Supplementary Material

Interpretable machine learning for early prediction of prognosis in sepsis: a discovery and validation study

Chang Hu, MD1,2*, Lu Li, MD1,2*, Weipeng Huang, MD1,2, Tong Wu, MD1,2, Qiancheng Xu, MD1,2, Juan Liu, PhD3#, Bo Hu, MD1,2#

1 Department of Critical Care Medicine, Zhongnan Hospital of Wuhan University, Wuhan 430071, Hubei, China
2 Clinical Research Center of Hubei Critical Care Medicine, Wuhan 430071, Hubei, China
3 School of Computer Science, Wuhan University, Wuhan 430072, Hubei, China

Email addresses: huchang@whu.edu.cn (Chang Hu), lulu189vip@163.com (Lu Li), huang7@whu.edu.cn (Weipeng Huang), annie_wutong@foxmail.com (Tong Wu), qianchengxu@whu.edu.cn (Qiancheng Xu), liujuan@whu.du.cn (Juan Liu), hobbier1979@163.com (Bo Hu)

* Chang Hu and Lu Li contributed equally and share the first authorship

#Corresponding Author:
Correspondence to: Bo Hu, MD; Zhongnan Hospital of Wuhan University; Wuhan 430071, Hubei, China; Email: hobbier1979@163.com
And also correspondence to: Juan Liu, PhD; School of Computer Science, Wuhan University, Wuhan 430072, Hubei, China; Email: liujuan@whu.edu.cn

Supplementary Tables and Figures cited in main text

- Table S1: All extracted variables in MIMIC-IV database (N=57).

- Table S2: Clinical features used for developing the models (N=25).

- Figure S1. Diagnostic criteria for sepsis.

- Figure S2. Study flowchart.

- Figure S3. Percentages of missing data for all included variables.

- Figure S4. Feature selection using the LASSO regression model.

- Figure S5. Calibration curve for in-hospital mortality for validation cohort in XGBoost.

Table S1. All extracted variables in MIMIC-IV database (N=57).

Variable	Category
Age	**Demographic characteristics (4)**
Gender	
Body weight	
Height	
Hypertension	**Medical history (9)**
Diabetes	
Congestive heart failure	
Cerebrovascular disease	
Chronic pulmonary disease	
Liver disease	
Renal disease	
Tumor	
Acquired immune deficiency syndrome	
Heart rate	**Vital signs (7)**
Systolic blood pressure	
Diastolic blood pressure	
Mean artery pressure	
Respiratory rate	
Body temperature	
SPO_2	
Blood glucose	**Laboratory findings (32)**
Lactate	
pH	
PCO_2	
PO_2	
Base excess	
White blood cell	
Anion gap	
Bicarbonate	
Blood urea nitrogen	
Serum calcium	
Serum chloride	
Serum creatinine	
Serum sodium	
Serum potassium	
Serum fibrinogen	
International normalized ratio	
Prothrombin time	
Partial thromboplastin time	
Alanine aminotransferase	
Alkaline phosphatase	

Aspartate aminotransferase	
Total bilirubin	
Amylase	
Creative phosphokinase	
Creatine kinase MB	
Lactate dehydrogenase	
Pao2/Fio2 ratio	
Hematocrit	
Hemoglobin	
Platelets	
Albumin	
Antibiotic	**Medical treatments (3)**
Ventilation	
Vasopressor	
Urine output	**Urine (1)**
GCS	**Severity of illness scores (1)**

GCS, Glasgow Coma Scale

Table S2. Clinical features used for developing the models (N=25).

Age	**Demographic characteristics (3)**
Body weight	
Height	
Hypertension	**Medical history (4)**
Cerebrovascular disease	
Liver disease	
Tumor	
Heart rate	**Vital signs (5)**
Systolic blood pressure	
Respiratory rate	
Body temperature	
SPO$_2$	
Lactate	**Laboratory findings (9)**
pH	
PO$_2$	
Hematocrit	
Anion gap	
Blood urea nitrogen	
International normalized ratio	
Prothrombin time	
Partial thromboplastin time	
Ventilation	**Medical treatments (2)**
Vasopressor	
Urine output	**Urine (1)**
GCS	**Severity of illness scores (1)**

