

**Early Management of Community-Acquired Sepsis in a Regional  
Thai Referral Hospital:  
a Prospective Observational Study**

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**Abstract**

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**Purpose:** The epidemiology and management of sepsis is poorly characterized in low- and middle-income countries. **Methods:** We performed a prospective observational cohort study of adults with community-acquired sepsis in a 1,420-bed regional referral hospital in northeast Thailand. Sepsis was defined as suspected infection plus organ dysfunction. **Results:** Between March 2013 and February 2014, 932 patients with sepsis were enrolled. Five hundred twelve (55%) were male and the mean age was 54 years. Eighty three percent of patients were transferred from other hospitals. Eighty four percent of patients were first evaluated in the Emergency Department, where median length of stay was 25 minutes. In the first day after presentation to the study hospital, the majority had blood cultures ordered (80%) and received antibiotics (84%). Most patients were admitted to the general medical wards; 15% were admitted to the intensive care unit (ICU) within the first hospital day. Patients admitted to the ICU had similar demographics and pre-existing co-morbidities but were more critically ill, and were and more likely to receive all measured sepsis management interventions. In-hospital mortality was 9% (87/932) and 28-day mortality was 22% (203/932). The 28-day mortality was significantly higher for patients admitted to the ICU on the first day (45% [63/139] vs. 18% [140/793],  $p < 0.001$ ). **Conclusions:** Sepsis in a regional referral hospital in rural Thailand, where some resources are limited, is commonly managed on general medical wards despite high rates of respiratory failure and shock. Twenty-eight-day mortality is comparable to some high-resource settings.

## ***Introduction***

Sepsis is the dysregulated host response to infection that results in life-threatening organ dysfunction [1]. Sepsis is a global problem; over 19 million cases of sepsis (formerly severe sepsis) and 5 million sepsis-related deaths are estimated to occur worldwide each year [2]. Although data are incomplete, the burden of sepsis is particularly heavy in resource-limited settings [3]. Thus it is critical to better characterize sepsis in such environments.

The management of sepsis is evolving, but current evidence and recommendations emphasize the importance of early recognition and initiation of antimicrobial therapies, and provision of necessary organ support [4]. While outcomes from sepsis have been improving in recent years, perhaps due to increased clinical awareness of sepsis [5,6], several randomized controlled clinical trials have not provided evidence that specific sepsis care protocols yield a benefit over usual clinical management [7–9]. Nearly all of these studies have been conducted in high resource settings.

There may be important differences in how and where patients with sepsis are managed in resource-limited settings. For example, emergency department capabilities and access to intensive care may be limited. Oxygen, antimicrobials, intravenous fluids, and vasoactive agents may not be available. To develop a better understanding of sepsis management in resource-limited settings, we analyzed the initial management of adult patients with community-acquired sepsis presenting to a tertiary referral hospital in rural Thailand, a middle-income country. We performed this analysis on data collected during the first year of a prospective observational study of patients with community-acquired sepsis.

Thailand is an upper-middle income country, spending \$228 USD on health per capita in 2014 (in comparison, the United States of America spent \$9,403 USD on health per capita in 2014) [10]. The median age is 37 years, and 48% of the population lives in urban areas [11]. Life expectancy at birth is 75

years, similar to that of the World Bank upper-middle income country group. The Thai Ministry of Public Health operates government health facilities and is responsible for development, implementation, monitoring, and evaluation of national health policy [12]. All Thai citizens are covered by a universal health insurance program, which has been in place since 2002. The universal insurance scheme is comprised of three individual programs – Civil Servant Medical Benefit Scheme (for civil servants and their dependents), Social Health Insurance Scheme (for private sector employees), and Universal Coverage Scheme (the rest of the population). Public hospitals account for 79% of total hospital beds in the country.

While non-communicable diseases account for 73% of all disability-adjusted life years (DALYs) lost to ill health in Thailand, infectious diseases continue to cause significant death and disability [13]. Lower respiratory tract infections are the leading cause of communicable disease, accounting for 5% of all health loss in terms of DALYs and 87 deaths per 100,000 population in 2015. HIV/AIDS, tuberculosis, diarrheal diseases, and meningitis are the next most common causes of morbidity and mortality due to communicable diseases (in DALYs). Other common infections in Thailand include dengue fever, viral hepatitis, and malaria.

While over 80% of the 5 million sepsis-related deaths each year are thought to occur in low- and middle-income countries (LMICs)[2], the vast majority of research on sepsis epidemiology, management, and outcomes is conducted in high-income countries. This is highly problematic, as there are important differences in the patient populations at risk, infecting pathogens, and available resources to treat sepsis in LMICs. Research on the epidemiology and management of sepsis in LMICs is critically important for the purposes of health services planning, to optimize care of patients with sepsis in low-resource settings in LMICs, and to inform future research.

