**Additional File 1**

**Biomarkers and clinical scores to identify patient populations at risk of delayed antibiotic administration or intensive care admission**

***Short title: Delayed antibiotic and ICU admission decisions in the ED***

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**Table S1. Initial clinical diagnoses and suspected infectious source**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Suspected source of infection** | **Patients**  **(*N*)** | **Hospital admission**  **(*N*, %)** | **ICU admission**  **(*N*, %)** | **28-day mortality**  ***(N*, %)** |
| Bone and Joint | 4 | 3 (0.6%) | 1 (4.3%) | 1 (3.3%) |
| Cardiac | 2 | 1 (0.2%) | 0 (0.0%) | 1 (3.3%) |
| Intra-abdominal | 93 | 71 (14.3%) | 4 (17.4%) | 7 (23.3%) |
| Appendicitis | 6 |  |  |  |
| Cholangitis | 11 |
| Cholecystitis | 8 |
| Diverticulitis | 10 |
| Gastroenteritis | 17 |
| Other | 41 |
| Respiratory - lower | 220 | 185 (37.1%) | 8 (34.8%) | 14 (46.7%) |
| IECOPD | 8 |  |  |  |
| Pneumonia | 90 |
| Unspecified respiratory infection | 101 |
| Other | 21 |
| Respiratory - upper | 18 | 7 (1.4%) | 0 (0.0%) | 0 (0.0%) |
| Tonsillitis | 7 |  |  |  |
| Other | 11 |
| Skin and Soft Tissue | 36 | 25 (5.0%) | 2 (8.7%) | 1 (3.3%) |
| Cellulitis | 24 |  |  |  |
| Other | 12 |
| Surgical | 16 | 11 (2.2%) | 3 (13.0%) | 0 (0.0%) |
| Unknown origin | 81 | 47 (9.4%) | 1 (4.3%) | 1 (3.3%) |
| Urogenital | 214 | 148 (29.7%) | 4 (17.4%) | 5 (16.7%) |
| Pyelonephritis | 34 |  |  |  |
| Urinary tract infection | 112 |
| Other | 68 |

Percentages for each outcome per suspected source of infection, represent the proportion of the number of events per outcome within the total patient cohort. In brief, there were a total of *N*=498 hospitalisation, *N*=23 ICU admission and *N*=30 28-day mortality events. *N:* Number; *ICU:* Intensive Care Unit; *IECOPD*: Infective Exacerbation of Chronic Obstructive Pulmonary Disease.

**Table S2. Characteristics of patients hospitalised at 72 hours**

|  |  |
| --- | --- |
| **Patient Characteristics** | **Total cohort**  **(*N*=380)** |
| **Demographics** | |
| Age (years) (mean, SD) | 71.2 (16.7) |
| Male Sex (*N*, %) | 218 (57.4%) |
| **Disposition** | |
| Hospital admission (*N*, %) | 380 (100.0%) |
| Hospital length of stay (days) (median, Q1-Q3) | 7 [5 - 12] |
| ICU admission (*N*, %) | 7 (1.8%) |
| Infection-related 28-day mortality (*N*, %) | 26 (6.8%) |
| Hospital mortality (*N*, %) | 29 (7.6%) |
| **Sepsis classification** | |
| Sepsis-2 (*N*, %) | 211 (57.3%) |
| Sepsis-3 (*N*, %) | 229 (73.9%) |
| **Comorbidities** | |
| Cardiovascular disease (*N*, %) | 171 (45.0%) |
| Diabetes (*N*, %) | 103 (27.1%) |
| Immunodeficiency (*N*, %) | 65 (17.1%) |
| Liver disease (*N*, %) | 34 (8.9%) |
| Malignancy (*N*, %) | 115 (30.3%) |
| Neurological disorders (*N*, %) | 91 (23.9%) |
| Respiratory disease (*N*, %) | 119 (31.3%) |
| Renal disease (*N*, %) | 93 (24.5%) |
| **Infectious source** | |
| Bone and Joint (*N*, %) | 3 (0.8%) |
| Cardiac (*N*, %) | 1 (0.3%) |
| Intra-abdominal (*N*, %) | 57 (15.0%) |
| Respiratory - lower (*N*, %) | 148 (38.9%) |
| Respiratory - upper (*N*, %) | 1 (0.3%) |
| Skin and Soft Tissue (*N*, %) | 21 (5.5%) |
| Surgical-related (*N*, %) | 11 (2.9%) |
| Unknown origin (*N*, %) | 34 (8.9%) |
| Urogenital (*N*, %) | 104 (27.4%) |
| **Blood cultures** | |
| Blood cultures taken (*N*, %) | 252 (66.3%) |
| Positive blood cultures (*N*, %) | 49 (12.9%) |
| **Biomarkers and severity scores** | |
| MR-proADM (nmol/L) (median, Q1-Q3) | 1.08 [0.70 - 1.61] |
| PCT (ng/mL) (median, Q1-Q3) | 0.28 [0.12 - 0.89] |
| Lactate (mmol/L) (median, Q1-Q3) | 1.7 [1.3 - 2.2] |
| CRP (mg/L) (median, Q1-Q3) | 7.4 [3.07 - 17.43] |
| SOFA (points) (median, Q1-Q3) | 1 [0 - 1] |
| qSOFA (points) (median, Q1-Q3) | 2 [1 - 3] |
| SIRS (points) (median, Q1-Q3) | 1 [1 - 2] |
| NEWS (points) (median, Q1-Q3) | 0 [0 - 1] |
| CRB-65 (points) (median, Q1-Q3) | 2 [1 - 4] |

Values expressed in percentages (%) indicate the proportion of patients for each variable. Data are presented as mean (standard deviation, SD) or median [first quartile (Q1) - third quartile (Q3)] where specified. The chi-square (χ2) test was used to determine significance between the cohorts for categorical variables, Student’s t-test for the variable of age, and Mann-Whitney U test for hospitalisation duration, biomarker and clinical score variables. *CRB-65*: Severity score for community-acquired pneumonia; *CRP*: C-reactive protein; *ICU*: Intensive Care Unit; *MR-proADM*: Mid-regional proadrenomedullin; *N*: Number; *NEWS*: National Early Warning Score; *PCR*: Polymerase Chain Reaction; *PCT*: Procalcitonin; *qSOFA*: quick Sequential Organ Failure Assessment; *SIRS*: Systemic Inflammatory Response Syndrome; *SOFA*: Sequential Organ Failure Assessment.

**Table S3. Univariate and Multivariate Logistic regression for antibiotic administration (ED treatment)**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Biomarker or clinical score** | **Patients (*N*)** | **Antibiotics**  **(*N*)** | **LR χ²** | **p-value** | **C-index** | **OR [95% CI]** |
| Univariate | MR-proADM | 684 | 505 | 115.2 | <0.001 | 0.77 | 4.9 [3.5 - 6.8] |
| PCT | 684 | 505 | 80.6 | <0.001 | 0.73 | 3.5 [2.5 - 4.8] |
| Lactate | 533 | 412 | 1.8 | 0.176 | 0.52 | 1.2 [0.9 - 1.5] |
| CRP | 646 | 480 | 78.9 | <0.001 | 0.65 | 2.4 [1.7 - 3.3] |
| SOFA | 684 | 505 | 87.3 | <0.001 | 0.71 | 3.1 [2.4 - 4.0] |
| qSOFA | 684 | 505 | 51.4 | <0.001 | 0.65 | 3.5 [2.3 - 5.3] |
| NEWS | 684 | 505 | 103.4 | <0.001 | 0.74 | 5.5 [3.6 - 8.2] |
| CRB-65 | 684 | 505 | 66.8 | <0.001 | 0.70 | 2.9 [2.2 - 3.9] |
| SIRS | 684 | 505 | 61.6 | <0.001 | 0.67 | 2.1 [1.7 - 2.5] |
| Multivariate | MR-proADM | 684 | 505 | 133.1 | <0.001 | 0.79 | 3.5 [2.4 - 5.2] |
| PCT | 684 | 505 | 130.2 | <0.001 | 0.78 | 2.7 [1.9 - 3.7] |
| Lactate | 533 | 412 | 79.7 | <0.001 | 0.75 | 0.9 [0.7 - 1.2] |
| CRP | 646 | 480 | 145.4 | <0.001 | 0.78 | 2.5 [1.9 - 3.1] |
| SOFA | 684 | 505 | 107.8 | <0.001 | 0.79 | 2.9 [2.2 - 5.1] |
| qSOFA | 684 | 505 | 112.9 | <0.001 | 0.78 | 2.8 [1.8 - 4.4] |
| NEWS | 684 | 505 | 151.3 | <0.001 | 0.79 | 4.5 [2.9 - 6.9] |
| CRB-65 | 684 | 505 | 92.9 | <0.001 | 0.73 | 2.5 [1.3 - 4.6] |
| SIRS | 684 | 505 | 140.7 | <0.001 | 0.78 | 2.1 [1.7 - 2.6] |

*CI*: Confidence Interval; *CRB-65*: Severity score for community-acquired pneumonia; *CRP*: C-reactive protein; *LR*: Likelihood ratio; *MR-proADM*: Mid-regional proadrenomedullin; *N*: Number; *NEWS*: National Early Warning Score; *OR*: Odds Ratio; *PCT*: Procalcitonin; *qSOFA*: quick Sequential Organ Failure Assessment; *SIRS*: Systemic Inflammatory Response Syndrome; *SOFA*: Sequential Organ Failure Assessment.