GCS, Glasgow Coma Scale

Figure S1. Diagnostic criteria for sepsis.
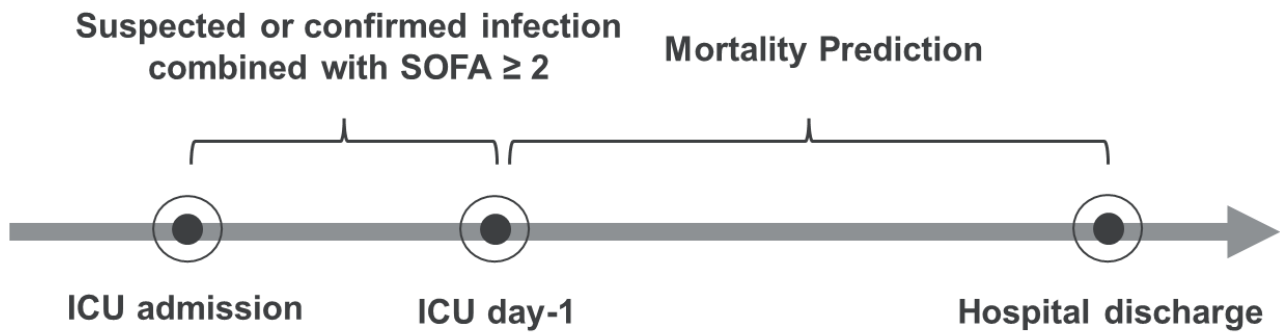
Patients were diagnosed with sepsis using the Sepsis-3 criteria in the first 24 hours of ICU admission: (i) with confirmed or suspected infection and (ii) with 2 or more SOFA points. Abbreviations: SOFA, Sequential Organ Failure Assessment; ICU, intensive care unit.
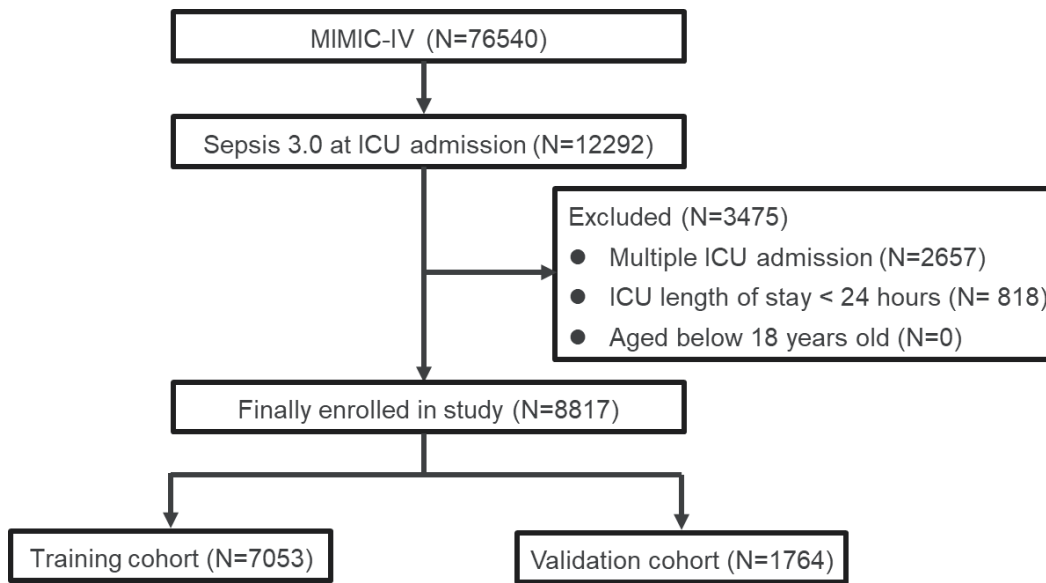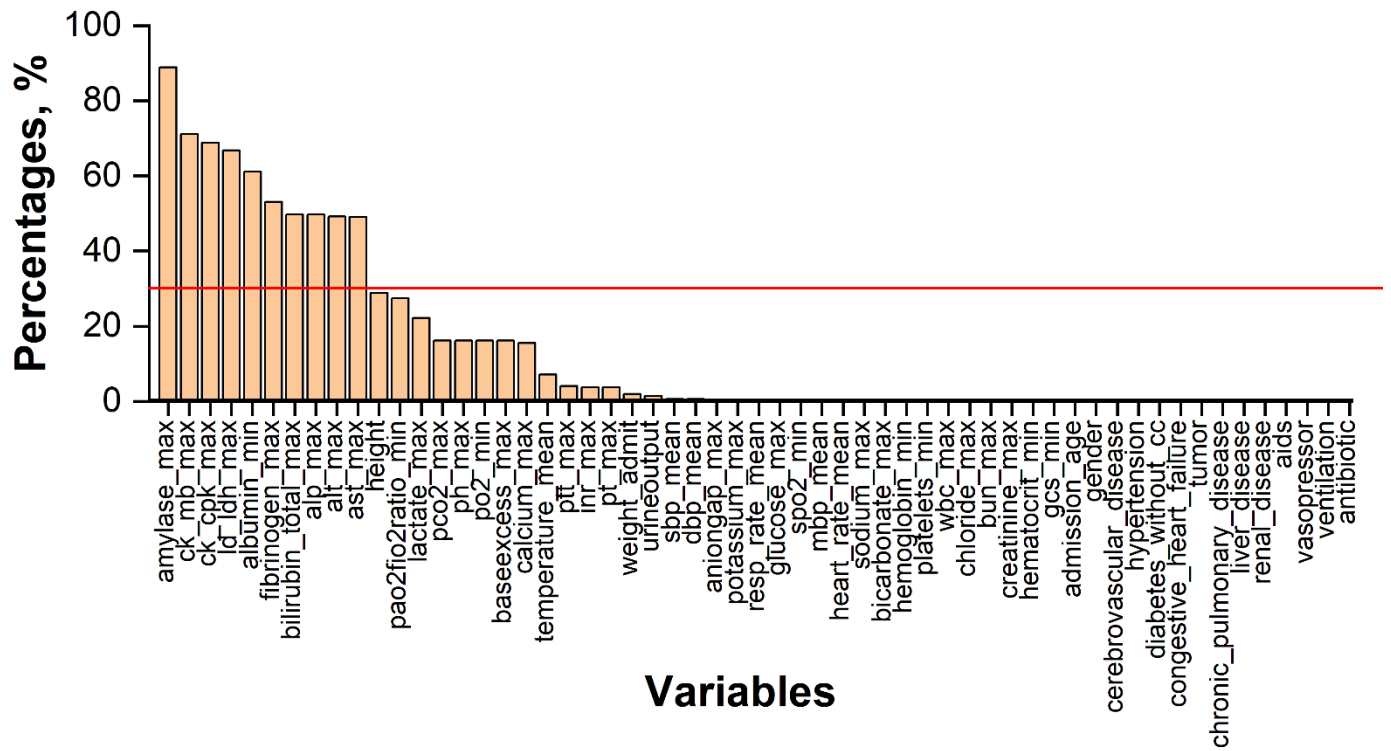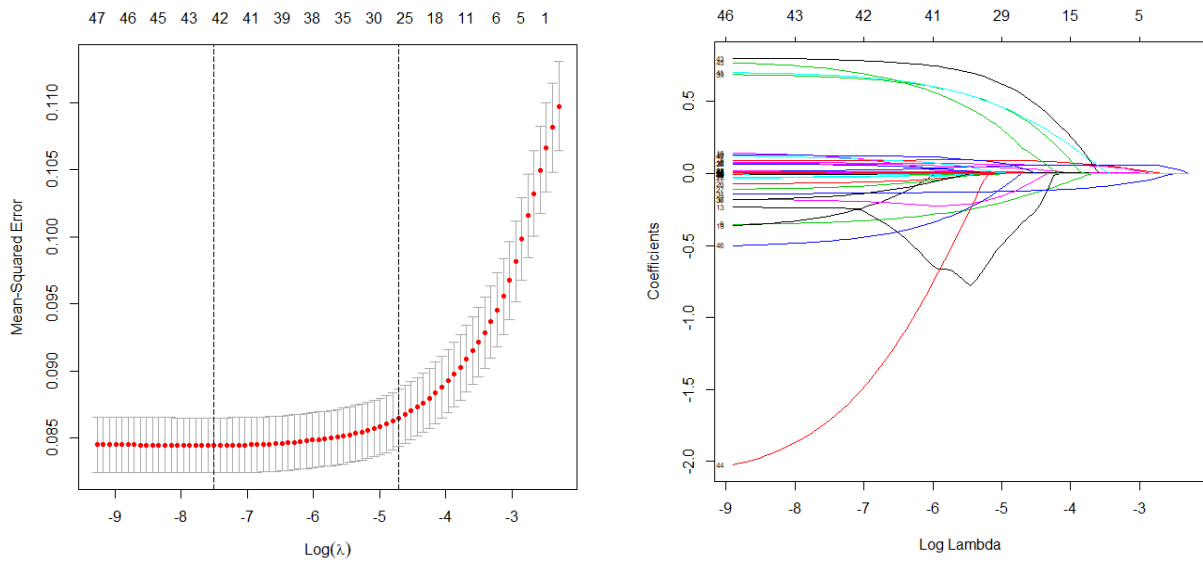
Figure S2. Study flowchart.

