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Sequential Organ Failure Assessment (SOFA) Score for predicting mortality in patients with sepsis in Vietnamese intensive care units: a multicentre, cross-sectional study

Son Ngoc Do,[1,2,3] Co Xuan Dao,[1,2,3] Tuan Anh Nguyen ,[2,4] My Ha Nguyen,[5] Dung Thi Pham,[6] Nga Thi Nguyen,[7] Dai Quang Huynh,[8,9] Quoc Trong Ai Hoang,[10] Cuong Van Bui,[1,2] Thang Dinh Vu,[11] Ha Nhat Bui,[12] Hung Tan Nguyen,[13] Hai Bui Hoang,[2,14] Thuy Thi Phuong Le,[15] Lien Thi Bao Nguyen,[16] Phuoc Thien Duong,[17] Tuan Dang Nguyen,[18] Vuong Hung Le,[19] Giang Thi Tra Pham,[20] Giang Thi Huong Bui,[1,2] Tam Van Bui,[7] Thao Thi Ngoc Pham ,[8,9] Chi Van Nguyen,[2,4] Anh Dat Nguyen,[2,4] Jason Phua,[21,22] Andrew Li,[22,23] Chinh Quoc Luong [2,3,4]

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MHN and DTP contributed equally.

SND, CXD, TAN, JP, AL and CQL are joint senior authors.

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For numbered affiliations see end of article.

Correspondence to
Dr Tuan Anh Nguyen;
bstuanccbm@gmail.com

ABSTRACT

Objectives To compare the accuracy of the Sequential Organ Failure Assessment (SOFA) and Acute Physiology and Chronic Health Evaluation II (APACHE II) Scores in predicting mortality among intensive care unit (ICU) patients with sepsis in a low-income and middle-income country.

Design A multicentre, cross-sectional study.

Setting A total of 15 adult ICUs throughout Vietnam.

Participants We included all patients aged ≥18 years who were admitted to ICUs for sepsis and who were still in ICUs from 00:00 to 23:59 of the specified study days (ie, 9 January, 3 April, 3 July and 9 October of the year 2019).

Primary and secondary outcome measures The primary outcome was hospital all-cause mortality (hospital mortality). We also defined the secondary outcome as all-cause deaths in the ICU (ICU mortality).

Results Of 252 patients, 40.1% died in hospitals, and 33.3% died in ICUs. SOFA Score (areas under the receiver operating characteristic curve (AUROC): 0.688 (95% CI 0.618 to 0.758); cut-off value≥7.5; P_{AUROC}<0.001) and APACHE II Score (AUROC: 0.689 (95% CI 0.622 to 0.756); cut-off value ≥20.5; P_{AUROC}<0.001) both had a poor discriminatory ability for predicting hospital mortality. However, the discriminatory ability for predicting ICU mortality of SOFA (AUROC: 0.713 (95% CI 0.643 to 0.783); cut-off value≥9.5; P_{AUROC}<0.001) was fair and was better than that of APACHE II Score (AUROC: 0.672 (95% CI 0.603 to 0.742); cut-off value≥18.5; P_{AUROC}<0.001). A SOFA Score≥8 (adjusted OR (AOR): 2.717; 95% CI 1.371 to 5.382) and an APACHE II Score≥21 (AOR: 2.668; 95% CI 1.338 to 5.321) were independently associated with an increased risk of hospital mortality. Additionally, a SOFA Score≥10 (AOR: 2.194; 95% CI 1.017 to 4.735) was an independent predictor of ICU mortality, in contrast to an APACHE II Score≥19, for which this role did not.

Conclusions In this study, SOFA and APACHE II Scores were worthwhile in predicting mortality among ICU patients with sepsis. However, due to better discrimination for predicting ICU mortality, the SOFA Score was preferable to the APACHE II Score in predicting mortality.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ An advantage of the present study was data from multi centres, which had little missing data.
⇒ Due to the absence of a national registry of intensive care units (ICUs) to allow systematic recruitment of units, we used a snowball method to identify suitable units, which might have led to the selection of centres with a greater interest in sepsis management.
⇒ Due to the study's real-world nature, we did not make a protocol for microbiological investigations. Moreover, we mainly evaluated resources used in ICUs; therefore, the data detailing the point-of-care testing and life-sustaining treatments were not available. Additionally, to improve the feasibility of conducting the study in busy ICUs, we opted not to collect data on antibiotic resistance and appropriateness.
⇒ Due to our independent variables (eg, Sequential Organ Failure Assessment Score that was greater than or equal to the cut-off value) that might be associated with primary outcome only measured on ICU admission, the mixed-effects logistic regression model could not be used to predict discrete outcome variables measured at two different times, that is, inside and outside the ICU settings.
⇒ Although the sample size was large enough, the CI was slightly wide (±6.03%), which might influence the normal distribution of the sample.

TRIAL REGISTRATION
Clinical trials registry – India: CTRI/2019/01/016898.

INTRODUCTION

Sepsis is a clinical syndrome which has physiological, biological and biochemical abnormalities caused by a dysregulated host response to infection and is a critical global health problem.[1 2] Sepsis is the most common cause of in-hospital deaths, with most of the burden in low-income and middle-income countries (LMICs), and extracts a high economic and social cost;[3–5] mortality rates remain high at 30%–45% and contribute to as much as 20% of all deaths worldwide.[2 4 6 7] There is no reference standard that allows easy, accurate diagnosis and prognosis of sepsis.[1 8] Although the 1991 International Consensus Definition Task Force proposed the systemic inflammatory response syndrome criteria to identify patients with a septic host response,[9] these criteria do not measure whether the response is injurious, and their utility is limited.[1 8]

The Acute Physiology and Chronic Health Evaluation II (APACHE II) Score was originally developed for critically ill patients in intensive care units (ICUs).[10] It has 12 physiological measures and extra points based on age and the presence of chronic disease.[10] The APACHE II Score was shown to have good prognostic value in acutely ill or surgical patients.[10 11] However, some limitations of the APACHE II Score are that (1) It is complex and cumbersome to use, (2) It does not differentiate between the sterile and infected necrosis, and finally, (3) It has a poor predictive value at 24 hours.[12]

In 2016, the Sepsis-3 Task Force proposed that for patients with suspected infection, an increase of 2 points or more in the Sequential Organ Failure Assessment (SOFA) Score could serve as clinical criteria for sepsis,[1] and the consensus has not changed since then.[13] This approach was justified based on content validity (SOFA reflects the facets of organ dysfunction) and predictive validity (the proposed criteria predict downstream events associated with the condition of interest).[14–17] However, the validity of this score was mainly derived from critically ill patients with suspected sepsis by interrogating over a million ICU electronic health record encounters from ICUs in high-income countries (HICs).[1 17 18] Moreover, the patients, pathogens and clinical capacity to manage sepsis differ considerably between HIC and LMIC settings.[7] Therefore, it's still unclear whether this score could be applied to different types of infections, locations within the hospital and countries.

Vietnam is an LMIC, ranked fifteenth in the world and third in South-East Asia by population with 96.462 million people.[19] Vietnam is also a hot spot for emerging infectious diseases in South-East Asia, including SARS-CoV-1,[20] avian influenza A(H5N1)[21 22] and the ongoing global COVID-19 outbreaks.[23 24] Additionally, severe dengue,[25] *Streptococcus suis* infection,[26] malaria[27] and increased antibiotic resistance are other major causes of sepsis in ICUs across Vietnam.[28 29] Despite its recent economic growth spurt,[30] Vietnam is still struggling to provide either enough resources or adequate diagnostic, prognostic and treatment strategies for patients with sepsis in both local and central settings.[31 32] In addition, within the healthcare system in Vietnam, central hospitals are responsible for receiving patients who have difficulties being treated in local hospital settings.[33] Therefore, the diagnosis, prognosis and initiation of treatment for patients with sepsis are often delayed.

In resource-limited settings, the early identification of infected patients who may go on to develop sepsis or who may be at risk of death from sepsis using accurate scoring systems is a way to decrease sepsis-associated mortality. Therefore, this study aimed to investigate the mortality rate and compare the accuracy of the SOFA Score and the APACHE II Score in predicting mortality in ICU patients with sepsis in Vietnam.

METHODS

Source of data

This multicentre observational, cross-sectional, point prevalence study is part of the Management of Severe sepsis in Asia's Intensive Care unitS (MOSAICS) II Study,[34–37] which enrolled patients on 9 January (Winter), 3 April (Spring), 3 July (Summer) and 9 October (Autumn) of the year 2019. All patients received a follow-up till hospital discharge, death in the ICU/hospital or up to 90 days postenrolment, whichever was earliest. In this study, we only used data from Vietnam. A total of 15 adult ICUs (excluding predominantly neurosurgical, coronary, and cardiothoracic ICUs) participated in the MOSAICS II study from 14 hospitals, of which 5 are central, and 9 are provincial, district, or private hospitals throughout Vietnam. Each ICU had one or two representatives who were part of the local study team and the MOSAICS II Study group, as shown in eAppendix 2 of a previously published paper.[36] Participation was voluntary and unfunded.

Participants

All patients admitted to participating ICUs on 1 of the 4 days (ie, 9 January, 3 April, 3 July and 9 October, 2019) which represented the different seasons of the year 2019 were screened for eligibility. We included all patients, aged ≥18 years, who were admitted to the ICUs for sepsis, and who were still in the ICUs from 00:00 to 23:59 of the study days. We defined sepsis as infection with a SOFA Score of 2 points or more from baseline (assumed to be 0 for patients without prior organ dysfunction).[1]

Data collection

We used a standardised classification and case record form (CRF) to collect data on common variables as shown in online supplemental file 1. The data dictionary of the MOSAICS II Study is available as an online supplement of previously published papers.[35 36] Data were

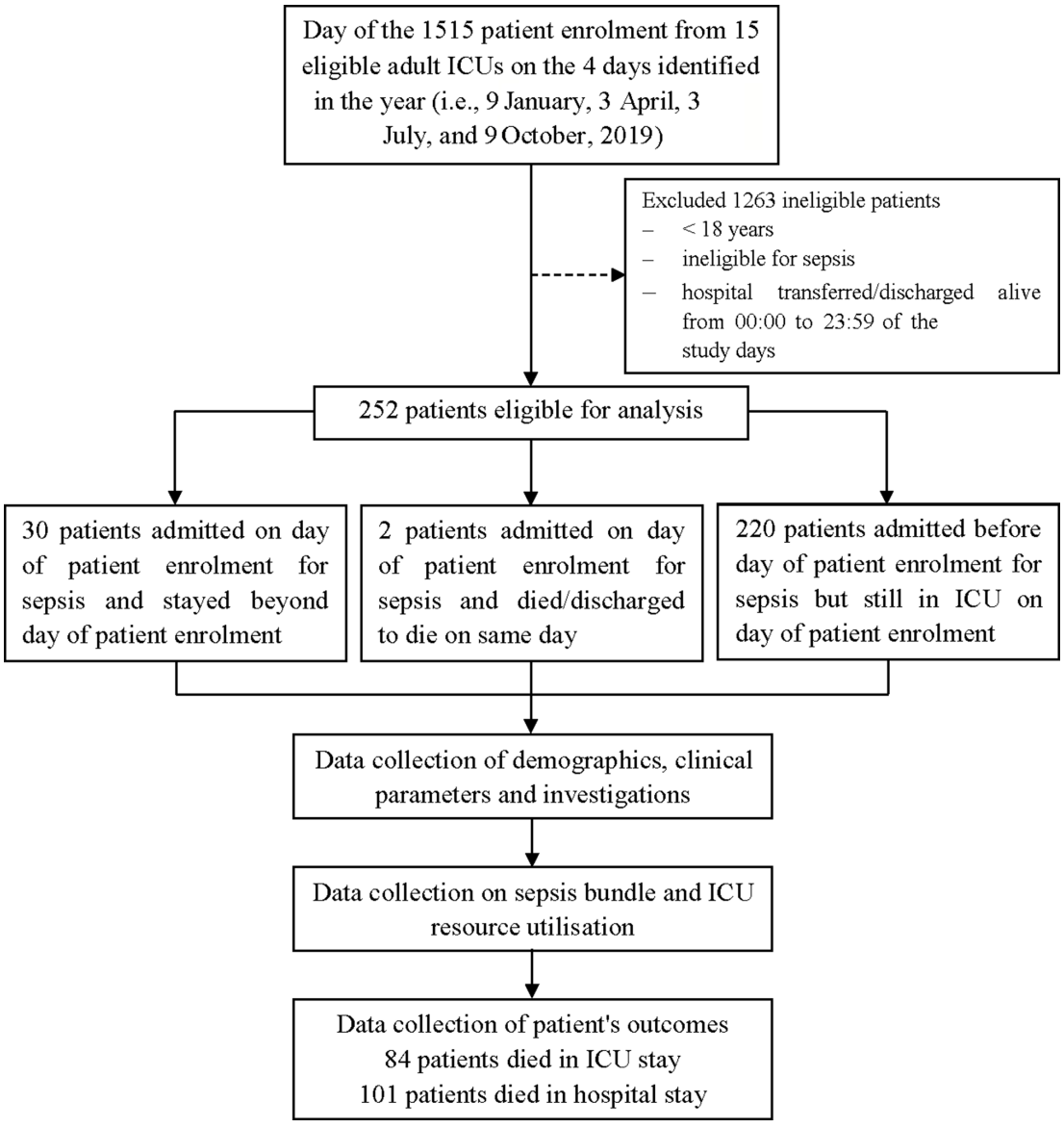

Figure 1 Flow chart of the study design, patient enrolment and follow-up. ICU, intensive care unit; discharged to die, defined as the patients who were in grave condition or dying and were classified with deaths in the ICU at the time of discharge.

entered by the representatives of the participating hospitals into the database of the MOSAICS II Study via the password-protected online CRFs. We checked the data for implausible outliers and missing fields and contacted ICU representatives for clarification. We then merged the data sets for the 14 hospitals.

Outcome measures

The primary outcome was hospital all-cause mortality (hospital mortality). We also defined the secondary outcomes as all-cause deaths in the ICU (ICU mortality) and the ICU and hospital lengths of stay (LOS).

Predictor measures

We defined exposure variables as the SOFA and the APACHE II Scores.[10 14] All data elements required for calculating the SOFA Score at the time of ICU admission and the APACHE II Score over the first 24 hours of ICU admission were prospectively collected on a CRF and entered into a database via the online CRF for later analysis.

We determined confounding factors as the variables of hospital and ICU characteristics collected on a questionnaire by representatives before patient enrolment, as shown in online supplemental file 2. We also determined confounding factors as variables collected on a CRF by investigators. The CRF contained four sections which is available in online supplemental file 1. The first section focused on baseline characteristics (demographics, documented comorbidities and details of admission). The second section comprised of vital signs on ICU admission, laboratory parameters, site of infection and microbiology. Only microorganisms detected via all cultures, serology, molecular and histological investigations, and deemed to be true pathogens rather than commensals or

Table 1 Baseline characteristics according to hospital survivability of patients with sepsis

Variables	All cases	Survived	Died	P value*
Hospital and ICU characteristics	n=252	n=151	n=101	
University affiliation, no. (%)	99 (39.3)	46 (30.5)	53 (52.5)	<0.001
Training programme in ICU, no. (%)	202 (80.2)	129 (85.4)	73 (72.3)	0.010
Demographics	n=252	n=151	n=101	
Age (years), median (IQR)	65 (52–76.75)	65 (53–76)	65 (52–78)	0.810‡
Sex (male), no. (%)	162 (64.3)	93 (61.6)	69 (68.3)	0.275
Documented comorbidities	n=252	n=151	n=101	
Cardiovascular disease, no. (%)	78 (31.0)	41 (27.2)	37 (36.6)	0.111
Chronic lung disease, no. (%)	30 (11.9)	18 (11.9)	12 (1.9)	0.992
Chronic neurological disease, no. (%)	36 (14.3)	28 (18.5)	8 (7.9)	0.018
Chronic kidney disease, no. (%)	23 (9.1)	14 (9.3)	9 (8.9)	0.922
Peptic ulcer disease, no. (%)	9 (3.6)	5 (3.3)	4 (4.0)	>0.999†
Chronic liver disease, no. (%)	27 (10.7)	14 (9.3)	13 (12.9)	0.365
Diabetes mellitus, no. (%)	67 (26.6)	40 (26.5)	27 (26.7)	0.966
Connective tissue disease, no. (%)	3 (1.2)	2 (1.3)	1 (1.0)	>0.999†
Immunosuppression, no. (%)	10 (4.0)	7 (4.6)	3 (3.0)	0.744
Haematological malignancies, no. (%)	5 (2.0)	3 (2.0)	2 (2.0)	>0.999†
Solid malignant tumours, no. (%)	12 (4.8)	6 (4.0)	6 (5.9)	0.551†
Vital signs (on admission into ICU)	n=252	n=151	n=101	
GCS, median (IQR)	13 (9–15)	14 (10–15)	10 (8–14)	<0.001‡
HR (beats per min), median (IQR)	110 (95.25–125.75)	110 (92–125)	110 (100–129.5)	0.083‡
Temperature (°C), mean (SD)	37.79 (1.01)	37.80 (1.08)	37.77 (0.91)	0.871‡
MBP (mmHg), mean(SD)	75.82 (22.08)	79.75 (22.88)	69.93 (19.51)	0.002‡
RR (breaths per min), median (IQR)	25 (22–30)	25 (22–30)	25 (20–30)	0.693‡
Blood investigations	n=252	n=151	n=101	
Total WBC ($x10^9$/L), mean (SD)	15.73 (9.20)	15.63 (8.67)	15.88 (9.98)	0.914‡
PLT ($x10^9$/L), mean (SD)	185.98 (137.85)	200.71 (129.67)	163.95 (147.15)	0.002‡
Hb (g/dL), mean (SD)	11.14 (2.59)	11.36 (2.68)	10.82 (2.44)	0.088‡
K^+ (mmol/L), mean (SD)	3.89 (0.79)	3.90 (0.80)	3.87 (0.77)	0.865‡
Na^+ (mmol/L), mean (SD)	136.05 (8.24)	135.62 (8.81)	136.69 (7.80)	0.068‡
Creatinine (µmol/L), mean (SD)	187.85 (151.92)	186.15 (171.60)	190.38 (117.27)	0.030‡
Bilirubin (µmol/l), mean (SD)	32.80 (61.49)	31.74 (72.67)	34.35 (40.09)	0.007‡
pH, mean (SD)	7.37 (0.50)	7.41 (0.64)	7.32 (0.14)	0.004‡
PaO_2 (mmHg), mean (SD)	116.17 (74.28)	110.23 (56.25)	124.73 (94.07)	0.665‡
PaO_2/FiO_2 ratio, mean (SD)	262.48 (149.58)	281.52 (149.39)	235.26 (146.32)	0.003‡
Severity of illness scores	n=252	n=151	n=101	
SOFA, median (IQR), n=250	7 (4.75–10)	6 (4-9)	9 (6-12)	<0.001‡
APACHE II, median (IQR)	18 (13–24)	15 (12–21)	22 (16–27)	<0.001‡
Septic shock	74 (29.4)	35 (23.2)	39 (38.6)	0.008
Site of Infection	n=252	n=151	n=101	
Respiratory, no. (%)	143 (56.7)	82 (54.3)	61 (60.4)	0.339
Urinary tract, no. (%)	37 (14.7)	30 (19.9)	7 (6.9)	0.004
Abdominal, no. (%)	61 (24.2)	34 (22.5)	27 (26.7)	0.444
Neurological, no. (%)	12 (4.8)	8 (5.3)	4 (4.0)	0.767†

Continued

Table 1 Continued

Variables	All cases	Survived	Died	P value*
Bones or joints, no. (%)	2 (0.8)	2 (1.3)	0 (0.0)	0.518†
Skin or cutaneous sites, no. (%)	19 (7.5)	7 (4.6)	12 (11.9)	0.033
Intravascular catheter, no. (%)	1 (0.4)	1 (0.7)	0 (0.0)	>0.999†
Infective endocarditis, no. (%)	1 (0.4)	0 (0.0)	1 (1.0)	0.401†
Primary bacteraemia, no. (%)	7 (2.8)	5 (3.3)	2 (2.0)	0.705†
Systemic, no. (%)	6 (2.4)	4 (2.6)	2 (2.0)	>0.999†
Microbiology	n=252	n=151	n=101	
No pathogens detected, no. (%)	67 (26.6)	47 (31.1)	20 (19.8)	0.046
Gram-negative bacteria, no. (%)	156 (61.9)	88 (58.3)	68 (67.3)	0.147
Gram-positive bacteria, no. (%)	34 (13.5)	22 (14.6)	12 (11.9)	0.540
Fungi, no. (%)	7 (2.8)	4 (2.6)	3 (3.0)	>0.999†
Viruses, no. (%)	2 (0.8)	0 (0.0)	2 (2.0)	0.160†
Other pathogens, no. (%)	4 (1.6)	3 (2.0)	1 (1.0)	0.651†

See tables S1–S4 (online supplemental file 3) for additional information.
*Comparison between the patients who survived and died using χ^2 test.
†Fisher's exact test.
‡Mann–Whitney U test.
APACHE II, Acute Physiology and Chronic Health Evaluation II; FiO_2, fraction of inspired oxygen; GCS, Glasgow Coma Scale; Hb, haemoglobin; HR, heart rate; ICU, intensive care unit; MBP, mean blood pressure; no, number; PaO_2, partial pressure of oxygen in the arterial blood; PLT, platelet count; RR, respiratory rate; SOFA, Sequential Organ Failure Assessment; WBC, white blood cell.

contaminants were recorded. The third section captured the timing of sepsis bundle elements referencing time zero, determined as follows: (A) Time of triage in the emergency department (ED) for those presenting with sepsis to the ED; (B) Time of clinical documentation of deterioration in the general wards or other non-ED areas for those who developed sepsis after hospital admission; (C) Time of ICU admission for those in which (A) or (B) could not be determined from the clinical documentation. The bundle elements were based on the Surviving Sepsis Campaign's 2018 update: antibiotics administration, blood cultures, lactate measurement, fluid administration (amount of fluids administered in the first and third hours from time zero) and vasopressor initiation.[38] The fourth section concerned life-sustaining treatments provided during the ICU stay.

Sample size

In the present study, hospital mortality served as the primary outcome. We, therefore, used the formula to determine the minimal sample size for estimating a population proportion with a confidence level of 95%, a CI (margin of error) of 6.03% and an assumed population proportion of 61.0%, based on the hospital mortality rate (61.0%) of our cohort reported in a previously published study.[39] Therefore, we should have at least 252 patients in our sample. Because of this, our sample size was sufficient and reflected a normal distribution.

$$n = \frac{z^2 x\hat{p}(1-\hat{p})}{\varepsilon^2}$$

where:

z is the z score (z score for a 95% confidence level is 1.96)

ε is the margin of error (ε for a CI of ±6.03% is 0.0603)

$\hat{p}$ is the population proportion ($\hat{p}$ for a population proportion of 61.0% is 0.61)

n is the sample size

Statistical analyses

We used IBM SPSS Statistics V.22.0 (IBM Corp, Armonk, New York, USA) for data analysis. We report data as numbers (no.) and percentages (%) for categorical variables and medians and IQRs or means and SDs for continuous variables. Comparisons were made between survival and death in the hospital and ICU for each variable, using the χ^2 test or Fisher's exact test for categorical variables and the Mann-Whitney U test, Kruskal-Wallis test, one-way analysis of variance for continuous variables.

Receiver operating characteristic (ROC) curves were plotted and the areas under the ROC curve (AUROC) were calculated to determine the discriminatory ability of the SOFA and APACHE II Scores for deaths in the hospital and ICU. The cut-off value of the SOFA and the APACHE II Scores was determined by the ROC curve analysis and defined as the cut-off point with the maximum value of Youden's Index (ie, sensitivity+specificity – 1). Based on the cut-off value of the scores, we assigned the patients to two groups: either a score that was less than the cut-off value or a score that was greater than or equal to the cut-off value.

We assessed factors associated with death in the hospital using logistic regression analysis. To reduce the number

of predictors and the multicollinearity issue and resolve the overfitting, we used different ways to select variables as follows: (A) We put all variables (including exposure and confounding factors) of hospital and ICU characteristics, baseline characteristics, clinical and laboratory characteristics, and treatments into the univariable logistic regression model; (B) We selected variables if the value of p was <0.05 in the univariable logistic regression analysis between survival and death in the hospital, as well as those that are clinically crucial to put in the multivariable logistic regression model. These variables included university affiliation, training programme in ICU, documented comorbidities (ie, cardiovascular disease, chronic neurological disease), the severity of illness (ie, SOFA and APACHE II Scores that were greater than or equal to the cut-off value), sites of infection (ie, urinary tract, abdominal, skin or cutaneous sites), pathogens detection (ie, no pathogens detected, Gram-negative bacteria), completion of the 1-hour or 3-hour sepsis bundle of care, completion of the initial administration of antibiotics within 1 hour or 3 hours, respiratory support (ie, mechanical ventilation (MV), high-flow nasal oxygen), and additional ICU support (ie, vasopressors/inotropes, renal replacement therapy (RRT), red blood cell transfusion, platelet transfusion, fresh frozen plasma transfusion, surgical source control, and non-surgical source control). Using a stepwise backward elimination method, we started with the full multivariable logistic regression model that included the selected variables. This method then deleted the variables stepwise from the full model until all remaining variables were independently associated with the risk of death in the hospital in the final model. Similarly, we used these methods of variable selection and analysis for assessing factors associated with death in the ICU. We presented the ORs and 95% CIs in the univariable logistic regression model and the adjusted ORs (AORs) and 95% CIs in the multivariable logistic regression model.