**Table S4. Bivariate MR-proADM Logistic regression models for antibiotic administration (ED treatment)**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Biomarker or clinical score model + MR-proADM** | **Patients (*N*)** | **Antibiotics**  **(*N*)** | **LR χ²** | **p-value** | **C-index** | **OR [95% CI]** |
| Bivariate  MR-proADM model | PCT | 684 | 505 | 103.2 | <0.001 | 0.78 | 3.6 [2.5 – 5.2] |
| Lactate | 533 | 412 | 85.6 | <0.001 | 0.77 | 5.3 [3.5 – 7.9] |
| CRP | 646 | 480 | 160.2 | <0.001 | 0.81 | 4.4 [3.1 – 6.4] |
| SOFA | 684 | 505 | 129.1 | <0.001 | 0.78 | 3.4 [2.3 – 5.0] |
| qSOFA | 684 | 505 | 129.1 | <0.001 | 0.78 | 4.1 [2.9 – 5.7] |
| NEWS | 684 | 505 | 157.1 | <0.001 | 0.80 | 3.3 [2.3 – 4.7] |
| CRB-65 | 684 | 505 | 125.7 | <0.001 | 0.78 | 3.7 [2.6 – 5.3] |
| SIRS | 684 | 505 | 145.3 | <0.001 | 0.79 | 4.1 [2.9 – 5.8] |

*CI*: Confidence Interval; *CRB-65*: Severity score for community-acquired pneumonia; *CRP*: C-reactive protein; *LR*: Likelihood ratio; *MR-proADM*: Mid-regional proadrenomedullin; *N*: Number; *NEWS*: National Early Warning Score; *OR*: Odds Ratio; *PCT*: Procalcitonin; *qSOFA*: quick Sequential Organ Failure Assessment; *SIRS*: Systemic Inflammatory Response Syndrome; *SOFA*: Sequential Organ Failure Assessment.

**Table S5. Univariate and Multivariate Logistic regression for hospitalisation requirement (ED presentation)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Biomarker or clinical score** | **Patients (*N*)** | **Hospitalisation**  **(*N*)** | **LR χ²** | **p-value** | **C-index** | **OR [95% CI]** |
| MR-proADM | 684 | 498 | 151.2 | <0.001 | 0.82 | 6.6 [4.6 - 9.4] |
| PCT | 684 | 498 | 78.0 | <0.001 | 0.73 | 3.3 [2.4 - 4.5] |
| Lactate | 533 | 420 | 2.7 | 0.098 | 0.53 | 1.2 [1.0 - 1.6] |
| CRP | 646 | 479 | 45.0 | <0.001 | 0.66 | 2.0 [1.6 - 2.5] |
| SOFA | 684 | 498 | 105.2 | <0.001 | 0.75 | 5.7 [3.7 - 9.4] |
| qSOFA | 684 | 498 | 62.2 | <0.001 | 0.65 | 4.1 [2.7 - 6.3] |
| NEWS | 684 | 498 | 114.5 | <0.001 | 0.75 | 6.0 [4.0 - 9.1] |
| CRB-65 | 684 | 498 | 74.0 | <0.001 | 0.69 | 2.5 [1.9 - 2.6] |
| SIRS | 684 | 498 | 58.6 | <0.001 | 0.68 | 2.0 [1.7 - 2.4] |
| MR-proADM | 684 | 498 | 169.7 | <0.001 | 0.81 | 5.2 [3.4 - 7.8] |
| PCT | 684 | 498 | 129.3 | <0.001 | 0.77 | 2.6 [1.9 - 3.6] |
| Lactate | 533 | 420 | 67.9 | <0.001 | 0.74 | 1.0 [0.7 - 1.3] |
| CRP | 646 | 479 | 114.1 | <0.001 | 0.76 | 1.9 [1.5 - 2.4] |
| SOFA | 684 | 498 | 132.2 | <0.001 | 0.77 | 3.8 [2.5 - 6.0] |
| qSOFA | 684 | 498 | 122.5 | <0.001 | 0.74 | 3.4 [2.2 - 5.4] |
| NEWS | 684 | 498 | 162.6 | <0.001 | 0.80 | 5.1 [3.3 - 8.0] |
| CRB-65 | 684 | 498 | 96.4 | <0.001 | 0.74 | 3.0 [1.6 - 5.6] |
| SIRS | 684 | 498 | 140.2 | <0.001 | 0.78 | 2.1 [1.7 - 2.6] |

*CI*: Confidence Interval; *CRB-65*: Severity score for community-acquired pneumonia; *CRP*: C-reactive protein; *LR*: Likelihood ratio; *MR-proADM*: Mid-regional proadrenomedullin; *N*: Number; *NEWS*: National Early Warning Score; *OR*: Odds Ratio; *PCT*: Procalcitonin; *qSOFA*: quick Sequential Organ Failure Assessment; *SIRS*: Systemic Inflammatory Response Syndrome; *SOFA*: Sequential Organ Failure Assessment.

**Table S6. Bivariate MR-proADM Logistic regression models for hospitalisation requirement (ED presentation)**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Biomarker or clinical score model + MR-proADM** | **Patients (*N*)** | **Hospitalisation**  **(*N*)** | **LR χ²** | **p-value** | **C-index** | **OR [95% CI]** |
| Bivariate  MR-proADM model | PCT | 684 | 498 | 159.4 | <0.001 | 0.80 | 5.2 [3.5 - 7.7] |
| Lactate | 533 | 420 | 94.7 | <0.001 | 0.78 | 6.3 [4.0 - 9.7] |
| CRP | 646 | 479 | 157.0 | <0.001 | 0.81 | 5.9 [4.0 - 8.8] |
| SOFA | 684 | 498 | 165.8 | <0.001 | 0.81 | 4.5 [3.0 - 6.8] |
| qSOFA | 684 | 498 | 167.7 | <0.001 | 0.80 | 5.4 [3.7 - 7.9] |
| NEWS | 684 | 498 | 193.1 | <0.001 | 0.82 | 4.5 [3.1 - 6.6] |
| CRB-65 | 684 | 498 | 159.4 | <0.001 | 0.80 | 5.1 [3.4 - 7.6] |
| SIRS | 684 | 498 | 175.9 | <0.001 | 0.81 | 5.7 [3.9 - 8.2] |

*CI*: Confidence Interval; *CRB-65*: Severity score for community-acquired pneumonia; *CRP*: C-reactive protein; *LR*: Likelihood ratio; *MR-proADM*: Mid-regional proadrenomedullin; *N*: Number; *NEWS*: National Early Warning Score; *OR*: Odds Ratio; *PCT*: Procalcitonin; *qSOFA*: quick Sequential Organ Failure Assessment; *SIRS*: Systemic Inflammatory Response Syndrome; *SOFA*: Sequential Organ Failure Assessment.

**Table S7. Univariate and Multivariate Logistic regression for ICU admission prediction (ED presentation)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Biomarker or clinical score** | **Patients (*N*)** | **ICU admission**  **(*N*)** | **LR χ²** | **p-value** | **C-index** | **OR [95% CI]** |
| MR-proADM | 684 | 23 | 25.4 | <0.001 | 0.79 | 4.1 [2.3 - 7.1] |
| PCT | 684 | 23 | 12.5 | <0.001 | 0.71 | 2.2 [1.5 - 3.4] |
| Lactate | 533 | 22 | 0.7 | 0.408 | 0.58 | 1.2 [ 0.8 - 1.9] |
| CRP | 646 | 23 | 7.6 | 0.006 | 0.67 | 2.1 [1.2 - 3.6] |
| SOFA | 684 | 23 | 7.4 | 0.006 | 0.70 | 2.2 [1.3 - 3.8] |
| qSOFA | 684 | 23 | 7.5 | 0.006 | 0.62 | 2.1 [1.3 - 3.4] |
| NEWS | 684 | 23 | 8.5 | 0.004 | 0.62 | 2.0 [1.3 - 3.2] |
| CRB-65 | 684 | 23 | 5.3 | 0.021 | 0.63 | 3.0 [1.2 - 7.5] |
| SIRS | 684 | 23 | 0.1 | 0.725 | 0.52 | 1.1 [0.7 - 1.6] |
| MR-proADM | 684 | 23 | 34.0 | <0.001 | 0.82 | 5.8 [3.1 - 10.8] |
| PCT | 684 | 23 | 14.8 | 0.022 | 0.74 | 2.2 [1.4 - 3.4] |
| Lactate | 533 | 22 | 4.0 | 0.673 | 0.60 | 1.3 [0.8 - 2.0] |
| CRP | 646 | 23 | 10.2 | 0.115 | 0.71 | 2.0 [1.2 - 3.5] |
| SOFA | 684 | 23 | 9.7 | 0.136 | 0.75 | 2.3 [1.3 - 4.2] |
| qSOFA | 684 | 23 | 10.5 | 0.105 | 0.66 | 2.2 [1.3 - 3.8] |
| NEWS | 684 | 23 | 12.4 | 0.053 | 0.65 | 2.2 [1.4 - 3.6] |
| CRB-65 | 684 | 23 | 11.2 | 0.083 | 0.67 | 1.7 [1.2 - 2.6] |
| SIRS | 684 | 23 | 3.2 | 0.785 | 0.60 | 1.1 [0.7 - 1.6] |

Patients admitted to the ICU after 28 days following initial ED presentation were not treated as an ICU positive event. *CI*: Confidence Interval; *CRB-65*: Severity score for community-acquired pneumonia; *CRP*: C-reactive protein; *LR*: Likelihood ratio; *MR-proADM*: Mid-regional proadrenomedullin; *N*: Number; *NEWS*: National Early Warning Score; *OR*: Odds Ratio; *PCT*: Procalcitonin; *qSOFA*: quick Sequential Organ Failure Assessment; *SIRS*: Systemic Inflammatory Response Syndrome; *SOFA*: Sequential Organ Failure Assessment.

