**Supplemental Material**

**e-Appendix1**

*Description of risk model development, variable selection, and transformation*

We developed four independent logistic regression models for the following outcomes: hospital mortality, 30-day mortality, 90-day mortality, and a composite of >72-hour ICU stay or hospital mortality. Variables we collected including sociodemographic and clinical characteristics (e.g., age, gender, race, insurance, clinical orders, laboratory values, vital signs in 24 hours from admission, diagnoses, and prior healthcare utilization), as well as variables collected for calculation of qSOFA, weighted Charlson Comorbidity index (CCI) score.

*Variable Manipulation*

We transformed all vital signs and laboratory values variables due to their longitudinal characteristics, i.e., multiple values recorded or ordered over time and missing value phenomenon. We used the following logic for variable transformation in all models:

1. Number of Abnormal Measurements Ratio in 24 hours from ED Admission:

The ratio was defined as number of abnormal measurements divided by total number of measurements within 24 hours from ED admission.

1. Converting continuous value variables to categorical variables:

We calculated 1st quantile, median, mean, 3rd quantile for both in-hospital morality and discharged survival patients’ group, and then categorized continuous variables to categorical variables based on those calculated values.

1. Missing value imputation:

We determined the frequency of missing data for each element. For variables with less than or equal to 1% missing data, we imputed mean value according to age at admission, gender, race, CCI, and BMI group (e-Table 1). To account for informative missingness, we converted variables with greater than 1% missing values to categorical format and classified missing values as “Not Available”.

We utilized backward elimination to select significant variables for all four models. Total number of variables was 183, and 78 of which were selected in Died in Hospital model, 87 of which were selected in Died-HOSP/ICU72 model, 84 of which were selected in Died30 model, and 99 of which were selected in Died90 model. Details regarding to selected variables for each model are shown in e-Table 2.

**ICU**

**1**

**3**

**4**

**Admission**

**Discharge**

**30d**

**90d**

**2: Composite**

**e-Figure 1**. Four competing outcome definitions: 1) Hospital mortality; 2) Composite of hospital mortality or intensive care unit length of stay >72 hours; 3) 30-day mortality; and 4) 90-day mortality

**e-Table 1.** Comprehensive characteristics of clinically suspected infection study cohort and number of missing values (%) for all variables.