For all analyses, significance levels were two-tailed, and we considered p<0.05 as statistically significant.

Patient and public involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

RESULTS

Data on 252 patients with sepsis were submitted to the database of the MOSAICS II Study (figure 1), in which there were little missing data.

Clinical characteristics and outcomes

In our study cohort, 64.3% (162/252) were men and the median age was 65 years (IQR: 52–76.75) (table 1). Among the total patients, the median SOFA Score was 7 (IQR: 4.75–10) at the time of ICU admission, the median APACHE II Score was 18 (IQR: 13–24) over the first 24 hours of ICU admission, and 29.4% (74/252) of patients had septic shock (table 1). Table 1 also shows that the most common documented comorbidities included cardiovascular disease (31.0%; 78/252), diabetes mellitus (26.6%; 67/252) and chronic neurological disease (14.3%; 36/252), the most common sites of infection included respiratory (56.7%; 143/252), abdominal cavity (24.2%; 61/252), urinary tract (14.7%; 37/252), and skin or cutaneous sites (7.5%; 19/252) and Gram-negative bacteria were isolated in 61.9% (156/252) of patients. Table 2 shows that MV was provided for 68.9% (173/251) of patients and RRT for 40.2% (101/251). Overall, 40.1% (101/252) of patients with sepsis died in the hospital, 33.3% (84/252) of whom died in the ICU (figure 1 and table 2). The median hospital and ICU LOS were 16 (IQR: 10–25) and 10 (IQR: 6–18) days, respectively (table 2). The clinical characteristics, severity of illness, sites of infection and microbiology, compliance with sepsis bundle elements, and life-sustaining treatments during ICU stay were compared between patients who survived and patients who died in the hospital and ICU, as shown in tables 1 and 2, and tables S1–S14 (online supplemental file 3).

Overall prognostic performance of the severity scoring systems

The SOFA Score (AUROC: 0.688 (95% CI 0.618 to 0.758); cut-off value≥7.5; sensitivity: 64.4%; specificity: 69.8%; P_{AUROC}<0.001) and APACHE II Score (AUROC: 0.689 (95% CI 0.622 to 0.756); cut-off value≥20.5; sensitivity: 61.4%; specificity: 71.8%; P_{AUROC}<0.001) both had a poor discriminatory ability for the hospital mortality (figure 2). The discriminatory ability for the ICU mortality of SOFA Score (AUROC: 0.713 (95% CI 0.643 to 0.783); cut-off value≥9.5; sensitivity: 53.6%; specificity: 80.1%; P_{AUROC}<0.001), however, was fair and was better than that of the APACHE II Score (AUROC: 0.672 (95% CI 0.603 to 0.742); cut-off value≥18.5; sensitivity: 69.0%; specificity: 60.8%; P_{AUROC}<0.001) (figure 3).

Risk factors for mortality

In the multivariable analysis, a SOFA Score of 8 and above (AOR: 2.717; 95% CI 1.371 to 5.382) and an APACHE II Score of 21 and above (AOR: 2.668; 95% CI 1.338 to 5.321) were independently associated with an increased risk of hospital mortality (table 3). Additionally, a SOFA Score of 10 and above (AOR: 2.801; 95% CI 1.332 to 5.891) was independently associated with an increased risk of ICU mortality, in contrast to an APACHE II Score of 19 and above, for which this independent association was not observed (table 4). Other factors were significantly or independently associated with the risk of hospital and ICU mortalities, as shown in tables 3 and 4, and tables S15–S18) (online supplemental file 3).

DISCUSSION

Of 252 patients with sepsis included in our analysis, two-fifths (40.1%) died in the hospital, and about a third

Table 2 Treatments and outcomes according to hospital survivability of patients with sepsis

Variables	All cases	Survived	Died	P value*
Completion of the sepsis bundle of care	n=241	n=146	n=95	
Completion of the sepsis bundle within 1 hour, no. (%)	87 (36.1)	53 (36.3)	34 (35.8)	0.936
Completion of the initial administration of antibiotics within 1 hour, no. (%)	173 (71.8)	109 (74.7)	64 (63.4)	0.219
Completion of the sepsis bundle within 3 hours, no. (%)	108 (44.8)	66 (45.2)	42 (44.2)	0.879
Completion of the initial administration of antibiotics within 3 hours, no. (%)	205 (85.1)	131 (89.7)	74 (77.9)	0.012
Life-sustaining treatments	n=251	n=150	n=101	
Respiratory support, no. (%)				
Mechanical ventilation	173 (68.9)	82 (54.7)	91 (90.1)	<0.001
Non-invasive ventilation	20 (8.0)	13 (8.7)	7 (6.9)	0.618
High-flow nasal oxygen	38 (15.1)	29 (19.3)	9 (8.9)	0.024
Additional ICU support, no. (%)				
Vasopressors/inotropes	163 (64.7)	82 (54.3)	81 (80.2)	<0.001
Renal replacement therapy	101 (40.2)	43 (28.7)	58 (57.4)	<0.001
Red blood cell transfusion	93 (37.1)	48 (32.0)	45 (44.6)	0.043
Platelet transfusion	50 (19.9)	20 (13.3)	30 (29.7)	0.001
Fresh frozen plasma transfusion	58 (23.1)	28 (18.7)	30 (29.7)	0.042
Surgical source control	25 (10.0)	19 (12.7)	6 (5.9)	0.081
Non-surgical source control	78 (31.1)	54 (36.0)	24 (23.8)	0.040
Outcomes	n=252	n=151	n=101	
Patient status, no. (%)				<0.001†
Alive on current hospital discharge	150 (59.5)	150 (99.3)	0 (0.0)	
Alive on discharge from current ICU stay, but died in current hospital stay	17 (6.7)	0 (0.0)	17 (16.8)	
Alive on discharge from current ICU stay, but still in current hospital stay after 90 days	1 (0.4)	1 (0.7)	0 (0.0)	
Still in current ICU stay after 90 days	0 (0.0)	0 (0.0)	0 (0.0)	
Died in current ICU stay	84 (33.3)	0 (0.0)	84 (83.2)	
Length of stay, median days (IQR)				
Hospital	16 (10–25)	17 (11–24.25)	13 (7–26)	0.027‡
ICU	10 (6–18)	[6–17]10.5 (6-17)	10 (5–21)	0.740‡

See tables S5–S7 (online supplemental file 3) for additional information.
*Comparison between the patients who survived and died using χ^2 test.
†Fisher's exact test.
‡Mann–Whitney U test.
ICU, intensive care unit; no, number.

(33.3%) died during the ICU stay (figure 1 and table 2). The SOFA and APACHE II Scores had a poor discriminatory ability for predicting hospital mortality (figure 2). However, the overall performance of the SOFA Score for predicting ICU mortality was fair and was better than that of the APACHE II Score (figure 3). A SOFA Score of 8 and above and an APACHE II Score of 21 and above were independently associated with an increased risk of hospital mortality (table 3). Additionally, a SOFA score of 10 and above was an independent predictor of ICU mortality, in contrast to an APACHE II score of 19 and above, for which this role did not appear (table 4).

In our study, the hospital mortality rate was lower than that of the MOSAICS I Study (44.5%; 572/1285),[40] as well as the rates previously reported from LMICs in South-East Asia, including Indonesia (68.3%; 41/60),[41] Thailand (42%; 263/627)[42] and Vietnam (61.0%; 75/123).[39] These findings may be because the diagnosis and treatment of sepsis have significantly changed over the previous 10 years to increase patient survival in sepsis and septic shock.[1 8 13 36 38 43 44] However, our study showed rates for ICU and hospital mortality that were higher than rates reported in the international Extended Study on Prevalence of Infection in Intensive Care III (EPIC III) (28% (99/352) and 31.1% (110/352) in LMICs, 26.4% (821/3114) and 32.7% (1019/3114) in upper-middle-income countries (UMICs), and 21.3% (950/4470) and 28.5% (1275/4470) in HICs).[45] These variations might be because EPIC III included ICU-acquired infection rather than only sepsis.[45] Despite the distinct inclusion criteria,

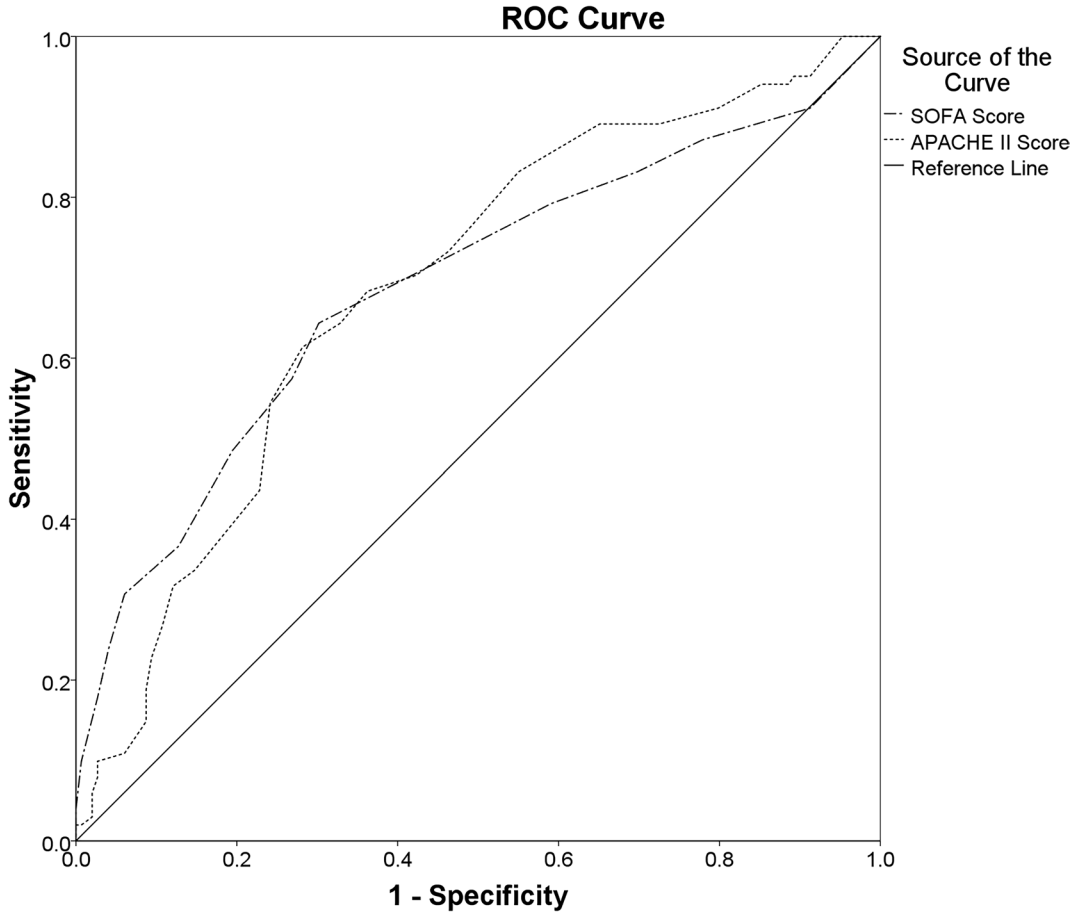

Figure 2 Comparisons of the AUROCs: Comparing the overall diagnostic performance of the SOFA Score (AUROC: 0.688 (95% CI 0.618 to 0.758); cut-off value≥7.5; sensitivity: 64.4%; specificity: 69.8%; P_{AUROC}<0.001) and the APACHE II Score (AUROC: 0.689 (95% CI 0.622 to 0.756); cut-off value≥20.5; sensitivity: 61.4%; specificity: 71.8%; P_{AUROC}<0.001) for predicting hospital mortality in ICU patients with sepsis. APACHE II, Acute Physiology and Chronic Health Evaluation II Score; AUROC, areas under the ROC curve; ICU, intensive care unit; ROC, receiver operating characteristics; SOFA, Sequential Organ Failure Assessment.

our median SOFA Score at the time of ICU admission was comparable to that of EPIC III (7 points (IQR: 4–11) in LMICs/UMICs/HICs).[45] However, patients in our study received invasive organ support treatments (ie, MV and RRT) during ICU stays more frequently than those in EPIC III (54.4% (4377/8045) and 15.7% (1253/8045)).[45] Previous studies showed that MV was a crucial predictor of mortality at any point throughout the ICU stay.[4 35] Additionally, the utilisation of RRT at any time during the ICU stay was also associated with a higher fatality rate.[4 35 46–48] Furthermore, *Acinetobacter baumannii* (17.9%, 45/252; table S4, online supplemental file 3), one of the most harmful pathogens, was more frequently isolated from patients in the present study than in those from the HIC cohort (4.4%; 137/3113) of the EPIC III Study.[45] The previous studies showed that *A. baumannii* infection was often due to a lack of strict infection control bundles[49] and associated with an increased risk of death.[50 51] The fact that our proportions for ICU and hospital mortality were higher than those reported in EPIC III suggested that patients, pathogens and clinical capacity to manage sepsis vary significantly between regions, particularly between HIC and LMIC settings.

In this study, we found a poor ability of both SOFA and APACHE II Scores to predict hospital mortality (figure 2). However, with the SOFA Score, the discrimination for predicting ICU mortality was fair, and it was better than those of the APACHE II Score (figure 3). The APACHE scoring system is among the most widely used, of which there are four versions (APACHE I through IV Scores). Although APACHE IV Score is the most up-to-date version, some centres still use older versions including APACHE II Score. In the present study, despite having a poor discriminatory ability for predicting hospital and ICU mortalities, an APACHE II Score of 21 and above was independently associated with an increased risk of deaths in hospitals (table 3). However, in contrast to a SOFA Score of 10 and above, an APACHE II Score of 19 and above was not an independent predictor of ICU mortality (table 4). Previous studies revealed that the APACHE II Score had a good prognostic value in acutely ill or surgical patients[10 11] but did not differentiate between

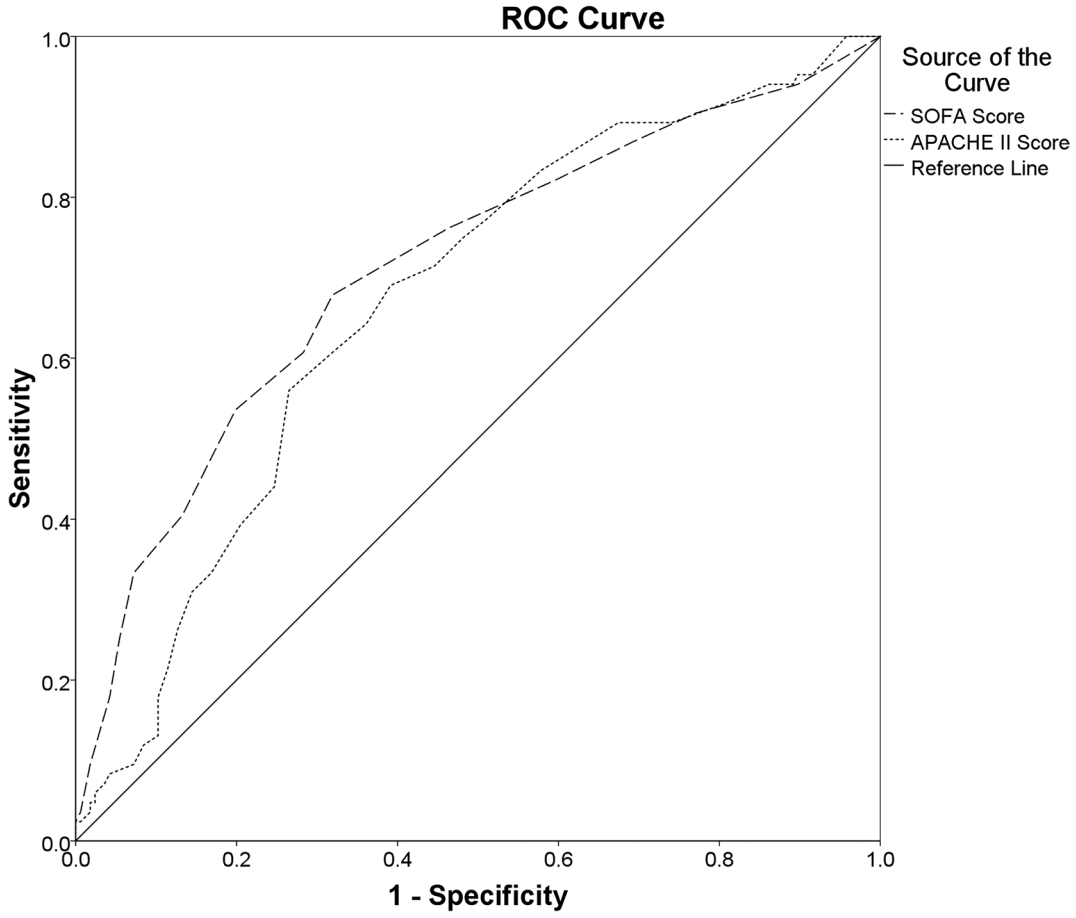

Figure 3 Comparisons of the AUROCs: Comparing the overall diagnostic performance of the SOFA Score (AUROC: 0.713 (95% CI 0.643 to 0.783); cut-off value≥9.5; sensitivity: 53.6%; specificity: 80.1%; P_{AUROC}<0.001) and the APACHE II Score (AUROC: 0.672 (95% CI 0.603 to 0.742); cut-off value≥18.5; sensitivity: 69.0%; specificity: 60.8%; P_{AUROC}<0.001) for predicting ICU mortality in ICU patients with sepsis. APACHE II, Acute Physiology and Chronic Health Evaluation II; AUROC, areas under the ROC curve; ICU, intensive care unit; ROC, receiver operating characteristics; SOFA, Sequential Organ Failure Assessment.

sterile and infected necrotising pancreatitis and had a poor predictive value for the severity of acute pancreatitis at 24 hours.[12]

In contrast, the SOFA Score was proposed for patients with a suspected infection that an increase of 2 points or more could serve as clinical criteria for sepsis.[1] In ICU patients with suspected infection, discrimination of the SOFA Score was fair for predicting hospital mortality, with an AUROC value of 0.74 (95% CI, 0.73 to 0.76; P_{AUROC}<0.001), reported in the previously published studies.[1 17] However, our study showed that the discriminatory ability of the SOFA Score was poor for predicting hospital mortality (figure 2). This difference might be due to our SOFA Score only calculated on ICU admission, in contrast to the SOFA Score in the previously published study that was calculated for the time window from 48 hours before to 24 hours after the onset of an infection, as well as on each calendar day.[17] This difference also might be because the burden and causes of sepsis and its management differ considerably between HIC and LMIC settings,[7 35 37] which might make the accuracy of critical illness severity scoring systems vary widely in the different countries, particularly between HICs and LMICs. However, our study revealed that the SOFA Score had a fair discriminatory ability for predicting ICU mortality (figure 3). Moreover, a SOFA Score of 8 and above and a score of 10 and above were independently associated with an increased risk of deaths in hospitals and ICUs, respectively (tables 3 and 4). Overall, this study shows that both SOFA and APACHE II Scores were worthwhile in predicting hospital and ICU mortalities in ICU patients with sepsis. However, because of having better discrimination for predicting ICU mortality, the SOFA Score was preferable to the APACHE II Score in predicting mortality.

The present study's data from many centres, which contained few missing data points, was a benefit (tables S19, online supplemental file 3). The following are some drawbacks of the current study, though: *first*, since there isn't a national registry of ICUs to enable systematic recruitment of units, we used the snowball method to find suitable units, which may have resulted in the selection of centres with a greater interest in managing sepsis; as a result, our data are subject to selection bias and might not accurately reflect intensive care in all of Vietnam; *second*, we did not create a protocol for microbiological

Table 3 Factors relating to hospital mortality in patients with sepsis

Factors	Univariable logistic regression analyses*				Multivariable logistic regression analyses†			
		95% CI for OR				95% CI for AOR		
	OR	Lower	Upper	P value	AOR	Lower	Upper	P value
Hospital and ICU characteristics								
University affiliation	2.520	1.495	4.248	0.001	NA	NA	NA	NA
Training programme in ICU	0.445	0.237	0.833	0.011	0.392	0.162	0.949	0.038
Documented comorbidities								
Cardiovascular disease	1.551	0.903	2.664	0.112	2.181	1.019	4.664	0.044
Chronic neurological disease	0.378	0.165	0.867	0.022	0.179	0.058	0.546	0.003
Severity of illness scores								
SOFA Score≥8	4.173	2.440	7.137	<0.001	2.717	1.371	5.382	0.004
APACHE II Score≥21	4.126	2.414	7.051	<0.001	2.668	1.338	5.321	0.005
Site of infection								
Urinary tract	0.300	0.126	0.714	0.006	0.312	0.105	0.932	0.037
Abdominal	1.256	0.701	2.249	0.444	NA	NA	NA	NA
Skin or cutaneous sites	2.774	1.053	7.309	0.039	NA	NA	NA	NA
Microbiology								
No pathogens detected	0.546	0.300	0.994	0.048	NA	NA	NA	NA
Gram-negative bacteria	1.475	0.871	2.498	0.148	NA	NA	NA	NA
Completion of sepsis bundle elements								
Completion of the sepsis bundle within 1 hour	0.978	0.571	1.675	0.936	NA	NA	NA	NA
Completion of the administration of antibiotics within 1 hour	0.701	0.397	1.237	0.220	NA	NA	NA	NA
Completion of the sepsis bundle within 3 hours	0.961	0.571	1.615	0.879	NA	NA	NA	NA
Completion of the administration of antibiotics within 3 hours	0.403	0.196	0.830	0.014	0.381	0.151	0.965	0.042
Life-sustaining treatments during ICU stay								
Respiratory support								
Mechanical ventilation	7.546	3.645	15.625	<0.001	4.391	1.912	10.085	<0.001
High-flow nasal oxygen	0.408	0.184	0.904	0.027	NA	NA	NA	NA
Additional ICU support								
Vasopressors/inotropes	3.408	1.899	6.116	<0.001	NA	NA	NA	NA
Renal replacement therapy	3.356	1.976	5.702	<0.001	NA	NA	NA	NA
Red blood cell transfusion	1.708	1.014	2.876	0.044	NA	NA	NA	NA
Platelet transfusion	2.746	1.455	5.185	0.002	NA	NA	NA	NA
Fresh frozen plasma transfusion	1.841	1.018	3.329	0.043	NA	NA	NA	NA
Surgical source control	0.435	0.168	1.132	0.088	NA	NA	NA	NA
Non-surgical source control	0.554	0.314	0.977	0.041	NA	NA	NA	NA
Constant					0.230			0.007

See tables S15 and S16 (online supplemental file 3) for additional information.
*Each variable of hospital and ICU characteristics, baseline characteristics, clinical and laboratory characteristics, and treatments was analysed in the univariable logistic regression model and was considered in the multivariable logistic regression model if the value of p was<0.05 in univariable logistic regression analysis between survival and death in the hospital, as well as clinically crucial factors.
†All selected variables were included in the multivariable logistic regression model with the stepwise backward elimination method. Variables, then, were deleted stepwise from the full model until all remaining variables were independently associated with death in the hospital.
AOR, adjusted OR; APACHE II, Acute Physiology and Chronic Health Evaluation II; ICU, intensive care unit; NA, not available; SOFA, Sequential Organ Failure Assessment.

investigations due to the study's real-world aspect. The data on point-of-care tests (such as lactate clearance) and life-sustaining therapies (such as fluid balance, steroid administration, and modalities of RRT and MV) were also missing since we primarily evaluated resources used in ICUs. Additionally, we decided not to gather information on antibiotic resistance and appropriateness to increase the practicality of performing the study in busy ICUs; *third*, the mixed-effects logistic regression model could not be used to predict the discrete outcome variables measured

Table 4 Factors relating to intensive care unit mortality in patients with sepsis

	Univariable logistic regression analyses*				Multivariable logistic regression analyses†			
		95% CI for OR				95% CI for AOR		
Factors	OR	Lower	Upper	P value	AOR	Lower	Upper	P value
Hospital and ICU characteristics								
University affiliation	2.260	1.322	3.862	0.003	2.562	1.164	5.639	0.019
Intensivist to patient ratio								
1 intensivist : 5 or fewer patients	Reference			0.082	NA			NA
1 intensivist : 6 to 8 patients	0.553	0.298	1.025	0.060	NA	NA	NA	NA
1 intensivist : 12 or more patients	1.750	0.540	5.668	0.351	NA	NA	NA	NA
Training programme in ICU	0.458	0.243	0.861	0.015	0.267	0.100	0.713	0.008
Documented comorbidities								
Cardiovascular disease	1.506	0.863	2.627	0.150	2.047	0.954	4.391	0.066
Chronic neurological disease	0.526	0.229	1.212	0.131	4.630	1.130	18.970	0.033
Solid malignant tumours	2.077	0.649	6.648	0.218	NA	NA	NA	NA
Severity of illness scores								
SOFA Score≥10	4.650	2.620	8.254	<0.001	2.801	1.332	5.891	0.007
APACHE II Score≥19	3.535	1.025	6.171	<0.001	NA	NA	NA	NA
Site of infection								
Urinary tract	0.340	0.136	0.851	0.021	0.276	0.087	0.878	0.029
Abdominal	1.416	0.779	2.575	0.254	NA	NA	NA	NA
Skin or cutaneous sites	2.387	0.931	6.123	0.070	3.074	0.982	9.629	0.054
Microbiology								
No pathogens detected	0.599	0.320	1.121	0.109	NA	NA	NA	NA
Gram-negative bacteria	1.258	0.729	2.171	0.409	NA	NA	NA	NA
Completion of sepsis bundle elements								
Completion of the sepsis bundle within 1 hour	0.931	0.532	1.630	0.802	NA	NA	NA	NA
Completion of the administration of antibiotics within 1 hour	0.671	0.374	1.202	0.180	NA	NA	NA	NA
Completion of the sepsis bundle within 3 hours	0.938	0.546	1.609	0.815	NA	NA	NA	NA
Completion of the administration of antibiotics within 3 hours	0.434	0.211	0.889	0.023	0.344	0.122	0.970	0.044
Life-sustaining treatments during ICU stay								
Respiratory support								
Mechanical ventilation	6.856	3.109	15.116	<0.001	3.086	1.180	8.072	0.022
High-flow nasal oxygen	0.257	0.096	0.685	0.007	NA	NA	NA	NA
Additional ICU support								
Vasopressors/inotropes	2.956	1.600	5.460	0.001	NA	NA	NA	NA
Renal replacement therapy	4.239	2.432	7.388	<0.001	3.433	1.669	7.058	0.001
Red blood cell transfusion	1.682	0.983	2.879	0.058	NA	NA	NA	NA
Platelet transfusion	2.966	1.571	5.597	0.001	NA	NA	NA	NA
Fresh frozen plasma transfusion	1.891	1.036	3.453	0.038	NA	NA	NA	NA
Surgical source control	0.599	0.230	1.562	0.295	NA	NA	NA	NA
Non-surgical source control	0.535	0.293	0.977	0.042	0.385	0.175	0.842	0.017
Constant					0.182			0.004

See tables S17 and S18 (online supplemental file 3) for additional information.
*Each variable of hospital and ICU characteristics, baseline characteristics, clinical and laboratory characteristics, and treatments was analysed in the univariable logistic regression model and was considered in the multivariable logistic regression model if the value of p was <0.05 in univariable logistic regression analysis between survival and death in the ICU, as well as clinically crucial factors.
†All selected variables were included in the multivariable logistic regression model with the stepwise backward elimination method. Variables, then, were deleted stepwise from the full model until all remaining variables were independently associated with death in the ICU.
AOR, adjusted OR; APACHE II, Acute Physiology and Chronic Health Evaluation II; ICU, intensive care unit; NA, not available; SOFA, Sequential Organ Failure Assessment.

at two different times, that is, inside and outside the ICU settings, due to our independent variables (eg, SOFA Score that was greater than or equal to the cut-off value), which might be associated with the primary outcome only measured on ICU admission; *finally*, even though the sample size was sufficient, the CI was a little bit broad (6.03%), which may have an impact on the sample's normal distribution. Therefore, more studies with bigger sample sizes may be required to strengthen the findings.