**Table S8. Bivariate MR-proADM Logistic regression models for ICU admission prediction (ED presentation)**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Biomarker or clinical score model + MR-proADM** | **Patients (*N*)** | **ICU admission**  **(*N*)** | **LR χ²** | **p-value** | **C-index** | **OR [95% CI]** |
| Bivariate  MR-proADM model | PCT | 684 | 23 | 25.4 | <0.001 | 0.79 | 3.8 [1.7 - 8.4] |
| Lactate | 533 | 22 | 18.4 | <0.001 | 0.76 | 3.6 [2.0 - 6.8] |
| CRP | 646 | 23 | 28.9 | <0.001 | 0.81 | 3.7 [2.1 - 6.4] |
| SOFA | 684 | 23 | 25.6 | <0.001 | 0.79 | 4.5 [2.2 - 9.3] |
| qSOFA | 684 | 23 | 25.8 | <0.001 | 0.79 | 3.7 [2.0 - 6.9] |
| NEWS | 684 | 23 | 26.1 | <0.001 | 0.78 | 3.7 [2.0 - 6.7] |
| CRB-65 | 684 | 23 | 25.4 | <0.001 | 0.79 | 4.1 [2.2 - 7.7] |
| SIRS | 684 | 23 | 26.5 | <0.001 | 0.80 | 4.4 [2.4 - 7.8] |

*CI*: Confidence Interval; *CRB-65*: Severity score for community-acquired pneumonia; *CRP*: C-reactive protein; *LR*: Likelihood ratio; *MR-proADM*: Mid-regional proadrenomedullin; *N*: Number; *NEWS*: National Early Warning Score; *OR*: Odds Ratio; *PCT*: Procalcitonin; *qSOFA*: quick Sequential Organ Failure Assessment; *SIRS*: Systemic Inflammatory Response Syndrome; *SOFA*: Sequential Organ Failure Assessment.

**Table S9.** **Univariate Cox regression for the prediction of 28-day mortality (ED presentation)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Biomarker or clinical score** | **Patients (*N*)** | **Mortality**  **(*N*)** | **LR χ²** | **p-value** | **C-index** | **HR [95% CI]** |
| MR-proADM | 684 | 30 | 36.6 | <0.001 | 0.84 | 4.1 [2.6 - 6.5] |
| PCT | 684 | 30 | 10.9 | <0.001 | 0.68 | 1.9 [1.3 - 2.7] |
| Lactate | 533 | 30 | 6.9 | <0.01 | 0.67 | 1.6 [1.2 - 2.2] |
| CRP | 646 | 28 | 0.0 | 0.994 | 0.50 | 1.0 [0.7 - 1.5] |
| SOFA | 684 | 30 | 36.2 | <0.001 | 0.84 | 3.9 [2.6 - 5.7] |
| qSOFA | 684 | 30 | 25.8 | <0.001 | 0.86 | 2.9 [2.0 - 4.2] |
| NEWS | 684 | 30 | 18.6 | <0.001 | 0.77 | 2.4 [1.7 - 3.4] |
| CRB-65 | 684 | 30 | 25.3 | <0.001 | 0.82 | 2.7 [1.9 - 4.0] |
| SIRS | 684 | 30 | 5.1 | 0.025 | 0.66 | 1.5 [1.1 - 2.0] |

*CI*: Confidence Interval; *CRB-65*: Severity score for community-acquired pneumonia; *CRP*: C-reactive protein; *HR*: Hazard Ratio; *LR*: Likelihood ratio; *MR-proADM*: Mid-regional proadrenomedullin; *N*: Number; *NEWS*: National Early Warning Score; *PCT*: Procalcitonin; *qSOFA*: quick Sequential Organ Failure Assessment; *SIRS*: Systemic Inflammatory Response Syndrome; *SOFA*: Sequential Organ Failure Assessment.

**Table S10. Bivariate MR-proADM Logistic regression models for the prediction of 28-day mortality (ED presentation)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Biomarker or clinical score model + MR-proADM** | **Patients (*N*)** | **Mortality**  **(*N*)** | **LR χ²** | **p-value** | **HR [95% CI]** |
| Bivariate  MR-proADM model | PCT | 684 | 30 | 38.1 | <0.001 | 5.7 [2.8 - 11.6] |
| Lactate | 533 | 30 | 30.4 | <0.001 | 3.3 [2.0 - 5.5] |
| CRP | 646 | 28 | 32.7 | <0.001 | 4.1 [2.5 - 6.6] |
| SOFA | 684 | 30 | 46.1 | <0.001 | 2.4 [1.4 - 4.2] |
| qSOFA | 684 | 30 | 43.6 | <0.001 | 3.0 [1.8 - 5.1] |
| NEWS | 684 | 30 | 40.3 | <0.001 | 3.4 [2.0 - 5.6] |
| CRB-65 | 684 | 30 | 42.1 | <0.001 | 3.0 [1.8 - 5.2] |
| SIRS | 684 | 30 | 37.1 | <0.001 | 3.9 [2.4 - 6.3] |

*CI*: Confidence Interval; *CRB-65*: Severity score for community-acquired pneumonia; *CRP*: C-reactive protein; *LR*: Likelihood ratio; *MR-proADM*: Mid-regional proadrenomedullin; *N*: Number; *NEWS*: National Early Warning Score; *OR*: Odds Ratio; *PCT*: Procalcitonin; *qSOFA*: quick Sequential Organ Failure Assessment; *SIRS*: Systemic Inflammatory Response Syndrome; *SOFA*: Sequential Organ Failure Assessment.

**Table S11. Univariate Cox regression for the prediction of 28-day mortality (72 hours)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Biomarker or clinical score** | **Patients (*N*)** | **Mortality**  **(*N*)** | **LR χ²** | **p-value** | **C-index** | **HR [95% CI]** |
| MR-proADM | 375 | 25 | 20.7 | <0.001 | 0.75 | 3.0 [1.9 - 4.7] |
| PCT | 370 | 25 | 5.9 | 0.015 | 0.62 | 1.6 [1.1 - 2.4] |
| Lactate | 266 | 24 | 0.0 | 0.908 | 0.59 | 1.0 [0.7 - 1.4] |
| CRP | 281 | 20 | 1.3 | 0.256 | 0.55 | 0.7 [0.5 - 1.2] |
| SOFA | 375 | 25 | 19.8 | <0.001 | 0.75 | 2.3 [1.7 - 3.2] |
| qSOFA | 376 | 25 | 3.9 | 0.049 | 0.68 | 1.7 [1.0 - 2.8] |
| NEWS | 376 | 25 | 8.8 | 0.003 | 0.68 | 1.8 [1.3 - 2.5] |
| CRB-65 | 376 | 25 | 7.1 | 0.008 | 0.71 | 1.8 [1.2 - 2.8] |
| SIRS | 376 | 25 | 4.6 | 0.031 | 0.67 | 1.6 [1.1 - 2.8] |

*CI*: Confidence Interval; *CRB-65*: Severity score for community-acquired pneumonia; *CRP*: C-reactive protein; *HR*: Hazard Ratio; *LR*: Likelihood ratio; *MR-proADM*: Mid-regional proadrenomedullin; *N*: Number; *NEWS*: National Early Warning Score; *PCT*: Procalcitonin; *qSOFA*: quick Sequential Organ Failure Assessment; *SIRS*: Systemic Inflammatory Response Syndrome; *SOFA*: Sequential Organ Failure Assessment.

**Table S12. Bivariate MR-proADM Logistic regression models for the prediction of 28-day mortality (72 hours)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Biomarker or clinical score model + MR-proADM** | **Patients (*N*)** | **Mortality**  **(*N*)** | **LR χ²** | **p-value** | **HR [95% CI]** |
| Bivariate  MR-proADM model | PCT | 375 | 25 | 21.9 | <0.001 | 3.2 [1.8 - 5.7] |
| Lactate | 370 | 25 | 13.4 | 0.001 | 2.5 [1.6 - 4.1] |
| CRP | 266 | 24 | 17.4 | <0.001 | 3.1 [1.8 - 5.3] |
| SOFA | 281 | 20 | 27.0 | <0.001 | 2.1 [1.2 - 3.6] |
| qSOFA | 375 | 25 | 21.8 | <0.001 | 2.8 [1.8 - 4.6] |
| NEWS | 376 | 25 | 24.7 | <0.001 | 2.7 [1.7 - 4.3] |
| CRB-65 | 376 | 25 | 23.1 | <0.001 | 2.8 [1.7 - 4.5] |
| SIRS | 376 | 25 | 22.7 | <0.001 | 2.8 [1.7 - 4.4] |

*CI*: Confidence Interval; *CRB-65*: Severity score for community-acquired pneumonia; *CRP*: C-reactive protein; *LR*: Likelihood ratio; *MR-proADM*: Mid-regional proadrenomedullin; *N*: Number; *NEWS*: National Early Warning Score; *OR*: Odds Ratio; *PCT*: Procalcitonin; *qSOFA*: quick Sequential Organ Failure Assessment; *SIRS*: Systemic Inflammatory Response Syndrome; *SOFA*: Sequential Organ Failure Assessment.

**Table S13. Treatment and outcome in patients with low biomarker or clinical score values (ED presentation)**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Biomarker**  **or score** | **Selected**  **cut-offs** | **Population**  **(*N*)** | **Antibiotic administration**  ***N* (%)** | **Mortality**  ***N* (%)** | **ICU admission**  ***N* (%)** | **Hospitalisation**  ***N* (%)** | **Length of hospitalisation**  **(days)** | **Infection related readmission**  ***N* (%)** |
| MR-proADM | <1.54 nmol/L\* | 475 | 313 (65.9%) | 4 (0.8%) | 8 (1.7%) | 307 (64.0%) | 2 [0 - 6] | 26 (5.5%) |
| MR-proADM | <1.77 nmol/L† | 525 | 360 (68.6%) | 6 (1.1%) | 9 (1.7%) | 353 (67.2%) | 2 [0 - 6] | 28 (5.3%) |
| PCT | <0.20 ng/mL† | 330 | 200 (60.6%) | 6 (1.8%) | 4 (1.2%) | 193 (58.5%) | 1 [0 - 6] | 20 (6.6%) |
| PCT | <0.25 ng/mL\* | 369 | 231 (62.6%) | 8 (2.2%) | 5 (1.4%) | 224 (60.7%) | 2 [0 - 6] | 21 (5.7%) |
| Lactate | <1.90 mmol/L† | 355 | 271 (76.3%) | 9 (2.5%) | 11 (3.1%) | 272 (76.6%) | 4 [0 - 7] | 27 (7.6%) |
| Lactate | <2.0 mmol/L\* | 371 | 284 (76.5%) | 13 (3.5%) | 13 (3.5%) | 286 (77.1%) | 4 [0 - 7] | 28 (7.5%) |
| CRP | <7.0 mg/L† | 251 | 148 (59.0%) | 7 (2.8%) | 3 (1.2%) | 155 (61.8%) | 3 [0 - 7] | 19 (7.6%) |
| SOFA | <2 points\* | 376 | 233 (62.0%) | 2 (0.5%) | 6 (1.6%) | 222 (59.0%) | 2 [0 - 6] | 24 (6.4%) |
| SOFA | <3 points† | 491 | 332 (67.6%) | 7 (1.4%) | 12 (2.4%) | 324 (66.0%) | 3 [0 - 7] | 33 (6.7%) |
| qSOFA | <1 point† | 452 | 300 (66.4%) | 5 (0.9%) | 10 (2.2%) | 291 (64.4%) | 2 [0 - 7] | 36 (8.0%) |
| qSOFA | <2 points\* | 637 | 458 (71.9%) | 23 (5.0%) | 19 (3.0%) | 451 (70.8%) | 3 [0 - 8] | 48 (7.5%) |
| NEWS | <4 points\* | 427 | 271 (63.5%) | 8 (1.9%) | 9 (2.1%) | 261 (61.1%) | 2 [0 - 6] | 35 (8.2%) |
| NEWS | <5 points† | 499 | 329 (65.9%) | 10 (2.0%) | 13 (2.6%) | 323 (64.7%) | 2 [0 - 6] | 39 (7.8%) |
| CRB-65 | <2 points\*\* | 502 | 345 (68.7%) | 11 (2.2%) | 12 (2.4%) | 332 (66.1%) | 2 [0 - 7] | 40 (8.0%) |
| SIRS | <2 points\*\* | 375 | 238 (63.5%) | 11 (2.9%) | 12 (3.2%) | 236 (62.9%) | 2 [0 - 6] | 30 (8.0%) |