|  |  |  |
| --- | --- | --- |
| **Variable** | **Overall** | **Missing, n (%)** |
| **Male Gender, n (%)** | 23868 (45.7)  | 0(0) |
| **Age at Admission, median (IQR)** | 60 [46, 71] | 0(0) |
| **Race, n (%)** |  | 335(0.64) |
|  Black | 13485 (25.8)  |  |
|  White | 35661 (68.3)  |  |
|  Other |  3038 (5.8)  |  |
| **Marital Status, n (%)** |  | 734(1.41) |
| Single | 16394 (31.4)  |  |
| Married | 19938 (38.2)  |  |
| Separated |  1918 (3.7)  |  |
| Divorced |  5728 (11.0)  |  |
| Widowed |  7472 (14.3)  |  |
| Unknown |  734 (1.4)  |  |
| **Insurance, n (%)** |  | 232(0.44) |
| Medicaid |  8820 (16.9)  |  |
| Medicare | 27125 (52.0)  |  |
| Commercial | 11242 (21.5)  |  |
| Self-Pay |  4331 (8.3)  |  |
| Other**/**Unknown |  666 (1.3) |  |
| **Facility, n (%)** |  | 0(0) |
|  Carolinas Medical Center | 12130 (23.2)  |  |
|  CMC Mercy |  4732 (9.1)  |  |
|  AH Anson |  113 (0.2)  |  |
|  AH Blue Ridge |  3835 (7.3)  |  |
|  AH Cleveland |  4113 (7.9)  |  |
|  AH Kings Mountain |  916 (1.8)  |  |
|  AH Lincoln |  3228 (6.2)  |  |
|  AH Northeast |  9255 (17.7)  |  |
|  AH Pineville |  6305 (12.1)  |  |
|  AH Stanly |  673 (1.3)  |  |
|  AH Union |  4006 (7.7)  |  |
|  AH University |  2878 (5.5)  |  |
| **ED Acuity, n (%)** |  | 8390(16.08) |
|  Nonurgent |  37 (0.1)  |  |
|  Emergent | 18597 (35.6)  |  |
|  Less Urgent |  1176 (2.3)  |  |
|  Urgent | 22840 (43.8)  |  |
|  Resuscitation |  1144 (2.2)  |  |
|  Unknown |  8390 (16.1)  |  |
| **BMI, median (IQR)** | 28.1 [23.7, 33.8]  | 26(0.05) |
| **Indicator of Any Encounter within Past 1 year with Charlson Comorbidity Diagnosis, n (%)** |  | 0(0) |
| Myocardial infarction |  4495 (8.6)  |  |
| Congestive heart failure |  8297 (15.9)  |  |
| Peripheral Arterial Disease |  6246 (12.0)  |  |
| Cerebrovascular  |  5694 (10.9)  |  |
| Dementia  |  2215 (4.2)  |  |
| Chronic obstructive pulmonary disease  | 17681 (33.9)  |  |
| Connective Tissue Disorder  |  2595 (5.0)  |  |
| Ulcerative Disease  |  1466 (2.8)  |  |
| Mild Liver Disease  |  6102 (11.7)  |  |
| Diabetes with No Complications  | 17056 (32.7)  |  |
| Diabetes with Complications  |  6376 (12.2)  |  |
| Hemiplegia  |  1975 (3.8)  |  |
| Renal  |  9911 (19.0)  |  |
| Malignancy  |  6563 (12.6)  |  |
| Moderate Liver Disease  |  1563 (3.0)  |  |
| Metastatic Solid  |  2225 (4.3)  |  |
| HIV/AIDS  |  963 (1.8)  |  |
| **Physiologic Measures and Laboratory Values, median (IQR)** |  |
| Minimum SBP | 102.0 [90.0, 115.0] | 16(0.03) |
| Maximum Temperature | 99.2 [98.6, 100.7] | 118(0.23) |
| Minimum MAP | 71.3 [62.0, 80.3] | 18(0.03) |
| Maximum WBC | 12.1 [8.6, 16.6] | 327(0.63) |
| Maximum Respiratory rate  |  23.0 [20.0, 28.0] | 5(0.01) |
| Minimum O2Sat | 93.0 [90.0, 95.0] | 10(0.02) |
| Minimum Platelets | 211.0 [156.0, 274.0] | 393(0.75) |
| Maximum Potassium  |  4.1 [3.8, 4.6] | 279(0.53) |
| Maximum Pulse  | 107.0 [94.0, 122.0] | 3(0.01) |
| Maximum Sodium  | 138.0 [136.0, 141.0] | 280(0.54) |
| Minimum GCS | 15.0 [14.0, 15.0] | 144(0.28) |
| Maximum BUN  | 18.0 [12.0, 29.0] | 377(0.72) |