CONCLUSIONS

Our cohort was a selected population of patients with sepsis admitted to the ICUs in Vietnam with a high mortality rate. The SOFA and APACHE II Scores were worthwhile in predicting mortality among ICU patients with sepsis. However, due to better discrimination for predicting ICU mortality, the SOFA Score was preferable to the APACHE II Score in predicting mortality.

Author affiliations
[1]Center for Critical Care Medicine, Bach Mai Hospital, Hanoi, Viet Nam
[2]Department of Emergency and Critical Care Medicine, Hanoi Medical University, Hanoi, Viet Nam
[3]Faculty of Medicine, University of Medicine and Pharmacy, Vietnam National University, Hanoi, Vietnam
[4]Center for Emergency Medicine, Bach Mai Hospital, Hanoi, Viet Nam
[5]Department of Health Organization and Management, Faculty of Public Health, Thai Binh University of Medicine and Pharmacy, Thai Binh City, Thai Binh, Viet Nam
[6]Department of Nutrition and Food Safety, Faculty of Public Health, Thai Binh University of Medicine and Pharmacy, Thai Binh City, Thai Binh, Viet Nam
[7]Department of Intensive Care and Poison Control, Vietnam-Czechoslovakia Friendship Hospital, Hai Phong City, Viet Nam
[8]Intensive Care Department, Cho Ray Hospital, Ho Chi Minh City, Viet Nam
[9]Department of Critical Care, Emergency Medicine and Clinical Toxicology, Faculty of Medicine, Ho Chi Minh City University of Medicine and Pharmacy, Ho Chi Minh City, Viet Nam
[10]Emergency Department, Hue Central General Hospital, Hue City, Thua Thien Hue, Viet Nam
[11]Intensive Care Unit, 115 People's Hospital, Ho Chi Minh City, Viet Nam
[12]Intensive Care Unit, Bai Chay General Hospital, Ha Long City, Quang Ninh, Viet Nam
[13]Intensive Care Unit, Da Nang Hospital, Da Nang City, Viet Nam
[14]Emergency and Critical Care Department, Hanoi Medical University Hospital, Hanoi Medical University, Hanoi, Viet Nam
[15]Intensive Care Unit, Dong Da General Hospital, Hanoi, Viet Nam
[16]Intensive Care Unit, Saint Paul General Hospital, Hanoi, Viet Nam
[17]Intensive Care Unit, Can Tho Central General Hospital, Can Tho, Viet Nam
[18]Intensive Care Unit, Vinmec Times City International Hospital, Hanoi, Viet Nam
[19]Intensive Care Unit, Thai Nguyen Central General Hospital, Thai Nguyen City, Thai Nguyen, Viet Nam
[20]Emergency Department, Thanh Nhan General Hospital, Hanoi, Viet Nam
[21]FAST and Chronic Programmes, Alexandra Hospital, National University Health System, Singapore
[22]Division of Respiratory and Critical Care Medicine, Department of Medicine, National University Hospital, National University Health System, Singapore
[23]Department of Intensive Care Medicine, Woodlands Health, Singapore

Twitter Chinh Quoc Luong @drchinh

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Contributors SND contributed to the conception, design of the work, acquisition, and interpretation of data for the work, and revised the draft critically for important intellectual content; CQL contributed to the conception, design of the work, acquisition, analysis, and interpretation of data for the work, and wrote the first draft of the work; CXD and TAN contributed to the design of the work, acquisition, interpretation of data for the work, and revised the draft critically for important intellectual content; DTP and MHN contributed to the design of the work, analysis, and interpretation of data for the work; NTN, DQH, QTAH, CVB, TDV, HNB, HTN, HBH, TTPL, LTBN, PTD, TDN, VHL and GTTP contributed to the acquisition and interpretation of data for the work; GTHB, TVB, TTNP, CVN and ADN contributed to the interpretation of data for the work; JP and AL contributed to the design of the work, interpretation of data for the work, and revised the draft critically for important intellectual content. All authors reviewed and edited the work and approved its final version. CQL is responsible for the overall content as the guarantor.

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Patient consent for publication Not applicable.

Ethics approval This study involves human participants. The Scientific and Ethics Committees of Bach Mai Hospital approved this study (approval number: 2919/QĐ–BM; project code: BM-2017-883-89). The authors also obtained permission from the heads of institutions and departments of all participating hospitals and their respective institutional review boards wherever available. The study was conducted according to the principles of the Declaration of Helsinki. In this non-intervention study, all collected information has received verbal informed consent from patients or, when unavailable, from family members at the ICUs, and witnessed by the on-duty medical staff. Written informed consent, however, was waived by the Bach Mai Hospital Scientific and Ethics Committees since it was not feasible to undergo such a methodical process of collection when the subject was comprised of an urgent situation in which a patient or a family member's condition was severe or life-threatening. Public notification of the study was made by public posting. All data analyses were based upon data sets kept in password-protected systems, and all final presented data have been made anonymous. Participants gave informed consent to participate in the study before taking part.

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ORCID iDs
Tuan Anh Nguyen http://orcid.org/0000-0002-3554-2526
Thao Thi Ngoc Pham http://orcid.org/0000-0002-8312-2390
Chinh Quoc Luong http://orcid.org/0000-0002-6409-577X

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MOSAICS II Study

Please fill in all blanks before submission

Country: _____ Hospital/ICU: _____

Patient Index Number: _____ Age of Patient: _____

Admission Date to your hospital (DD/MM/YYYY): _____ Gender (Tick one): ☐ Male ☐ Female

Admission Date to your ICU (DD/MM/YYYY): _____

1. Comorbidities *Please circle yes or no*

Cardiovascular disease	Ischaemic heart disease (IHD), heart failure	Yes/No
Chronic Lung Disease	Chronic obstructive pulmonary disease (COPD), asthma, bronchiectasis, post-tuberculosis related lung disease, interstitial lung disease (ILD), excluding primary or secondary lung malignancy. Patients who are undergoing treatment for tuberculosis or non-tuberculosis mycobacterium (NTM) prior to ICU admission should be included in this category	Yes/No
Chronic neurological disease	Strokes, neuromuscular disease, epilepsy, movement disorders, excluding brain tumors	Yes/No
Chronic Kidney Disease	Kidney damage ≥ 3 months (abnormal blood/urine composition or radiological renal abnormalities or glomerular filtration rate < 60mL/min/1.73m2), excluding renal cell carcinoma	Yes/No
Peptic Ulcer Disease	Gastric and duodenal ulcers	Yes/No
Chronic liver disease	Prolonged course of hepatic disease > 6 months, excluding hepatocellular cancer	Yes/No
Diabetes mellitus	Any type of diabetes mellitus	Yes/No
Human immunodeficiency virus (HIV) infection	Positive HIV serology with or without acquired immunodeficiency syndrome (AIDS)-defining illness	Yes/No
Connective tissue disease	Presence of appropriate clinical symptoms and high titres of specific autoantibodies that fulfill the criteria of different connective tissue diseases. Examples include systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), gout, systemic sclerosis, scleroderma	Yes/No
Immunosuppression	Patients on long term steroids or other immunosuppressants (excluding patients with haematological conditions or other malignancies)	Yes/No
Haematological malignancies	Include leukaemia, lymphoma, multiple myeloma	Yes/No
Solid malignant tumours	Such as breast, colon, lung, prostate, skin, etc	Yes/No
Others (Please specify):		

1a. Type of Admission (Tick one):

☐ Medical
☐ Elective Surgical
☐ Unscheduled Surgical

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1b. Source of Admission (Tick one):

- ☐ Emergency Department
- ☐ Operating Room
- ☐ General Wards
- ☐ Other ICUs or High-dependency Units
- ☐ Inter-hospital Transfer
- ☐ Others

2. Vital Signs (Upon admission into ICU)

Mean blood or arterial pressure (mmHg):		Systolic blood pressure (mmHg):	
Heart rate (beats per min):		Temperature (degree Celsius):	
Respiratory rate (breaths per min):		Glasgow Coma Scale:	

3. Blood Investigations

Record those that are obtained within the first 24 hours of ICU admission. The results closest to the time of ICU admission should be the ones recorded. If no such investigations are available within the 1st 24 hours of ICU admission, record the results which are obtained within 4 hours prior to ICU admission, with preference being given to those closest to the time of ICU admission

Total white cell count ($x10^9$/L):		Platelets ($x10^9$/L):	
Haemoglobin (g/dl):		Haematocrit (%):	
Potassium (mmol/l):		Sodium (mmol/l):	
Creatinine (umol/l):		Bilirubin (umol/l):	
pH:		PaO_2 (mmHg):	
FiO_2:		PaO_2/FiO_2 ratio:	

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Oxygen tank flow rate in liters/min	**FiO_2**
Nasal cannula	
0 L/min	0.21
1 L/min	0.24
2 L/min	0.28
3 L/min	0.32
4 L/min	0.36
5 L/min	0.40
6 L/min	0.44
Face mask	
5 L/min	0.4
6 L/min	0.5
7-8 L/min	0.6
Nasopharyngeal catheter	
4 L/min	0.4
5 L/min	0.5
6 L/min	0.6
Venturi mask	FiO_2 as set on the apparatus
Face mask with reservoir	
6 L/min	0.6
7 L/min	0.7
8 L/min	0.8
9 L/min	0.9
10 L/min	0.95
15 L/min (non-rebreather mask)	1.0
High flow nasal cannula, non-invasive ventilation, mechanical ventilation	
Regardless of inspiratory flow, positive end-expiratory pressure (PEEP)	FiO_2 as set on the apparatus

4. Severity of Illness Scores

qSOFA at time of ICU admission _____ SOFA at time of ICU admission _____

SIRS at time of ICU admission _____ APACHE II (over first 24 hours of ICU admission) _____

5. Site of Infection

Definition of infections

- *Pneumonia requires the presence of radiographic infiltrates and features including fever or hypothermia, leukocytosis or leukopenia and purulent respiratory secretions.*
- *Intra-abdominal infections include but are not limited to intra-abdominal abscesses, peritonitis, biliary tract infections, pancreatic infections, enteritis, and colitis.*
- *Urinary tract infection requires typical features of fever, urgency, frequency, dysuria, pyuria and haematuria, together with confirmatory radiological features and/or positive culture results.*
- *Soft tissue and skin infections include surgical site infections, septic arthritis, cellulitis and necrotizing fasciitis.*
- *Catheter-related blood stream infection is defined as bacteremia with an intravascular device in situ and no other apparent source for the bloodstream infection, with culture results.*
- *Systemic infections refer to infections without a clear primary site of infection, as is often the case in infections such as dengue and malaria.*

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Please tick all that apply

- ☐ Respiratory
- ☐ Urinary Tract
- ☐ Abdominal
- ☐ Neurological
- ☐ Bones or Joints
- ☐ Skin or Cutaneous Sites
- ☐ Intravascular Catheter
- ☐ Infective Endocarditis
- ☐ Primary Bacteraemia
- ☐ Systemic
- ☐ Others, Please Specify: _____

6. Positive Cultures

Please tick all that apply

Gram-positive	**Gram-negative**	**Fungal**
☐ Methicillin-sensitive *Staphylococcus aureus*	☐ *Klebsiella pneumoniae*	☐ *Candida albicans*
☐ Methicillin-resistant *Staphylococcus aureus*	☐ *Escherichia coli*	☐ *Candida* non-albicans
☐ *Streptococcus pneumoniae*	☐ *Pseudomonas aeruginosa*	☐ *Aspergillus* species
☐ Other *Streptococcus* species	☐ *Acinetobacter baumannii*	
☐ *Enterococcus*	☐ *Bulkholderia pseudomallei*	
	☐ *Enterobacter cloacae*	
	☐ *Haemophilus influenza*	
	☐ *Salmonella* species	
	☐ *Citrobacter* species	
	☐ *Stenotrophomonas maltophilia*	
	☐ *Proteus* species	
	☐ *Bacteroides fragilis*	

- ☐ Negative Cultures
- ☐ Others, Please Specify: _____

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7. Positive Serologies, Molecular, or Histological Tests

Please tick all that apply

Tetanus		☐
Tuberculosis	Positive culture from any medium	☐
	Histological diagnosis	☐
	Polymerase chain reaction (PCR) tests	☐
Non-tuberculous mycobacteria	Positive culture from any medium	☐
	Histological diagnosis	☐
Aspergillosis		☐
Blastomycosis		☐
Histoplasmosis	Antigen testing (Urine)	☐
	Antigen testing (Serum)	☐
Cryptococcus		☐
Malaria	Thick and thin blood films	☐
	Rapid diagnostic tests (Serum)	☐
Measles	Serum serology (presence of IgM)	☐
	PCR tests	☐
Chikungunya	Serum	☐
	CSF serology (presence of IgM)	☐
	PCR tests	☐
Dengue	Serum antigen	☐
	Serology (presence of IgM)	☐
	PCR tests	☐
Influenza	PCR tests	☐
	Immunofluorescence assays from BAL	☐
	Endotracheal aspirate	☐
	Nasopharyngeal swabs	☐
	Nasal swabs	☐
	Throat swabs	☐
Other respiratory viruses apart from influenza	PCR tests	☐
	Immunofluorescence assays from BAL	☐
	Endotracheal aspirate	☐
	Nasopharyngeal swabs	☐
	Nasal swabs	☐
	Throat swabs	☐
Rabies		☐
Leptospirosis		☐
Q fever		☐
Rickettsia	Serum	☐
	Eschar serology (presence of IgM)	☐

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Please circle yes or no

7a. Clinical diagnosis made and persisted with due to strong clinical suspicion even though cultures, serologies, molecular, and/or histological tests were performed and negative	Yes / No
7b. Clinical diagnosis made and persisted with due to strong clinical suspicion because cultures, serologies, molecular, and/or histological tests are not available in the ICU	Yes / No

8. Measurements around Time Zero

8a. Time Zero (DD/MM/YY (HH:MM)) : _____(_____)

Time zero is the onset of sepsis. This is determined according to the patient's location within the hospital when sepsis is diagnosed:

i. For patients presenting to the emergency department with sepsis, time zero is defined as the time of triage.

ii. For patients who develop sepsis in the wards or other non-emergency department units, time zero is determined by searching the clinical documentation for the time of diagnosis of sepsis. This may include, for example, a physician's note or timed and dated orders, a timed and dated note of a nurse's discussion of sepsis with a physician, or timed records initiating referral to the ICU for sepsis.

iii. If no time and date can be found by searching the chart, the default time of presentation is the time of admission to the ICU.

iv. In the rare event that the patient does not present with sepsis in the emergency department, but deteriorates and develops sepsis in the emergency department while being observed or while waiting for a hospital bed, time zero is determined by searching the clinical documentation for the time of diagnosis of sepsis. This may include, for example, a physician's note or timed and dated orders, a timed and dated note of a nurse's discussion of sepsis with a physician, or timed records initiating referral to the ICU for sepsis.

For the following questions, please circle yes or no

<u>Blood Culture</u>

8.1. Was blood culture performed between 1 hour before time zero to 24 hours after time zero?	Yes / No

8.2. If yes, time of blood culture (DD/MM/YY (HHMM)) : _____(_____)

<u>Lactate Measurement</u>

8.3. Was lactate measured between 1 hour before time zero to 24 hours after time zero?	Yes / No

8.3a. If yes:

Time of lactate measurement (DD/MM/YY (HHMM)) : _____(_____)

Lactate value (mmol/l): _____

Antibiotic Administration

8.4: Was antibiotic administered between 1 hour before time zero to 24 hours after time zero? Yes / No

8.4.a: If yes, time of antibiotic administration (DD/MM/YY (HHMM)) : _____(_____)

Fluid Bolus

8.5: Was there any episode of hypotension (SBP < 90 mmHg or mean blood pressure or MAP < 65 mmHg) between time zero and 1 hour after time zero? Yes / No

8.5.a: If the answer to 8.5 is no, was there any episode of hypotension (SBP < 90 mmHg or mean blood pressure or MAP < 65 mmHg) between time zero and 3 hours after time zero? Yes / No

8.5.b: If answer to questions 8.5 & 8.5.a is yes, was any vasopressor started between 1 hour before time zero to 24 hours after time zero? Yes / No

8.5.c: If answer to 8.5.b is yes, time of starting vasopressor (DD/MM/YY (HHMM)) : _____(_____)

8.5.d: Amount of fluid bolus administered within 1 hour from time zero (mLs): _____

8.5.e: Amount of fluid bolus administered within 3 hours from time zero (mLs): _____

9. Resources used in ICU (Anytime during ICU stay)

For the following questions, please circle yes or no

9.1: Vasopressors / Intropes Yes / No

9.2: Mechanical ventilation (MV), performed through a laryngeal mask, an endotracheal, endobronchial or tracheostomy tube Yes / No

If answer is no, skip next question

9.3: If yes, duration of MV, defined as from the time of starting invasive MV until the patient has been successfully extubated or breathing on a tracheostomy mask for ≥ 48 hours, whichever comes first (days) _____

9.4: Noninvasive ventilation (NIV) using NIPPV or CPAP (excludes NIV used peri-intubation and extubation) Yes / No

If answer is no, skip next question

9.5: If yes, duration of NIV, defined as from the time of starting NIV until the patient has been successfully weaned off for > 24 hours or required subsequent intubation, whichever comes first (days) _____

9.6: High-flow nasal cannula (HFNC) (excludes HFNC used peri-intubation and extubation) Yes / No

If answer is no, skip next question

9.7: If yes, duration of HFNC, defined as from the time of starting HFNC until patient has been successfully weaned off for > 24 hours or required subsequent intubation, whichever comes first (days)	_____
9.8: Renal replacement therapy (IHD, PD, SLED or CRRT)	Yes / No
9.9: Transfusion of packed red blood cells	Yes / No
9.10: Transfusion of platelets	Yes / No
9.11: Transfusion of fresh frozen plasma	Yes / No
9.12: Non-surgical source control measure implemented e.g. removal of infected intravascular or other catheters, insertion of ascitic drains, pleural drains, percutaneous drains, and others	Yes / No
9.13: Surgical source control measure implemented e.g. debridement of infected necrotic tissue	Yes / No

9.14: Time of first source control measure, if any (DD/MM/YY (HHMM)) : _____(_____)

10. Limitations of Life-Sustaining Treatments

Please tick all that apply

- ☐ Do-not-resuscitate (DNR) order
- ☐ Withdrawal of life-sustaining treatments
- ☐ Withholding of life-sustaining treatments

11. Outcome

Please pick only one

- ☐ Alive upon current hospital stay discharge
- ☐ Alive upon discharge from current ICU stay, but died in current hospital stay
- ☐ Died in current ICU stay

Discharge date from current ICU stay or death date in your current ICU stay	(DD/MM/YYYY): _____
Discharge date from current hospital stay or death date in your current hospital stay	(DD/MM/YYYY): _____

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ICU Questionnaire

Please fill in all blanks before submission

Name of person entering data: _____

Country: _____ Hospital: _____ ICU: _____

Type of hospital (tick one): ☐ Rural ☐ Urban

University or university-affiliated hospital (tick one): ☐ Yes ☐ No

* *Rural is defined as non-metropolitan areas, catering to patients not in the city as defined by the country's healthcare system*

Number of beds in hospital: _____

Number of beds in ICU: _____

Type of ICU (tick one):

- ☐ Medical
- ☐ Surgical
- ☐ Mixed medical & surgical
- ☐ Others (excluding paediatric, coronary and neurosurgical ICUs)

Nurse to ICU patient ratio (Tick one; only 1 choice allowed, choose the ratio most frequently seen in your ICU)

- ☐ 1 or more nurses : 1 patient
- ☐ 1 nurse : 2 patients
- ☐ 1 nurse : 3 patients
- ☐ 1 nurse : 4 or more patients

Nature of ICU (Tick one; only 1 choice allowed)

- ☐ Closed ICU = All patients are cared for by 1 team of intensivists in collaboration with a primary service. Only intensivists have admitting privileges to the ICU
- ☐ Open ICU = Any physician can admit patients to the ICU. The primary service (not intensivists) takes main responsibility for care of patients. If an ICU functions as an open ICU some of the time, and as a closed ICU some of the time, please tick "Open ICU"

Only for closed ICUs: Intensivist to ICU patient ratio (Tick one; only 1 choice allowed, choose the ratio most frequently seen in your ICU)

- ☐ 1 intensivist : 5 or fewer patients
- ☐ 1 intensivist: 6 to 8 patients
- ☐ 1 intensivist: 9 to 11 patients
- ☐ 1 intensivist: 12 to 14 patients
- ☐ 1 intensivist: 15 or more patients

Is the ICU part of an accredited intensive care fellowship programme? (Tick one)

- ☐ Yes
- ☐ No

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Capabilities (Tick all that apply)

- ☐ Able to perform routine blood, urine, stool, CSF, synovial, fluid cultures
- ☐ Able to process AFB smear and cultures
- ☐ Able to perform PCR testing for tuberculosis
- ☐ Able to perform serology or PCR testing for dengue
- ☐ Able to perform serology or PCR testing for influenza
- ☐ Able to test for galactomannan
- ☐ Able to perform blood film identification for malaria

Possible additional practices in the general ward outside of the ICU and outside of any high dependency or intermediate care ward or dialysis unit (Tick all that apply)

- ☐ Able to support patients on noninvasive ventilation in the general ward
- ☐ Able to support patients on invasive mechanical ventilation in the general ward
- ☐ Able to support patients on vasopressor/inotrope infusions in the general ward
- ☐ Able to support patients on dialysis/renal replacement therapy in the general ward

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SUPPLEMENTARY RESULTS

Article title: Sequential Organ Failure Assessment (SOFA) score for predicting mortality in patients with sepsis in Vietnamese intensive care units: A multicentre, cross-sectional study

TABLE OF CONTENT

Table S12. Completion of sepsis bundle elements according to intensive care unit survivability of patients with sepsis

Table S13. Completion of the sepsis bundle of care and the initial administration of antibiotics according to intensive care unit survivability of patients with sepsis

Table S14. Life-sustaining treatments during ICU stay and outcomes according to intensive care unit survivability of patients with sepsis

Table S15. Factors associated with hospital mortality in patients with sepsis: univariable regression analyses

Table S16. Factors associated with hospital mortality in patients with sepsis: multivariable logistic regression analyses (backward elimination)

Table S17. Factors associated with intensive care unit mortality in patients with sepsis: univariable regression analyses

Table S18. Factors associated with intensive care unit mortality in patients with sepsis: multivariable logistic regression analyses (backward elimination)

Table S19. Breakdown of missing data

TABLES

Table S1. Hospital and intensive care unit characteristics according to hospital survivability of patients with sepsis

Variable	All cases n=252	Survived n=151	Died n=101	p[a]
Participating hospital, no. (%)				NA
115 People's	25 (9.9)	6 (4.0)	19 (18.8)	
Bach Mai	26 (10.3)	14 (9.3)	12 (11.9)	
Bai Chay	14 (5.6)	10 (6.6)	4 (4.0)	
Can Tho	7 (2.8)	1 (0.7)	6 (5.9)	
Cho Ray	41 (16.3)	19 (12.6)	22 (21.8)	
Da Nang	12 (4.8)	6 (4.0)	6 (5.9)	
Dong Da	9 (3.6)	6 (4.0)	3 (3.0)	
Hanoi Medical University	12 (4.8)	6 (4.0)	6 (5.9)	
Hue	39 (15.5)	26 (17.2)	13 (12.9)	

Saint Paul	9 (3.6)	9 (6.0)	0 (0.0)	
Thai Nguyen	2 (0.8)	1 (0.7)	1 (1.0)	
Thanh Nhan	1 (0.4)	0 (0.0)	1 (1.0)	
Vietnam–Czechoslovakia Friendship	48 (19.0)	40 (26.5)	8 (7.9)	
Vinmec Times City International	7 (2.8)	7 (4.6)	0 (0.0)	
Hospital characteristics				
Type of hospital, no. (%)				NA
Rural	0 (0.0)	0 (0.0)	0 (0.0)	
Urban	252 (100)	151 (100)	101 (100)	
University affiliation, no. (%)				<0.001
No	153 (60.7)	105 (69.5)	48 (47.5)	
Yes	99 (39.3)	46 (30.5)	53 (52.5)	
ICU characteristics				
Nature of ICU, no. (%)				NA
Open	0 (0.0)	0 (0.0)	0 (0.0)	
Closed	252 (100)	151 (100)	101 (100)	
Type of ICU, no. (%)				0.589
Medical	110 (43.7)	68 (45.0)	42 (41.6)	
Surgical	0 (0.0)	0 (0.0)	0 (0.0)	
Mixed	142 (56.3)	83 (55.0)	59 (58.4)	
Nurse to patient ratio, no. (%)				0.079
1 or more nurses : 1 patient	7 (2.8)	7 (4.6)	0 (0.0)	
1 nurse : 2 patients	187 (74.2)	111 (73.5)	76 (75.2)	
1 nurse : 3 patients	0 (0.0)	0 (0.0)	0 (0.0)	
1 nurse : 4 or more patients	58 (23.0)	33 (21.9)	25 (24.8)	
Intensivist to patient ratio, no. (%)				0.446
1 intensivist : 5 or fewer patients	165 (65.5)	96 (63.6)	69 (68.3)	
1 intensivist : 6 to 8 patients	75 (29.8)	49 (32.5)	26 (25.7)	
1 intensivist : 9 to 11 patients	0 (0.0)	0 (0.0)	0 (0.0)	
1 intensivist : 12 or more patients	12 (4.8)	6 (4.0)	6 (5.9)	
Training programme in ICU, no. (%)				0.010
No	50 (19.8)	22 (14.6)	28 (27.7)	
Yes	202 (80.2)	129 (85.4)	73 (72.3)	

[a]Comparison between the patients who survived and died using the Chi-squared test; *Fisher's exact test; **Mann–Whitney U test.