## *Specific Aims*

Despite the very high burden of sepsis in LMICs, little data exist on the epidemiology of sepsis in these settings. To address this critical knowledge gap, I will describe the presentation, initial management, and outcomes of adult patients with community-acquired sepsis at a large regional referral hospital in northeast Thailand. I will accomplish this overall study objective via the following three specific aims, using the Ubon-Sepsis cohort, a prospectively-enrolled cohort of adult patients with community-acquired sepsis admitted to Sunpasithiprasong Hospital in Ubon Ratchathani, Thailand.

**Aim 1.** Describe the characteristics and outcomes of patients in the first year of the Ubon-Sepsis cohort.

**Aim 2.** Describe the initial management of patients in the first year of the Ubon-Sepsis cohort.

Aim 2a. Describe the clinical management prior to transfer, for those patients who were transferred from another hospital to Sunpasithiprasong.

Aim 2b. Describe the clinical management in the Sunpasithiprasong Hospital Emergency Department (ED).

Aim 2c. Describe the clinical management in the first day of admission to Sunpasithiprasong Hospital, stratified by admission ward (intensive care unit (ICU) vs non-ICU).

**Aim 3.** Assess the clinical characteristics present at the time of presentation to the Emergency Department associated with admission to the intensive care unit.

## ***Methods***

### **Study design and study site**

We conducted a prospective observational study of community-acquired sepsis at Sunpasitthiprasong Hospital, Ubon Ratchathani, Thailand from March 2013 to December 2016. Ubon Ratchathani is the largest province in northeast Thailand with a population of 1.8 million, covers an area of 16,113 km<sup>2</sup>, and is bordered by Cambodia to the south and Laos to the east. Sunpasitthiprasong Hospital is a public tertiary-care hospital with 1,200 non-intensive care unit (ICU) beds and 220 ICU beds, providing care to people living within its catchment area and acting as a referral hospital for smaller district hospitals. Severely ill patients presenting to district hospitals are often referred to Sunpasitthiprasong Hospital, which is equipped with microbiology facilities and specialty physicians.

### **Study participants**

We prospectively enrolled patients  $\geq 18$  years of age who were admitted with a primary diagnosis of infection made by the attending physician, were within 24 hours of admission to the study hospital, and had at least three Surviving Sepsis Campaign diagnostic criteria for sepsis documented in the medical record (Supplemental Table 1) [14]. As this study was limited to community-acquired sepsis only, we excluded patients who were suspected of having hospital-acquired infections, had a hospital stay within 30 days prior to this admission, or were transferred from other hospitals with a total duration of hospitalization  $>72$  hours. The study is registered on [clinicaltrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT02217592) (NCT02217592). For this analysis, we evaluated patients enrolled from March 2013 to February 2014 with sepsis (formerly severe sepsis), defined as infection plus the presence of organ dysfunction. At the time of study enrollment, consensus definitions of sepsis (Sepsis-2) differentiated between sepsis, systemic inflammatory response syndrome in the presence of a suspected or confirmed infection, and severe sepsis, the additional presence of organ dysfunction [15]. In January 2016, updated consensus definitions were released (Sepsis-3), dispensing

with the term severe sepsis and changing the definition of sepsis to life-threatening organ dysfunction due to dysregulated immune response to infection [1].

Organ dysfunction was determined by the presence of at least one of the following features at the time of study enrollment: systolic blood pressure (SBP) < 90mmHg, mean arterial pressure (MAP) <70mmHg, SBP drop >40mmHg (since initial presentation), or vasopressor use; pulse oximetry <90%, arterial partial pressure of oxygen (PaO<sub>2</sub>) <60mmHg, ratio of PaO<sub>2</sub> to fraction of inspired oxygen (FiO<sub>2</sub>) <300, or mechanical ventilation; platelet count <100,000 u/L, international normalized ratio (INR) >1.5, or partial thromboplastin time (PTT) >60 sec; Glasgow Coma Scale (GCS) ≤14; acute oliguria, creatinine increase >0.5 mg/dL, or creatinine >2 mg/dL without history of chronic kidney disease; total bilirubin >4 mg/dL; and venous lactate >3 mmol/L. These are standard markers of organ dysfunction in the field of critical care medicine and are largely based on the Surviving Sepsis Campaign criteria[14].

Trained research nurses sequentially screened all medical patients admitted with a primary diagnosis of infection by conducting ward rounds and reviewing admission logs in the emergency department (ED), medical wards and medical ICUs twice on every working day. In addition, ED staff notified the study team directly about potentially eligible patients. Patient eligibility for the study was determined only from the data documented in the medical charts.