\* denotes the use of a pre-established cut-off, † donates use of the optimised cut-off, and \*\* indicates that both the pre-established and optimised cut-offs were identical. *CI*:Confidence interval; *CRB-65*: Severity score for community-acquired pneumonia; *CRP*: C-reactive protein; ICU: Intensive Care Unit; MR*-proADM*: Mid-regional proadrenomedullin; *N*: Number; *NEWS*: National Early Warning Score; *PCT*: Procalcitonin; *qSOFA*: quick Sequential Organ Failure Assessment; *SOFA*: Sequential Organ Failure Assessment.

**Table S14. Treatment and outcome in patients with high biomarker or clinical score values (ED presentation)**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Biomarker**  **or score** | **Selected**  **cut-offs** | **Population**  **(*N*)** | **Antibiotic administration**  ***N* (%)** | **Mortality**  ***N* (%)** | **ICU admission**  ***N* (%)** | **Hospitalisation**  **N (%)** | **Length of hospitalisation**  **(days)** | **Infection related readmission**  ***N* (%)** |
| MR-proADM | ≥1.54 nmol/L\* | 209 | 192 (91.9%) | 26 (12.4%) | 15 (7.2%) | 191 (91.4%) | 7 [3 - 12] | 25 (12.0%) |
| MR-proADM | ≥1.77 nmol/L† | 159 | 145 (91.2%) | 24 (15.1%) | 14 (8.8%) | 145 (91.2%) | 7 [4 - 13] | 23 (14.5%) |
| PCT | ≥0.20 ng/mL† | 354 | 305 (86.2%) | 24 (6.8%) | 19 (5.4%) | 305 (86.2%) | 5 [2 - 10] | 31 (8.9%) |
| PCT | ≥0.25 ng/mL\* | 315 | 274 (87.0%) | 22 (7.0%) | 18 (5.7%) | 274 (87.0%) | 5 [2 - 10] | 30 (9.5%) |
| Lactate | ≥1.90 mmol/L† | 178 | 141 (79.2%) | 21 (11.8%) | 11 (6.2%) | 148 (83.1%) | 5 [2 - 10] | 12 (6.7%) |
| Lactate | ≥2.0 mmol/L\* | 162 | 128 (79.0%) | 17 (10.5%) | 9 (5.6%) | 134 (82.7%) | 5 [1.5 - 10] | 11 (6.8%) |
| CRP | ≥7.0 mg/L† | 395 | 332 (84.0%) | 21 (5.3%) | 20 (5.1%) | 324 (82.0%) | 4 [2 - 8] | 31 (7.8%) |
| SOFA | ≥2 points\* | 308 | 273 (88.6%) | 28 (9.1%) | 17 (5.5%) | 276 (89.6%) | 6 [3 - 10] | 27 (8.8%) |
| SOFA | ≥3 points† | 193 | 173 (89.6%) | 23 (11.9%) | 11 (5.7%) | 174 (90.2%) | 7 [4 - 11] | 18 (10.4%) |
| qSOFA | ≥1 point† | 232 | 205 (88.4%) | 25 (12.2%) | 13 (5.6%) | 207 (89.2%) | 6 [3 - 11] | 15 (6.5%) |
| qSOFA | ≥2 points\* | 47 | 47 (100.0%) | 7 (14.9%) | 4 (8.5%) | 47 (100.0%) | 7 [4 - 13] | 0 (0.0%) |
| NEWS | ≥4 points\* | 257 | 234 (91.1%) | 22 (8.6%) | 14 (5.4%) | 237 (92.2%) | 6 [3 - 11] | 16 (6.2%) |
| NEWS | ≥5 points† | 185 | 176 (95.1%) | 20 (10.8%) | 10 (5.4%) | 175 (94.6%) | 7 [4 - 12] | 12 (6.5%) |
| CRB-65 | ≥2 points\*\* | 182 | 160 (87.9%) | 19 (10.4%) | 11 (6.0%) | 166 (91.2%) | 7 [3 - 12] | 11 (6.0%) |
| SIRS | ≥2 points\*\* | 309 | 267 (86.4%) | 19 (6.1%) | 11 (3.6%) | 262 (84.8%) | 5 [2 - 10] | 21 (6.8%) |

\* denotes the use of a pre-established cut-off, † donates use of the optimised cut-off, and \*\* indicates that both the pre-established and optimised cut-offs were identical. *CI*:Confidence interval; *CRB-65*: Severity score for community-acquired pneumonia; *CRP*: C-reactive protein; *ICU*: Intensive Care Unit; *MR-proADM*: Mid-regional proadrenomedullin; *N*: Number; *NEWS*: National Early Warning Score; *PCT*: Procalcitonin; *qSOFA*: quick Sequential Organ Failure Assessment; *SOFA*: Sequential Organ Failure Assessment.

**Table S15. Treatment and outcome in patients with low biomarker or score values (72 hours)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Biomarker**  **or score** | **Selected**  **cut-offs** | **Population**  **(*N*)** | **Mortality**  ***N* (%)** | **ICU admission**  ***N* (%)** | **Length of hospitalisation**  **(days)** | **Infection related readmission**  ***N* (%)** |
| MR-proADM | <1.57 nmol/L† | 273 | 8 (2.9%) | 3 (1.1%) | 7 [5 - 10] | 22 (8.1%) |
| PCT | <1.78 ng/mL† | 296 | 13 (4.3%) | 6 (2.0%) | 7 [5 - 11] | 24 (8.1%) |
| Lactate | <1.7 mmol/L† | 121 | 6 (5.0%) | 2 (1.7%) | 7 [5 - 13] | 11 (9.1%) |
| CRP | <16.4 mg/L† | 202 | 14 (6.9%) | 3 (1.5%) | 7 [4 - 10] | 15 (7.4%) |
| SOFA | <2 points† | 183 | 3 (1.6%) | 3 (1.6%) | 7 [5 - 12] | 25 (13.7%) |
| qSOFA | <1 point† | 351 | 22 (6.3%) | 7 (2.0%) | 7 [4- 1 2] | 29 (8.3%) |
| NEWS | <4 points† | 268 | 11 (4.1%) | 7 (2.6%) | 7 [4.25 - 12.75] | 23 (8.6%) |
| CRB-65 | <1 point† | 90 | 1 (1.1%) | 1 (1.1%) | 7 [5 - 11] | 12 (13.3%) |
| SIRS | <1 point† | 158 | 7 (4.4%) | 5 (3.2%) | 6 [4 - 11] | 14 (8.9%) |

† donates use of the optimised cut-off. *CRB-65*: Severity score for community-acquired pneumonia; *CRP*: C-reactive protein; *ICU*: Intensive Care Unit; *MR-proADM*: Mid-regional proadrenomedullin; *N*: Number; *NEWS*: National Early Warning Score; *PCT*: Procalcitonin; *qSOFA*: quick Sequential Organ Failure Assessment; *SOFA*: Sequential Organ Failure Assessment.

**Table S16. Treatment and outcome in patients with high biomarker or score values (72 hours)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Biomarker**  **or score** | **Selected**  **cut-offs** | **Population**  **(*N*)** | **Mortality**  ***N* (%)** | **ICU admission**  ***N* (%)** | **Length of hospitalisation**  **(days)** | **Infection related readmission**  ***N* (%)** |
| MR-proADM | ≥1.57 nmol/L† | 102 | 17 (16.7%) | 4 (3.9%) | 9.5 [6 - 19.25] | 9 (8.8%) |
| PCT | ≥1.78 ng/mL† | 74 | 12 (16.2%) | 1 (1.4%) | 8.5 [6 - 13.75] | 6 (8.1%) |
| Lactate | ≥1.7 mmol/L† | 145 | 18 (12.4%) | 5 (3.4%) | 8 [4 - 10] | 12 (8.3%) |
| CRP | ≥16.4 mg/L† | 79 | 6 (7.6%) | 0 (0.0%) | 7.5 [5 - 14] | 7 (8.9%) |
| SOFA | ≥2 points† | 192 | 22 (11.5%) | 4 (2.1%) | 8 [5 - 14] | 18 (9.4%) |
| qSOFA | ≥1 point† | 119 | 13 (10.9%) | 0 (0.0%) | 8 [6 - 14] | 9 (7.6%) |
| NEWS | ≥4 points† | 108 | 14 (13.0%) | 0 (0.0%) | 9 [6 - 14] | 8 (7.4%) |
| CRB-65 | ≥1 point† | 286 | 24 (8.4%) | 6 (2.1%) | 7 [5 - 13] | 20 (7.0%) |
| SIRS | ≥1 point† | 218 | 18 (8.3%) | 2 (0.9%) | 8 [5 - 14] | 17 (7.8%) |

† donates use of the optimised cut-off. *CRB-65*: Severity score for community-acquired pneumonia; *CRP*: C-reactive protein; *ICU*: Intensive Care Unit; *MR-proADM*: Mid-regional proadrenomedullin; *N*: Number; *NEWS*: National Early Warning Score; *PCT*: Procalcitonin; *qSOFA*: quick Sequential Organ Failure Assessment; *SOFA*: Sequential Organ Failure Assessment.