| Maximum Chloride  | 104.0 [101.0, 108.0] | 280(0.54) |
| Minimum CO2  | 24.0 [21.0, 26.0] | 310(0.59) |
| Maximum Creatinine  |  1.1 [0.8, 1.6] | 293(0.56) |
| Maximum Glucose  | 146.0 [115.0, 210.0] | 237(0.45) |
| Minimum Hematocrit  | 34.0 [30.0, 39.0] | 198(0.38) |
| Minimum HGB  | 11.3 [9.7, 12.8] | 197(0.38) |
| Minimum MCH  | 29.0 [28.0, 31.0] | 334(0.64) |
| Maximum MCHC  | 33.0 [33.0, 34.0] | 290(0.56) |
| Minimum MCV  | 89.0 [85.0, 93.0] | 329(0.63) |
| Maximum MPV  |  8.6 [7.9, 9.4] | 344(0.66) |
| Minimum RBC  |  3.9 [3.4, 4.4] | 329(0.63) |
| Maximum RDW  | 14.9 [13.8, 16.6] | 330(0.63) |
| Maximum Lactate  |  1.7 [1.2, 2.8] | 19696(37.74) |
| Maximum BNP  | 193.0 [69.0, 515.0] | 40025(76.7) |
| Maximum AST  | 28.0 [20.0, 45.0] | 11387(21.82) |
| Maximum ALT  | 23.0 [16.0, 37.0] | 11490(22.02) |
| Minimum Albumin |  3.0 [2.6, 3.5] | 10949(20.98) |
| Maximum Calcium  |  8.8 [8.4, 9.2] | 2077(3.98) |
| Maximum Troponin  |  0.0 [0.0, 0.1] | 30953(59.32) |
| Maximum PTT  | 30.9 [27.6, 36.0] | 50571(96.91) |
| Maximum Pain  |  8.0 [7.0, 10.0] | 13255(25.4) |
| Minimum Braden | 19.0 [16.0, 21.0] | 1834(3.51) |
| Maximum Shock index  |  0.9 [0.7, 1.1] | 35337(67.72) |
| Maximum FiO2  |  28.0 [21.0, 85.0] | 33559(64.31) |
| Maximum ALP  | 85.0 [66.0, 116.0] | 11382(21.81) |
|  |  |  |
| Maximum CRP  |  1.6 [0.6, 4.2] | 48954(93.81) |
| Maximum CVP  |  15.0 [11.0, 20.0] | 50038(95.89) |
| Maximum FALL RISK SCORE, n (%) |  | 906(1.7) |
|  No Risk | 3505 (6.7) |  |
|  Low Risk | 22673 (43.4) |  |
|  High Risk | 25100 (48.1) |  |
| Maximum INR  |  1.2 [1.1, 1.4] | 28956(55.49) |
| Minimum PaO2 |  38.0 [28.0, 56.0] | 23530(45.09) |
| Maximum Eosinophils |  1.0 [0.0, 2.0] | 7518(14.41) |
| Maximum Basophils  |  0.0 [0.0, 1.0] | 7550(14.47) |
| Maximum Lymphocytes  | 13.0 [8.0, 21.0] | 7416(14.21) |
| Maximum Monocytes  |  7.0 [5.0, 10.0] | 7423(14.22) |
| Maximum Neutrophils  |  80.0 [70.0, 87.0] | 7508(14.39) |
| \* Physiologic measures and laboratory values captured within 24 hours from Emergency Department presentation.\*Abbreviations: ED=Emergency Department; BMI=Body Mass Index; qSOFA= Quick Sepsis Related Organ Failure Assessment; CCI=Charlson Comorbidity Index Score; HIV/AIDS=Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome; SBP=Systolic Blood Pressure; MAP=Mean Arterial Pressure; WBC=White Blood Cell Count; O2Sat=O2 Saturation; GCS=Glasgow Coma Scale; BUN=Blood Urea Nitrogen; CO2=Carbon Dioxide; HGB=Hemoglobin; MCH=Mean Corpuscular Hemoglobin; MCHC=Mean Corpuscular Hemoglobin Concentration; MCV=Mean Corpuscular Volume; MPV=Mean Platelet Volume; RBC=Red Blood Cell Count; RDW=Red Blood Cell Distribution Width; BNP=Brain Natriuretic Peptide; AST=Aspartate Aminotransferase Test; ALT=Alanine Aminotransferase; PTT=Partial Thromboplastin Time; FiO2=Fraction Inspired O2; ALP=Alkaline Phosphatase; CRP=C-Reactive Protein; CVP=Central Venous Pressure; GGT=Gamma-Glutamyl Transpeptidase; INR=International Normalized Ratio; PaO2=Partial Pressure of Carbon Dioxide;  |