Abbreviations: **ICU**, intensive care unit; **NA**, not available; **no.**, number.

Table S2. Baseline characteristics according to hospital survivability of patients with sepsis

Variable	All cases n=252	Survived n=151	Died n=101	p[a]
Age (year), median (IQR)	65 (52-	65 (53-76)	65 (52-78)	0.810**

	76.75)			
Age (year), no. (%)				0.865*
< 20	3 (1.2)	2 (1.3)	1 (1.0)	
20 - 39	19 (7.5)	10 (6.6)	9 (8.9)	
40 - 59	74 (29.4)	43 (28.5)	31 (30.7)	
≥ 60	156 (61.9)	96 (63.6)	60 (59.4)	
Sex (male), no. (%)	162 (64.3)	93 (61.6)	69 (68.3)	0.275
Collection batch, no. (%)				0.007
Collection 1 (Jan)	80 (31.7)	58 (38.4)	22 (21.8)	
Collection 2 (April)	62 (24.6)	27 (17.9)	35 (34.7)	
Collection 3 (July)	54 (21.4)	32 (21.2)	22 (21.8)	
Collection 4 (Oct)	56 (22.2)	34 (22.5)	22 (21.8)	
Admission type, no. (%)				0.195*
Medical	236 (93.7)	138 (91.4)	98 (97.0)	
Elective surgical	2 (0.8)	2 (1.3)	0 (0.0)	
Unscheduled surgical	14 (5.6)	11 (7.3)	3 (3.0)	
Admission source, no. (%)				0.505*
Emergency department	138 (54.8)	87 (57.6)	51 (50.5)	
Operating room	4 (1.6)	3 (2.0)	1 (1.0)	
General wards	56 (22.2)	33 (21.9)	23 (22.8)	
Other ICUs or HDU	16 (6.3)	10 (6.6)	6 (5.9)	
Inter-hospital transfer	37 (14.7)	18 (11.9)	19 (18.8)	
Others	1 (0.4)	0 (0.0)	1 (1.0)	
Comorbidities, no. (%)				
Cardiovascular disease	78 (31.0)	41 (27.2)	37 (36.6)	0.111
Chronic lung disease	30 (11.9)	18 (11.9)	12 (1.9)	0.992
Chronic neurological disease	36 (14.3)	28 (18.5)	8 (7.9)	0.018
Chronic kidney disease	23 (9.1)	14 (9.3)	9 (8.9)	0.922
Peptic ulcer disease	9 (3.6)	5 (3.3)	4 (4.0)	>0.999*
Chronic liver disease	27 (10.7)	14 (9.3)	13 (12.9)	0.365
Diabetes mellitus	67 (26.6)	40 (26.5)	27 (26.7)	0.966
HIV infection	0 (0.0)	0 (0.0)	0 (0.0)	NA
Connective tissue disease	3 (1.2)	2 (1.3)	1 (1.0)	>0.999*
Immunosuppression	10 (4.0)	7 (4.6)	3 (3.0)	0.744*
Haematological malignancies	5 (2.0)	3 (2.0)	2 (2.0)	>0.999*
Solid malignant tumours	12 (4.8)	6 (4.0)	6 (5.9)	0.551*

[a]Comparison between the patients who survived and died using the Chi-squared test; *Fisher's exact test; **Mann–Whitney U test.

Abbreviations: **HIV**, human immunodeficiency virus; **ICU**, intensive care unit; **IQR**, interquartile range; **NA**, not available; **no.**, number.

Table S3. Clinical and laboratory characteristics and severity of illness according to hospital survivability of patients with sepsis

Variable	All cases	Survived	Died	p[a]
Vital signs (on admission into ICU)				
GCS, median (IQR)	13 (9-15)	14 (10-15)	10 (8-14)	<0.001**
HR (beats per min), median (IQR)	110 (95.25-125.75)	110 (92-125)	110 (100-129.5)	0.083**
Temperature (^{o}C), mean (SD)	37.79 (1.01)	37.80 (1.08)	37.77 (0.91)	0.871**
MBP (mmHg), mean(SD)	75.82 (22.08)	79.75 (22.88)	69.93 (19.51)	0.002**
SBP (mmHg), mean (SD)	106.45 (29.96)	111.39 (29.44)	99.07 (29.35)	0.004**
RR (breaths per min), median (IQR)	25 (22-30)	25 (22-30)	25 (20-30)	0.693**
Blood investigations				
Total WBC (x10^9/L), mean (SD)	15.73 (9.20)	15.63 (8.67)	15.88 (9.98)	0.914**
PLT (x10^9/L), mean (SD)	185.98 (137.85)	200.71 (129.67)	163.95 (147.15)	0.002**
Hb (g/dL), mean (SD)	11.14 (2.59)	11.36 (2.68)	10.82 (2.44)	0.088**
Hct (%), mean (SD)	34.31 (7.75)	35.08 (7.92)	33.17 (7.38)	0.031**
K^+ (mmol/L), mean (SD)	3.89 (0.79)	3.90 (0.80)	3.87 (0.77)	0.865**
Na^+ (mmol/L), mean (SD)	136.05 (8.24)	135.62 (8.81)	136.69 (7.80)	0.068**
Creatinine (µmol/L), mean (SD)	187.85 (151.92)	186.15 (171.60)	190.38 (117.27)	0.030**
Bilirubin (µmol/l), mean (SD)	32.80 (61.49)	31.74 (72.67)	34.35 (40.09)	0.007**
pH, mean (SD)	7.37 (0.50)	7.41 (0.64)	7.32 (0.14)	0.004**
PaO_2 (mmHg), mean (SD)	116.17 (74.28)	110.23 (56.25)	124.73 (94.07)	0.665**
FiO_2, mean (SD)	0.50 (0.22)	0.44 (0.18)	0.58 (0.24)	<0.001**
PaO_2/FiO_2 ratio, mean (SD)	262.48 (149.58)	281.52 (149.39)	235.26 (146.32)	0.003**
Severity of illness scores				
qSOFA, median (IQR)	2 (1-2)	2 (1-2)	2 (2-3)	0.001**
qSOFA, no. (%)				0.055
0 - 1	69 (27.4)	48 (31.8)	21 (20.8)	
2 - 3	183 (72.6)	103 (68.2)	80 (79.2)	
SIRS, median (IQR)	3 (2-4)	3 (2-4)	3 (2-4)	0.937**
SOFA, median (IQR)	7 (4.75-10)	6 (4-9)	9 (6-12)	<0.001**
SOFA, no. (%)				<0.001
0 - 1	0 (0.0)	0 (0.0)	0 (0.0)	

2 - 3	46 (18.4)	33 (22.1)	13 (12.9)	
4 - 5	36 (14.4)	28 (18.8)	8 (7.9)	
6 - 7	58 (23.2)	43 (28.9)	15 (14.9)	
8 - 9	32 (12.8)	16 (10.7)	16 (15.8)	
10 - 11	38 (15.2)	20 (13.4)	18 (17.8)	
12 - 14	29 (11.6)	8 (5.4)	21 (20.8)	
> 14	11 (4.4)	1 (0.7)	10 (9.9)	
SOFA, no. (%)				<0.001
< 8	140 (56.0)	113 (68.1)	27 (32.1)	
≥ 8[b]	110 (44.0)	53 (31.9)	57 (67.9)	
APACHE II, median (IQR)	18 (13-24)	15 (12-21)	22 (16-27)	<0.001**
APACHE II, no. (%)				<0.001
0 - 4	3 (1.2)	3 (2.0)	0 (0.0)	
5 - 9	22 (8.7)	16 (10.6)	6 (5.9)	
10 - 14	61 (24.2)	50 (33.1)	11(10.9)	
15 - 19	52 (20.6)	33 (21.9)	19 (18.8)	
20 - 24	58 (23.0)	27 (17.9)	31 (30.7)	
25 - 29	28 (11.1)	9 (6.0)	19 (18.8)	
30 - 34	19 (7.5)	10 (6.6)	9 (8.9)	
> 34	9 (3.6)	3 (2.0)	6 (5.9)	
APACHE II, no. (%)				<0.001
< 21	148 (58.7)	115 (68.5)	33 (39.3)	
≥ 21[b]	104 (41.3)	53 (31.5)	51 (60.7)	
Septic Shock	74 (29.4)	35 (23.2)	39 (38.6)	0.008

[a]Comparison between the patients who survived and died using the Chi-squared test; *Fisher's exact test; **Mann–Whitney U test.

[b] The cut-off value of the SOFA or APACHE II score, which was determined by receiver operator characteristic curve analysis, for predicting death in the hospital.

Abbreviations: **APACHE II**: Acute Physiology and Chronic Health Evaluation II Score; **FiO_2**: fraction of inspired oxygen; **GCS**: Glasgow Coma Scale; **Hb**: haemoglobin; **HR**: heart rate; **ICU**: intensive care unit; **IQR**: interquartile range; **MBP**: mean blood pressure; **no.**: number; **PaO_2**: partial pressure of oxygen in the arterial blood; **PLT**: platelet count; **RR**: respiratory rate; **SD**: standard deviation; **SOFA**: Sequential Organ Failure Assessment Score; **WBC**: white blood cell.

Table S4. Sites of infection and microbiology according to hospital survivability of patients with sepsis

Variable	All cases n=252	Survived n=151	Died n=101	p[a]
Site of Infection				
Respiratory, no. (%)	143 (56.7)	82 (54.3)	61 (60.4)	0.339
Urinary tract, no. (%)	37 (14.7)	30 (19.9)	7 (6.9)	0.004
Abdominal, no. (%)	61 (24.2)	34 (22.5)	27 (26.7)	0.444
Neurological, no. (%)	12 (4.8)	8 (5.3)	4 (4.0)	0.767*

Bones or joints, no. (%)	2 (0.8)	2 (1.3)	0 (0.0)	0.518*
Skin or cutaneous sites, no. (%)	19 (7.5)	7 (4.6)	12 (11.9)	0.033
Intravascular catheter, no. (%)	1 (0.4)	1 (0.7)	0 (0.0)	>0.999*
Infective endocarditis, no. (%)	1 (0.4)	0 (0.0)	1 (1.0)	0.401*
Primary bacteraemia, no. (%)	7 (2.8)	5 (3.3)	2 (2.0)	0.705*
Systemic, no. (%)	6 (2.4)	4 (2.6)	2 (2.0)	>0.999*
Microbiology				
No pathogens detected, no. (%)	67 (26.6)	47 (31.1)	20 (19.8)	0.046
Gram negative bacteria, no. (%)	156 (61.9)	88 (58.3)	68 (67.3)	0.147
Klebsiella pneumonia	27 (10.7)	16 (10.6)	11 (10.9)	0.941
Acinetobacter baumannii	45 (17.9)	21 (13.9)	24 (23.8)	0.045
Escherichia coli	44 (17.5)	26 (17.2)	18 (17.8)	0.902
Pseudomonas aeruginosa	24 (9.5)	17 (11.3)	7 (6.9)	0.251
Stenotrophomonas maltophilia	2 (0.8)	0 (0.0)	2 (2.0)	0.160*
Proteus species	47 (18.7)	25 (16.6)	22 (21.8)	0.297
Enterobacter cloacae	3 (1.2)	3 (2.0)	0 (0.0)	0.277*
Bulkholderia pseudomallei	1 (0.4)	0 (0.0)	1 (1.0)	0.221*
Others	0 (0.0)	0 (0.0)	0 (0.0)	NA
Gram positive bacteria, no. (%)	34 (13.5)	22 (14.6)	12 (11.9)	0.540
Enterococcus	5 (2.0)	5 (3.3)	0 (0.0)	0.085*
MSSA	5 (2.0)	3 (2.0)	2 (2.0)	>0.999*
MRSA	10 (4.0)	6 (4.0)	4 (4.0)	>0.999*
Other Streptococcus species	12 (4.8)	6 (4.0)	6 (5.9)	0.551*
Streptococcus pneumonia	2 (0.8)	2 (1.3)	0 (0.0)	0.518*
Fungi, no. (%)	7 (2.8)	4 (2.6)	3 (3.0)	>0.999
Candida species	7 (2.8)	4 (2.6)	3 (3.0)	>0.999*
Aspergillus species	0 (0.0)	0 (0.0)	0 (0.0)	NA
Others	0 (0.0)	0 (0.0)	0 (0.0)	NA
Viruses, no. (%)	2 (0.8)	0 (0.0)	2 (2.0)	0.160*
Influenza	1 (0.4)	0 (0.0)	1 (1.0)	0.401*
Dengue	1 (0.4)	0 (0.0)	1 (1.0)	0.401*
Others	0 (0.0)	0 (0.0)	0 (0.0)	NA
Other pathogens, no. (%)				
Anaerobes	0 (0.0)	0 (0.0)	0 (0.0)	NA
Mycobacterium tuberculosis	4 (1.6)	3 (2.0)	1 (1.0)	0.651*
Malaria	0 (0.0)	0 (0.0)	0 (0.0)	NA

[a]Comparison between the patients who survived and died using the Chi-squared test; *Fisher's exact test; **Mann–Whitney U test.

Abbreviations: **MRSA**: methicillin-resistant Staphylococcus aureus; **MSSA**: methicillin-susceptible Staphylococcus aureus; **NA**, not available; **no.**, number.

Table S5. Completion of sepsis bundle elements according to the hospital survivability of patients with sepsis

Variable	All cases n=252	Survived n=151	Died n=101	p[a]
Timing of antibiotics administration				
Performed within 24 hours, no. (%)	n=225	n=141	n=84	0.348
0-60 minutes	173 (76.9)	109 (77.3)	64 (76.2)	
61-120 minutes	21 (9.3)	13 (9.2)	8 (9.5)	
121-180 minutes	14 (6.2)	11 (7.8)	3 (3.6)	
>180 minutes	17 (7.6)	8 (5.7)	9 (10.7)	
Not performed within 24 hours, no. (%)	0 (0.0)	0 (0.0)	0 (0.0)	NA
Timing of antibiotics administration, median (IQR), minutes	30 (11-60)	35 (13.5-60)	30 (10-60)	0.794**
Timing of obtaining blood cultures				
Performed within 24 hours, no. (%)	n=197	n=114	n=83	0.838
0-60 minutes	135 (68.5)	77 (67.5)	58 (69.9)	
61-120 minutes	14 (7.1)	7 (6.1)	7 (8.4)	
121-180 minutes	10 (5.1)	6 (5.3)	4 (4.8)	
>180 minutes	38 (19.3)	24 (21.1)	14 (16.9)	
Not performed within 24 hours, no. (%)	0 (0.0)	0 (0.0)	0 (0.0)	NA
Timing of obtaining blood cultures, median (IQR), minutes	30.0 (15-114.5)	30 (14-130.5)	30 (15-90)	0.493**
Timing of obtaining lactate measurement				
Performed within 24 hours, no. (%)	n=198	n=121	n=77	0.790*
0-60 minutes	141 (71.2)	85 (70.2)	56 (72.7)	
61-120 minutes	10 (5.1)	6 (5.0)	4 (5.2)	
121-180 minutes	6 (3.0)	5 (4.1)	1 (1.3)	
>180 minutes	41 (20.7)	25 (20.7)	16 (20.8)	
Not performed within 24 hours, no. (%)	0 (0.0)	0 (0.0)	0 (0.0)	NA
Timing of obtaining lactate measurement, median (IQR), minutes	30 (10-92)	30 (10-139.5)	30 (10-75.5)	0.583**

[a]Comparison between the patients who survived and died using the Chi-squared test; *Fisher's exact test; **Mann–Whitney U test.

Abbreviations: **IQR**: interquartile range; **NA**, not available; **no.**: number.

Table S6. Completion of the sepsis bundle of care and the initial administration of antibiotics according to the hospital survivability of patients with sepsis

Variable	All cases n=252	Survived n=151	Died n=101	p[a]
Completion of the sepsis bundle within 1 hour, no. (%), n=241	87 (36.1)	53 (36.3)	34 (35.8)	0.936
Completion of the initial administration of antibiotics within 1 hour, no. (%), n=241	173 (71.8)	109 (74.7)	64 (63.4)	0.219
Permutations of the completed elements within 1 hour, no. (%)	n=241	n=146	n=95	0.196
No elements completed	20 (8.3)	12 (8.2)	8 (8.4)	
Antibiotics only	44 (18.3)	30 (20.5)	14 (14.7)	
Blood cultures only	13 (5.4)	9 (6.2)	4 (4.2)	
Lactate only	23 (9.5)	11 (7.5)	12 (12.6)	
Antibiotics + Lactate	17 (7.1)	14 (9.6)	3 (3.2)	
Antibiotics + Blood cultures	25 (10.4)	12 (8.2)	13 (13.7)	
Blood cultures + Lactate	12 (5.0)	5 (3.4)	7 (7.4)	
Antibiotics + Blood cultures + Lactate	87 (36.1)	53 (36.3)	34 (35.8)	
Completion of the sepsis bundle within 3 hours, no. (%), n=241	108 (44.8)	66 (45.2)	42 (44.2)	0.879
Completion of the initial administration of antibiotics within 3 hours, no. (%), n=241	205 (85.1)	131 (89.7)	74 (77.9)	0.012
Permutation of the completed elements of 3-hour sepsis bundle, no. (%)	n=241	n=146	n=95	0.028
No elements completed	8 (3.3)	3 (2.1)	5 (5.3)	
Antibiotics only	37 (15.4)	28 (19.2)	9 (9.5)	
Blood cultures only	5 (2.1)	2 (1.4)	3 (3.2)	
Lactate only	16 (6.6)	8 (5.5)	8 (8.4)	
Antibiotics + Lactate	24 (10.0)	19 (13.0)	5 (5.3)	
Antibiotics + Blood cultures	36 (14.9)	18 (12.3)	18 (18.9)	
Blood cultures + Lactate	7 (2.9)	2 (1.4)	5 (5.3)	
Antibiotics + Blood cultures + Lactate	108 (44.8)	66 (45.2)	42 (44.2)	

[a]Comparison between the patients who survived and died using the Chi-squared test; *Fisher's exact test; **Mann–Whitney U test.

Abbreviations: **no.**: number.

Table S7. Life-sustaining treatments during ICU stay and outcomes according to hospital survivability of patients with sepsis

Variable	All cases n=252	Survived n=151	Died n=101	P
Life-sustaining treatments during ICU stay				
Respiratory support, no. (%) and median (IQR), days				
Mechanical ventilation	173/251 (68.9)	82/150 (54.7)	91/101 (90.1)	<0.001
Duration of mechanical ventilation	8 (4-15)	9 (4-15)	7(3-14)	0.153**
Non-invasive ventilation	20/251 (8.0)	13/150 (8.7)	7/101 (6.9)	0.618
Duration of non-invasive ventilation	2 (2-3.75)	2 (1-2)	5 (2-7)	0.004**
High-flow nasal oxygen	38/251 (15.1)	29/150 (19.3)	9/101 (8.9)	0.024
Duration of high-flow nasal oxygen	2 (1-3)	2 (1-3)	2 (1-3)	>0.999**
Additional ICU support, no. (%)				
Vasopressors/inotropes	163 (64.7)	82 (54.3)	81 (80.2)	<0.001
Renal replacement therapy	101/251 (40.2)	43/150 (28.7)	58/101 (57.4)	<0.001
Red blood cell transfusion	93/251 (37.1)	48/150 (32.0)	45/101 (44.6)	0.043
Platelet transfusion	50/251 (19.9)	20/150 (13.3)	30/101 (29.7)	0.001
Fresh frozen plasma transfusion	58/251 (23.1)	28/150 (18.7)	30/101 (29.7)	0.042
Surgical source control	25/251 (10.0)	19/150 (12.7)	6/101 (5.9)	0.081*
Non-surgical source control	78/251 (31.1)	54/150 (36.0)	24/101 (23.8)	0.040
Length of of surgical source control, median (IQR), minutes	295.0 (190.0-637.5)	290.0 (105.0-630.0)	430.0 (270.0-1587.5)	0.241**
Length of of surgical source control, n (%)	n=24	n=19	n=5	0.208*
<12 hours	23 (95.8)	19 (100)	4 (80.0)	
12-24 hours	1 (4.2)	0 (0.0)	1 (20.0)	
>24 hours	0 (0.0)	0 (0.0)	0 (0.0)	
Outcomes				
Patient status, no. (%)				<0.001*

Alive upon current hospital discharge	150 (59.5)	150 (99.3)	0 (0.0)	
Alive upon discharge from current ICU stay, but died in current hospital stay	17 (6.7)	0 (0.0)	17 (16.8)	
Alive upon discharge from current ICU stay, but still in current hospital stay after 90 days	1 (0.4)	1 (0.7)	0 (0.0)	
Still in current ICU stay after 90 days	0 (0.0)	0 (0.0)	0 (0.0)	
Died in current ICU stay	84 (33.3)	0 (0.0)	84 (83.2)	
Length of stay, median days (IQR)				
Hospital	16 (10-25)	17 (11-24.25)	13 (7-26)	0.027**
ICU	10 (6-18)	10.5 (6-17)	10 (5-21)	0.740**

[a]Comparison between the patients who survived and died using the Chi-squared test; *Fisher's exact test; **Mann–Whitney U test.

Abbreviations: **ICU**: intensive care unit; **IQR**: interquartile range; **no.**: number.

Table S8. Hospital and intensive care unit characteristics according to intensive care unit survivability of patients with sepsis

Variable	All cases n=252	Survived n=168	Died n=84	p[a]
Participating hospital, no. (%)				NA
115 People's	25 (9.9)	7 (4.2)	18 (21.4)	
Bach Mai	26 (10.3)	16 (9.5)	10 (11.9)	
Bai Chay	14 (5.6)	10 (6.0)	4 (4.8)	
Can Tho	7 (2.8)	4 (2.4)	3 (3.6)	
Cho Ray	41 (16.3)	22 (13.1)	19 (22.6)	
Da Nang	12 (4.8)	6 (3.6)	6 (7.1)	
Dong Da	9 (3.6)	6 (3.6)	3 (3.6)	
Hanoi Medical University	12 (4.8)	6 (3.6)	6 (7.1)	
Hue	39 (15.5)	31 (18.5)	8 (9.5)	
Saint Paul	9 (3.6)	9 (5.4)	0 (0.0)	
Thai Nguyen	2 (0.8)	1 (0.6)	1 (1.2)	
Thanh Nhan	1 (0.4)	1 (0.6)	0 (0.0)	
Vietnam–Czechoslovakia Friendship	48 (19.0)	42 (25.0)	6 (7.1)	
Vinmec Times City International	7 (2.8)	7 (4.2)	0 (0.0)	
Hospital characteristics				
Type of hospital, no. (%)				NA

Rural	0 (0.0)	0 (0.0)	0 (0.0)	
Urban	252 (100)	168 (100)	84 (100)	
University affiliation, no. (%)				0.003
No	153 (60.7)	113 (67.3)	40 (47.6)	
Yes	99 (39.3)	55 (32.7)	44 (52.4)	
ICU characteristics				
Nature of ICU, no. (%)				NA
Open	0 (0.0)	0 (0.0)	0 (0.0)	
Closed	252 (100)	168 (100)	84 (100)	
Type of ICU, no. (%)				0.857
Medical	110 (43.7)	74 (44.0)	36 (42.9)	
Surgical	0 (0.0)	0 (0.0)	0 (0.0)	
Mixed	142 (56.3)	94 (56.0)	48 (57.1)	
Nurse to patient ratio, no. (%)				0.124
1 or more nurses : 1 patient	7 (2.8)	7 (4.2)	0 (0.0)	
1 nurse : 2 patients	187 (74.2)	120 (71.4)	67 (79.8)	
1 nurse : 3 patients	0 (0.0)	0 (0.0)	0 (0.0)	
1 nurse : 4 or more patients	58 (23.0)	41 (24.4)	17 (20.2)	
Intensivist to patient ratio, no. (%)				0.077
1 intensivist : 5 or fewer patients	165 (65.5)	105 (62.5)	60 (71.4)	
1 intensivist : 6 to 8 patients	75 (29.8)	57 (33.9)	18 (21.4)	
1 intensivist : 9 to 11 patients	0 (0.0)	0 (0.0)	0 (0.0)	
1 intensivist : 12 to 14 patients	12 (4.8)	6 (3.6)	6 (7.1)	
Training programme in ICU, no. (%)				0.014
No	50 (19.8)	26 (15.5)	24 (28.6)	
Yes	202 (80.2)	142 (84.5)	60 (71.4)	

[a]Comparison between the patients who survived and died using the Chi-squared test; *Fisher's exact test; **Mann–Whitney U test.