**Table S17. Patient subgroups stratified by lactate and MR-proADM**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Patient populations stratified by Lactate and MR-proADM | | | | | | | |
| **Patient subgroups** | MR-proADM  (nmol/L) | Lactate  (mmol/L) | MR-proADM  (nmol/L) | Lactate  (mmol/L) | MR-proADM  (nmol/L) | Lactate  (mmol/L) | MR-proADM  (nmol/L) | Lactate  (mmol/L) |
| <1.77 | <2.0 | ≥1.77 | <2.0 | <1.77 | ≥2.0 | ≥1.77 | ≥2.0 |
| **Population** *N* (%) | 296 (55.5%) | | 75 (14.1%) | | 98 (18.4%) | | 64 (12.0%) | |
| **Antibiotic administration** *N* (%) | 214 (72.3%) | | 70 (94.7%) | | 71 (72.4%) | | 57 (89.1%) | |
| **Time to antibiotic administration** (mins) (median [Q1-Q4]) | 182 [90 - 329] | | 180 [116 - 300] | | 120 [56 - 240] | | 120 [60 - 203] | |
| **Antibiotic administration <180 mins** *N* (%) | 86 (40.2%) | | 32 (45.7%) | | 44 (62.0%) | | 38 (66.7%) | |
| **Hospitalisation** *N* (%) | 217 (73.3%) | | 69 (92.0%) | | 76 (77.6%) | | 58 (90.6%) | |
| **Length of hospitalisation** (days) (median [Q1-Q4]) | 2 [0 - 7] | | 7 [4 - 13.5] | | 3 [0 - 7.5] | | 7 [4 - 13] | |
| **Infection related readmission** *N* (%) | 17 (5.7%) | | 11 (14.7%) | | 3 (3.1%) | | 8 (12.5%) | |
| **ICU admission** *N* (%) | 7 (2.4%) | | 6 (8.0%) | | 2 (2.0%) | | 7 (10.9%) | |
| **Time to ICU admission** (days) (median [Q1-Q4]) | 13 [2 - 17] | | 1 [0 - 4.75] | | NA | | 0 [0 - 0] | |
| **Number of immediate ICU admissions** *N* (%) | 1 (4.5%) | | 3 (13.6%) | | 1 (4.5%) | | 4 (18.2%) | |
| **Number of delayed ICU admissions** *N* (%) | 1 (4.5%) | | 3 (13.6%) | | 1 (4.5%) | | 2 (9.1%) | |
| **Number of late ICU admissions** *N* (%) | 5 (22.7%) | | 0 (0.0%) | | 0 (0.0%) | | 1 (4.5%) | |
| **Infection-related 28-day mortality** *N* (%) | 3 (1.0%) | | 10 (13.3%) | | 3 (3.1%) | | 14 (21.9%) | |
| **Hospital mortality** *N* (%) | 4 (1.4%) | | 10 (13.3%) | | 6 (6.1%) | | 14 (21.9%) | |
| **Disease progression** *N* (%) | 24 (8.1%) | | 20 (26.7%) | | 8 (8.2%) | | 24 (37.5%) | |

Number of immediate, delayed or late ICU admissions are expressed as a percentage of the total number of ICU admissions. *ICU*: Intensive Care Unit; *MR-proADM*: Mid-regional proadrenomedullin; *N*: Number.

**Table S18. Patient subgroups stratified by qSOFA and MR-proADM**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Patient populations stratified by qSOFA and MR-proADM | | | | | | | |
| **Patient subgroups** | MR-proADM  (nmol/L) | qSOFA  (points) | MR-proADM  (nmol/L) | qSOFA  (points) | MR-proADM  (nmol/L) | qSOFA  (points) | MR-proADM  (nmol/L) | qSOFA  (points) |
| <1.77 | <2 | ≥1.77 | <2 | <1.77 | ≥2 | ≥1.77 | ≥2 |
| **Population** *N* (%) | 506 (74.0%) | | 131 (19.2%) | | 19 (2.8%) | | 28 (4.1%) | |
| **Antibiotic administration** *N* (%) | 341 (67.4%) | | 117 (89.3%) | | 19 (100.0%) | | 28 (100.0%) | |
| **Time to antibiotic administration** (mins) (median [Q1-Q4]) | 210 [120 - 360] | | 210 [120 - 360] | | 180 [120 - 234] | | 120 [85 - 221] | |
| **Antibiotic administration <180 mins** *N* (%) | 132 (38.7%) | | 44 (37.6%) | | 9 (47.4%) | | 18 (64.3%) | |
| **Hospitalisation** *N* (%) | 334 (66.0%) | | 117 (89.3%) | | 19 (100.0%) | | 28 (100.0%) | |
| **Length of hospitalisation** (days) (median [Q1-Q4]) | 2 [0 - 7] | | 7 [4 - 12] | | 7 [5 - 8] | | 8 [3.75 - 19.25] | |
| **Infection related readmission** *N* (%) | 28 (5.5%) | | 20 (15.3%) | | 0 (0.0%) | | 3 (10.7%) | |
| **ICU admission** *N* (%) | 9 (1.8%) | | 10 (7.6%) | | 0 (0.0%) | | 4 (14.3%) | |
| **Time to ICU admission** (days) (median [Q1-Q4]) | 13 [2 - 9] | | 1 [0 - 5] | | NA | | 0 [0 - 0] | |
| **Number of immediate ICU admissions** *N* (%) | 2 (8.7%) | | 3 (13.0%) | | 0 (0.0%) | | 4 (17.4%) | |
| **Number of delayed ICU admissions** *N* (%) | 2 (8.7%) | | 6 (26.1%) | | 0 (0.0%) | | 0 (0.0%) | |
| **Number of late ICU admissions** *N* (%) | 5 (21.7%) | | 1 (4.3%) | | 0 (0.0%) | | 0 (0.0%) | |
| **Infection-related 28-day mortality** *N* (%) | 6 (1.2%) | | 17 (13.0%) | | 0 (0.0%) | | 7 (25.0%) | |
| **Hospital mortality** *N* (%) | 8 (1.6%) | | 17 (13.0%) | | 2 (10.5%) | | 8 (28.6%) | |
| **Disease progression** *N* (%) | 32 (6.3%) | | 34 (26.0%) | | 1 (5.3%) | | 12 (42.9%) | |

Number of immediate, delayed or late ICU admissions are expressed as a percentage of the total number of ICU admissions. *ICU*: Intensive Care Unit; *MR-proADM*: Mid-regional proadrenomedullin; *N*: Number; *qSOFA*: quick Sequential Organ Failure Assessment.

**Table S19. Patient subgroups stratified by CRB-65 and MR-proADM**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Patient populations stratified by CRB-65 and MR-proADM | | | | | | | |
| **Patient subgroups** | MR-proADM  (nmol/L) | CRB-65  (points) | MR-proADM  (nmol/L) | CRB-65  (points) | MR-proADM  (nmol/L) | CRB-65  (points) | MR-proADM  (nmol/L) | CRB-65  (points) |
| <1.77 | <2 | ≥1.77 | <2 | <1.77 | ≥2 | ≥1.77 | ≥2 |
| **Population** *N* (%) | 423 (61.8%) | | 79 (11.5%) | | 102 (14.9%) | | 80 (11.7%) | |
| **Antibiotic administration** *N* (%) | 273 (64.5%) | | 72 (91.1%) | | 87 (85.3%) | | 73 (91.3%) | |
| **Time to antibiotic administration** (mins) (median [Q1-Q4]) | 183 [120 - 330] | | 180 [120 - 300] | | 240 [150 - 355] | | 182 [97.5 - 300] | |
| **Antibiotic administration <180 mins** *N* (%) | 114 (41.8%) | | 30 (41.7%) | | 26 (30.0%) | | 36 (49.3%) | |
| **Hospitalisation** *N* (%) | 262 (61.9%) | | 70 (88.6%) | | 91 (89.2%) | | 75 (93.8%) | |
| **Length of hospitalisation** (days) (median [Q1-Q4]) | 13 [1 - 18] | | 6 [4 - 10.75] | | 6 [2 - 9.5] | | 8 [4 - 16.5] | |
| **Infection related readmission** *N* (%) | 25 (5.9%) | | 15 (19.0%) | | 3 (2.9%) | | 8 (10.0%) | |
| **ICU admission** *N* (%) | 7 (1.7%) | | 5 (6.3%) | | 2 (2.0%) | | 9 (11.3%) | |
| **Time to ICU admission** (days) (median [Q1-Q4]) | 2 [0 - 6] | | 0 [0 - 0] | | NA | | 0 [0 - 2] | |
| **Number of immediate ICU admissions** *N* (%) | 2 (8.7%) | | 3 (13.0%) | | 0 (0.0%) | | 4 (17.4%) | |
| **Number of delayed ICU admissions** *N* (%) | 1 (4.3%) | | 2 (8.7%) | | 1 (4.3%) | | 4 (17.4%) | |
| **Number of late ICU admissions** *N* (%) | 4 (17.4%) | | 0 (0.0%) | | 1 (4.3%) | | 1 (4.3%) | |
| **Infection-related 28-day mortality** *N* (%) | 4 (0.9%) | | 7 (8.9%) | | 2 (2.0%) | | 17 (21.3%) | |
| **Hospital mortality** *N* (%) | 4 (0.9%) | | 7 (8.9%) | | 6 (5.9%) | | 18 (22.5%) | |
| **Disease progression** *N* (%) | 23 (5.4%) | | 18 (22.8%) | | 10 (12.5%) | | 28 (35.0%) | |

