (233527)	53.8 (169018)	54.3 (188640)	57.2 (162381)	53.4 (843816)
Site of Infection						
Respiratory	22.9 (39108)	28.8 (129624)	32.7 (102896)	33.8(117339)	34.4 (97768)	31.1 (486735)
Blood	10.4 (17662)	9.4 (42317)	7.0 (22060)	6.2 (21419)	5.2 (14724)	7.5 (118182)
Endocarditis	1.9 (3292)	1.7 (7517)	1.3 (4096)	1.1 (3712)	0.7 (2105)	1.3 (20722)
Central nervous system	1.2 (1968)	1.3 (5718)	0.7 (2327)	0.4 (1413)	0.2 (507)	0.8 (11933)
Gastrointestinal	11.9 (20311)	13.5 (60577)	13.4 (42260)	12.6 (43765)	10.5 (29903)	12.6 (196816)
Genitourinary	44.6 (53373)	30.5 (137350)	37.2 (117059)	44.1 (153307)	50.0 (142147)	38.5 (603236)
Skin and soft tissues	16.5 (28108)	15.8 (70882)	11.6 (36502)	8.6 (29945)	6.6 (18797)	11.8 (184234)
Bone and Joint	4.0 (6740)	5.2 (23502)	3.4 (10684)	2.3 (7978)	1.5 (4171)	3.4 (53075)
Device-related	5.0 (8601)	5.4 (24522)	5.2 (16224)	4.6 (15988)	3.7 (10414)	4.8 (75749)
None of the above	22.9 (39127)	21.1 (94926)	20.0 (62820)	18.9 (65492)	18.4 (52276)	20.1 (314641)

Table 3

Independent risk factors for sepsis mortality in multivariate logistic regression analysis.

		95% Confidence Interval	
Characteristics	**OR**	**Lo**	**Hi**
Age ≥65	1.82	1.80	1.84
Male	0.89	0.88	0.90
Number of Failed Organs (0 Reference)			
1	3.32	3.25	3.39
2	8.79	8.62	8.97
≥ 3	24.28	23.79	24.78
Route of Admission SNF/IC	1.32	1.31	1.34
Myocardial Infarction	1.31	1.29	1.32
Congestive Heart Failure	1.21	1.20	1.23
Dementia	1.07	1.05	1.09
Liver Disease	1.57	1.55	1.60
Diabetes	0.80	0.79	0.81
Renal Disease	0.70	0.69	0.71
Metastatic Carcinoma	3.04	2.99	3.10
Site of Infection Respiratory	1.23	1.21	1.24
Site of Infection Central nervous system	1.07	1.01	1.13
Site of Infection Gastrointestinal/abdominal	1.44	1.42	1.46
Site of Infection Urinary (including Genital)	0.68	0.67	0.69
Site of Infection Skin and soft tissues	0.72	0.71	0.74
Cause (Gram Positive reference)			
Cause Gram Negative	0.85	0.83	0.87
Cause Other Bacteria (including Anaerobes)	0.88	0.82	0.94
Cause Fungi	1.63	1.57	1.69
Cause Two or more of above	1.03	1.00	1.06
Cause None of the Above	1.58	1.55	1.60