**e-Table 2**. Variables Selected for each Model by Backward Elimination.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Variable | Died in Hospital | Died in Hospital or >72-hour ICU stay | 30-Day Mortality | 90-Day Mortality |
| Gender | x | x | x | x |
| Indicator of Any Encounter within Past 1 Year with Myocardial infarction Diagnosis Code |  |  |  |  |
| Indicator of Any Encounter within Past 1 Year with Congestive heart failure Diagnosis Code | x | x | x | x |
| Indicator of Any Encounter within Past 1 Year with Peripheral Arterial Disease Diagnosis Code | x | x | x | x |
| Indicator of Any Encounter within Past 1 Year with Cerebrovascular Diagnosis Code | x | x |  |  |
| Indicator of Any Encounter within Past 1 Year with Dementia Diagnosis Code |  |  |  | x |
| Indicator of Any Encounter within Past 1 Year with Chronic obstructive pulmonary disease Diagnosis Code |  |  |  |  |
| Indicator of Any Encounter within Past 1 Year with Connective Tissue Disorder Diagnosis Code | x |  | x |  |
| Indicator of Any Encounter within Past 1 Year with Ulcerative Disease Diagnosis Code |  |  |  |  |
| Indicator of Any Encounter within Past 1 Year with Mild Liver Disease Diagnosis Code |  |  |  |  |
| Indicator of Any Encounter within Past 1 Year with Diabetes with No Complications Diagnosis Code |  |  |  |  |
| Indicator of Any Encounter within Past 1 Year with Diabetes with Complications Diagnosis Code |  |  |  |  |
| Indicator of Any Encounter within Past 1 Year with Hemiplegia Diagnosis Code | x |  | x | x |
| Indicator of Any Encounter within Past 1 Year with Renal Diagnosis Code |  |  |  |  |
| Indicator of Any Encounter within Past 1 Year with Malignancy Diagnosis Code | x | x | x | x |
| Indicator of Any Encounter within Past 1 Year with Moderate Liver Disease Diagnosis Code |  | x |  | x |
| Indicator of Any Encounter within Past 1 Year with Metastatic Solid Diagnosis Code | x |  | x | x |
| Indicator of Any Encounter within Past 1 Year with HIV/AIDS Diagnosis Code |  |  |  |  |
| Ratio of Abnormal Lactate in 24 Hours | x | x | x | x |
| Ratio of Abnormal white blood cells Counts in 24 Hours | x |  | x | x |
| Ratio of Abnormal Temperature in 24 Hours |  | x |  | x |
| Ratio of Abnormal Respiratory rate in 24 Hours  | x | x | x | x |
| Ratio of Abnormal DBP in 24 Hours |  | x |  | x |
| Ratio of Abnormal SBP in 24 Hours | x | x | x | x |
| Ratio of Abnormal MAP in 24 Hours |  | x |  |  |
| Ratio of Abnormal GCS in 24 Hours |  |  | x | x |
| Ratio of Abnormal O2Sat in 24 Hours | x | x | x | x |
| Ratio of Abnormal Platelets in 24 Hours | x | x | x | x |
| Ratio of Abnormal Potassium in 24 Hours |  |  |  |  |
| Ratio of Abnormal Pulse in 24 Hours | x | x | x | x |
| Ratio of Abnormal Sodium in 24 Hours | x |  | x | x |
| Ratio of Abnormal BUN in 24 Hours | x |  | x | x |
| Ratio of Abnormal Chloride in 24 Hours | x | x | x | x |
| Ratio of Abnormal CO2 in 24 Hours | x |  | x | x |
| Ratio of Abnormal Creatinine in 24 Hours |  |  |  |  |
| Ratio of Abnormal Glucose in 24 Hours |  | x |  |  |
| Ratio of Abnormal Hematocrit in 24 Hours | x | x |  | x |
| Ratio of Abnormal HGB in 24 Hours  |  |  | x | x |
| Ratio of Abnormal MCH in 24 Hours |  |  |  |  |
| Ratio of Abnormal MCHC in 24 Hours |  |  | x | x |
| Ratio of Abnormal MCV in 24 Hours | x |  | x | x |
| Ratio of Abnormal MPV in 24 Hours |  |  | x |  |
| Ratio of Abnormal RDW in 24 Hours |  |  |  | x |
| Ratio of Abnormal RBC in 24 Hours |  |  |  |  |
| Indicator of Any Chemo Drug Ordered in Last 90 Days  |  |  |  | x |
| Indicator of Any Cardiovascular Disease Agent Ordered in Last 90 Days |  |  |  | x |
| Indicator of Any Antidiabetic Agent Ordered in Last 90 Days | x | x | x |  |
| Indicator of Any Anti-Infective Agent Ordered in Last 90 Days |  |  |  |  |
| Indicator of Any Respiratory Agent Ordered in Last 90 Days  |  |  |  |  |
| Month of Admission | x | x | x | x |
| Indicator of ICU Admission in 24 Hours | x | x |  |  |
| Indicator of Ventilator Use in 24 Hours | x | x | x | x |
| Number of ED Visit During 6 Months Prior to Admission |  |  |  |  |
| Age at Admission | x | x | x | x |
| Race | x | x | x | x |
| Marital Status | x | x | x | x |
| Insurance | x | x | x | x |
| ED Acuity | x | x | x | x |
| Facility | x | x | x | x |
| Initial Admission Type (Inpatient/Observation)  | x | x | x | x |
| Number of Ambulatory Visit During 6 Months Prior to Admission  |  |  |  |  |
| Number of Outpatient Visit During 6 Months Prior to Admission |  |  | x |  |
| Number of inpatient Visit During 6 Months Prior to Admission |  | x | x | x |
| Number of Admitted in Observation During 6 Months Prior to Admission |  | x |  |  |
| Number of Medications on Multum Level 1--Alternative Medicines Category, 1 Year Prior to Admission |  | x | x | x |
| Number of Medications on Multum Level 1-- Anticonvulsants Category, 1 Year Prior to Admission | x | x | x | x |
| Number of Medications on Multum Level 1-- Antidiabetic Agents Category, 1 Year Prior to Admission |  |  |  |  |
| Number of Medications on Multum Level 1-- Antihyperlipidemic Agents Category, 1 Year Prior to Admission |  |  |  |  |
| Number of Medications on Multum Level 1-- Anti-Infectives Category, 1 Year Prior to Admission |  |  |  |  |