Number of immediate, delayed or late ICU admissions are expressed as a percentage of the total number of ICU admissions. *ICU*: Intensive Care Unit; *MR-proADM*: Mid-regional proadrenomedullin; *N*: Number; *CRB-65:* severity sore for community acquired Pneumonia

**Table S20. Patient subgroups based on antibiotic administration using NEWS and MR-proADM**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Low NEWS, Low MR-proADM subgroup** | | **Low NEWS, High MR-proADM subgroup** | |
|  | **Patients receiving antibiotics**  **(*N*=266)** | **Patients not receiving antibiotics**  **(*N*=159)** | **Patients receiving antibiotics**  **(*N*=63)** | **Patients not receiving antibiotics**  **(*N*=11)** |
| Hospitalisation | 225 (84.6%) | 35 (22.0%) | 58 (92.1%) | 5 (45.5%) |
| ICU admission | 6 (2.3%) | 1 (0.6%) | 3 (4.8%) | 3 (27.3%) |
| Hospital readmission | 16 (0.6%) | 9 (5.7%) | 9 (14.3%) | 6 (54.5%) |
| 28-day Mortality | 0 (0.0%) | 0 (0.0%) | 9 (14.3%) | 1 (9.1%) |

Patients with respective NEWS and MR-proADM cut-offs of <5 points and <1.77 nmol/L were designated as “low”, whereas patients with NEWS and MR-proADM cut-offs of ≥5 points and ≥1.77 nmol/L were designated as “high”. *ICU*: Intensive Care Unit; *MR-proADM*: Mid-regional proadrenomedullin; *N*: Number; *NEWS*: National Early Warning Score

**Table S21. Patient subgroups based on antibiotic administration using qSOFA and MR-proADM**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Low qSOFA, Low MR-proADM subgroup** | | **Low qSOFA, High MR-proADM subgroup** | |
|  | **Patients receiving antibiotics**  **(*N*=341)** | **Patients not receiving antibiotics**  **(*N*=165)** | **Patients receiving antibiotics**  **(*N*=117)** | **Patients not receiving antibiotics**  **(*N*=14)** |
| Hospitalisation | 298 (87.4%) | 36 (21.8%) | 110 (94.0%) | 7 (50.0%) |
| ICU admission | 8 (2.3%) | 1 (0.6%) | 6 (5.1%) | 4 (28.6%) |
| Hospital readmission | 19 (5.6%) | 9 (5.4%) | 15 (12.8%) | 5 (35.7%) |
| 28-day Mortality | 6 (1.8%) | 0 (0.0%) | 15 (12.8%) | 2 (14.3%) |

Patients with respective qSOFA and MR-proADM cut-offs of <2 points and <1.77 nmol/L were designated as “low”, whereas patients with qSOFA and MR-proADM cut-offs of ≥2 points and ≥1.77 nmol/L were designated as “high”. *ICU*: Intensive Care Unit; *MR-proADM*: Mid-regional proadrenomedullin; *N*: Number; *qSOFA*: quick Sequential Organ Failure Assessment.

**Table S22. Low NEWS patient subgroups classified according to Lactate and PCT kinetics between ED presentation and 72 hours**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Patient populations stratified by NEWS and either lactate or PCT | | | | | | | |
| **Patient subgroups** | Lactate  (mmol/L) | NEWS  (points) | Lactate  (mmol/L) | NEWS  (points) | PCT  (ng/mL) | NEWS  (points) | PCT  (ng/mL) | NEWS  (points) |
| <1.90 | <5 | ≥1.90 | <5 | <0.20 | <5 | ≥0.20 | <5 |
| **Population** *N (%)* | 258 (37.7%) | | 101 (14.8%) | | 279 (40.8%) | | 220 (32.2%) | |
| **Infection related 28-day mortality** *N* (%) | 3 (1.2%) | | 7 (6.9%) | | 0 (0.0%) | | 10 (4.5%) | |
| **NEWS: Surviving patients** | | | | | | | | |
| ED admission (points) | 1.83 {1.36) | | 2.05 (1.38) | | 1.54 (1.28) | | 2.11 (1.30) | |
| 72 hours (points) | 1.72 (1.88) | | 1.71 (1.77) | | 1.52 (1.72) | | 1.77 (1.85) | |
| p-value | 0.498 | | 0.202 | | 0.064 | | 0.012 | |
| **NEWS: Non-surviving patients** | | | | | | | | |
| ED admission (points) | 2.67 (1.15) | | 2.57 (0.97) | | NA | | 2.60 (0.97) | |
| 72 hours (points) | 2.67 (3.79) | | 3.14 (1.77) | | NA | | 3.00 (2.31) | |
| p-value | 1.000 | | 0.469 | | NA | | 0.565 | |
| **Biomarker: Surviving patients** | | | | | | | | |
| ED admission | 1.25 (0.33) | | 2.94 (2.26) | | 0.09 (0.05) | | 3.94 (11.05) | |
| 72 hours | 2.22 (3.66) | | 2.38 (3.42) | | 0.17 (0.22) | | 3.67 (11.90) | |
| p-value | <0.001 | | 0.284 | | 0.010 | | 0.268 | |
| **Biomarker: Non-surviving patients** | | | | | | | | |
| ED admission | 1.33 (0.29) | | 2.93 (1.78) | | NA | | 9.92 (15.65) | |
| 72 hours | 1.26 (0.12) | | 1.97 (0.23) | | NA | | 6.64 (8.71) | |
| p-value | 0.691 | | 0.183 | | NA | | 0.553 | |

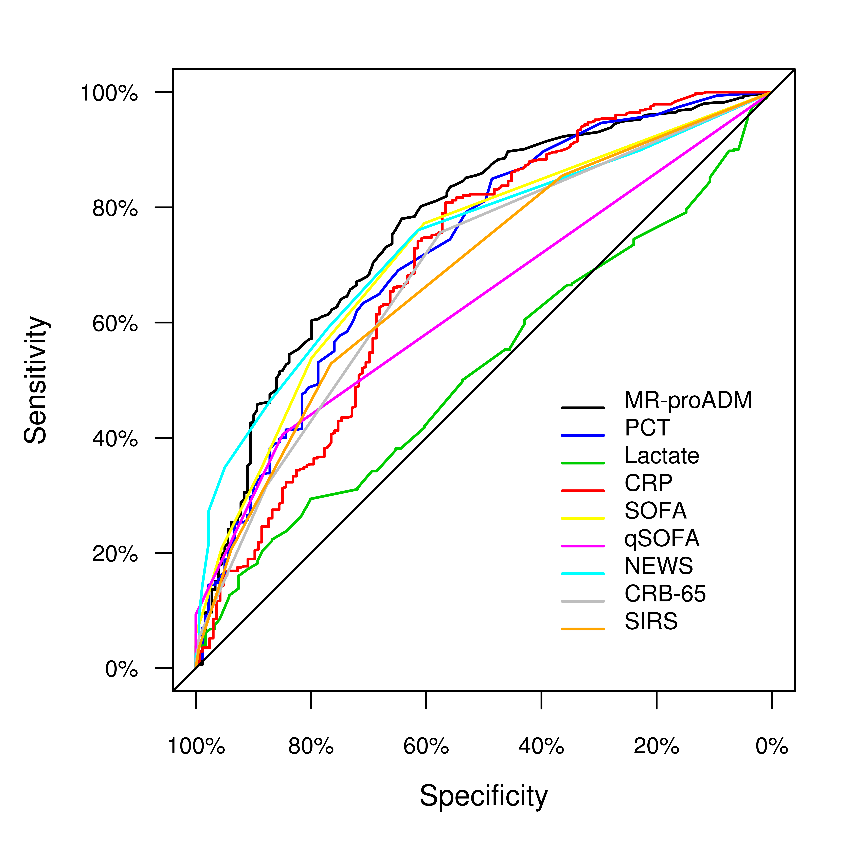
*ED*: Emergency Department; *N*: Number; *NEWS*: National Early Warning Score; *PCT*: Procalcitonin;

**Table S23. qSOFA and MR-proADM values upon presentation and 72 hours within stratified subgroups**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | | Patient populations stratified by qSOFA and MR-proADM | | | | | | | |
| **Patient subgroups** | | | MR-proADM  (nmol/L) | qSOFA  (points) | MR-proADM  (nmol/L) | qSOFA  (points) | MR-proADM  (nmol/L) | qSOFA  (points) | MR-proADM  (nmol/L) | qSOFA  (points) |
| <1.77 | <2 | ≥1.77 | <2 | <1.77 | ≥2 | ≥1.77 | ≥2 |
| **Population**  *N* (%) | | | 506 (74.0%) | | 131 (19.2%) | | 19 (2.8%) | | 28 (4.1%) | |
| **Infection related 28-day mortality**  *N* (%) | | | 6 (1.2%) | | 17 (13.0%) | | 0 (0.0%) | | 7 (25.0%) | |
| **Disease progression: qSOFA** | **Total cohort** | Admission (points) | 0.44 (0.50) | | 0.61 (0.49) | | 2.00 (0.00) | | 2.20 (0.42) | |
| 72 hours (points) | 0.38 (0.61) | | 0.51 (0.69) | | 0.87 (0.63) | | 0.87 (0.63) | |
| p-value | 0.749 | | 0.115 | | <0.001 | | <0.001 | |
| **Surviving patients** | Admission (points) | 0.41 (0.50) | | 0.53 (0.50) | | 2.24 (0.44) | | 2.24 (0.44) | |
| 72 hours (points) | 0.38 (0.61) | | 0.45 (0.65) | | 0.95 (0.62) | | 0.95 (0.62) | |
| p-value | 0.867 | | 0.184 | | <0.001 | | <0.001 | |
| **Non-surviving patients** | Admission (points) | 0.60 (0.55) | | 0.87 (0.35) | | NA | | 2.14 (0.38) | |
| 72 hours (points) | 0.80 (0.84) | | 0.60 (0.74) | | NA | | 0.50 (0.58) | |
| p-value | 0.704 | | 0.165 | | NA | | 0.014 | |
| **Disease progression: MR-proADM** | **Total cohort** | Admission (nmol/L) | 1.17 (0.38) | | 3.11 (1.28) | | 1.37 (0.32) | | 3.63 (1.82) | |
| 72 hours (nmol/L) | 1.03 (0.48) | | 2.35 (1.58) | | 1.24 (0.47) | | 2.23 (1.64) | |
| p-value | 0.010 | | 0.001 | | 0.348 | | 0.002 | |
| **Surviving patients** | Admission (nmol/L) | 1.68 (0.37) | | 3.09 (1.24) | | 1.37 (0.32) | | 3.82 (1.79) | |
| 72 hours (nmol/L) | 1.01 (0.48) | | 2.04 (1.07) | | 1.24 (0.47) | | 2.29 (1.85) | |
| p-value | 0.010 | | <0.001 | | 0.348 | | 0.002 | |
| **Non-surviving patients** | Admission (nmol/L) | 1.30 (0.29) | | 2.98 (1.16) | | NA | | 2.20 (0.46) | |
| 72 hours (nmol/L) | 0.94 (0.48) | | 3.17 (2.53) | | NA | | 2.04 (0.60) | |
| p-value | 0.256 | | 0.617 | | NA | | 0.467 | |

All NEWS and MR-proADM values are expressed as mean (standard deviation). *MR-proADM*: Mid-regional proadrenomedullin; *N*: Number; *qSOFA*: quick Sequential Organ Failure Assessment.