### **Study team point-of-care assessments**

After enrollment, each patient was evaluated by the study team at the bedside using four point-of-care assessments: a whole blood lactate rapid diagnostic test (RDT) (Lactate Pro 2, Arkray Global Business Inc., Australia), a whole blood glucose RDT (ACCU-CHECK Performa, Roche Diagnostic, Germany), pulse oximetry (Nellcor N-65, Covidien plc., Ireland) and GCS. The results were reported to the treating physicians. The study did not involve any clinical interventions; all treatment was provided by attending

physicians and the medical teams. Mortality at 28 days after enrollment was evaluated via study nurse report or telephone contact if subjects were no longer hospitalized and had been discharged alive.

We conducted the study in full compliance with the principles of good clinical practice and the ethical principles of the Declaration of Helsinki. The study protocol and related documents were approved by Sunpasithprasong Hospital Ethics Committee (039/2556), the Ethics Committee of the Faculty of Tropical Medicine of Mahidol University (MUTM2012-024-01), the University of Washington Institutional Review Board (42988), and the Oxford Tropical Research Ethics Committee of the University of Oxford (OXTREC172-12).

### **Statistical analysis**

For continuous data, means and standard deviations (SDs) are reported where the data followed a normal distribution and medians and interquartile ranges (IQRs) are reported where the data followed a non-normal distribution. The t-test was used for comparison of continuous data. For categorical data, counts and percentages are reported and the Chi-square test or Fisher's exact test (when any cell had a value less than 10) was used for comparisons. We assessed the clinical characteristics present at the time of presentation to the Emergency Department associated with admission to the ICU using a multivariable logistic regression model. Covariates in the models, chosen *a priori*, included age, sex, presence of at least one co-morbidity, pulse oximetry, SBP, GCS score, creatinine, bilirubin, platelets, presence of respiratory failure, receipt of adrenergic agent, transfer from ED or inpatient status at another medical facility, and nighttime admission. We performed a Kaplan-Meier analysis to assess 28-day survival by admitting location. All analyses were performed using Stata version 14.1 (StataCorp, College Station, TX, USA).

### **Role of the funding source**

This study was funded by the National Heart, Lung and Blood Institute of the National Institutes of Health (R01HL113382 and T32HL007287) and the Wellcome Trust (090219/Z/09/Z). All study activities, including data collection, data analysis, data interpretation, and writing of the report were performed solely by the participating authors without the sponsors' involvement.

## ***Results***

### **Baseline characteristics**

We enrolled 1,211 patients from March 2013 through February 2014. Vital status at 28 days after enrollment was unavailable for 3 (0.2%) patients, and 1 (0.08%) withdrew consent after enrollment; these patients were excluded from analysis. Nine hundred thirty two (77%) met the definition of sepsis, exhibiting organ dysfunction as described above, and were retained for further analysis. The characteristics of the patients at enrollment are shown in [Table 1](#). The majority of patients (N=512, 55%) were male and the mean age was 54 years (SD 20). Three hundred ninety three (42%) patients had a pre-existing medical condition. The mean lowest recorded systolic blood pressure was 91 mm Hg (SD 22) and mean platelet count was 149,940 cells/ $\mu$ L (SD 122,338 cells/ $\mu$ L).

### **Prior management**

Of the 932 patients with sepsis, 773 (83%) were transferred to Sunpasitthiprasong Hospital from one of 19 healthcare facilities. Of these patients, 35 (5%) had blood cultures ordered and 472 (61%) were prescribed at least one antibiotic prior to transfer. Ceftriaxone was the most commonly prescribed antibiotic (N=385, 50%). Three hundred fifty three (46%) patients received intravenous (IV) fluid at the referring facility. Two hundred sixty nine (35%) of patients received an IV adrenergic agent, most commonly dopamine.

### **Emergency Department management**

Of 932 patients, 783 (84%) were first evaluated in the ED and the rest were evaluated in the outpatient department. The median length of stay in the ED was 25 mins (IQR 20-40 mins), and 693 (89%) were transferred from other facilities. Of the 783 patients evaluated in the ED, 579 (74%) had blood cultures ordered and 514 (66%) were prescribed at least one antibiotic prior to study enrollment ([Table 2](#)). Ceftriaxone was the most commonly prescribed antibiotic (346/783, 44%). For the 479 patients for whom

data were available, the median time from presentation to antibiotic administration was 4.5 hrs (IQR 2.3-7.3 hrs), indicating that most antibiotics were administered after patients left the ED. There was no difference in time to first antibiotic administration between patients who were or were not transferred from other facilities. Two hundred ninety four (38%) patients were prescribed IV fluid in the ED; the mean volume received was 733mL (SD 557). Two hundred eighty seven (37%) patients were prescribed an IV adrenergic agent, most commonly dopamine. Ninety seven (12%) patients were mechanically ventilated in the ED, mostly with an electrical ventilator (78/97); the remainder were mechanically ventilated with a gas-powered ventilator.