Abbreviations: **ICU**, intensive care unit; **NA**, not available; **no.**, number.

Table S9. Baseline characteristics according to intensive care unit survivability of patients with sepsis

Variable	All cases n=252	Survived n=168	Died n=84	p[a]
Age (year), median (IQR)	65 (52-76.75)	65 (52-76)	65 (52-77)	0.971**
Age (year), no. (%)				0.844*
< 20	3 (1.2)	2 (1.2)	1 (1.2)	
20 - 39	19 (7.5)	11 (6.5)	8 (9.5)	
40 - 59	74 (29.4)	49 (29.2)	25 (29.8)	
≥ 60	156 (61.9)	106 (63.1)	50 (59.5)	
Sex (male), no. (%)	162 (64.3)	104 (61.9)	58 (69.0)	0.265

Collection batch, no. (%)				0.034
Collection 1 (Jan)	80 (31.7)	61 (36.3)	19 (22.6)	
Collection 2 (April)	62 (24.6)	33 (19.6)	29 (34.5)	
Collection 3 (July)	54 (21.4)	35 (20.8)	19 (22.6)	
Collection 4 (Oct)	56 (22.2)	39 (23.2)	17 (20.2)	
Admission type, no. (%)				0.393*
Medical	236 (93.7)	155 (92.3)	81 (96.4)	
Elective surgical	2 (0.8)	2 (1.2)	0 (0.0)	
Unscheduled surgical	14 (5.6)	11 (6.5)	3 (3.6)	
Admission source, no. (%)				0.351*
Emergency department	138 (54.8)	94 (56.0)	44 (52.4)	
Operating room	4 (1.6)	3 (1.8)	1 (1.2)	
General wards	56 (22.2)	39 (23.2)	17 (20.2)	
Other ICUs or HDU	16 (6.3)	12 (7.1)	4 (4.8)	
Inter-hospital transfer	37 (14.7)	20 (11.9)	17 (20.2)	
Others	1 (0.4)	0 (0.0)	1 (1.2)	
Comorbidities, no. (%)				
Cardiovascular disease	78 (31.0)	47 (28.0)	31 (36.9)	0.148
Chronic lung disease	30 (11.9)	21 (12.5)	9 (10.7)	0.680
Chronic neurological disease	36 (14.3)	28 (16.7)	8 (9.5)	0.127
Chronic kidney disease	23 (9.1)	16 (9.5)	7 (8.3)	0.757
Peptic ulcer disease	9 (3.6)	6 (3.6)	3 (3.6)	>0.999*
Chronic liver disease	27 (10.7)	17 (10.1)	10 (11.9)	0.670
Diabetes mellitus	67 (26.6)	44 (26.2)	23 (27.4)	0.840
HIV infection	0 (0.0)	0 (0.0)	0 (0.0)	NA
Connective tissue disease	3 (1.2)	2 (1.2)	1 (1.2)	>0.999*
Immunosuppression	10 (4.0)	7 (4.2)	3 (3.6)	>0.999*
Haematological malignancies	5 (2.0)	3 (1.8)	2 (2.4)	>0.999*
Solid malignant tumours	12 (4.8)	6 (3.6)	6 (7.1)	0.222

[a]Comparison between the patients who survived and died using the Chi-squared test; *Fisher's exact test; **Mann–Whitney U test.

Abbreviations: **HIV**, human immunodeficiency virus; **ICU**, intensive care unit; **IQR**, interquartile range; **NA**, not available; **no.**, number.

Table S10. Clinical and laboratory characteristics and severity of illness according to intensive care unit survivability of patients with sepsis

Variable	All cases n=252	Survived n=168	Died n=84	p[a]
Vital signs (on admission into ICU)				
GCS, median (IQR)	13 (9-15)	14 (10-15)	10 (8-14)	<0.001**
HR (beats per min), median (IQR)	110 (95.25-125.75)	109 (92-121)	111.5 (100-130)	0.008**

Temperature (^{o}C), mean (SD)	37.79 (1.01)	37.82 (1.07)	37.72 (0.88)	0.485**
MBP (mmHg), mean (SD)	75.82 (22.08)	78.95 (22.80)	69.54 (19.21)	0.001**
SBP (mmHg), mean (SD)	106.45 (29.96)	110.64 (29.48)	98.08 (29.33)	0.002**
RR (breaths per min), median (IQR)	25 (22-30)	25 (22-30)	25 (20.25-30)	>0.999**
Blood investigations				
Total WBC (x10^{9}/L), mean (SD)	15.73 (9.20)	15.70 (8.64)	15.79 (10.28)	0.941**
PLT (x10^{9}/L), mean (SD)	185.98 (137.85)	203.72 (131.99)	150.49 (143.17)	0.004**
Hb (g/dL), mean (SD)	11.14 (2.59)	11.33 (2.62)	10.77 (2.50)	0.104**
Hct (%), mean (SD)	34.31 (7.75)	34.85 (7.76)	33.24 (7.67)	0.122**
K^{+} (mmol/L), mean (SD)	3.89 (0.79)	3.89 (0.80)	3.87 (0.77)	0.838**
Na^{+} (mmol/L), mean (SD)	136.05 (8.24)	135.21 (8.72)	137.74 (6.92)	0.021**
Creatinine (µmol/L), mean (SD)	187.85 (151.92)	188.47 (169.24)	186.60 (110.29)	0.927**
Bilirubin (µmol/l), mean (SD)	32.80 (61.49)	31.40 (69.33)	35.52 (42.65)	0.629**
pH, mean (SD)	7.37 (0.50)	7.40 (0.61)	7.32 (0.13)	0.249**
PaO_2 (mmHg), mean (SD)	116.17 (74.28)	111.80 (64.31)	124.49 (90.14)	0.206**
FiO_2, mean (SD)	0.50 (0.22)	0.45 (0.20)	0.57 (0.24)	<0.001**
PaO_2/FiO_2 ratio, mean (SD)	262.48 (149.58)	273.45 (149.45)	241.73 (148.49)	0.116**
Severity of illness scores				
qSOFA, median (IQR)	2 (1-2)	2 (1-2)	2 (2-3)	0.001**
qSOFA, no. (%)				0.036
0 - 1	69 (27.4)	53 (31.5)	16 (19.0)	
2 - 3	183 (72.6)	115 (68.5)	68 (81.0)	
SIRS, median (IQR)	3 (2-4)	3 (3-3.75)	3 (2-4)	0.792**
SOFA, median (IQR)	7 (4.75-10)	6 (4-9)	10 (7-12.75)	<0.001**
SOFA, no. (%)				<0.001
0 - 1	0 (0.0)	0 (0.0)	0 (0.0)	
2 - 3	46 (18.4)	38 (22.9)	8 (9.5)	
4 - 5	36 (14.4)	29 (17.5)	7 (8.3)	
6 - 7	58 (23.2)	46 (27.7)	12 (14.3)	
8 - 9	32 (12.8)	20 (12.0)	12 (14.3)	
10 - 11	38 (15.2)	21 (12.7)	17 (20.2)	
12 - 14	29 (11.6)	9 (5.4)	20 (23.8)	

> 14	11 (4.4)	3 (1.8)	8 (9.5)	
SOFA, no. (%)				<0.001
< 10	172 (68.8)	120 (80.5)	52 (51.5)	
≥ 10[b]	78 (31.2)	29 (19.5)	49 (48.5)	
APACHE II, median (IQR)	18 (13-24)	16 (12-22)	22 (16.25-27)	<0.001**
APACHE II, no. (%)				<0.001
0 - 4	3 (1.2)	3 (1.8)	0 (0.0)	
5 - 9	22 (8.7)	17 (10.1)	5 (6.0)	
10 - 14	61 (24.2)	52 (31.0)	9 (10.7)	
15 - 19	52 (20.6)	36 (21.4)	16 (19.0)	
20 - 24	58 (23.0)	32 (19.0)	26 (31.0)	
25 - 29	28 (11.1)	11 (6.5)	17 (20.2)	
30 - 34	19 (7.5)	13 (7.7)	6 (7.1)	
> 34	9 (3.6)	4 (2.4)	5 (6.0)	
APACHE II, no. (%)				<0.001
< 19	129 (51.2)	97 (64.2)	32 (31.7)	
≥ 19[b]	123 (48.8)	54 (35.8)	69 (68.3)	
Sheptic Shock	74 (29.4)	43 (25.6)	31 (36.9)	0.063

[a]Comparison between the patients who survived and died using the Chi-squared test; *Fisher's exact test; **Mann–Whitney U test.

[b]The cut-off value of the SOFA or APACHE II score, which was determined by receiver operator characteristic curve analysis, for predicting death in the intensive care unit.

Abbreviations: **APACHE II**: Acute Physiology and Chronic Health Evaluation II Score; **FiO_2**: fraction of inspired oxygen; **GCS**: Glasgow Coma Scale; **Hb**: haemoglobin; **HR**: heart rate; **ICU**: intensive care unit; **IQR**: interquartile range; **MBP**: mean blood pressure; **no.**: number; **PaO_2**: partial pressure of oxygen in the arterial blood; **PLT**: platelet count; **RR**: respiratory rate; **SD**: standard deviation; **SOFA**: Sequential Organ Failure Assessment Score; **WBC**: white blood cell.

Table S11. Sites of infection and microbiology according to intensive care unit survivability of patients with sepsis

Variable	All cases n=252	Survived n=168	Died n=84	p[a]
Site of Infection				
Respiratory, no. (%)	143 (56.7)	93 (55.4)	50 (59.5)	0.529
Urinary tract, no. (%)	37 (14.7)	31 (18.5)	6 (7.1)	0.017
Abdominal, no. (%)	61 (24.2)	37 (22.0)	24 (28.6)	0.253
Neurological, no. (%)	12 (4.8)	9 (5.4)	3 (3.6)	0.756*
Bones or joints, no. (%)	2 (0.8)	2 (1.2)	0 (0.0)	0.554*
Skin or cutaneous sites, no. (%)	19 (7.5)	9 (5.4)	10 (11.9)	0.063
Intravascular catheter, no. (%)	1 (0.4)	1 (0.6)	0 (0.0)	>0.999*
Infective endocarditis, no. (%)	1 (0.4)	0 (0.0)	1 (1.2)	0.333*
Primary bacteraemia, no. (%)	7 (2.8)	6 (3.6)	1 (.2)	0.430*

Systemic, no. (%)	6 (2.4)	4 (2.4)	2 (2.4)	>0.999*
Microbiology				
No pathogens detected, no. (%)	67 (26.6)	50 (29.8)	17 (20.2)	0.107
Gram negative bacteria, no. (%)	156 (61.9)	101 (60.1)	55 (65.5)	0.409
Klebsiella pneumonia	27 (10.7)	17 (10.1)	10 (11.9)	0.666
Acinetobacter baumannii	45 (17.9)	24 (14.3)	21 (25.0)	0.036
Escherichia coli	44 (17.5)	31 (18.5)	13 (15.5)	0.557
Pseudomonas aeruginosa	24 (9.5)	18 (10.7)	6 (7.1)	0.363
Stenotrophomonas maltophilia	2 (0.8)	1 (0.6)	1 (1.2)	>0.999*
Proteus species	47 (18.7)	30 (17.9)	17 (20.2)	0.647
Enterobacter cloacae	3 (1.2)	3 (1.8)	0 (0.0)	0.553*
Bulkholderia pseudomallei	1 (0.4)	1 (0.6)	0 (0.0)	>0.999
Other	0 (0.0)	0 (0.0)	0 (0.0)	NA
Gram positive bacteria, no. (%)	34 (13.5)	23 (13.7)	11 (13.1)	0.896
Enterococcus	5 (2.0)	5 (3.0)	0 (0.0)	0.173*
MSSA	5 (2.0)	3 (1.8)	2 (2.4)	>0.999*
MRSA	10 (4.0)	7 (4.2)	3 (3.6)	>0.999*
Other Streptococcus species	12 (4.8)	6 (3.6)	6 (7.1)	0.222*
Streptococcus pneumonia	2 (0.8)	2 (1.2)	0 (0.0)	0.554*
Fungi, no. (%)	7 (2.8)	4 (2.4)	3 (3.6)	0.689*
Candida species	7 (2.8)	4 (2.4)	3 (3.6)	0.689*
Aspergillus species	0 (0.0)	0 (0.0)	0 (0.0)	NA
Others	0 (0.0)	0 (0.0)	0 (0.0)	NA
Viruses, no. (%)	2 (0.8)	0 (0.0)	2 (2.4)	0.110*
Influenza	1 (0.4)	0 (0.0)	1 (1.2)	0.333*
Others	0 (0.0)	0 (0.0)	0 (0.0)	NA
Dengue	1 (0.4)	0	1 (1.2)	0.333*
Other pathogens, no. (%)				
Anaerobes	0 (0.0)	0 (0.0)	0 (0.0)	NA
Mycobacterium tuberculosis	4 (1.6)	3 (1.8)	1 (1.2)	>0.999*
Malaria	0 (0.0)	0 (0.0)	0 (0.0)	NA

[a]Comparison between the patients who survived and died using the Chi-squared test; *Fisher's exact test; **Mann–Whitney U test.
Abbreviations: **MRSA**: methicillin-resistant Staphylococcus aureus; **MSSA**: methicillin-susceptible Staphylococcus aureus; **NA**, not available; **no.**, number.

Table S12. Completion of sepsis bundle elements according to intensive care unit survivability of patients with sepsis

Variable	All cases n=252	Survived n=168	Died n=84	p[a]
Timing of antibiotics administration				
Performed within 24 hours, no. (%)				0.686

0-60 minutes	173 (76.9)	120 (77.4)	53 (75.7)	
61-120 minutes	21 (9.3)	14 (9.0)	7 (10.0)	
121-180 minutes	14 (6.2)	11 (7.1)	3 (4.3)	
>180 minutes	17 (7.6)	10 (6.5)	7 (10.0)	
Not performed within 24 hours, no. (%)	0 (0.0)	0 (0.0)	0 (0.0)	NA
Timing of antibiotics administration, median (IQR), minutes	30 (11-60)	35 (15-60)	30 (10-61.25)	0.590**
Timing of obtaining blood cultures				
Performed within 24 hours, no. (%)	n=197	n=128	n=69	0.545*
0-60 minutes	135 (68.5)	87 (68.0)	48 (69.6)	
61-120 minutes	14 (7.1)	7 (5.5)	7 (10.1)	
121-180 minutes	10 (5.1)	7 (5.5)	3 (4.3)	
>180 minutes	38 (19.3)	27 (21.1)	11 (15.9)	
Not performed within 24 hours, no. (%)	0 (0.0)	0 (0.0)	0 (0.0)	NA
Timing of obtaining blood cultures, median (IQR), minutes	30.0 (15-114.5)	30 (15-133.5)	30 (10-90)	0.371**
Timing of obtaining lactate measurement				
Performed within 24 hours, no. (%)	n=198	n=135	n=63	0.827*
0-60 minutes	141 (71.2)	95 (70.4)	46 (73.0)	
61-120 minutes	10 (5.1)	6 (4.4)	4 (6.3)	
121-180 minutes	6 (3.0)	5 (3.7)	1 (1.6)	
>180 minutes	41 (20.7)	29 (21.5)	12 (19.0)	
Not performed within 24 hours, no. (%)	0 (0.0)	0 (0.0)	0 (0.0)	NA
Timing of obtaining lactate measurement, median (IQR), minutes	30 (10-92)	30 (11-159)	30 (10-75)	0.381**

[a]Comparison between the patients who survived and died using the Chi-squared test; *Fisher's exact test; **Mann–Whitney U test.

Abbreviations: **IQR**: interquartile range; **NA**, not available; **no.**: number.

Table S13. Completion of the sepsis bundle of care and the initial administration of antibiotics according to intensive care unit survivability of patients with sepsis

Variable	All cases n=252	Survived n=168	Died n=84	p[a]
Completion of the sepsis bundle within 1 hour, no. (%), n=241	87 (36.1)	59 (36.6)	28 (35.0)	0.802
Completion of the initial administration of antibiotics within 1 hour, no. (%), n=241	173 (71.8)	120 (74.5)	53 (66.3)	0.178

Permutations of the completed elements within 1 hour, no. (%)	n=241	n=161	n=80	0.311
No elements completed	20 (8.3)	13 (8.1)	7 (8.8)	
Antibiotics only	44 (18.3)	32 (19.9)	12 (15.0)	
Blood cultures only	13 (5.4)	9 (5.6)	4 (5.0)	
Lactate only	23 (9.5)	12 (7.5)	11 (13.8)	
Antibiotics + Lactate	17 (7.1)	15 (9.3)	2 (2.5)	
Antibiotics + Blood cultures	25 (10.4)	14 (8.7)	11 (13.8)	
Blood cultures + Lactate	12 (5.0)	7 (4.3)	5 (6.3)	
Antibiotics + Blood cultures + Lactate	87 (36.1)	59 (36.6)	28 (35.0)	
Completion of the sepsis bundle within 3 hours, no. (%), n=241	108 (44.8)	73 (45.3)	35 (43.8)	0.815
Completion of the initial administration of antibiotics within 3 hours, no. (%), n=241	205 (85.1)	143 (88.8)	62 (77.5)	0.020
Permutation of the completed elements of 3-hour sepsis bundle, no. (%)	n=241	n=161	n=80	0.089*
No elements completed	8 (3.3)	4 (2.5)	4 (5.0)	
Antibiotics only	37 (15.4)	29 (18.0)	8 (10.0)	
Blood cultures only	5 (2.1)	2 (1.2)	3 (3.8)	
Lactate only	16 (6.6)	9 (5.6)	7 (8.8)	
Antibiotics + Lactate	24 (10.0)	20 (12.4)	4 (5.0)	
Antibiotics + Blood cultures	36 (14.9)	21 (13.0)	15 (18.8)	
Blood cultures + Lactate	7 (2.9)	3 (1.9)	4 (5.0)	
Antibiotics + Blood cultures + Lactate	108 (44.8)	73 (45.3)	35 (43.8)	

[a]Comparison between the patients who survived and died using the Chi-squared test; *Fisher's exact test; **Mann–Whitney U test.

Abbreviations: **no.**: number.

Table S14. Life-sustaining treatments during ICU stay and outcomes according to intensive care unit survivability of patients with sepsis

Variable	All cases n=252	Survived n=168	Died n=84	p[a]
Life-sustaining treatments during ICU stay				
Respiratory support, no. (%) and median (IQR), days				
Mechanical ventilation	173/251 (68.9)	97/167 (58.1)	76/84 (90.5)	<0.001
Duration of mechanical	8 (4-15)	9 (4-15)	7 (3-15)	0.502**

ventilation				
Non-invasive ventilation	20/251 (8.0)	14 (8.4)	6 (7.1)	0.732
Duration of non-invasive ventilation	2 (2-3.75)	2 (1-2)	5 (3.5-11.25)	0.002**
High-flow nasal oxygen	38/251 (15.1)	33/167 (19.8)	5/84 (6.0)	0.004
Duration of high-flow nasal oxygen	2 (1-3)	2 (1-3)	3 (2.25-11.25)	0.146
Additional ICU support, no. (%)				
Vasopressors/inotropes	163 (64.7)	96 (57.1)	67 (79.8)	<0.001
Renal replacement therapy	101/251 (40.2)	48/167 (28.7)	43/84 (63.1)	<0.001
Red blood cell transfusion	93/251 (37.1)	55/167 (32.9)	38/84 (45.2)	0.057
Platelet transfusion	50/251 (19.9)	23/167 (13.8)	27/84 (32.1)	0.001
Fresh frozen plasma transfusion	58/251 (23.1)	32/167 (19.2)	26/84 (31.0)	0.037
Surgical source control	25/251 (10.0)	19/167 (11.4)	6/84 (7.1)	0.290
Non-surgical source control	78/251 (31.1)	59/167 (35.3)	19/84 (22.6)	0.040
Length of of surgical source control, median (IQR), minutes	290 (105-630)	290 (105-630)	430 (270-1587)	0.241**
Length of of surgical source control, n (%)	n=24	n=19	n=5	0.208
<12 hours	23 (95.8)	19 (100)	4 (80.0)	
12-24 hours	1 (4.2)	0 (0.0)	1 (20.0)	
>24 hours	0 (0.0)	0 (0.0)	0 (0.0)	
Outcomes				
Patient status, no. (%)				<0.001*
Alive upon current hospital discharge	150 (59.5)	150 (89.3)	0 (0.0)	
Alive upon discharge from current ICU stay, but died in current hospital stay	17 (6.7)	17 (10.1)	0 (0.0)	
Alive upon discharge from current ICU stay, but still in current hospital stay after 90 days	1 (0.4)	1 (0.6)	0 (0.0)	
Still in current ICU stay after 90 days	0 (0.0)	0 (0.0)	0 (0.0)	
Died in current ICU stay, no.	84 (33.3)	0 (0.0)	84 (100)	

(%)				
Mortality, no. (%)				
Hospital	101 (40.1)	17 (10.1)	84 (100)	<0.001
Length of stay, median days (IQR)				
Hospital	16 (10-25)	17 (11-26)	13 (6-22)	0.002**
ICU	10 (6-18)	10 (6-17)	10 (5-20.5)	0.688**

[a]Comparison between the patients who survived and died using the Chi-squared test; *Fisher's exact test; **Mann–Whitney U test.

Abbreviations: **ICU**: intensive care unit; **IQR**: interquartile range; **no.**: number.