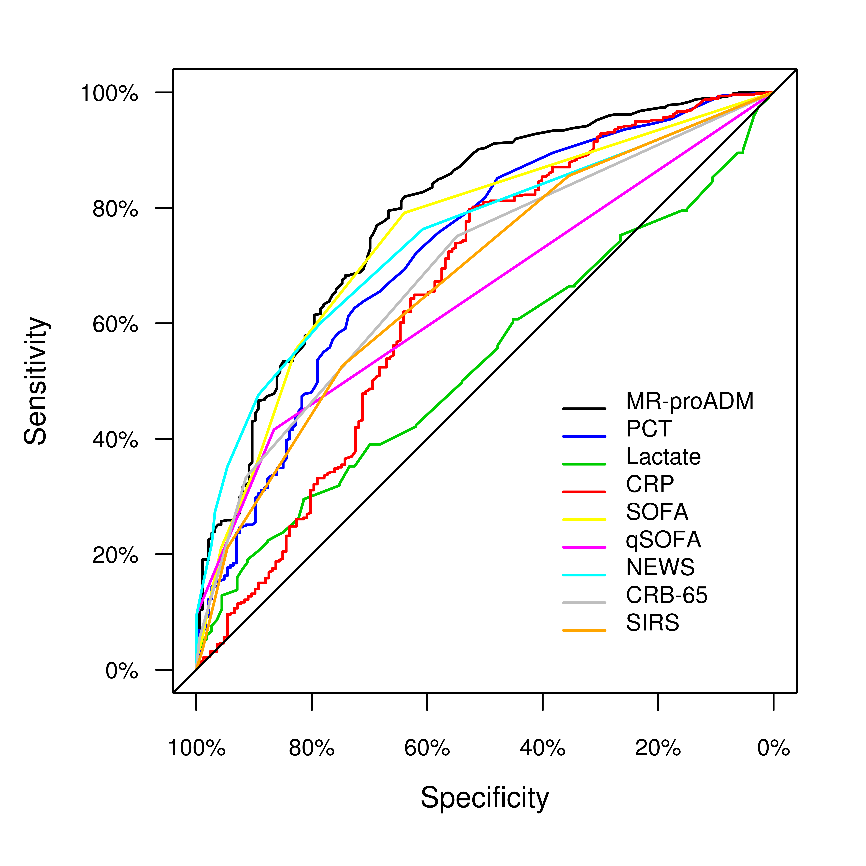
**Supplementary Figures**

**Figure S1. AUROC analysis for antibiotic requirement during treatment within the ED**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Biomarkers and clinical scores** | **AUC** | **Cut-off** | **Sensitivity** | **Specificity** | **PPV** | **NPV** | **LR+** | **LR-** | **OR** |
| ED admission | MR-proADM | 0.77 [0.73-0.81] | 0.80 | 0.78 [0.74-0.81] | 0.64 [0.57-0.71] | 0.86 [0.83-0.89] | 0.51 [0.44-0.57] | 2.18 [1.78-2.67] | 0.34 [0.28-0.42] | 6.4 [4.4 - 9.2] |
| PCT | 0.73 [0.69-0.77] | 0.18 | 0.63 [0.59-0.67] | 0.71 [0.64-0.77] | 0.86 [0.82-0.89] | 0.41 [0.35-0.46] | 2.18 [1.72-2.77] | 0.52 [0.45-0.60] | 4.3 [2.9 - 6.2] |
| Lactate | 0.52 [0.47-0.58] | 2.06 | 0.29 [0.25-0.34] | 0.80 [0.72-0.86] | 0.83 [0.77-0.89] | 0.25 [0.21-0.30] | 1.48 [1.00-2.18] | 0.88 [0.79-0.98] | 1.6 [1.0 - 2.7] |
| CRP | 0.70 [0.65-0.75] | 4.07 | 0.81 [0.77-0.84] | 0.57 [0.49-0.64] | 0.84 [0.81-0.87] | 0.51 [0.43-0.58] | 1.86 [1.56-2.23] | 0.34 [0.27-0.42] | 5.5 [3.8 - 8.1] |
| SOFA | 0.73 [0.69-0.77] | 1 | 0.77 [0.73-0.81] | 0.60 [0.53-0.67] | 0.85 [0.81-0.88] | 0.48 [0.42-0.55] | 1.95 [1.62-2.35] | 0.38 [0.31-0.46] | 5.2 [3.6 - 7.4] |
| qSOFA | 0.64 [0.60-0.67] | 1 | 0.41 [0.36-0.45] | 0.85 [0.79-0.89] | 0.88 [0.84-0.92] | 0.34 [0.29-0.38] | 2.69 [1.87-3.87] | 0.70 [0.64-0.77] | 3.8 [2.5 - 6.0] |
| NEWS | 0.74 [0.70-0.78] | 2 | 0.76 [0.72-0.80] | 0.61 [0.54-0.68] | 0.85 [0.81-0.88] | 0.48 [0.41-0.54] | 1.97 [1.63-2.39] | 0.39 [0.32-0.47] | 5.1 [3.5 - 7.3] |
| CRB-65 | 0.69 [0.65-0.73] | 1 | 0.76 [0.72-0.79] | 0.58 [0.50-0.65] | 0.83 [0.80-0.87] | 0.46 [0.39-0.52] | 1.78 [1.49-2.13] | 0.42 [0.35-0.52] | 4.2 [2.9 - 6.0] |
| SIRS | 0.69 [0.64-0.73] | 2 | 0.53 [0.49-0.57] | 0.77 [0.70-0.82] | 0.86 [0.82-0.90] | 0.37 [0.32-0.42] | 2.25 [1.71-2.97] | 0.62 [0.54-0.70] | 3.7 [2.5 - 5.4] |

*CRB-65*: Severity score for community-acquired pneumonia; *CRP*: C-reactive protein; *MR-proADM*: Mid-regional proadrenomedullin; *NEWS*: National Early Warning Score; *PCT*: Procalcitonin; *qSOFA*: quick Sequential Organ Failure Assessment; *SOFA*: Sequential Organ Failure Assessment.

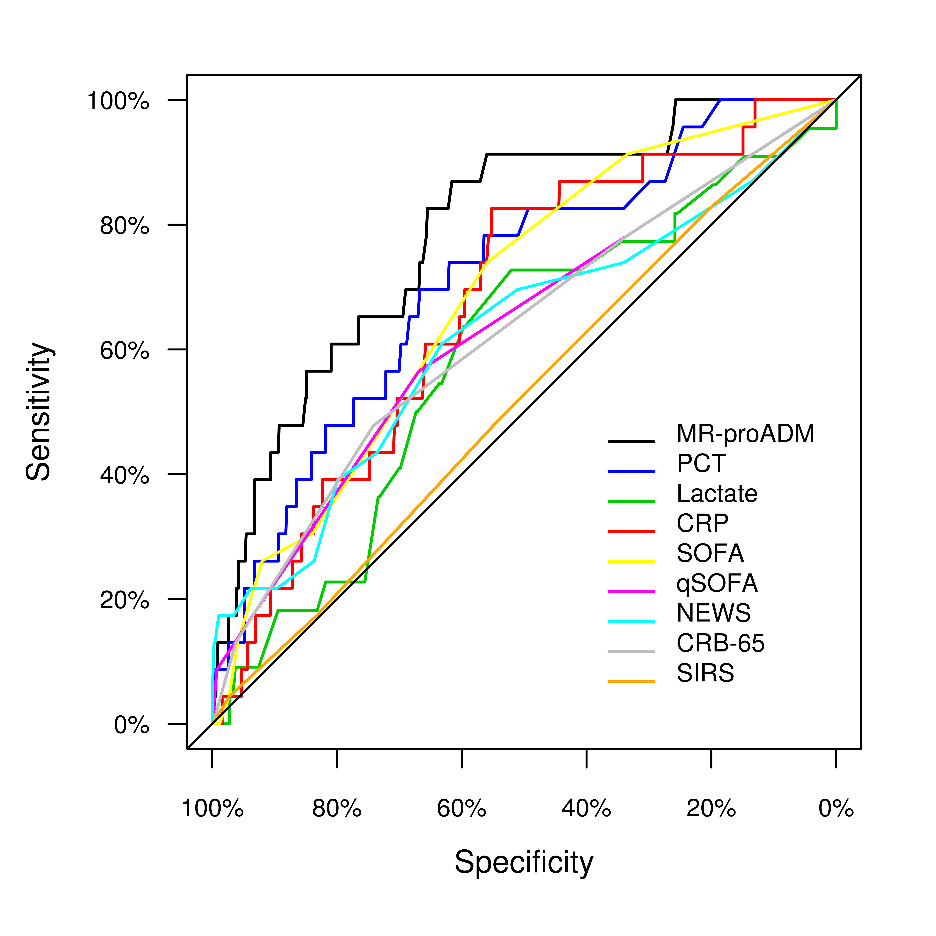
**Figure S2. AUROC analysis for hospitalisation requirement upon ED presentation**