### **Admission ward and management during the first hospital day**

Of all 932 patients with sepsis evaluated in either the ED or the OPD, 65 (7.0%) were admitted immediately to the ICU. An additional 74 patients (8%) were transferred to the ICU by the first hospital day; a total of 139 patients (15%) were managed in the ICU at some point in the first day of their admission. The remaining patients were managed on general medical wards. Patients admitted to the ICU during the first hospital day were more likely than those admitted to the general medical wards during the same time period to receive all measured interventions, including antibiotics, fluids, blood cultures, mechanical ventilation, vasopressors, placement of a urinary catheter, and dialysis ([Table 3](#)). Nonetheless, one-third (N=261, 33%) of patients on the general medical wards received an adrenergic agent and many (N=137, 17%) received mechanical ventilation within the first day. The ventilators used on the wards were primarily gas powered (128/137, 93%) but the ventilators used in the ICUs were primarily electrical (109/118, 93%).

### **Outcomes**

Overall in-hospital mortality was 9% (87/932) but differed significantly for patients admitted to the ICU (21%; 29/139) compared to those admitted to the general medical wards during the first day of their hospitalization (7%; 58/793,  $p<0.001$ ). Overall 28-day mortality was 22% (203/932) and was higher for

patients admitted to the ICU (45%; 63/139) than patients admitted to the general medical ward (18%; 140/793,  $p<0.001$ ). Survival curves demonstrated that the majority of deaths in patients admitted to the ICU occurred within a week of admission ([Figure 1](#)). The majority of patients who died after hospital discharge but within 28 days of enrollment were discharged in a moribund condition (87%; 101/116), with a median time to death of 5 days after discharge (IQR 2-13 days).

### **Clinical characteristics associated with ICU admission**

The availability of ICU beds is far exceeded by the number of septic patients. To determine how access to this restricted resource is allocated, we performed univariable and multivariable analysis of patient characteristics present on presentation associated with ICU admission ([Table 4](#), [Table 5](#)). Patients admitted to the ICU were similar to those admitted to the general medical wards with respect to age, sex, and underlying medical conditions. However, patients admitted to the ICU were more hypoxemic, had lower GCS, and had higher plasma levels of creatinine and bilirubin ( $p<0.001$ ). They were also more likely to have respiratory failure and to be receiving an adrenergic agent. After controlling for other variables, younger age (OR 0.97 per each 1 year higher age, 95% CI 0.96-0.99), lower SpO<sub>2</sub> (OR 0.91 per each 1% higher SpO<sub>2</sub>, 95% CI 0.87-0.95), respiratory failure (OR 3.32, 95% CI 1.59-6.92), and use of an adrenergic agent (OR 2.72, 95% CI 1.28-5.76) prior to hospital admission were significantly associated with admission to the ICU within the first day after study enrollment.

## ***Discussion***

This prospective observational study of adults with community-acquired sepsis at a regional Thai referral hospital provides important new data about patient characteristics and management in this setting. The most salient findings are that ED stay was remarkably short, perhaps because nearly all of the patients seen in the ED were transferred from other hospitals, but the majority of patients were prescribed antibiotics and had blood cultures ordered. In addition, the large majority of patients were admitted to general medical wards rather than to the ICU. Those who were admitted to the ICU were more critically ill, with higher rates of hypoxemia, altered mental status, and renal and liver dysfunction, and had higher mortality. While mechanical ventilation and adrenergic agents were implemented frequently on both the general medical wards and in the ICU, initiation of hemodialysis was uncommon. Patients received modest volumes of IV fluid resuscitation in the first day of hospitalization. Sepsis in this setting is a frequently fatal condition, with a 28-day mortality rate of 22%.

While there are several well-equipped ICUs in the study hospital, these are chronically near capacity. This may partly reflect the fact that long-term acute care facilities in are not available in this region, as some chronically ventilated patients must remain in the ICU due to lack of alternative disposition options. Because the ICUs have so little admitting capacity, critically ill patients often must be admitted to the medical wards. Indeed, during the first day of hospitalization 74% of patients receiving adrenergic agents were admitted to the ward vs the ICU (261/351), and more patients with respiratory failure requiring mechanical ventilation were admitted to the ward than to the ICU (137/255, 54%). Despite this, the sicker patients were generally admitted to the ICU, with significant differences in multiple markers of organ dysfunction between the two groups.