Table S15. Factors associated with hospital mortality in patients with sepsis: univariable regression analyses

Factors	Number of patients	OR	95.0% CI for OR		P
			Lower	Upper	
Participating hospital					
115 People's	25	Ref.			0.004
Bach Mai	26	0.271	0.082	0.898	0.033
Bai Chay	14	0.126	0.029	0.554	0.006
Can Tho	7	1.895	0.189	19.039	0.587
Cho Ray	41	0.366	0.121	1.103	0.074
Da Nang	12	0.316	0.074	1.356	0.121
Dong Da	9	0.158	0.030	0.832	0.030
Hanoi Medical University	12	0.316	0.074	1.356	0.121
Hue	39	0.158	0.051	0.491	0.001
Saint Paul	9	0.000	0.000	NA	0.999
Thai Nguyen	2	0.316	0.017	5.854	0.439
Thanh Nhan	1	510149957.2	0.000	NA	>0.999
Vietnam–Czechoslovakia Friendship	48	0.063	0.019	0.208	<0.001
Vinmec Times City International	7	0.000	0.000	NA	0.999
Hospital characteristics					
University affiliation					
No	153	Ref.			NA
Yes	99	2.520	1.495	4.248	0.001
ICU characteristics					
Type of ICU					
Medical	110	Ref.			NA
Mixed	142	1.151	0.692	1.915	0.589
Nurse to patient ratio					
1 nurse : 4 or more patients	58	Ref.			0.946
1 or more nurses : 1 patient	7	0.000	0.000	-	0.999

1 nurse : 2 patients	187	0.904	0.498	1.640	0.739
Intensivist to patient ratio					
1 intensivist : 5 or fewer patients	165	Ref.			0.449
1 intensivist : 6 to 8 patients	75	0.738	0.419	1.302	0.294
1 intensivist : 12 or more patients	12	1.391	0.430	4.497	0.581
Training programme in ICU					
No	50	Ref.			NA
Yes	202	0.445	0.237	0.833	0.011
Baseline characteristics					
Age (year)	252	1.001	0.986	1.016	0.921
Age (year) group					
< 20	3	Ref.			0.863
20 - 39	19	1.800	0.139	23.374	0.653
40 - 59	74	1.442	0.125	16.617	0.769
≥ 60	156	1.250	0.111	14.086	0.857
Sex (male)	162	1.345	0.790	2.290	0.275
Collection batch					
Collection 1 (Jan)	80	Ref.			0.008
Collection 2 (April)	62	3.418	1.694	6.896	0.001
Collection 3 (July)	54	1.812	0.872	3.768	0.111
Collection 4 (Oct)	56	1.706	0.825	3.529	0.150
Admission type					
Medical	236	Ref.			0.355
Elective surgical	2	0.000	0.000	NA	0.999
Unscheduled surgical	14	0.384	0.104	1.413	0.150
Admission source					
Emergency department	138	Ref.			0.714
Operating room	4	0.569	0.058	5.612	0.629
General wards	56	1.189	0.630	2.243	0.593
Other ICUs or HDU	16	1.024	0.351	2.983	0.966
Inter-hospital transfer	37	1.801	0.866	3.742	0.115
Others	1	2755810063	0.000	NA	>0.999
Comorbidities					
Cardiovascular disease	78	1.551	0.903	2.664	0.112
Chronic lung disease	30	0.996	0.458	2.169	0.992
Chronic neurological disease	36	0.378	0.165	0.867	0.022
Chronic kidney disease	23	0.957	0.398	2.304	0.922
Peptic ulcer disease	9	1.204	0.315	4.597	0.786
Chronic liver disease	27	1.446	0.649	3.220	0.367
Diabetes mellitus	67	1.012	0.573	1.790	0.966

Connective tissue disease	3	0.745	0.067	8.326	0.811
Immunosuppression	10	0.630	0.159	2.495	0.510
Haematological malignancies	5	0.997	0.164	6.073	0.997
Solid malignant tumours	12	1.526	0.478	4.873	0.475
Vital signs					
GCS	251	0.849	0.786	0.918	<0.001
HR (beats per min)	252	1.010	0.997	1.022	0.140
Temperature (^{o}C)	252	0.975	0.760	1.252	0.845
MBP (mmHg)	252	0.978	0.965	0.991	0.001
SBP (mmHg)	252	0.986	0.977	0.995	0.002
RR (breaths per min)	252	0.987	0.944	1.031	0.555
Blood investigations					
Total WBC (x10^9/L)	252	1.003	0.976	1.031	0.833
PLT (x10^9/L)	252	0.998	0.996	1.000	0.040
Hb (g/dL)	251	0.922	0.835	1.018	0.109
Hct (%)	252	0.968	0.936	1.001	0.057
K^+ (mmol/L)	252	0.961	0.697	1.324	0.805
Na^+ (mmol/L)	252	1.016	0.985	1.048	0.313
Creatinine (µmol/L)	252	1.000	0.999	1.002	0.828
Bilirubin (µmol/l)	232	1.001	0.996	1.005	0.752
pH	248	0.045	0.005	0.389	0.005
PaO_2 (mmHg)	244	1.003	0.999	1.006	0.142
FiO_2	245	26.892	7.081	102.133	<0.001
PaO_2/FiO_2 ratio	243	0.998	0.996	1.000	0.020
Severity of illness scores					
qSOFA	252	1.697	1.203	2.393	0.003
qSOFA					
0 - 1	69	Ref.			NA
2 - 3	183	1.775	0.984	3.203	0.057
SIRS	252	1.004	0.776	1.300	0.974
SOFA	250	1.219	1.130	1.315	<0.001
SOFA					
2 - 3	46	Ref.			<0.001
4 - 5	36	0.725	0.263	2.000	0.535
6 - 7	58	0.886	0.371	2.114	0.784
8 - 9	32	2.538	0.987	6.528	0.053
10 - 11	38	2.285	0.925	5.642	0.073
12 - 14	29	6.663	2.363	18.793	<0.001
> 14	11	25.385	2.947	218.685	0.003
SOFA					
< 8	140	Ref.			NA
≥ 8	110	4.173	2.440	7.137	<0.001

APACHE II	252	1.088	1.050	1.127	<0.001
APACHE II					
0 - 4	3	Ref.			<0.001
5 - 9	22	605807962.9	0.000	NA	0.999
10 - 14	61	355407338.2	0.000	NA	0.999
15 - 19	52	930129397.5	0.000	NA	0.999
20 - 24	58	1854819442	0.000	NA	0.999
25 - 29	28	3410474458	0.000	NA	0.999
30 - 34	19	1453939111	0.000	NA	0.999
> 34	9	3230975802	0.000	NA	0.999
APACHE II					<0.001
< 21	148	Ref.			NA
≥ 21	104	4.126	2.414	7.051	<0.001
Site of Infection					
Respiratory	143	1.283	0.769	2.140	0.339
Urinary tract	37	0.300	0.126	0.714	0.006
Abdominal	61	1.256	0.701	2.249	0.444
Neurological	12	0.737	0.216	2.516	0.626
Bones or joints	2	0.000	0.000	NA	0.999
Skin or cutaneous sites	19	2.774	1.053	7.309	0.039
Intravascular catheter	1	0.000	0.000	NA	1.000
Infective endocarditis	1	2439367045	0.000	NA	>0.999
Primary bacteraemia	7	0.590	0.112	3.101	0.533
Systemic	6	0.742	0.133	4.131	0.734
Microbiology					
Pathogens detection					
No pathogens detected	67	0.546	0.300	0.994	0.048
Gram negative bacteria	156	1.475	0.871	2.498	0.148
Gram positive bacteria	34	0.791	0.372	1.679	0.541
Fungi	7	1.125	0.246	5.137	0.879
Viruses	2	2464007117	0.000	NA	0.999
Other pathogens	4	0.493	0.051	4.810	0.543
Completion of sepsis bundle elements					
Timing of antibiotics administration					
0-60 minutes	173	Ref.			0.367
61-120 minutes	21	1.048	0.412	2.665	0.921
121-180 minutes	14	0.464	0.125	1.727	0.252
>180 minutes	17	1.916	0.704	5.214	0.203
Timing of obtaining blood cultures					

0-60 minutes	135	Ref.			0.939
61-120 minutes	14	1.328	0.441	3.995	0.614
121-180 minutes	10	0.885	0.239	3.281	0.855
>180 minutes	38	0.774	0.369	1.626	0.500
Timing of obtaining lactate measurement					
0-60 minutes	141	Ref.			0.763
61-120 minutes	10	1.012	0.273	3.748	0.986
121-180 minutes	6	0.304	0.035	2.668	0.282
>180 minutes	41	0.971	0.476	1.981	0.936
Completion of the sepsis bundle within 1 hour	87	0.978	0.571	1.675	0.936
Completion of the administration of antibiotics within 1 hour	173	0.701	0.397	1.237	0.220
Permutations of the completed elements within 1 hour					
No elements completed	20	Ref.			0.228
Antibiotics only	44	0.700	0.234	2.096	0.524
Blood cultures only	13	0.667	0.152	2.926	0.591
Lactate only	23	1.636	0.487	5.500	0.426
Antibiotics + Lactate	17	0.321	0.069	1.491	0.147
Antibiotics + Blood cultures	25	1.625	0.491	5.341	0.424
Blood cultures + Lactate	12	2.100	0.490	8.998	0.318
Antibiotics + Blood cultures + Lactate	87	0.962	0.357	2.597	0.939
Completion of the sepsis bundle within 3 hours	108	0.961	0.571	1.615	0.879
Completion of the administration of antibiotics within 3 hours	205	0.403	0.196	0.830	0.014
Permutation of the completed elements of 3-hour sepsis bundle					
No elements completed	8	Ref.			0.049
Antibiotics only	37	0.193	0.038	0.971	0.046
Blood cultures only	5	0.900	0.091	8.899	0.928
Lactate only	16	0.600	0.106	3.400	0.564
Antibiotics + Lactate	24	0.158	0.028	0.897	0.037
Antibiotics + Blood cultures	36	0.600	0.124	2.894	0.525
Blood cultures + Lactate	7	0.500	0.170	13.225	0.715
Antibiotics + Blood cultures + Lactate	108	0.382	0.087	1.682	0.203
Life-sustaining treatments during ICU stay					

Respiratory support					
Mechanical ventilation	173	7.546	3.645	15.625	<0.001
Duration of mechanical ventilation	167	0.998	0.969	1.028	0.909
Non-invasive ventilation	20	0.785	0.302	2.041	0.619
Duration of non-invasive ventilation	20	4.738	1.076	20.863	0.040
High-flow nasal oxygen	38	0.408	0.184	0.904	0.027
Duration of high-flow nasal oxygen	33	1.154	0.862	1.546	0.336
Additional ICU support					
Vasopressors/inotropes	163	3.408	1.899	6.116	<0.001
Renal replacement therapy	101	3.356	1.976	5.702	<0.001
Red blood cell transfusion	93	1.708	1.014	2.876	0.044
Platelet transfusion	50	2.746	1.455	5.185	0.002
Fresh frozen plasma transfusion	58	1.841	1.018	3.329	0.043
Surgical source control	25	0.435	0.168	1.132	0.088
Non-surgical source control	78	0.554	0.314	0.977	0.041

Abbreviations: **APACHE II**, Acute Physiology and Chronic Health Examination II; **CI**: confidence interval; **ICU**, intensive care unit; **NA**: not available; **OR**: odds ratio; **qSOFA**, quick Sequential (Sepsis-Related) Organ Failure Assessment; **Ref.**, reference; **SIRS**, systemic inflammatory response syndrome; **SOFA**, Sequential (Sepsis-Related) Organ Failure Assessment.

Table S16. Factors associated with hospital mortality in patients with sepsis: multivariable logistic regression analyses (backward elimination)

Step	Factors	Number of patients	Adjusted OR	95.0% CI for adjusted OR		P
				Lower	Upper	
1	University affiliation					
	No	153	Ref.			NA
	Yes	99	2.062	0.922	4.612	0.078
	Training program in ICU					
	No	50	Ref.			NA
	Yes	202	0.308	0.103	0.923	0.035
	Cardiovascular disease	78	2.307	1.005	5.295	0.049
	Chronic neurological disease	36	0.239	0.070	0.821	0.023
	SOFA					
	< 8	140	Ref.			NA
	≥ 8	110	2.042	0.888	4.695	0.093
	APACHE II					
	< 21	148	Ref.			NA

	≥ 21	104	2.463	1.134	5.348	0.023
	Urinary Tract	37	0.231	0.065	0.821	0.024
	Abdominal	61	0.968	0.382	2.452	0.945
	Skin or Cutaneous Sites	19	2.817	0.810	9.792	0.103
	Pathogens detection					
	No pathogens detected	67	1.248	0.340	4.584	0.738
	Gram-negative bacteria	156	1.980	0.611	6.414	0.254
	Completion of the sepsis bundle within 1 hour	87	1.533	0.411	5.724	0.525
	Completion of the administration of antibiotics within 1 hour	173	2.106	0.409	10.828	0.373
	Completion of the sepsis bundle within 3 hours	108	0.808	0.214	3.053	0.754
	Completion of the administration of antibiotics within 3 hours	205	0.212	0.038	1.179	0.076
	Respiratory support					
	Mechanical ventilation	173	3.789	1.408	10.196	0.008
	High-flow nasal oxygen	38	0.931	0.305	2.837	0.899
	Additional ICU support					
	Vasopressors/inotropes	163	0.987	0.387	2.516	0.979
	Renal replacement therapy	101	1.513	0.665	3.442	0.323
	Red blood cell transfusion	93	1.022	0.456	2.291	0.959
	Platelet transfusion	50	0.905	0.358	2.289	0.834
	Fresh frozen plasma transfusion	58	1.625	0.668	3.952	0.285
	Surgical source control	25	0.369	0.108	1.260	0.112
	Non-surgical source control	78	0.454	0.206	0.998	0.049
	Constant		0.147			0.018
2	University affiliation					
	No	153	Ref.			NA
	Yes	99	2.064	0.924	4.607	0.077
	Training program in ICU					
	No	50	Ref.			NA
	Yes	202	0.307	0.104	0.905	0.032
	Cardiovascular disease	78	2.308	1.007	5.292	0.048
	Chronic neurological disease	36	0.24	0.071	0.813	0.022
	SOFA					

	< 8	140	Ref.			NA
	≥ 8	110	2.035	0.916	4.521	0.081
	APACHE II					
	< 21	148	Ref.			NA
	≥ 21	104	2.459	1.142	5.295	0.022
	Urinary Tract	37	0.231	0.065	0.820	0.023
	Abdominal	61	0.968	0.382	2.452	0.946
	Skin or Cutaneous Sites	19	2.816	0.810	9.787	0.103
	Pathogens detection					
	No pathogens detected	67	1.246	0.342	4.538	0.739
	Gram-negative bacteria	156	1.977	0.615	6.352	0.253
	Completion of the sepsis bundle within 1 hour	87	1.533	0.411	5.723	0.525
	Completion of the administration of antibiotics within 1 hour	173	2.107	0.410	10.831	0.372
	Completion of the sepsis bundle within 3 hours	108	0.808	0.214	3.049	0.753
	Completion of the administration of antibiotics within 3 hours	205	0.212	0.038	1.178	0.076
	Respiratory support					
	Mechanical ventilation	173	3.775	1.461	9.753	0.006
	High-flow nasal oxygen	38	0.930	0.305	2.832	0.898
	Additional ICU support					
	Renal replacement therapy	101	1.511	0.670	3.406	0.320
	Red blood cell transfusion	93	1.020	0.459	2.269	0.961
	Platelet transfusion	50	0.906	0.359	2.286	0.835
	Fresh frozen plasma transfusion	58	1.626	0.669	3.952	0.284
	Surgical source control	25	0.369	0.108	1.257	0.111
	Non-surgical source control	78	0.454	0.206	0.998	0.049
	Constant		0.147			0.018
3	University affiliation					
	No	153	Ref.			NA
	Yes	99	2.062	0.924	4.602	0.077
	Training program in ICU					
	No	50	Ref.			NA
	Yes	202	0.308	0.105	0.904	0.032

	Cardiovascular disease	78	2.306	1.007	5.282	0.048
	Chronic neurological disease	36	0.241	0.071	0.812	0.022
	SOFA					
	< 8	140	Ref.			NA
	≥ 8	110	2.033	0.916	4.514	0.081
	APACHE II					
	< 21	148	Ref.			NA
	≥ 21	104	2.457	1.142	5.283	0.022
	Urinary Tract	37	0.230	0.065	0.819	0.023
	Abdominal	61	0.969	0.383	2.453	0.947
	Skin or Cutaneous Sites	19	2.814	0.810	9.776	0.104
	Pathogens detection					
	No pathogens detected	67	1.240	0.345	4.461	0.742
	Gram-negative bacteria	156	1.975	0.615	6.346	0.253
	Completion of the sepsis bundle within 1 hour	87	1.534	0.411	5.727	0.524
	Completion of the administration of antibiotics within 1 hour	173	2.106	0.410	10.830	0.373
	Completion of the sepsis bundle within 3 hours	108	0.807	0.214	3.042	0.751
	Completion of the administration of antibiotics within 3 hours	205	0.212	0.038	1.179	0.076
	Respiratory support					
	Mechanical ventilation	173	3.782	1.469	9.739	0.006
	High-flow nasal oxygen	38	0.929	0.305	2.822	0.896
	Additional ICU support					
	Renal replacement therapy	101	1.518	0.688	3.349	0.301
	Platelet transfusion	50	0.911	0.372	2.233	0.839
	Fresh frozen plasma transfusion	58	1.631	0.677	3.927	0.275
	Surgical source control	25	0.370	0.109	1.254	0.110
	Non-surgical source control	78	4.454	0.207	0.998	0.049
	Constant		0.147			0.017
4	University affiliation					
	No	153	Ref.			NA
	Yes	99	2.056	0.926	4.564	0.077
	Training program in ICU					
	No	50	Ref.			NA

	Yes	202	0.307	0.105	0.900	0.031
	Cardiovascular disease	78	2.316	1.021	5.254	0.045
	Chronic neurological disease	36	0.241	0.071	0.813	0.022
	SOFA					
	< 8	140	Ref.			NA
	≥ 8	110	2.026	0.920	4.461	0.080
	APACHE II					
	< 21	148	Ref.			NA
	≥ 21	104	2.459	1.143	5.290	0.021
	Urinary Tract	37	0.233	0.068	0.794	0.020
	Skin or Cutaneous Sites	19	2.831	0.826	9.710	0.098
	Pathogens detection					
	No pathogens detected	67	1.232	0.348	4.361	0.747
	Gram-negative bacteria	156	1.976	0.615	6.343	0.253
	Completion of the sepsis bundle within 1 hour	87	1.540	0.414	5.727	0.519
	Completion of the administration of antibiotics within 1 hour	173	2.097	0.410	10.738	0.374
	Completion of the sepsis bundle within 3 hours	108	0.802	0.215	2.989	0.742
	Completion of the administration of antibiotics within 3 hours	205	0.213	0.038	1.181	0.077
	Respiratory support					
	Mechanical ventilation	173	3.785	1.471	9.741	0.006
	High-flow nasal oxygen	38	0.930	0.306	2.824	0.899
	Additional ICU support					
	Renal replacement therapy	101	1.509	0.697	3.268	0.297
	Platelet transfusion	50	0.915	0.376	2.227	0.844
	Fresh frozen plasma transfusion	58	1.626	0.678	3.897	0.276
	Surgical source control	25	0.366	0.113	1.180	0.092
	Non-surgical source control	78	0.454	0.207	0.998	0.050
	Constant		0.147			0.017
5	University affiliation					
	No	153	Ref.			NA
	Yes	99	2.062	0.930	4.572	0.075
	Training program in ICU					
	No	50	Ref.			NA

	Yes	202	0.302	0.106	0.858	0.025
	Cardiovascular disease	78	2.311	1.019	5.240	0.045
	Chronic neurological disease	36	0.242	0.072	0.814	0.022
	SOFA					
	< 8	140	Ref.			NA
	≥ 8	110	2.016	0.919	4.425	0.080
	APACHE II					
	< 21	148	Ref.			NA
	≥ 21	104	2.465	1.147	5.297	0.021
	Urinary Tract	37	0.233	0.068	0.794	0.020
	Skin or Cutaneous Sites	19	2.839	0.829	9.727	0.097
	Pathogens detection					
	No pathogens detected	67	1.225	0.347	4.325	0.753
	Gram-negative bacteria	156	1.962	0.614	6.268	0.255
	Completion of the sepsis bundle within 1 hour	87	1.525	0.414	5.622	0.526
	Completion of the administration of antibiotics within 1 hour	173	2.123	0.418	10.771	0.364
	Completion of the sepsis bundle within 3 hours	108	0.811	0.220	2.992	0.783
	Completion of the administration of antibiotics within 3 hours	205	0.212	0.038	1.178	0.076
	Respiratory support					
	Mechanical ventilation	173	3.838	1.525	9.658	0.004
	Additional ICU support					
	Renal replacement therapy	101	1.519	0.705	3.269	0.286
	Platelet transfusion	50	0.914	0.376	2.226	0.844
	Fresh frozen plasma transfusion	58	1.638	0.689	3.897	0.264
	Surgical source control	25	0.369	0.116	1.180	0.093
	Non-surgical source control	78	0.456	0.208	1.000	0.050
	Constant		0.146			0.016
6	University affiliation					
	No	153	Ref.			NA
	Yes	99	2.036	0.927	4.473	0.077
	Training program in ICU					
	No	50	Ref.			NA
	Yes	202	0.305	0.108	0.862	0.025

	Cardiovascular disease	78	2.311	1.020	5.232	0.045
	Chronic neurological disease	36	0.244	0.073	0.818	0.022
	SOFA					
	< 8	140	Ref.			NA
	≥ 8	110	1.999	0.915	4.368	0.082
	APACHE II					
	< 21	148	Ref.			NA
	≥ 21	104	2.457	1.145	5.272	0.021
	Urinary Tract	37	2.457	1.145	5.272	0.021
	Skin or Cutaneous Sites	19	0.231	0.068	0.786	0.019
	Pathogens detection					
	No pathogens detected	67	1.236	0.351	4.357	0.741
	Gram-negative bacteria	156	1.966	0.615	6.283	0.254
	Completion of the sepsis bundle within 1 hour	87	1.523	0.413	5.613	0.527
	Completion of the administration of antibiotics within 1 hour	173	2.107	0.416	10.676	0.368
	Completion of the sepsis bundle within 3 hours	108	0.810	0.220	2.987	0.752
	Completion of the administration of antibiotics within 3 hours	205	0.215	0.039	1.187	0.078
	Respiratory support					
	Mechanical ventilation	173	3.822	1.520	9.610	0.004
	Additional ICU support					
	Renal replacement therapy	101	1.507	0.702	3.235	0.293
	Fresh frozen plasma transfusion	58	1.596	0.698	3.649	0.268
	Surgical source control	25	0.367	0.115	1.171	0.090
	Non-surgical source control	78	0.460	0.211	1.003	0.051
	Constant		0.145			0.016
7	University affiliation					
	No	153	Ref.			NA
	Yes	99	2.024	0.923	4.435	0.078
	Training program in ICU					
	No	50	Ref.			NA
	Yes	202	0.302	0.107	0.853	0.024
	Cardiovascular disease	78	2.310	1.020	5.230	0.045
	Chronic neurological disease	36	0.246	0.074	0.826	0.023

	SOFA					
	< 8	140	Ref.			NA
	≥ 8	110	1.952	0.907	4.201	0.087
	APACHE II					
	< 21	148	Ref.			NA
	≥ 21	104	2.504	1.176	5.329	0.017
	Urinary Tract	37	0.233	0.069	0.789	0.019
	Skin or Cutaneous Sites	19	2.892	0.845	9.897	0.091
	Pathogens detection					
	No pathogens detected	67	1.249	0.355	4.398	0.729
	Gram-negative bacteria	156	1.967	0.614	6.299	0.255
	Completion of the sepsis bundle within 1 hour	87	1.284	0.600	2.751	0.520
	Completion of the administration of antibiotics within 1 hour	173	2.172	0.433	10.903	0.346
	Completion of the administration of antibiotics within 3 hours	205	0.215	0.039	1.195	0.079
	Respiratory support					
	Mechanical ventilation	173	3.840	1.528	9.649	0.004
	Additional ICU support					
	Renal replacement therapy	101	1.513	0.705	3.248	0.288
	Fresh frozen plasma transfusion	58	1.614	0.710	3.671	0.253
	Surgical source control	25	0.375	0.119	1.186	0.095
	Non-surgical source control	78	0.461	0.211	1.005	0.052
	Constant		0.139			0.013
8	University affiliation					
	No	153	Ref.			NA
	Yes	99	2.038	0.931	4.460	0.075
	Training program in ICU					
	No	50	Ref.			NA
	Yes	202	0.306	0.109	0.862	0.025
	Cardiovascular disease	78	2.249	1.010	5.010	0.047
	Chronic neurological disease	36	0.250	0.075	0.836	0.024
	SOFA					
	< 8	140	Ref.			NA
	≥ 8	110	1.945	0.905	4.178	0.088
	APACHE II					

	< 21	148	Ref.			NA
	≥ 21	104	2.504	1.177	5.329	0.017
	Urinary Tract	37	0.237	0.071	0.798	0.020
	Skin or Cutaneous Sites	19	2.731	0.833	8.952	0.097
	Pathogens detection					
	Gram-negative bacteria	156	1.684	0.789	3.593	0.178
	Completion of the sepsis bundle within 1 hour	87	1.267	0.594	2.704	0.540
	Completion of the administration of antibiotics within 1 hour	173	2.200	0.436	11.099	0.340
	Completion of the administration of antibiotics within 3 hours	205	0.213	0.038	1.188	0.078
	Respiratory support					
	Mechanical ventilation	173	3.815	1.519	9.584	0.004
	Additional ICU support					
	Renal replacement therapy	101	1.511	0.704	3.241	0.290
	Fresh frozen plasma transfusion	58	1.604	0.706	3.644	0.259
	Surgical source control	25	0.380	0.121	1.196	0.098
	Non-surgical source control	78	0.461	0.212	1.006	0.052
	Constant		0.163			0.005
9	University affiliation					
	No	153	Ref.			NA
	Yes	99	2.074	0.949	4.532	0.067
	Training program in ICU					
	No	50	Ref.			NA
	Yes	202	0.309	0.110	0.870	0.026
	Cardiovascular disease	78	2.215	0.997	4.920	0.051
	Chronic neurological disease	36	0.252	0.076	0.842	0.025
	SOFA					
	< 8	140	Ref.			NA
	≥ 8	110	1.968	0.916	4.228	0.083
	APACHE II					
	< 21	148	Ref.			NA
	≥ 21	104	2.487	1.170	5.283	0.018
	Urinary Tract	37	0.248	0.074	0.830	0.024
	Skin or Cutaneous Sites	19	2.715	0.831	8.875	0.098
	Pathogens detection					

	Gram-negative bacteria	156	1.669	0.782	3.561	0.186
	Completion of the administration of antibiotics within 1 hour	173	1.988	0.411	9.618	0.393
	Completion of the administration of antibiotics within 3 hours	205	0.214	0.039	1.180	0.077
	Respiratory support					
	Mechanical ventilation	173	3.742	1.496	9.363	0.005
	Additional ICU support					
	Renal replacement therapy	101	1.486	0.695	3.174	0.307
	Fresh frozen plasma transfusion	58	1.558	0.691	3.513	0.285
	Surgical source control	25	0.374	0.119	1.176	0.092
	Non-surgical source control	78	0.466	0.214	1.013	0.054
	Constant		0.182			0.005
10	University affiliation					
	No	153	Ref.			NA
	Yes	99	2.024	.931	4.396	0.075
	Training program in ICU					
	No	50	Ref.			NA
	Yes	202	0.324	0.116	0.903	0.031
	Cardiovascular disease	78	2.168	0.980	4.793	0.056
	Chronic neurological disease	36	0.249	0.075	0.829	0.023
	SOFA					
	< 8	140	Ref.			NA
	≥ 8	110	2.023	0.946	4.326	0.069
	APACHE II					
	< 21	148	Ref.			NA
	≥ 21	104	2.529	1.194	5.355	0.015
	Urinary Tract	37	0.264	0.080	0.871	0.029
	Skin or Cutaneous Sites	19	2.731	0.841	8.868	0.095
	Pathogens detection					
	Gram-negative bacteria	156	1.589	0.752	3.360	0.225
	Completion of the administration of antibiotics within 3 hours	205	0.387	0.143	1.050	0.062
	Respiratory support					
	Mechanical ventilation	173	3.878	1.558	9.657	0.004
	Additional ICU support					