| Number of Medications on Multum Level 1-- Antineoplastics Category, 1 Year Prior to Admission |  |  |  |  |
| Number of Medications on Multum Level 1-- Antiparkinson Agents Category, 1 Year Prior to Admission |  |  |  |  |
| Number of Medications on Multum Level 1-- Antituberculosis Agents Category, 1 Year Prior to Admission |  |  | x |  |
| Number of Medications on Multum Level 1-- Biologicals Category, 1 Year Prior to Admission |  |  |  |  |
| Number of Medications on Multum Level 1-- Cardiovascular Agents Category, 1 Year Prior to Admission |  |  |  |  |
| Number of Medications on Multum Level 1-- Central Nervous System Agents Category, 1 Year Prior to Admission |  |  |  |  |
| Number of Medications on Multum Level 1-- Coagulation Modifiers Category, 1 Year Prior to Admission |  | x |  |  |
| Number of Medications on Multum Level 1-- Dermatological Agents Category, 1 Year Prior to Admission |  | x |  |  |
| Number of Medications on Multum Level 1-- Gastrointestinal Agents Category, 1 Year Prior to Admission |  |  |  |  |
| Number of Medications on Multum Level 1-- Genitourinary Tract Agents Category, 1 Year Prior to Admission |  |  |  |  |
| Number of Medications on Multum Level 1-- Hormones/Hormone Modifiers Category, 1 Year Prior to Admission |  |  |  |  |
| Number of Medications on Multum Level 1-- Immunologic Agents Category, 1 Year Prior to Admission |  |  |  |  |
| Number of Medications on Multum Level 1-- interferons Category, 1 Year Prior to Admission |  |  |  |  |
| Number of Medications on Multum Level 1-- Metabolic Agents Category, 1 Year Prior to Admission |  |  | x | x |
| Number of Medications on Multum Level 1-- Miscellaneous Agents Category, 1 Year Prior to Admission |  | x | x | x |
| Number of Medications on Multum Level 1-- Nutritional Products Category, 1 Year Prior to Admission |  |  |  | x |
| Number of Medications on Multum Level 1-- Plasma Expanders Category, 1 Year Prior to Admission |  |  |  |  |
| Number of Medications on Multum Level 1-- Psychotherapeutic Agents Category, 1 Year Prior to Admission | x | x |  |  |
| Number of Medications on Multum Level 1-- Radiologic Agents Category, 1 Year Prior to Admission |  |  |  |  |
| Number of Medications on Multum Level 1-- Respiratory Agents Category, 1 Year Prior to Admission | x |  |  |  |
| Number of Medications on Multum Level 1-- topical Agents Category, 1 Year Prior to Admission |  | x | x |  |
| Number of 30-Day Readmission to inpatient/Observation 1 Year Prior to Admission |  |  |  |  |
| Number of 30-Day Readmission to ED 1 Year Prior to Admission |  |  |  |  |
| Against Medical Advice 1 Year Prior to Admission | x | x |  |  |
| BMI |  |  | x | x |
| Number of Drug Ordered 1 Year Prior to Admission | x | x | x | x |
| Minimum BNP within 24 Hours from Admission |  |  |  |  |
| Maximum AST within 24 Hours from Admission | x | x | x | x |
| Maximum ALT within 24 Hours from Admission | x | x | x | x |
| Minimum Albumin within 24 Hours from Admission | x | x | x | x |
| Maximum Calcium within 24 Hours from Admission |  | x | x |  |
| Maximum Troponin within 24 Hours from Admission | x | x | x | x |
| Maximum PTT within 24 Hours from Admission | x |  | x | x |
| Minimum Pain within 24 Hours from Admission | x | x | x | x |
| Maximum Lactate within 24 Hours from Admission | x |  | x | x |
| Minimum Braden within 24 Hours from Admission | x | x | x | x |
| Maximum O2 Flow within 24 Hours from Admission |  | x |  | x |
| Maximum Shock index within 24 Hours from Admission |  | x | x |  |
| Maximum FiO2 within 24 Hours from Admission | x | x | x | x |
| Maximum ALP within 24 Hours from Admission | x |  | x | x |
| Maximum BASOPHILS within 24 Hours from Admission |  | x |  | x |
| Maximum CRP within 24 Hours from Admission |  |  |  |  |
| Maximum CVP within 24 Hours from Admission |  | x |  |  |
| Minimum Eosinophils within 24 Hours from Admission |  | x |  | x |
| Maximum INR within 24 Hours from Admission | x | x | x | x |
| Maximum Lymphocytes within 24 Hours from Admission | x | x | x | x |
| Maximum Monocytes within 24 Hours from Admission | x |  | x |  |
| Maximum Neutrophils within 24 Hours from Admission |  | x | x | x |
| Minimum PaO2 within 24 Hours from Admission |  |  | x | x |
| Average Hospitalization Length of Stay 1 Year Prior to Admission |  |  |  |  |
| Indicator of Any Encounter within Past 1 Year with Blood Transfusion Procedure Code |  | x |  | x |
| Indicator of Any Encounter within Past 1 Year with Nutrition Related Procedure Code |  |  |  | x |
| Indicator of Any Encounter within Past 1 Year with Hip Fracture Diagnosis Code |  |  | x | x |
| Indicator of Any Encounter within Past 1 Year with Urinary Related Procedure Code | x |  | x |  |
| Indicator of Any Encounter within Past 1 Year with Skin Ulcer Diagnosis Code |  |  |  |  |
| Indicator of Any Encounter within Past 1 Year with Pneumonia Diagnosis Code |  | x |  | x |
| Indicator of Any Encounter within Past 1 Year with Bone Marrow Diagnosis Code |  |  |  | x |
| Indicator of Any Encounter within Past 1 Year with Depression Diagnosis Code |  |  | x |  |
| Indicator of Any Encounter within Past 1 Year with Respiratory Failure Diagnosis Code |  | x | x | x |