Over 80% of medical ward patients and over 90% of ICU patients in our study received at least one antibiotic in the first day of hospitalization. This is similar to findings by Auma et al, who reported that

87% of hospitalized adults with sepsis at a public referral hospital in Uganda received antibiotics [16]. While most patients received an antibiotic in the first day of hospitalization, it is notable that 151 (16%) did not; of those who did not receive antibiotics within the first day of admission at the study hospital, 5 died during their hospitalization. A higher proportion of ICU patients than non-ICU patients received antibiotics in the first day of admission. In this group of hospitalized sepsis patients, all patients should receive early antibiotics, and ideally the rate of antibiotic administration should not differ between general and intensive care settings. This difference perhaps reflects a lower patient-to-provider ratio in the ICUs; further assessment of the determinants of this difference could potentially inform future sepsis management guidelines and implementation. Blood cultures are recommended before starting antimicrobial therapy per the Surviving Sepsis Campaign 2016 International Guidelines [4]. Greater than 70% of patients in this study had blood cultures ordered by their treating teams in the first day of admission. This is significantly higher than reported in other observational studies of sepsis patients in low- and middle-income countries (LMICs). Conde et al reported that, among patients in 19 different hospitals in Brazil, only 16.3% of patients in public hospitals and 34.1% of patients in private hospitals had blood cultures performed [17]. Patients in our study received less fluid as part of their initial resuscitation than in the usual care arms of several recent studies of patients with sepsis and septic shock [7,9,18].

While overall hospital mortality in this study was low, at 9.3%, many patients who were discharged alive were in a moribund condition and, due to cultural preference, were sent home with the expectation that they would die shortly after discharge. Thus, in this study, 28-day mortality may be the more robust measurement and the best point of comparison with other studies. Our overall 28-day mortality rate of 22% is similar to or lower than the in-hospital mortality rate reported by several other groups in LMICs. For example, Andrews et al reported 33% in-hospital mortality and 45% 28-day mortality for hospitalized adults with sepsis in the usual care arm of a randomized clinical trial in Zambia, and Waitt et al reported 50% in-hospital mortality for hospitalized adults with sepsis in Malawi [19,20]. The 28-day mortality rate

in this study was also similar to the in-hospital mortality rates reported in several studies of patients in high-resource settings. Rhee et al reported 15% in-hospital mortality and 6.2% discharge to hospice among adult patients with sepsis in 409 U.S. hospitals in 2014, and there was 18.9% in-hospital mortality among patients in the usual care arm of the ProCESS trial [9,21]. This comparable mortality to higher resource settings despite limited resources and different management practices could be due to several contributing factors, such as different causative pathogens [22], different characteristics of the study population and study subjects, and other factors. Further studies are needed to evaluate these contributing factors and to assess the impact of different sepsis management strategies in diverse settings.

This study has several limitations. First, we are unlikely to have enrolled all sepsis patients presenting during the study period. Although study staff consecutively screened all patients admitted to the medical wards on working days, screening was based upon a clinical diagnosis of suspected infection listed in the patient's chart. It is possible that patients with sepsis were initially misdiagnosed with conditions such as congestive heart failure or exacerbation of chronic obstructive pulmonary disease, and their infections were not identified until after they were excluded from the study based on screening. Additionally, we did not enroll surgical, obstetric, or pediatric patients. Second, some unique characteristics of this study population may limit generalizability. In particular, our population had a very low HIV prevalence relative to some LMIC settings and had much lower rates of other important comorbidities, such as cancer or heart disease, relative to some HIC settings. Perhaps the most unique feature of this population was the very high percentage of patients who were transferred from other facilities, exceeding levels even in some tertiary or quaternary referral hospitals elsewhere. As the study site is highly resourced relative to some more rural hospital settings in Thailand, caution must be taken with application of the results to other settings within the country, as well. Third, as an observational study, our data are limited to those routinely collected by clinicians in the study hospital, and availability of laboratory data or other invasive testing likely reflects common clinical practice in this LMIC setting.

There are several strengths of this study. The size, larger than many studies of sepsis management and outcomes in LMICs to date, is a major strength. We consecutively enrolled patients, limiting potential bias due to convenience sampling. We have an excellent follow-up rate, with only three of 1,211 (0.2%) patients missing vital status at 28 days after enrollment. Following patients to 28 days after enrollment, and not just tracking vital status at hospital discharge, allowed us to capture a more robust measure of case fatality in this population. Additionally, while this is a single-center study, over 80% of patients were transferred to the study hospital from one of 19 referral centers, and we were able to assess management at the referral centers in addition to management after arrival at the study hospital.

In conclusion, this prospective observational study of patients with sepsis at a regional Thai referral hospital provides important information about the characteristics, management, and outcomes of patients at a large public LMIC referral hospital. This study is among the largest published prospective analyses of patients with sepsis in a LMIC, and provides important information for clinicians, researchers, and public health professionals working in this arena.