	Renal replacement therapy	101	1.434	0.676	3.041	0.348
	Fresh frozen plasma transfusion	58	1.534	0.682	3.451	0.301
	Surgical source control	25	0.392	0.126	1.220	0.106
	Non-surgical source control	78	0.462	0.212	1.006	0.052
	Constant		0.184			0.006
11	University affiliation					
	No	153	Ref.			NA
	Yes	99	2.059	0.949	4.464	0.067
	Training program in ICU					
	No	50	Ref.			NA
	Yes	202	0.320	0.115	0.887	0.028
	Cardiovascular disease	78	2.212	1.002	4.881	0.049
	Chronic neurological disease	36	0.234	0.070	0.779	0.018
	SOFA					
	< 8	140	Ref.			NA
	≥ 8	110	2.239	1.080	4.641	0.030
	APACHE II					
	< 21	148	Ref.			NA
	≥ 21	104	2.608	1.234	5.510	0.012
	Urinary Tract	37	0.275	0.084	0.900	0.033
	Skin or Cutaneous Sites	19	2.766	0.865	8.848	0.086
	Pathogens detection					
	Gram-negative bacteria	156	1.646	0.783	3.461	0.188
	Completion of the administration of antibiotics within 3 hours	205	0.401	0.149	1.077	0.070
	Respiratory support					
	Mechanical ventilation	173	4.050	1.637	10.023	0.002
	Additional ICU support					
	Fresh frozen plasma transfusion	58	1.666	0.758	3.659	0.204
	Surgical source control	25	0.370	0.120	1.142	0.084
	Non-surgical source control	78	0.480	0.223	1.033	0.060
	Constant		0.184			0.006
12	University affiliation					
	No	153	Ref.			NA
	Yes	99	1.963	0.913	4.223	0.084
	Training program in ICU					

	No	50	Ref.			NA
	Yes	202	0.357	0.133	0.961	0.042
	Cardiovascular disease	78	2.208	1.005	4.852	0.049
	Chronic neurological disease	36	0.224	0.068	0.737	0.014
	SOFA					
	< 8	140	Ref.			NA
	≥ 8	110	2.430	1.184	4.989	0.016
	APACHE II					
	< 21	148	Ref.			NA
	≥ 21	104	2.584	1.224	5.452	0.013
	Urinary Tract	37	0.307	0.097	0.967	0.044
	Skin or Cutaneous Sites	19	2.803	0.878	8.950	0.082
	Pathogens detection					
	Gram-negative bacteria	156	1.728	0.828	3.606	0.145
	Completion of the administration of antibiotics within 3 hours	205	0.393	0.147	1.050	0.063
	Respiratory support					
	Mechanical ventilation	173	4.138	1.678	10.200	0.002
	Additional ICU support					
	Surgical source control	25	0.371	0.118	1.167	0.090
	Non-surgical source control	78	0.507	0.236	1.086	0.080
	Constant		0.177			0.004
13	University affiliation					
	No	153	Ref.			NA
	Yes	99	1.966	0.917	4.213	0.082
	Training program in ICU					
	No	50	Ref.			NA
	Yes	202	0.379	0.143	1.009	0.052
	Cardiovascular disease	78	2.308	1.060	5.027	0.035
	Chronic neurological disease	36	0.226	0.070	.731	0.013
	SOFA					
	< 8	140	Ref.			NA
	≥ 8	110	2.403	1.176	4.908	0.016
	APACHE II					
	< 21	148	Ref.			NA
	≥ 21	104	2.341	1.129	4.856	0.022
	Urinary Tract	37	0.315	0.101	.986	0.047
	Skin or Cutaneous Sites	19	2.465	0.787	7.716	0.121
	Completion of the administration of antibiotics	205	0.359	0.135	0.957	0.041

	within 3 hours					
	Respiratory support					
	Mechanical ventilation	173	4.556	1.860	11.160	0.001
	Additional ICU support					
	Surgical source control	25	0.382	0.122	1.194	0.098
	Non-surgical source control	78	0.564	0.267	1.191	0.133
	Constant		0.226			0.010
14	University affiliation					
	No	153	Ref.			NA
	Yes	99	1.967	0.921	4.200	0.080
	Training program in ICU					
	No	50	Ref.			NA
	Yes	202	0.338	0.131	0.870	0.025
	Cardiovascular disease	78	2.177	1.005	4.719	0.049
	Chronic neurological disease	36	0.206	0.066	0.645	0.007
	SOFA					
	< 8	140	Ref.			NA
	≥ 8	110	2.359	1.160	4.797	0.018
	APACHE II					
	< 21	148	Ref.			NA
	≥ 21	104	2.631	1.295	5.345	0.007
	Urinary Tract	37	0.282	0.092	0.865	0.027
	Skin or Cutaneous Sites	19	2.195	0.707	6.809	0.174
	Completion of the administration of antibiotics within 3 hours	205	0.395	0152	1.029	0.057
	Respiratory support					
	Mechanical ventilation	173	4.070	1.696	9.770	0.002
	Additional ICU support					
	Surgical source control	25	0.384	0.124	1.192	0.098
	Constant		0.224			0.008
15	University affiliation					
	No	153	Ref.			NA
	Yes	99	2.024	0.953	4.299	0.066
	Training program in ICU					
	No	50	Ref.			NA
	Yes	202	0.308	0.121	0.788	0.014
	Cardiovascular disease	78	2.218	1.026	4.795	0.043
	Chronic neurological disease	36	0.196	0.063	0.609	0.005
	SOFA					
	< 8	140	Ref.			NA

	≥ 8	110	2.358	1.161	4.789	0.018
	APACHE II					
	< 21	148	Ref.			NA
	≥ 21	104	2.625	1.296	5.316	0.007
	Urinary Tract	37	0.280	0.091	0.863	0.027
	Completion of the administration of antibiotics within 3 hours	205	0.400	0.155	1.032	0.058
	Respiratory support					
	Mechanical ventilation	173	3.893	1.644	9.220	0.002
	Additional ICU support					
	Surgical source control	25	0.406	0.131	1.264	0.120
	Constant		0.264			0.015
16	University affiliation					
	No	153	Ref.			NA
	Yes	99	1.852	0.884	3.879	0.103
	Training program in ICU					
	No	50	Ref.			NA
	Yes	202	0.312	0.123	0.787	0.014
	Cardiovascular disease	78	2.286	1.065	4.909	0.034
	Chronic neurological disease	36	0.206	0.067	0.637	0.006
	SOFA					
	< 8	140	Ref.			NA
	≥ 8	110	2.450	1.217	4.929	0.012
	APACHE II					
	< 21	148	Ref.			NA
	≥ 21	104	2.665	1.327	5.352	0.006
	Urinary Tract	37	0.283	0.094	0.852	0.025
	Completion of the administration of antibiotics within 3 hours	205	0.377	0.147	0.969	0.043
	Respiratory support					
	Mechanical ventilation	173	3.754	1.592	8.856	0.003
	Constant		0.248			0.010
17	Training program in ICU					
	No	50	Ref.			NA
	Yes	202	0.392	0.162	0.949	0.038
	Cardiovascular disease	78	2.181	1.019	4.664	0.044
	Chronic neurological disease	36	0.179	0.058	0.546	0.003
	SOFA					
	< 8	140	Ref.			NA
	≥ 8	110	2.717	1.371	5.382	0.004

	APACHE II					
	< 21	148	Ref.			NA
	≥ 21	104	2.668	1.338	5.321	0.005
	Urinary Tract	37	0.312	0.105	0.932	0.037
	Completion of the administration of antibiotics within 3 hours	205	0.381	0.151	0.965	0.042
	Respiratory support					
	Mechanical ventilation	173	4.391	1.912	10.085	<0.001
	Constant		0.230			0.007

Abbreviations: **AOR**: adjusted odds ratio; **APACHE II**, Acute Physiology and Chronic Health Examination II; **CI**: confidence interval; **ICU**, intensive care unit; **NA**: not available; **Ref.**, reference; **SOFA**, Sequential (Sepsis-Related) Organ Failure Assessment.

Table S17. Factors associated with intensive care unit mortality in patients with sepsis: univariable regression analyses

Factors	Number of patients	OR	95.0% CI for OR		P
			Lower	Upper	
Participating hospital					
115 People's	25	Ref.			0.005
Bach Mai	26	0.243	0.075	0.789	0.019
Bai Chay	14	0.156	0.036	0.664	0.012
Can Tho	7	0.292	0.052	1.650	0.163
Cho Ray	41	0.336	0.116	0.976	0.045
Da Nang	12	0.389	0.093	1.624	0.195
Dong Da	9	0.194	0.038	1.000	0.050
Hanoi Medical University	12	0.389	0.093	1.624	0.195
Hue	39	0.100	0.031	0.323	<0.001
Saint Paul	9	0.000	0.000	NA	0.999
Thai Nguyen	2	0.389	0.021	7.111	0.524
Thanh Nhan	1	0.000	0.000	NA	>0.999
Vietnam–Czechoslovakia Friendship	48	0.056	0.016	0.189	<0.001
Vinmec Times City International	7	0.000	0.000	NA	0.999
Hospital characteristics					
University affiliation					
No	153	Ref.			NA
Yes	99	2.260	1.322	3.862	0.003
ICU characteristics					
Type of ICU					
Medical	110	Ref.			NA

Mixed	142	1.050	0.619	1.781	0.857
Nurse to patient ratio					
1 nurse : 4 or more patients	58	Ref.			0.660
1 or more nurses : 1 patient	7	0.000	0.000	NA	0.999
1 nurse : 2 patients	187	1.347	0.710	2.553	0.362
Intensivist to patient ratio					
1 intensivist : 5 or fewer patients	165	Ref.			0.082
1 intensivist : 6 to 8 patients	75	0.553	0.298	1.025	0.060
1 intensivist : 12 or more patients	12	1.750	0.540	5.668	0.351
Training programme in ICU					
No	50	Ref.			NA
Yes	202	0.458	0.243	0.861	0.015
Baseline characteristics					
Age (year)	252	0.998	0.983	1.014	0.802
Age (year) group					
< 20	3	Ref.			
20 - 39	19	1.455	0.112	18.956	0.775
40 - 59	74	1.020	0.088	11.805	0.987
≥ 60	156	0.943	0.084	10.651	0.962
Sex (male)	162	0.728	0.417	1.272	0.265
Collection batch					
Collection 1 (Jan)	80	Ref.			0.038
Collection 2 (April)	62	2.821	1.377	5.779	0.005
Collection 3 (July)	54	1.743	0.815	3.725	0.152
Collection 4 (Oct)	56	1.399	0.649	3.016	0.391
Admission type					
Medical	236	Ref.			0.620
Elective surgical	2	0.000	0.000	NA	0.999
Unscheduled surgical	14	0.522	0.142	1.924	0.329
Admission source					
Emergency department	138	Ref.			0.615
Operating room	4	0.712	0.072	7.041	0.772
General wards	56	0.931	0.475	1.825	0.836
Other ICUs or HDU	16	0.712	0.217	2.333	0575
Inter-hospital transfer	37	1.816	0.867	3.802	0.114
Others	1	3451241756	0.000	NA	>0.999
Comorbidities					
Cardiovascular disease	78	1.506	0.863	2.627	0.150
Chronic lung disease	30	0.840	0.367	1.924	0.680

Chronic neurological disease	36	0.526	0.229	1.212	0.131
Chronic kidney disease	23	0.864	0.341	2.188	0.757
Peptic ulcer disease	9	1.000	0.244	4.101	>0.999
Chronic liver disease	27	1.200	0.524	2.750	0.666
Diabetes mellitus	67	1.063	0.589	1.917	0.840
Connective tissue disease	3	1.000	0.089	11.188	>0.999
Immunosuppression	10	0.852	0.215	3.381	0.820
Haematological malignancies	5	1.341	0.220	8.186	0.750
Solid malignant tumours	12	2.077	0.649	6.648	0.218
Vital signs					
GCS	251	0.589	0.794	0.930	<0.001
HR (beats per min)	252	1.017	1.003	1.030	0.014
Temperature (^{o}C)	252	0.910	0.700	1.184	0.484
MBP (mmHg)	252	0.978	0.965	0.992	0.002
SBP (mmHg)	252	0.985	0.976	0.995	0.002
RR (breaths per min)	252	0.993	0.949	1.040	0.774
Blood investigations					
Total WBC (x10^9/L)	252	1.001	0.973	1.030	0.941
PLT (x10^9/L)	252	0.997	0.994	0.999	0.005
Hb (g/dL)	251	0.918	0.828	1.018	0.105
Hct (%)	252	0.973	0.940	1.007	0.123
K^+ (mmol/L)	252	0.966	0.692	1.348	0.837
Na^+ (mmol/L)	252	1.038	1.005	1.073	0.025
Creatinine (µmol/L)	252	1.000	0.998	1.002	0.926
Bilirubin (µmol/l)	232	1.001	0.997	1.005	0.631
pH	248	0.131	0.016	1.108	0.062
PaO_2 (mmHg)	244	1.002	0.999	1.006	0.212
FiO_2	245	11.704	3.405	40.224	<0.001
PaO_2/FiO_2 ratio	243	0.998	0.997	1.000	0.119
Severity of illness scores					
qSOFA	252	1.768	1.231	2.540	0.002
qSOFA					
0 - 1	69	Ref.			NA
2 - 3	183	1.959	1.039	3.694	0.038
SIRS	252	1.045	0.798	1.368	0.750
SOFA	250	1.244	1.149	1.346	<0.001
SOFA					
2 - 3	46	Ref.			<0.001
4 - 5	36	1.147	0.373	3.527	0.811
6 - 7	58	1.239	0.459	3.343	0.672
8 - 9	32	2.850	1.002	8.109	0.050
10 - 11	38	3.845	1.422	10.401	0.008

12 - 14	29	10.556	3.529	31.569	<0.001
> 14	11	12.667	2.742	58.517	0.001
SOFA					
< 10	172	Ref.			NA
≥ 10	78	4.650	2.620	8.254	<0.001
APACHE II	252	1.076	1.039	1.114	<0.001
APACHE II					
0 - 4	3	Ref.			0.002
5 - 9	22	475125698.2	0.000	NA	0.999
10 - 14	61	2795931999.3	0.000	NA	0.999
15 - 19	52	7179677216	0.000	NA	0.999
20 - 24	58	1312534741	0.000	-NA	0.999
25 - 29	28	2496569578	0.000	NA	0.999
30 - 34	19	745581864.8	0.000	NA	0.999
> 34	9	2019284217	0.000	NA	0.999
APACHE II					
< 19	129	Ref.			NA
≥ 19	123	3.535	1.025	6.171	<0.001
Site of Infection					
Respiratory	143	1.186	0.697	2.018	0.529
Urinary tract	37	0.340	0.136	0.851	0.021
Abdominal	61	1.416	0.779	2.575	0.254
Neurological	12	0.654	0.172	2.483	0.533
Bones or joints	2	0.000	0.000	NA	0.999
Skin or cutaneous sites	19	2.387	0.931	6.123	0.070
Intravascular catheter	1	0.000	0.000	NA	>0.999
Infective endocarditis	1	3269876834	0.000	NA	>0.999
Primary bacteraemia	7	0.325	0.039	2.747	0.302
Systemic	6	1.000	0.179	5.573	>0.999
Microbiology					
Pathogens detection					
No pathogens detected	67	0.599	0.320	1.121	0.109
Gram negative bacteria	156	1.258	0.729	2.171	0.409
Gram positive bacteria	34	0.950	0.439	2.055	0.896

Fungi	7	1.519	0.332	6.946	0.590
Viruses	2	3309753384	0.000	NA	0.999
Other pathogens	4	0.663	0.068	6.469	0.723
Completion of sepsis bundle elements					
Timing of antibiotics administration					
0-60 minutes	173	Ref.			0.693
61-120 minutes	21	1.132	0.432	2.966	0.801
121-180 minutes	14	0.617	0.165	2.304	0.473
>180 minutes	17	1.585	0.572	4.389	0.376
Timing of obtaining blood cultures					
0-60 minutes	135	Ref.			0.557
61-120 minutes	14	1.812	0.600	5.474	0.292
121-180 minutes	10	0.777	0.192	3.143	0.723
>180 minutes	38	0.738	0.337	1.618	0.449
Timing of obtaining lactate measurement					
0-60 minutes	141	Ref.			0.785
61-120 minutes	10	1.377	0.370	5.119	0.633
121-180 minutes	6	0.413	0.047	3.638	0.426
>180 minutes	41	0.855	0.400	1.826	0.685
Completion of the sepsis bundle within 1 hour	87	0.931	0.532	1.630	0.802
Completion of the initial administration of antibiotics within 1 hour	173	0.671	0.374	1.202	0.180
Permutations of the completed elements within 1 hour					
No elements completed	20	Ref.			0.368
Antibiotics only	44	0.696	0.224	2.163	0.532
Blood cultures only	13	0.825	0.185	3.676	0.801
Lactate only	23	1.702	0.497	5.826	0.397
Antibiotics + Lactate	17	0.248	0.044	1.408	0.115
Antibiotics + Blood cultures	25	1.459	0.434	4.901	0.541
Blood cultures + Lactate	12	1.327	0.305	5.770	0.706
Antibiotics + Blood cultures + Lactate	87	0.881	0.317	2.452	0.809
Completion of the sepsis bundle within 3 hours	108	0.938	0.546	1.609	0.815

Completion of the initial administration of antibiotics within 3 hours	205	0.434	0.211	0.889	0.023
Permutation of the completed elements of 3-hour sepsis bundle					
No elements completed	8	Ref.			0.141
Antibiotics only	37	0.276	0.056	1.355	0.113
Blood cultures only	5	1.500	0.156	14.420	0.725
Lactate only	16	0.778	0.142	4.265	0.772
Antibiotics + Lactate	24	0.200	0.035	1.154	0.072
Antibiotics + Blood cultures	36	0.714	0.154	3.319	0.668
Blood cultures + Lactate	7	1.333	0.173	10.254	0.782
Antibiotics + Blood cultures + Lactate	108	0.479	0.113	2.030	0.318
Life-sustaining treatments during ICU stay					
Respiratory support					
Mechanical ventilation	173	6.856	3.109	15.116	<0.001
Duration of mechanical ventilation	167	1.005	0.976	1.036	0.722
Non-invasive ventilation	20	0.841	0.311	2.273	0.732
Duration of non-invasive ventilation	20	7.408	1.097	50.015	0.040
High-flow nasal oxygen	38	0.257	0.096	0.685	0.007
Duration of high-flow nasal oxygen	33	1.369	0.953	1.967	0.089
Additional ICU support					
Vasopressors/inotropes	163	2.956	1.600	5.460	0.001
Renal replacement therapy	101	4.239	2.432	7.388	<0.001
Red blood cell transfusion	93	1.682	0.983	2.879	0.058
Platelet transfusion	50	2.966	1.571	5.597	0.001
Fresh frozen plasma transfusion	58	1.891	1.036	3.453	0.038
Surgical source control	25	0.599	0.230	1.562	0.295
Non-surgical source control	78	0.535	0.293	0.977	0.042

Abbreviations: **APACHE II**, Acute Physiology and Chronic Health Examination II; **CI**: confidence interval; **ICU**, intensive care unit; **NA**: not available; **OR**: odds ratio; **qSOFA**, quick Sequential (Sepsis-Related) Organ Failure Assessment; **Ref.**, reference; **SIRS**, systemic inflammatory response syndrome; **SOFA**, Sequential (Sepsis-Related) Organ Failure Assessment.

Table S18. Factors associated with intensive care unit mortality in patients with sepsis: multivariable logistic regression analyses (backward elimination)

Step	Factors	Number of patients	Adjusted OR	95.0% CI for adjusted OR		p
				Lower	Upper	
1	University affiliation					
	No	153	Ref.			NA
	Yes	99	2.512	1.020	6.188	0.045
	Intensivist to patient ratio					
	1 intensivist : 5 or fewer patients	165	Ref.			0.111
	1 intensivist : 6 to 8 patients	75	3.315	1.069	10.286	0.038
	1 intensivist : 12 or more patients	12	1.278	0.244	6.712	0.772
	Training program in ICU					
	No	50	Ref.			NA
	Yes	202	0.277	0.095	0.807	0.019
	Cardiovascular disease	78	2.026	0.870	4.718	0.102
	Chronic neurological disease	36	0.815	0.240	2.773	0.744
	Solid malignant tumors	12	5.711	1.256	25.979	0.024
	SOFA					
	< 10	172	Ref.			NA
	≥ 10	78	3.022	1.267	7.208	0.013
	APACHE II					
	< 19	129	Ref.			NA
	≥ 19	123	1.623	0.676	3.900	0.279
	Urinary Tract	37	0.191	0.050	0.723	0.015
	Abdominal	61	0.852	0.314	2.308	0.752
	Skin or Cutaneous Sites	19	3.648	0.948	14.032	0.060
	Pathogens detection					
	No pathogens detected	67	1.298	0.336	5.018	0.706
	Gram-negative bacteria	156	1.413	0.432	4.628	0.568
	Completion of the sepsis bundle within 1 hour	87	0.946	0.228	3.937	0.940
	Completion of the administration of antibiotics within 1 hour	173	1.622	0.293	8.964	0.579
	Completion of the sepsis bundle within 3 hours	108	0.898	0.214	3.771	0.884
	Completion of the	205	0.239	0.037	1.545	0.133

	administration of antibiotics within 3 hours					
	Respiratory support					
	Mechanical ventilation	173	2.813	0.939	8.432	0.065
	High-flow nasal oxygen	38	0.181	0.035	0.925	0.040
	Additional ICU support					
	Vasopressors/inotropes	163	0.899	0.327	2.471	0.836
	Renal replacement therapy	101	3.551	1.471	8.569	0.005
	Red blood cell transfusion	93	0.612	0.258	1.451	0.264
	Platelet transfusion	50	1.384	0.536	3.569	0.502
	Fresh frozen plasma transfusion	58	1.427	0.573	3.553	0.445
	Surgical source control	25	0.662	0.182	2.404	0.531
	Non-surgical source control	78	0.322	0.132	0.783	0.012
	Constant		0.118			0.013
2	University affiliation					
	No	153	Ref.			NA
	Yes	99	2.507	1.019	6.170	0.045
	Intensivist to patient ratio					
	1 intensivist : 5 or fewer patients	165	Ref.			0.108
	1 intensivist : 6 to 8 patients	75	3.295	1.074	10.110	0.037
	1 intensivist : 12 or more patients	12	1.288	0.249	6.675	0.763
	Training program in ICU					
	No	50	Ref.			NA
	Yes	202	0.278	0.096	0.807	0.019
	Cardiovascular disease	78	2.030	0.873	4.720	0.100
	Chronic neurological disease	36	0.813	0.239	2.758	0.739
	Solid malignant tumors	12	5.677	1.259	25.608	0.024
	SOFA					
	< 10	172	Ref.			NA
	≥ 10	78	3.031	1.275	7.208	0.012
	APACHE II					
	< 19	129	Ref.			NA
	≥ 19	123	1.617	0.677	3.860	0.279

	Urinary Tract	37	0.190	0.050	0.720	0.015
	Abdominal	61	0.855	0.317	2.304	0.757
	Skin or Cutaneous Sites	19	3.633	0.949	13.907	0.060
	Pathogens detection					
	No pathogens detected	67	1.297	0.335	5.012	0.707
	Gram-negative bacteria	156	1.418	0.434	4.629	0.563
	Completion of the administration of antibiotics within 1 hour	173	1.624	0.294	8.977	0.578
	Completion of the sepsis bundle within 3 hours	108	0.858	0.377	1.954	0.716
	Completion of the administration of antibiotics within 3 hours	205	0.239	0.037	1.544	0.133
	Respiratory support					
	Mechanical ventilation	173	2.813	0.938	8.432	0.065
	High-flow nasal oxygen	38	0.182	0.036	0.925	0.040
	Additional ICU support					
	Vasopressors/inotropes	163	0.898	0.327	2.469	0.835
	Renal replacement therapy	101	3.544	1.470	8.540	0.005
	Red blood cell transfusion	93	0.611	0.258	1.450	0.264
	Platelet transfusion	50	1.384	0.537	3.570	0.501
	Fresh frozen plasma transfusion	58	1.425	0.572	3.550	0.446
	Surgical source control	25	0.659	0.182	2.380	0.524
	Non-surgical source control	78	0.322	0.132	0.782	0.012
	Constant		0.118			0.013
3	University affiliation					
	No	153	Reference			NA
	Yes	99	2.509	1.019	6.180	0.045
	Intensivist to patient ratio					
	1 intensivist : 5 or fewer patients	165	Reference			0.108
	1 intensivist : 6 to 8 patients	75	3.300	1.076	10.120	0.037
	1 intensivist : 12 or more patients	12	1.311	0.256	6.722	0.746
	Training program in ICU					