| Indicator of Any Encounter within Past 1 Year with Sepsis Diagnosis Code | x | x | x | x |
| Indicator of Any Encounter within Past 1 Year with Malnutrition Diagnosis Code |  |  |  |  |
| Indicator of Any Encounter within Past 1 Year with Fall-Related PRIMARY Diagnosis Code |  |  |  |  |
| Indicator of Any Encounter within Past 1 Year with Syncope Diagnosis Code |  |  |  |  |
| Minimum SBP within 24 from Admission (Imputed) |  |  |  |  |
| Minimum GCS within 24 from Admission (Imputed) | x | x | x | x |
| Minimum MAP within 24 from Admission (Imputed) |  | x |  |  |
| Minimum CO2 within 24 from Admission (Imputed) | x | x | x |  |
| Minimum Hematocrit within 24 from Admission (Imputed) |  | x |  |  |
| Minimum HGB within 24 from Admission (Imputed) |  |  |  |  |
| Minimum MCH within 24 from Admission (Imputed) | x |  |  |  |
| Minimum MCV within 24 from Admission (Imputed) | x |  | x | x |
| Minimum O2Sat within 24 from Admission (Imputed) |  |  | x | x |
| Minimum Platelets within 24 from Admission (Imputed) |  |  | x | x |
| Minimum RBC within 24 from Admission (Imputed) |  |  |  |  |
| Maximum TEMP within 24 from Admission (Imputed) | x | x | x | x |
| Maximum WBC within 24 from Admission (Imputed) |  |  |  |  |
| Maximum Respiratory rate within 24 from Admission (Imputed) |  |  |  |  |
| Maximum BUN within 24 from Admission (Imputed) |  | x | x | x |
| Maximum Chloride within 24 from Admission (Imputed) | x | x | x | x |
| Maximum Creatinine within 24 from Admission (Imputed) | x |  | x | x |
| Maximum Glucose within 24 from Admission (Imputed) | x | x | x | x |
| Maximum MCHC within 24 from Admission (Imputed) | x |  |  |  |
| Maximum MPV within 24 from Admission (Imputed) |  | x | x |  |
| Maximum Potassium within 24 from Admission (Imputed) | x | x | x | x |
| Maximum Pulse within 24 from Admission (Imputed) |  |  |  |  |
| Maximum RDW within 24 from Admission (Imputed) | x | x | x | x |
| Maximum Sodium within 24 from Admission (Imputed) | x |  | x | x |
| Maximum FALL RISK SCORE (Combine Morse Score) within 24 Hours from Admission |  | x | x | x |
| Number of Medications on Multum Level 1--Alternative Medicines Category, within 24 Hours from Admission |  | x |  |  |
| Number of Medications on Multum Level 1-- Anticonvulsants Category, within 24 Hours from Admission |  |  |  |  |
| Number of Medications on Multum Level 1-- Antidiabetic Agents Category, within 24 Hours from Admission |  |  |  |  |
| Number of Medications on Multum Level 1-- Antihyperlipidemic Agents Category, within 24 Hours from Admission |  |  |  |  |
| Number of Medications on Multum Level 1-- Anti-Infectives Category, within 24 Hours from Admission | x | x | x | x |
| Number of Medications on Multum Level 1-- Antineoplastics Category, within 24 Hours from Admission |  |  | x |  |
| Number of Medications on Multum Level 1-- Antiparkinson Agents Category, within 24 Hours from Admission |  |  |  |  |
| Number of Medications on Multum Level 1-- Antituberculosis Agents Category, within 24 Hours from Admission |  |  |  |  |
| Number of Medications on Multum Level 1-- Biologicals Category, within 24 Hours from Admission |  |  |  | x |
| Number of Medications on Multum Level 1-- Cardiovascular Agents Category, within 24 Hours from Admission |  |  |  |  |
| Number of Medications on Multum Level 1-- Central Nervous System Agents Category, within 24 Hours from Admission |  |  | x | x |
| Number of Medications on Multum Level 1-- Coagulation Modifiers Category, within 24 Hours from Admission | x | x | x | x |
| Number of Medications on Multum Level 1-- Dermatological Agents Category, within 24 Hours from Admission |  |  |  | x |
| Number of Medications on Multum Level 1-- Gastrointestinal Agents Category, within 24 Hours from Admission |  | x |  |  |
| Number of Medications on Multum Level 1-- Genitourinary Tract Agents Category, within 24 Hours from Admission |  | x |  |  |
| Number of Medications on Multum Level 1-- Hormones/Hormone Modifiers Category, within 24 Hours from Admission |  |  |  | x |
| Number of Medications on Multum Level 1-- Immunologic Agents Category, within 24 Hours from Admission | x | x | x | x |
| Number of Medications on Multum Level 1-- interferons Category, within 24 Hours from Admission |  |  |  |  |
| Number of Medications on Multum Level 1-- Metabolic Agents Category, within 24 Hours from Admission |  | x |  |  |
| Number of Medications on Multum Level 1-- Miscellaneous Agents Category, within 24 Hours from Admission | x |  |  |  |
| Number of Medications on Multum Level 1-- Nutritional Products Category, within 24 Hours from Admission |  |  |  |  |
| Number of Medications on Multum Level 1-- Plasma Expanders Category, within 24 Hours from Admission | x | x | x | x |
| Number of Medications on Multum Level 1-- Psychotherapeutic Agents Category, within 24 Hours from Admission |  |  |  | x |
| Number of Medications on Multum Level 1-- Radiologic Agents Category, within 24 Hours from Admission | x | x | x | x |
| Number of Medications on Multum Level 1-- Respiratory Agents Category, within 24 Hours from Admission |  |  |  |  |
| Number of Medications on Multum Level 1-- topical Agents Category, within 24 Hours from Admission |  | x |  |  |