## Figures and Tables

**Table 1. Characteristics at enrollment for 932 adult Thai patients with community-acquired sepsis enrolled in the Ubon-Sepsis study from March 2013-February 2014**

Variable	All Patients N=932
Male, <i>n</i> (%)	512 (55)
Age (yrs), mean (SD)	54 (20)
Co-morbidities, <i>n</i> (%)	393 (42)
Cancer	11 (1)
Cerebrovascular disease	21 (2)
Chronic kidney disease	79 (8)
Diabetes mellitus	155 (17)
Dyslipidemia	32 (3)
Heart disease	50 (5)
HIV	19 (2)
Hypertension	181 (19)
Liver disease	30 (3)
Lung disease	72 (8)
SpO <sub>2</sub> (%), mean (SD) <sup>a</sup>	95 (7.2)
SBP (mm Hg), mean (SD) <sup>a</sup>	91 (22)
GCS, mean (SD) <sup>a</sup>	14 (2.4)
Creatinine (mg/dL), mean (SD) <sup>a,b</sup>	2.1 (1.8)
Bilirubin (mg/dL), mean (SD) <sup>a,c</sup>	2.0 (3.5)
Platelets (cells/ $\mu$ L), mean (SD) <sup>a,d</sup>	149,940 (122,338)

<sup>a</sup> Lowest SpO<sub>2</sub>, SBP, GCS, and platelets, and highest creatinine and bilirubin values up to the time of study enrollment are presented

**Table 2. Emergency Department management of 783 adult Thai patients with community-acquired sepsis**

Therapy	Patients Treated in ED N = 783
Antibiotic, <i>n</i> (%)	514 (66)
Ceftriaxone	346 (44)
Ceftazidime	131 (17)
Clindamycin	86 (11)
Doxycycline	71 (9)
IV crystalloid, <i>n</i> (%)	294 (38)
IV crystalloid volume (mL), mean (SD) <sup>a</sup>	733 (557)
Blood culture, <i>n</i> (%)	579 (74)
Arterial blood gas, <i>n</i> (%)	8 (1)
Adrenergic agent, <i>n</i> (%)	287 (37)
Mechanical ventilation, <i>n</i> (%)	97 (12)

<sup>a</sup> Of patients who received any IV crystalloid

**Table 3. Management during first day of hospitalization for 793 adult Thai patients admitted to general medical wards and 139 adult Thai patients admitted to the ICU with community-acquired sepsis**

Therapy	General Ward N=793	ICU N=139	P value
Antibiotic, <i>n</i> (%)	651 (82)	130 (94)	<0.001
IV crystalloid, <i>n</i> (%)	386 (49)	109 (78)	<0.001
IV crystalloid volume (mL), mean (SD) <sup>a</sup>	969 (775)	2031 (1673)	<0.001
Blood culture, <i>n</i> (%)	623 (79)	120 (86)	0.04
Urinary catheterization, <i>n</i> (%)	388 (49)	131 (94)	<0.001
Acute dialysis, <i>n</i> (%)	3 (0.4)	3 (2)	0.05
Adrenergic agent, <i>n</i> (%)	261 (33)	90 (65)	<0.001
Mechanical ventilation, <i>n</i> (%)	137 (17)	118 (85)	<0.001

Management of general ward and ICU patients was compared using t-tests for continuous variables and Chi-squared tests for categorical variables. <sup>a</sup> Of patients who received any IV crystalloid.

**Table 4. Patient characteristics present upon presentation by for 793 Thai adults admitted to the general medical wards and 139 adults admitted to the ICU with sepsis**

Variable	General ward N=793	ICU N=139	P value
Male, <i>n</i> (%)	429 (54)	83 (60)	0.22
Age (yrs), mean (SD)	54 (20)	56 (19)	0.38
Co-morbidities, <i>n</i> (%)	333 (42)	60 (43)	0.80
Cancer	10 (1)	1 (0.7)	1.00
Cerebrovascular disease	17 (2)	4 (3)	0.53
Chronic kidney disease	69 (9)	10 (7)	0.55
Diabetes mellitus	125 (16)	30 (22)	0.08
Dyslipidemia	28 (4)	4 (3)	1.00
Heart disease	41 (5)	9 (6)	0.54
HIV	18 (2)	1 (0.7)	0.34
Hypertension	154 (20)	27 (21)	0.91
Liver disease	26 (3)	4 (3)	1.00
Lung disease	60 (8)	12 (9)	0.67
SpO <sub>2</sub> (%), mean (SD) <sup>a</sup>	96 (7.8)	91 (10)	<0.001
SBP (mm Hg), mean (SD) <sup>a</sup>	95 (27)	90 (27)	0.05
GCS, mean (SD) <sup>a</sup>	14.2 (2.2)	13.5 (2.7)	0.005
Creatinine (mg/dL), mean (SD) <sup>a,b</sup>	2.1 (1.8)	2.8 (2.0)	<0.001
Bilirubin (mg/dL), mean (SD) <sup>a,c</sup>	1.8 (3.4)	3.0 (4.8)	0.002
Platelets (cells/ $\mu$ L), mean (SD) <sup>a,d</sup>	154,410 (121,353)	163,462 (136,771)	0.44
Respiratory failure, <i>n</i> (%)	61 (8)	43 (31)	<0.001
Receiving adrenergic agents, <i>n</i> (%)	246 (31)	70 (50)	<0.001
Referred from another facility, <i>n</i> (%)	641 (81)	132 (95)	<0.001
Initial presentation to outpatient department, <i>n</i> (%)	145 (18)	3 (2)	<0.001
Night time admission, <i>n</i> (%)	278 (38)	38 (29)	0.06