	No	50	Ref.			NA
	Yes	202	0.272	0.095	0.778	0.015
	Cardiovascular disease	78	2.043	0.881	4.741	0.096
	Chronic neurological disease	36	0.821	.243	2.776	0.751
	Solid malignant tumors	12	5.733	1.272	25.841	0.023
	SOFA					
	< 10	172	Ref.			NA
	≥ 10	78	2.957	1.285	6.806	0.011
	APACHE II					
	< 19	129	Ref.			NA
	≥ 19	123	1.604	0.674	3.817	0.285
	Urinary Tract	37	0.190	0.050	0.719	0.015
	Abdominal	61	0.856	0.318	2.307	0.759
	Skin or Cutaneous Sites	19	3.605	0.945	13.751	0.060
	Pathogens detection					
	No pathogens detected	67	1.277	0.333	4.893	0.721
	Gram-negative bacteria	156	1.405	0.432	4.570	0.572
	Completion of the administration of antibiotics within 1 hour	173	1.624	0.293	9.016	0.579
	Completion of the sepsis bundle within 3 hours	108	0.851	0.375	1.931	0.700
	Completion of the administration of antibiotics within 3 hours	205	0.240	0.037	1.553	0.134
	Respiratory support					
	Mechanical ventilation	173	2.722	.951	7.789	0.062
	High-flow nasal oxygen	38	0.181	.036	0.924	0.040
	Additional ICU support		3.464	1.478	8.117	0.004
	Renal replacement therapy	101	0.604	0.256	1.425	0.250
	Red blood cell transfusion	93	1.393	0.541	3.586	0.492
	Platelet transfusion	50	1.431	0.574	3.566	0.442
	Fresh frozen plasma transfusion	58	0.656	0.182	2.368	0.520
	Surgical source control	25	0.323	0.133	0.784	0.013
	Non-surgical source control	78	0.118			0.013
	Constant		0.118			0.013

4	University affiliation					
	No	153	Ref.			NA
	Yes	99	2.478	1.010	6.083	0.048
	Intensivist to patient ratio					
	1 intensivist : 5 or fewer patients	165	Ref.			0.112
	1 intensivist : 6 to 8 patients	75	3.255	1.064	9.957	0.039
	1 intensivist : 12 or more patients	12	1.303	0.253	6.710	0.751
	Training program in ICU					
	No	50	Ref.			NA
	Yes	202	0.269	0.094	0.768	0.014
	Cardiovascular disease	78	2.084	0.905	4.797	0.084
	Chronic neurological disease	36	0.822	0.242	2.793	0.754
	Solid malignant tumors	12	5.847	1.309	26.112	0.021
	SOFA					
	< 10	172	Ref.			NA
	≥ 10	78	2.880	1.274	6.511	0.011
	APACHE II					
	< 19	129	Ref.			NA
	≥ 19	123	1.632	0.690	3.861	0.265
	Urinary Tract	37	0.201	0.056	0.720	0.014
	Skin or Cutaneous Sites	19	3.688	0.969	14.039	0.056
	Pathogens detection					
	No pathogens detected	67	1.227	0.329	4.575	0.761
	Gram-negative bacteria	156	1.400	0.432	4.540	0.575
	Completion of the administration of antibiotics within 1 hour	173	1.580	0.286	8.710	0.600
	Completion of the sepsis bundle within 3 hours	108	0.844	0.373	1.909	0.684
	Completion of the administration of antibiotics within 3 hours	205	0.246	0.038	1.582	0.140
	Respiratory support					
	Mechanical ventilation	173	2.714	0.949	7.757	0.062
	High-flow nasal oxygen	38	0.187	0.037	0.940	0.042
	Additional ICU support					
	Renal replacement	101	3.332	1.478	7.513	0.004

	therapy					
	Red blood cell transfusion	93	.604	0.256	1.427	0.251
	Platelet transfusion	50	1.425	0.558	3.634	0.459
	Fresh frozen plasma transfusion	58	1.405	0.567	3.481	0.463
	Surgical source control	25	0.624	0.180	2.158	0.456
	Non-surgical source control	78	0.328	0.136	0.792	0.013
	Constant		0.118			0.013
5	University affiliation					
	No	153	Ref.			NA
	Yes	99	2.509	1.026	6.136	.044
	Intensivist to patient ratio					
	1 intensivist : 5 or fewer patients	165	Ref.			0.116
	1 intensivist : 6 to 8 patients	75	3.206	1.054	9.756	0.040
	1 intensivist : 12 or more patients	12	1.291	0.251	6.635	0.759
	Training program in ICU					
	No	50	Ref.			NA
	Yes	202	0.272	0.096	0.775	0.015
	Cardiovascular disease	78	2.036	0.898	4.615	0.089
	Chronic neurological disease	36	0.829	0.244	2.816	0.764
	Solid malignant tumors	12	5.850	1.314	26.056	0.020
	SOFA					
	< 10	172	Ref.			NA
	≥ 10	78	2.848	1.265	6.412	0.011
	APACHE II					
	< 19	129	Ref.			NA
	≥ 19	123	1.629	0.689	3.853	0.267
	Urinary Tract	37	0.205	0.058	0.725	0.014
	Skin or Cutaneous Sites	19	3.469	0.968	12.432	0.056
	Pathogens detection					
	Gram-negative bacteria	156	1.221	0.560	2.663	0.615
	Completion of the administration of antibiotics within 1 hour	173	1.592	0.289	8.754	0.593
	Completion of the sepsis bundle within 3 hours	108	0.836	0.370	1.885	0.665

	Completion of the administration of antibiotics within 3 hours	205	0.244	0.038	1.567	0.137
	Respiratory support					
	Mechanical ventilation	173	2.709	0.947	7.751	0.063
	High-flow nasal oxygen	38	0.191	0.038	0.950	0.043
	Additional ICU support					
	Renal replacement therapy	101	3.356	1.489	7.564	0.003
	Red blood cell transfusion	93	0.593	0.253	1.388	0.228
	Platelet transfusion	50	1.416	0.556	3.605	0.466
	Fresh frozen plasma transfusion	58	1.403	0.567	3.475	0.464
	Surgical source control	25	0.634	0.184	2.180	0.470
	Non-surgical source control	78	0.327	0.136	0.790	0.013
	Constant		0.137			0.004
6	University affiliation					
	No	153	Ref.			NA
	Yes	99	2.571	1.065	6.206	0.036
	Intensivist to patient ratio					
	1 intensivist : 5 or fewer patients	165	Ref.			0.109
	1 intensivist : 6 to 8 patients	75	3.251	1.071	9.872	0.037
	1 intensivist : 12 or more patients	12	1.285	0.250	6.610	0.764
	Training program in ICU					
	No	50	Ref.			NA
	Yes	202	0.276	0.098	0.780	0.015
	Cardiovascular disease	78	1.990	0.891	4.444	0.093
	Solid malignant tumors	12	6.020	1.364	26.577	0.018
	SOFA					
	< 10	172	Ref.			NA
	≥ 10	78	2.887	1.288	6.473	0.010
	APACHE II					
	< 19	129	Ref.			NA
	≥ 19	123	1.596	0.681	3.740	0.282
	Urinary Tract	37	0.202	0.057	0.711	0.013
	Skin or Cutaneous Sites	19	3.549	0.993	12.684	0.051

	Pathogens detection					
	Gram-negative bacteria	156	1.223	0.560	2.670	0.613
	Completion of the administration of antibiotics within 1 hour	173	1.614	0.293	8.895	0.582
	Completion of the sepsis bundle within 3 hours	108	0.834	0.370	1.881	0.662
	Completion of the administration of antibiotics within 3 hours	205	0.236	0.037	1.506	0.127
	Respiratory support					
	Mechanical ventilation	173	2.690	0.942	7.683	0.065
	High-flow nasal oxygen	38	0.186	0.038	0.923	0.040
	Additional ICU support					
	Renal replacement therapy	101	3.418	1.530	7.635	0.003
	Red blood cell transfusion	93	0.584	0.250	1.360	0.212
	Platelet transfusion	50	1.425	0.559	3.629	0.458
	Fresh frozen plasma transfusion	58	1.413	0.572	3.490	0.454
	Surgical source control	25	0.637	0.185	2.194	0.475
	Non-surgical source control	78	0.320	0.134	0.764	0.010
	Constant		0.133			0.003
7	University affiliation					
	No	153	Ref.			NA
	Yes	99	2.552	1.059	6.147	0.037
	Intensivist to patient ratio					
	1 intensivist : 5 or fewer patients	165	Ref.			0.119
	1 intensivist : 6 to 8 patients	75	3.055	1.044	8.936	0.041
	1 intensivist : 12 or more patients	12	1.177	0.241	5.750	0.840
	Training program in ICU					
	No	50	Ref.			NA
	Yes	202	0.273	0.096	0.771	0.014
	Cardiovascular disease	78	2.003	.897	4.474	0.090
	Solid malignant tumors	12	5.845	1.351	25.290	0.018
	SOFA					

	< 10	172	Ref.			NA
	≥ 10	78	2.858	1.279	6.385	0.010
	APACHE II					
	< 19	129	Ref.			NA
	≥ 19	123	1.598	0.682	3.742	0.280
	Urinary Tract	37	0.201	0.057	0.704	0.012
	Skin or Cutaneous Sites	19	3.628	1.018	12.937	0.047
	Pathogens detection					
	Gram-negative bacteria	156	1.229	0.563	2.679	0.605
	Completion of the administration of antibiotics within 1 hour	173	1.735	0.326	9.238	0.518
	Completion of the administration of antibiotics within 3 hours	205	.239	0.038	1.521	0.130
	Respiratory support					
	Mechanical ventilation	173	2.709	0.947	7.747	0.063
	High-flow nasal oxygen	38	0.198	0.041	0.951	0.043
	Additional ICU support					
	Renal replacement therapy	101	3.411	1.528	7.616	0.003
	Red blood cell transfusion	93	0.596	0.258	1.378	0.227
	Platelet transfusion	50	1.393	0.551	3.524	0.484
	Fresh frozen plasma transfusion	58	1.449	0.592	3.550	0.417
	Surgical source control	25	0.653	0.191	2.230	0.497
	Non-surgical source control	78	0.322	0.135	0.769	0.011
	Constant		0.123			0.002
8	University affiliation					
	No	153	Ref.			NA
	Yes	99	2.564	1.064	6.175	0.036
	Intensivist to patient ratio					
	1 intensivist : 5 or fewer patients	165	Ref.			0.107
	1 intensivist : 6 to 8 patients	75	3.128	1.073	9.113	0.037
	1 intensivist : 12 or more patients	12	1.195	0.246	5.798	0.825
	Training program in ICU					

	No	50	Ref.			NA
	Yes	202	0.272	0.096	0.768	0.014
	Cardiovascular disease	78	2.040	0.916	4.543	0.081
	Solid malignant tumors	12	5.796	1.343	25.024	0.019
	SOFA					
	< 10	172	Ref.			NA
	≥ 10	78	2.820	1.266	6.282	0.011
	APACHE II					
	< 19	129	Ref.			NA
	≥ 19	123	1.578	0.676	3.683	0.292
	Urinary Tract	37	0.201	0.057	0.707	0.012
	Skin or Cutaneous Sites	19	3.434	0.981	12.023	0.054
	Completion of the administration of antibiotics within 1 hour	173	1.625	0.314	8.406	0.562
	Completion of the administration of antibiotics within 3 hours	205	0.249	0.040	1.552	0.136
	Respiratory support					
	Mechanical ventilation	173	2.821	0.997	7.981	0.051
	High-flow nasal oxygen	38	0.201	0.042	0.963	0.045
	Additional ICU support					
	Renal replacement therapy	101	3.429	1.538	7.645	0.003
	Red blood cell transfusion	93	0.618	0.271	1.409	0.252
	Platelet transfusion	50	1.384	0.549	3.492	0.491
	Fresh frozen plasma transfusion	58	1.477	.604	3.609	0.392
	Surgical source control	25	0.667	0.195	2.282	0.519
	Non-surgical source control	78	0.332	0.140	0.786	0.012
	Constant		0.133			0.002
9	University affiliation					
	No	153	Ref.			NA
	Yes	99	2.518	1.049	6.042	0.039
	Intensivist to patient ratio					
	1 intensivist : 5 or fewer patients	165	Ref.			0.115
	1 intensivist : 6 to 8 patients	75	3.042	1.050	8.811	0.040

	1 intensivist : 12 or more patients	12	1.151	0.239	5.554	0.861
	Training program in ICU					
	No	50	Ref.			NA
	Yes	202	0.282	0.101	0.788	0.016
	Cardiovascular disease	78	2.010	0.905	4.464	0.086
	Solid malignant tumors	12	5.854	1.368	25.056	0.017
	SOFA					
	< 10	172	Ref.			NA
	≥ 10	78	2.858	1.287	6.346	0.010
	APACHE II					
	< 19	129	Ref.			NA
	≥ 19	123	1.590	0.683	3.700	0.282
	Urinary Tract	37	0.207	0.059	0.727	0.014
	Skin or Cutaneous Sites	19	3.541	1.009	12.428	0.048
	Completion of the administration of antibiotics within 3 hours	205	0.381	0.126	1.158	0.089
	Respiratory support					
	Mechanical ventilation	173	2.862	1.012	8.090	0.047
	High-flow nasal oxygen	38	0.200	0.042	0.954	0.043
	Additional ICU support					
	Renal replacement therapy	101	3.380	1.515	7.538	0.003
	Red blood cell transfusion	93	0.612	0.268	1.397	0.244
	Platelet transfusion	50	1.390	0.553	3.492	0.484
	Fresh frozen plasma transfusion	58	1.464	0.599	3.575	0.403
	Surgical source control	25	0.690	0.203	2.347	0.553
	Non-surgical source control	78	0.331	0.140	.784	0.012
	Constant		0.133			0.002
10	University affiliation					
	No	153	Ref.			NA
	Yes	99	2.422	1.020	5.752	0.045
	Intensivist to patient ratio					
	1 intensivist : 5 or fewer patients	165	Ref.			0.106
	1 intensivist : 6 to 8 patients	75	3.115	1.077	9.013	0.036

	1 intensivist : 12 or more patients	12	1.195	0.250	5.713	0.824
	Training program in ICU					
	No	50	Ref.			NA
	Yes	202	0.279	0.100	0.778	0.015
	Cardiovascular disease	78	2.035	0.920	4.503	0.080
	Solid malignant tumors	12	5.880	1.367	25.293	0.017
	SOFA					
	< 10	172	Ref.			NA
	≥ 10	78	2.853	1.287	6.324	0.010
	APACHE II					
	< 19	129	Ref.			NA
	≥ 19	123	1.616	0.697	3.747	0.263
	Urinary Tract	37	0.205	0.058	.719	0.013
	Skin or Cutaneous Sites	19	3.452	1.002	11.897	0.050
	Completion of the administration of antibiotics within 3 hours	205	0.378	0.125	1.143	0.085
	Respiratory support					
	Mechanical ventilation	173	2.854	1.009	8.070	0.048
	High-flow nasal oxygen	38	0.205	0.043	0.977	0.047
	Additional ICU support					
	Renal replacement therapy	101	3.464	1.561	7.691	0.002
	Red blood cell transfusion	93	0.599	0.264	1.358	0.220
	Platelet transfusion	50	1.394	0.556	3.494	0.479
	Fresh frozen plasma transfusion	58	1.467	0.601	3.585	0.400
	Non-surgical source control	78	0.333	0.140	0.789	0.012
	Constant		0.129			0.001
11	University affiliation					
	No	153	Ref.			NA
	Yes	99	2.581	1.108	6.011	0.028
	Intensivist to patient ratio					
	1 intensivist : 5 or fewer patients	165	Ref.			0.109
	1 intensivist : 6 to 8 patients	75	3.074	1.064	8.886	0.038
	1 intensivist : 12 or	12	1.112	0.237	5.207	0.893

	more patients					
	Training program in ICU					
	No	50	Ref.			NA
	Yes	202	0.269	0.097	0.747	0.012
	Cardiovascular disease	78	1.999	0.905	4.414	0.087
	Solid malignant tumors	12	5.912	1.384	25.250	0.016
	SOFA					
	< 10	172	Ref.			NA
	≥ 10	78	2.913	1.318	6.435	0.008
	APACHE II					
	< 19	129	Ref.			NA
	≥ 19	123	1.596	0.691	3.687	0.274
	Urinary Tract	37	0.215	0.062	0.746	0.015
	Skin or Cutaneous Sites	19	3.527	1.029	12.091	0.045
	Completion of the administration of antibiotics within 3 hours	205	0.369	0.122	1.111	0.076
	Respiratory support					
	Mechanical ventilation	173	2.892	1.022	8.188	0.045
	High-flow nasal oxygen	38	0.203	0.043	0.963	0.045
	Additional ICU support					
	Renal replacement therapy	101	3.524	1.591	7.808	0.002
	Platelet transfusion	50	0.646	0.294	1.419	0.277
	Fresh frozen plasma transfusion	58	1.567	0.657	3.735	0.311
	Non-surgical source control	78	0.322	0.136	0.759	0.010
	Constant		0.133			0.002
12	University affiliation					
	No	153	Ref.			NA
	Yes	99	2.431	1.058	5.588	0.036
	Intensivist to patient ratio					
	1 intensivist : 5 or fewer patients	165	Ref.			0.117
	1 intensivist : 6 to 8 patients	75	3.020	1.051	8.677	0.040
	1 intensivist : 12 or more patients	12	1.182	0.252	5.547	0.833
	Training program in ICU					
	No	50	Ref.			NA

	Yes	202	0.298	0.111	0.803	0.017
	Cardiovascular disease	78	1.969	0.897	4.322	0.091
	Solid malignant tumors	12	5.678	1.355	23.795	0.018
	SOFA					
	< 10	172	Ref.			NA
	≥ 10	78	3.035	1.378	6.684	0.006
	APACHE II					
	< 19	129	Ref.			NA
	≥ 19	123	1.571	0.683	3.609	0.288
	Urinary Tract	37	0.241	0.073	0.800	0.020
	Skin or Cutaneous Sites	19	3.518	1.019	12.146	0.047
	Completion of the administration of antibiotics within 3 hours	205	.354	0.118	1.060	0.064
	Respiratory support					
	Mechanical ventilation	173	2.888	1.021	8.170	0.046
	High-flow nasal oxygen	38	0.194	0.041	0.912	0.038
	Additional ICU support					
	Renal replacement therapy	101	3.725	1.694	8.192	0.001
	Platelet transfusion	50	0.715	0.334	1.531	0.388
	Non-surgical source control	78	0.333	0.142	0.781	0.011
	Constant		0.132			0.001
13	University affiliation					
	No	153	Ref.			NA
	Yes	99	2.375	1.035	5.448	0.041
	Intensivist to patient ratio					
	1 intensivist : 5 or fewer patients	165	Ref.			0.123
	1 intensivist : 6 to 8 patients	75	2.983	1.037	8.576	0.043
	1 intensivist : 12 or more patients	12	1.189	.252	5.610	0.827
	Training program in ICU					
	No	50	Ref.			NA
	Yes	202	0.298	0.111	0.801	0.016
	Cardiovascular disease	78	1.987	0.907	4.352	0.086
	Solid malignant tumors	12	5.332	1.285	22.125	0.021
	SOFA					
	< 10	172	Ref.			NA

	≥ 10	78	2.958	1.347	6.497	0.007
	APACHE II					
	< 19	129	Ref.			NA
	≥ 19	123	1.601	0.697	3.680	0.268
	Urinary Tract	37	0.244	0.075	0.798	0.020
	Skin or Cutaneous Sites	19	3.524	1.029	12.061	0.045
	Completion of the administration of antibiotics within 3 hours	205	0.370	0.126	1.088	0.071
	Respiratory support					
	Mechanical ventilation	173	2.736	0.976	7.669	0.056
	High-flow nasal oxygen	38	0.203	0.043	0.950	0.043
	Additional ICU support					
	Renal replacement therapy	101	3.332	1.586	7.000	0.001
	Non-surgical source control	78	0.328	0.140	0.767	0.010
	Constant		0.129			0.001
14	University affiliation					
	No	153	Ref.			NA
	Yes	99	2.474	1.085	5.643	0.031
	Intensivist to patient ratio					
	1 intensivist : 5 or fewer patients	165	Ref.			0.165
	1 intensivist : 6 to 8 patients	75	2.591	0.945	7.101	0.064
	1 intensivist : 12 or more patients	12	0.929	0.212	4.076	0.923
	Training program in ICU					
	No	50	Ref.			NA
	Yes	202	0.287	0.107	0.769	0.013
	Cardiovascular disease	78	2.140	.989	4.630	0.053
	Solid malignant tumors	12	4.904	1.197	20.082	0.027
	SOFA					
	< 10	172	Ref.			NA
	≥ 10	78	3.194	1.473	6.925	0.003
	Urinary Tract	37	0.259	0.080	0.838	0.024
	Skin or Cutaneous Sites	19	3.642	1.079	12.295	0.037
	Completion of the administration of antibiotics within 3 hours	205	0.360	0.123	1.055	0.063

	Respiratory support					
	Mechanical ventilation	173	3.156	1.159	8.593	0.025
	High-flow nasal oxygen	38	0.211	0.045	0.992	0.049
	Additional ICU support					
	Renal replacement therapy	101	3.504	1.675	7.331	0.001
	Non-surgical source control	78	0.311	0.134	0.719	0.006
	Constant		0.151			0.002
15	University affiliation					
	No	153	Ref.			NA
	Yes	99	2.580	1.167	5.703	0.019
	Training program in ICU					
	No	50	Ref.			NA
	Yes	202	0.297	0.110	0.802	0.017
	Cardiovascular disease	78	2.088	0.973	4.478	0.059
	Solid malignant tumors	12	4.586	1.141	18.434	0.032
	SOFA					
	< 10	172	Ref.			NA
	≥ 10	78	2.840	1.347	5.985	0.006
	Urinary Tract	37	0.277	0.087	0.880	0.030
	Skin or Cutaneous Sites	19	2.937	0.928	9.289	0.067
	Completion of the administration of antibiotics within 3 hours	205	0.326	0.115	0.923	0.035
	Respiratory support					
	Mechanical ventilation	173	2.765	1.041	7.345	0.041
	High-flow nasal oxygen	38	0.432	0.116	1.618	0.213
	Additional ICU support					
	Renal replacement therapy	101	3.302	1.604	6.799	0.001
	Non-surgical source control	78	0.382	.174	0.840	0.017
	Constant		0.200			0.006
16	University affiliation					
	No	153	Ref.			NA
	Yes	99	2.562	1.164	5.639	0.019
	Training program in ICU					
	No	50	Ref.			NA
	Yes	202	0.267	0.100	0.713	0.008

	Cardiovascular disease	78	2.047	0.954	4.391	0.066
	Solid malignant tumors	12	4.630	1.130	18.970	0.033
	SOFA					
	< 10	172	Ref.			NA
	≥ 10	78	2.801	1.332	5.891	0.007
	Urinary Tract	37	0.276	0.087	0.878	0.029
	Skin or Cutaneous Sites	19	3.074	0.982	9.629	0.054
	Completion of the administration of antibiotics within 3 hours	205	0.344	0.122	0.970	0.044
	Respiratory support					
	Mechanical ventilation	173	3.086	1.180	8.072	0.022
	Additional ICU support					
	Renal replacement therapy	101	3.433	1.669	7.058	0.001
	Non-surgical source control	78	0.385	0.175	0.842	0.017
	Constant		0.182			0.004

Abbreviations: **AOR**: adjusted odds ratio; **APACHE II**, Acute Physiology and Chronic Health Examination II; **CI**: confidence interval; **ICU**, intensive care unit; **NA**: not available; **Ref.**, reference; **SOFA**, Sequential (Sepsis-Related) Organ Failure Assessment.

Table S19. Breakdown of missing data

Variables	Number of patients with missing data
Hospital characteristics	
Type of hospital	0
University affiliation	0
ICU characteristics	
Nature of ICU	0
Type of ICU	0
Nurse to patient ratio	0
Intensivist to patient ratio	0
Training programme in ICU	0
Baseline characteristics	
Age (year)	0
Sex	0
Collection batch	0

Admission type	0
Admission source	0
Comorbidities	0
Vital signs (on admission into ICU)	
GCS	1
HR (beats per min)	0
Temperature (^{o}C)	0
MBP (mmHg), mean(SD)	0
SBP (mmHg), mean (SD)	0
RR (breaths per min), median (IQR)	0
Blood investigations	
Total WBC (x10^9/L)	0
PLT (x10^9/L)	0
Hb (g/dL)	1
Hct (%)	0
K^+ (mmol/L)	0
Na^+ (mmol/L)	0
Creatinine (µmol/L)	0
Bilirubin (µmol/l)	20
pH, mean (SD)	3
PaO_2 (mmHg)	8
FiO_2 (mmHg)	7
PaO_2/FiO_2 ratio	9
Severity of illness scores	
qSOFA	0
SIRS	0
SOFA	2
APACHE II	0
Site of Infection	
Respiratory	0
Urinary tract	0
Abdominal	0

Neurological	0
Bones or joints	0
Skin or cutaneous sites	0
Intravascular catheter	0
Infective endocarditis	0
Primary bacteraemia	0
Systemic	0
Measurements around time zero	
Blood culture	0
Lactate measurement	0
Antibiotic administration	0
Fluid bolus	2
Resources used in ICU (anytime during ICU stay)	
Vasopressors/Intropes	0
Mechanical ventilation	1
Noninvasive ventilation	1
High-flow nasal cannula	1
Renal replacement therapy	1
Red blood cell transfusion	1
Platelet transfusion	1
Fresh frozen plasma transfusion	1
Surgical source control	1
Non-surgical source control	1
In-hospital time course (DD/MM/YY (HHMM))	
Admission date to the hospital	0
Admission date to the ICU	0
Time zero	0
Time of blood culture	2
Time of lactate measurement	1
Time of antibiotic administration	2

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Time of starting vasopressor	3
Time of first source control measure	0
Discharge date from current ICU stay or death date in your current ICU stay	1
Discharge date from current hospital stay or death date in your current hospital stay	1