**eTable 3.** Model performance across different selection of outcomes on training dataset.

|  |  |
| --- | --- |
| **Model** | **Outcome** |
|  | **Died Hosp** | **ICU72/Died-Hosp** | **Died30** | **Died90** |
| **Died-Hosp** | 0.89 (0.88-0.90)*a* | 0.87 (0.86-0.87) b | 0.86 (0.85-0.87) b | 0.82 (0.81-0.83) b |
| **ICU72/Died-Hosp** | - | 0.91 (0.91-0.92)*a* | 0.81 (0.81-0.82) b | 0.76 (0.75-0.77) b |
| **Died30** | - | - | 0.87 (0.86-0.88) *a* | 0.85 (0.85-0.86)b |
| **Died90** | - | - | - | 0.86 (0.85-0.86)*a* |
| Abbreviations: Died-Hosp=hospital mortality; ICU72/Died-Hosp=composite of >72-hour ICU stay or hospital mortality; Died30=30-day mortality; Died90=90-day mortality.Model discrimination presented as area under receiver operating characteristic curve (AUC) and 95% confidence intervals (CI).*a* AUC and 95%CI generated by k-fold cross-validation (k=10).*b* AUC and 95%CI generated by DeLong’s method. |

**eFigure 1:** Calibration Plots for Died-Hosp, ICU72/ Died-Hosp, Died30, and Died90 Model against outcomes of interest on training dataset. Calibration plots are depicted for each model and outcome pair (Died-Hosp=hospital mortality, ICU72/Died-Hosp=composite of >72-hour ICU stay or hospital mortality, Died30=30-day mortality, Died90=90-day mortality)