Figure S3. Percentages of missing data for all included variables.

Variables with above 30% missing values were removed from further analysis.

**Figure S4. Feature selection using the LASSO regression model.**

(A) LASSO coefficient profiles of the 47 baseline features.

(B) Tuning parameter (λ) selection in the LASSO model used 5-fold cross-validation via minimum criteria.

LASSO, least absolute shrinkage and selection operator.

Figure S5. Calibration curve for in-hospital mortality for validation cohort in XGBoost.
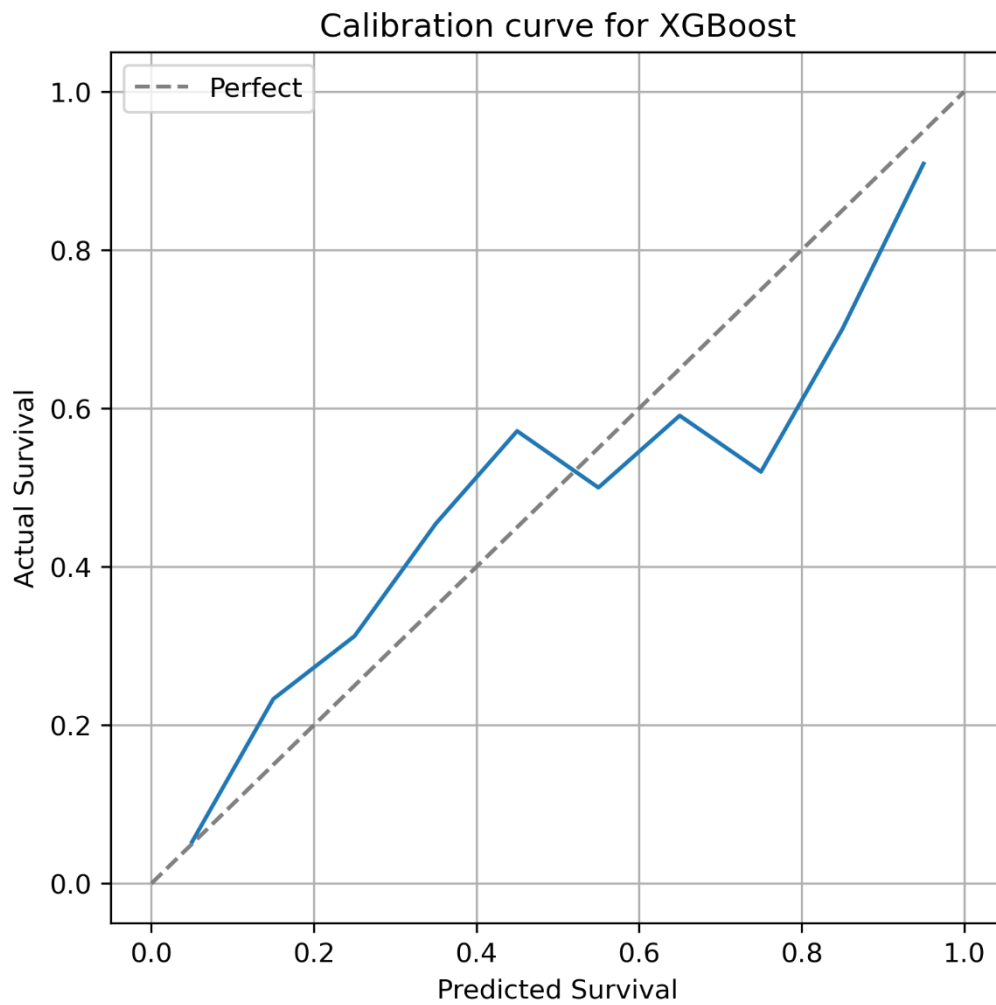
The dotted line indicates the ideal reference line where predicted probabilities would match the observed survival rates. The blue line represents the performance of the XGBoost. The closer the blue line is to the dotted line, the more accurately the model predicts in-hospital mortality.

XGBoost, eXtreme Gradient Boosting.