Characteristics of patients admitted to the general medical ward and ICU were compared using t-tests for continuous variables and Chi-squared tests for categorical variables. <sup>a</sup> Lowest SpO<sub>2</sub>, SBP, GCS, and platelets; highest creatinine and bilirubin values; and clinical management up to the time of admission are presented

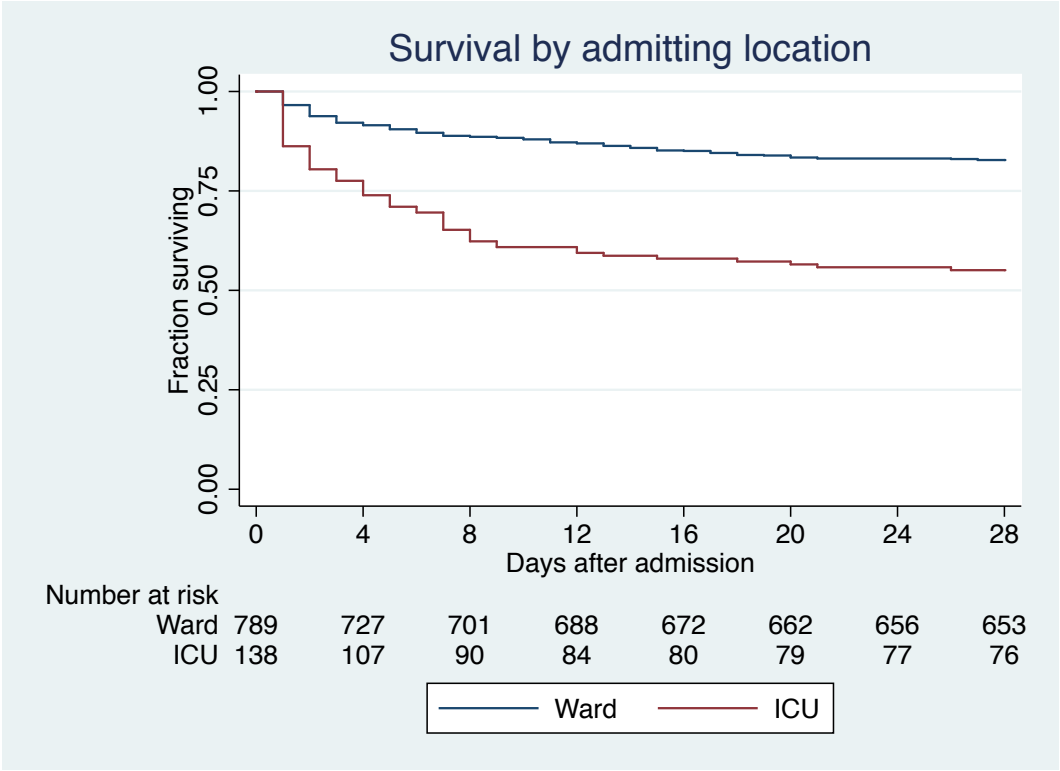
**Table 5. Association between patient characteristics at presentation and ICU admission**