RMSE=12

RMSE=5

RMSE=8

RMSE=4

RMSE=30

RMSE=36

RMSE=2

RMSE=6

RMSE=28

RMSE=3

The x-axis of all inner plots is the expected risk (%) for each of the outcomes of interest while the y-axis represents observed risk (%) for each of the outcomes. The identity line is indicated with a dashed line and represents a perfectly calibrated model, in which the observed number of events are equal to the predicted number of events. The solid line indicates the actual number of observed events across the range of predicted risk values (i.e., 0-100). The area within the 95% confidence band around each of the observed estimates are shaded gray. RMSE is the root mean square error between prediction models (solid-line) and the perfectly calibrated model (dash-line). The circles illustrate examples comparing observed 90-day mortality versus expected risk predicted by Died-Hosp (a), ICU72/Died-Hosp (b), and Died30 (c) models. At expected risks of 25%, Died-Hosp and Died30 models underpredicted the 90-day mortality risk (observed risk=45% and 38%, respectively) while the ICU72/Died-Hosp model overpredicted the 90-day mortality risk (observed risk=17%).

**e-Appendix2**

**TRIPOD CHECKLIST: Prediction Model Development and Validation**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Section/Topic | Item | Development or Validation? | Checklist Item | Page |
| Title and abstract |
| Title | 1 | D;V | Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted | 1 |
| Abstract | 2 | D;V | Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions. | 3 |
| Introduction |
| Background and Objectives | 3a | D;V | Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models | 6 |
| 3b | D;V | Specify the objectives, including whether the study describes the development or validation of the model or both | 6-7 |
| Method |
| Source of data | 4a | D;V | Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable | 7 |
|  | 4b | D;V | Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up | 7-8 |
| Participants | 5a | D;V | Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centers | 7-8 |
|  | 5b | D;V | Describe eligibility criteria for participants | 7-8 |
|  | 5c | D;V | Give details of treatments received, if relevant | n/a |
| Outcome | 6a | D;V | Clearly define the outcome that is predicted by the prediction model, includinghow and when assessed | 8 |
|  | 6b | D;V | Report any actions to blind assessment of the outcome to be predicted | n/a |
| Predictors | 7a | D;V | Clearly define all predictors used in developing the multivariable prediction model,including how and when they were measured | 8, Suppl |
|  | 7b | D;V | Report any actions to blind assessment of predictors for the outcome and other predictors | n/a |
| Sample size | 8 | D;V | Explain how the study size was arrived at | 7 |
| Missing data | 9 | D;V | Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method | 8-9, Suppl. |
| Statistical analysis methods | 10a | D | Describe how predictors were handled in the analyses | 8-10 |
|  | 10b | D | Specify type of model, all model-building procedures (including any predictor selection), and method for internal validation | 8, Suppl. |
|  | 10c | V | For validation, describe how the predictions were calculated | 8, Suppl. |
|  | 10d | D;V | Specify all measures used to assess model performance and, if relevant, to compare multiple models | 9 |
|  | 10e | V | Describe any model updating (e.g., recalibration) arising from the validation, if done | n/a |
| Risk groups | 11 | D;V | Provide details on how risk groups were created, if done | 8 |
| Development vs. validation | 12 | V | For validation, identify any differences from the development data in setting, eligibility criteria, outcome, and predictors | 8 |
| Results |
| Participants | 13a | D;V | Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of thefollow-up time. A diagram may be helpful | n/a |
|  | 13b | D;V | Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missingdata for predictors and outcome | 10 |
|  | 13c | V | For validation, show a comparison with the development data of the distribution of important variables (demographics, predictors and outcome) | 10-11 |
| Model development | 14a | D | Specify the number of participants and outcome events in each analysis | 10 |
|  | 14b | D | If done, report the unadjusted association between each candidate predictor and outcome | 9 |
| Model specification | 15a | D | Present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point) | n/a |
|  | 15b | D | Explain how to use the prediction model  | n/a |
| Model Performance | 16 | D;V | Report performance measures (with CIs) for the prediction model | 10 |
| Model updating | 17 | V | If done, report the results from any model updating (i.e., model specification, model performance) | n/a |
| Discussion |
| Limitations | 18 | D;V | Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data) | 13 |
| Interpretation | 19a | V | For validation, discuss the results with reference to performance in the development data, and any other validation data | 11-12 |
|  | 19b | D;V | Give an overall interpretation of the results, considering objectives, limitations, results from similar studies, and other relevant evidence | 12-14 |
| Implications | 20 | D;V | Discuss the potential clinical use of the model and implications for future research | 14 |
| Other information |
| Supplementary information | 21 | D;V | Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets | Online Suppl. |
| Funding | 22 | D;V | Give the source of funding and the role of the funders for the present study | 15 |