Variable	Number of Patients with Observation	Unadjusted OR (95% CI)	P value	Adjusted OR (95% CI) <sup>a</sup> N = 314	P value
Male sex	932	1.26 (0.87-1.81)	0.22	0.62 (0.35 – 1.12)	0.12
Age (yrs)	932	1.00 (1.00-1.01)	0.38	0.97 (0.96 – 0.99)	<b>0.005</b>
Presence of at least one co-morbidity	932	1.05 (0.73-1.51)	0.80	0.81 (0.42 – 1.56)	0.53
SpO <sub>2</sub> (%) <sup>b</sup>	729	0.94 (0.92-0.96)	<b>&lt;0.001</b>	0.91 (0.87 – 0.95)	<b>&lt;0.001</b>
SBP (mm Hg) <sup>b</sup>	928	0.99 (0.99-1.00)	0.05	1.00 (0.99 – 1.02)	0.54
GCS <sup>b</sup>	629	0.90 (0.84-0.97)	<b>0.006</b>	0.98 (0.87 – 1.11)	0.77
Creatinine (mg/dL) <sup>b</sup>	732	1.18 (1.08-1.30)	<b>&lt;0.001</b>	1.14 (0.99 – 1.32)	0.07
Bilirubin (mg/dL) <sup>b</sup>	546	1.07 (1.02-1.13)	<b>0.005</b>	1.05 (0.98 – 1.13)	0.13
Platelets (cells/ $\mu$ L) <sup>b</sup>	850	1.00 (1.00-1.00)	0.44	1.00 (1.00 – 1.00)	0.43
Respiratory failure	932	5.38 (3.45-8.38)	<b>&lt;0.001</b>	3.32 (1.59 – 6.92)	<b>0.001</b>
Receiving adrenergic agent	932	2.26 (1.57-3.25)	<b>&lt;0.001</b>	2.72 (1.28 – 5.76)	<b>0.009</b>
Referred from another facility	930	4.41 (2.02-9.63)	<b>&lt;0.001</b>	0.56 (0.10 – 3.32)	0.53
Night time admission	872	0.68 (0.45-1.02)	0.06	1.12 (0.57 – 2.19)	0.75

<sup>a</sup> Using logistic regression, each variable controlled for all other variables

<sup>b</sup> Lowest SpO<sub>2</sub>, SBP, GCS, and platelets; highest creatinine and bilirubin values; and clinical management up to the time of admission are presented

**Figure 1. Kaplan-Meier curve demonstrating 28-day survival of 932 Thai adults admitted with community-acquired sepsis, by admitting location**



**Supplemental Table 1. Modified Surviving Sepsis Campaign diagnostic criteria for sepsis.**

<b>Infection, documented or suspected, and some of the following:</b>
<b>General variables</b>
Fever or hypothermia (body temperature $>38.3^{\circ}\text{C}$ or $<36^{\circ}\text{C}$ ) <sup>a</sup>
Heart rate $>90/\text{min}$
Tachypnea (respiratory rate $>20/\text{min}$ ) <sup>b</sup>
Altered mental status (Glasgow Coma Scale $<15$ ) <sup>c</sup>
Significant edema or positive fluid balance ( $>20$ mL/kg over 24 hr)
Hyperglycemia (plasma glucose $>140$ mg/dL) in the absence of diabetes
<b>Inflammatory variables</b>
Leukocytosis (WBC count $>12,000$ u/L), Leukopenia (WBC count $<4,000$ u/L), or immature forms $>10\%$ <sup>d</sup>
Plasma C-reactive protein $>2$ SD above the normal value
Plasma procalcitonin $>2$ SD above the normal value
<b>Hemodynamic variables</b>
Arterial hypotension (SBP $<90$ mmHg, MAP $<70$ mmHg or an SBP decrease $>40$ mmHg)
<b>Organ dysfunction variables</b>
Low oxygen saturation determined by pulse oximetry ( $\text{SpO}_2 <95\%$ ) <sup>e</sup>
Arterial hypoxemia ( $\text{PaO}_2/\text{FiO}_2 <300$ )
Acute oliguria (urine output $<0.5$ mL/kg/hr for at least 2 hrs) <sup>f</sup>
Creatinine increase $>0.5$ mg/dL
Coagulation abnormalities (INR $>1.5$ or aPTT $>60$ s)
Ileus (absent bowel sounds)
Thrombocytopenia (platelet count $<100,000$ u/L)
Hyperbilirubinemia (plasma total bilirubin $>4$ mg/dL)
<b>Tissue perfusion variables</b>
Hyperlactatemia ( $>1$ mmol/L)
Decreased capillary refill or mottling

Adapted from Dellinger et al, Surviving Sepsis Campaign: International Guideline for Management of Severe Sepsis and Septic Shock, 2012 [14]

<sup>a</sup> Fever and hypothermia were consolidated into a single variable.

<sup>b</sup> Respiratory rate  $>20/\text{min}$  was defined for the tachypnea variable.

<sup>c</sup> Glasgow Coma Scale  $<15$  was defined for the altered mental status variable.

<sup>d</sup> Leukocytosis, Leukopenia, and immature forms  $>10\%$  were consolidated into a single variable.

<sup>e</sup> Low oxygen saturation determined by pulse oximetry ( $\text{SpO}_2 <95\%$ ) was added.

<sup>f</sup> The condition of ‘despite adequate fluid resuscitation’ for this criterion was omitted.

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