|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Biomarkers and clinical scores** | **AUC** | **Cut-off** | **Sensitivity** | **Specificity** | **PPV** | **NPV** | **LR+** | **LR-** | **OR** |
| ED admission | MR-proADM | 0.79 [0.75-0.83] | 0.8 | 0.80 [0.76-0.83] | 0.67 [0.60-0.73] | 0.86 [0.83-0.89] | 0.55 [0.48-0.61] | 2.39 [1.94-2.94] | 0.31 [0.25-0.38] | 7.8 [5.3 - 11.3] |
| PCT | 0.73 [0.68-0.77] | 0.19 | 0.63 [0.58-0.67] | 0.73 [0.66-0.78] | 0.86 [0.82-0.89] | 0.42 [0.37-0.48] | 2.28 [1.79-2.91] | 0.51 [0.45-0.59] | 4.4 [3.1 - 6.4] |
| Lactate | 0.53 [0.48-0.59] | 2.06 | 0.30 [0.25-0.34] | 0.81 [0.73-0.88] | 0.86 [0.79-0.90] | 0.24 [0.20-0.28] | 1.59 [1.05-2.40] | 0.87 [0.78-0.96] | 1.8 [1.1 - 3.1] |
| CRP | 0.66 [0.61-0.71] | 3.97 | 0.80 [0.76-0.83] | 0.53 [0.45-0.60] | 0.83 [0.79-0.86] | 0.48 [0.40-0.55] | 1.69 [1.43-1.99] | 0.38 [0.31-0.48] | 4.4 [3.0 - 6.4] |
| SOFA | 0.75 [0.71-0.79] | 1 | 0.79 [0.75-0.82] | 0.64 [0.57-0.71] | 0.85 [0.82-0.88] | 0.53 [0.47-0.60] | 2.20 [1.80-2.67] | 0.33 [0.27-0.40] | 6.7 [4.7 - 9.7] |
| qSOFA | 0.65 [0.62-0.68] | 1 | 0.42 [0.37-0.46] | 0.87 [0.81-0.91] | 0.89 [0.85-0.93] | 0.36 [0.31-0.40] | 3.09 [2.12-4.52] | 0.68 [0.61-0.74] | 4.6 [2.9 - 7.2] |
| NEWS | 0.75 [0.71-0.79] | 3 | 0.60 [0.56-0.64] | 0.78 [0.72-0.84] | 0.88 [0.84-0.91] | 0.42 [0.37-0.48] | 2.79 [2.10-3.71] | 0.51 [0.45-0.58] | 5.5 [3.7 - 8.1] |
| CRB-65 | 0.69 [0.66-0.73] | 1 | 0.75 [0.71-0.79] | 0.55 [0.48-0.62] | 0.82 [0.78-0.85] | 0.45 [0.39-0.52] | 1.66 [1.41-1.96] | 0.45 [0.37-0.55] | 3.7 [2.6 - 5.2] |
| SIRS | 0.68 [0.64-0.72] | 2 | 0.53 [0.48-0.57] | 0.75 [0.68-0.80] | 0.85 [0.80-0.88] | 0.37 [0.32-0.42] | 2.08 [1.60-2.70] | 0.63 [0.56-0.72] | 3.3 [2.3 - 4.8] |

*CRB-65*: Severity score for community-acquired pneumonia; *CRP*: C-reactive protein; *MR-proADM*: Mid-regional proadrenomedullin; *NEWS*: National Early Warning Score; *PCT*: Procalcitonin; *qSOFA*: quick Sequential Organ Failure Assessment; *SOFA*: Sequential Organ Failure Assessment.

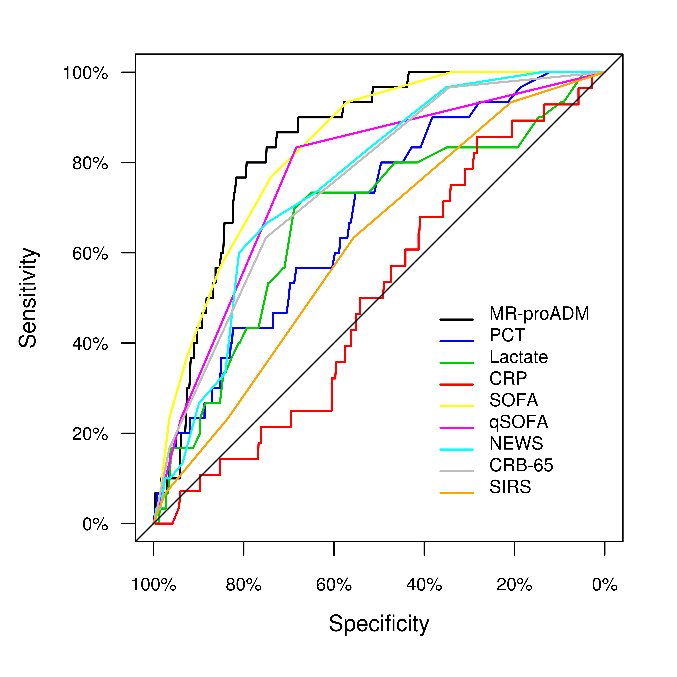
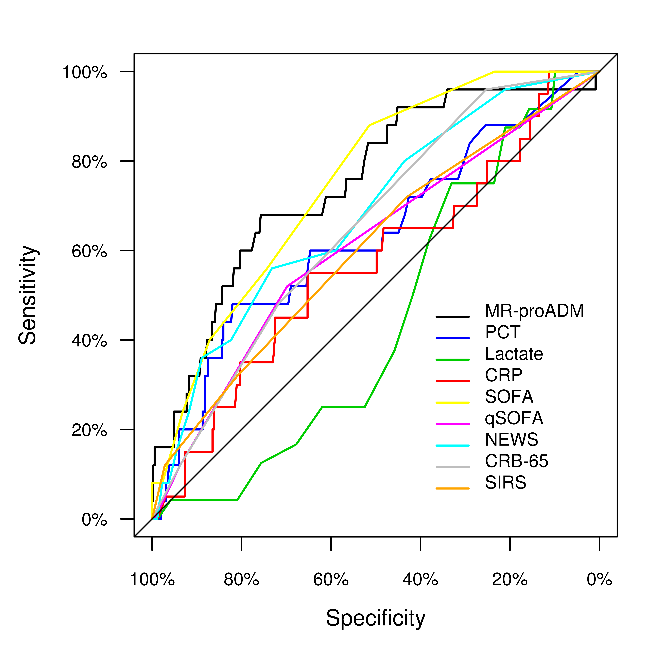
**Figure S3. AUROC analysis for ICU admission within 28 days of initial ED presentation**



|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Biomarkers and clinical scores** | **AUC** | **Cut-off** | **Sensitivity** | **Specificity** | **PPV** | **NPV** | **LR+** | **LR-** | **OR** |
| ED admission | MR-proADM | 0.79 [0.70-0.88] | 1.26 | 0.87 [0.68-0.95] | 0.62 [0.58-0.65] | 0.07 [0.05-0.11] | 0.99 [0.98-1.00] | 2.26 [1.88-2.72] | 0.21 [0.07-0.61] | 10.7 [3.1 - 36.3] |
| PCT | 0.71 [0.61-0.82] | 0.47 | 0.70 [0.49-0.84] | 0.67 [0.63-0.70] | 0.07 [0.04-0.11] | 0.98 [0.97-0.99] | 2.09 [1.56-2.80] | 0.46 [0.25-0.85] | 4.6 [1.9 - 11.3] |
| Lactate | 0.59 [0.47-0.71] | 1.6 | 0.73 [0.52-0.87] | 0.52 [0.48-0.56] | 0.06 [0.04-0.10] | 0.98 [0.95-0.99] | 1.52 [1.16-1.99] | 0.52 [0.26-1.04] | 2.9 [1.1 - 7.5] |
| CRP | 0.67 [0.57-0.78] | 12.2 | 0.83 [0.63-0.93] | 0.55 [0.51-0.59] | 0.06 [0.04-0.10] | 0.99 [0.97-1.00] | 1.84 [1.50-2.27] | 0.31 [0.13-0.77] | 5.9 [2.0 - 17.4] |
| SOFA | 0.68 [0.58-0.78] | 2 | 0.74 [0.54-0.87] | 0.56 [0.52-0.60] | 0.06 [0.03-0.09] | 0.98 [0.97-0.99] | 1.68 [1.30-2.17] | 0.47 [0.23-0.93] | 3.6 [1.4 - 9.2] |
| qSOFA | 0.63 [0.52-0.74] | 1 | 0.57 [0.37-0.74] | 0.67 [0.63-0.70] | 0.06 [0.03-0.09] | 0.98 [0.96-0.99] | 1.71 [1.17-2.48] | 0.65 [0.41-1.04] | 2.6 [1.1 - 6.1] |
| NEWS | 0.62 [0.49-0.75] | 4 | 0.61 [0.41-0.78] | 0.63 [0.59-0.67] | 0.05 [0.03-0.09] | 0.98 [0.96-0.99] | 1.66 [1.18-2.33] | 0.62 [0.37-1.03] | 2.7 [1.1 - 6.3] |
| CRB-65 | 0.62 [0.53-0.75] | 2 | 0.48 [0.29-0.67] | 0.74 [0.71-0.77] | 0.06 [0.03-0.10] | 0.98 [0.96-0.99] | 1.85 [1.18-2.89] | 0.70 [0.47-1.04] | 2.6 [1.1 - 6.1] |
| SIRS | 0.52 [0.40-0.64] | 1 | 0.83 [0.63-0.93] | 0.20 [0.17-0.24] | 0.03 [0.02-0.05] | 0.97 [0.93-0.99] | 1.04 [0.86-1.25] | 0.86 [0.35-2.12] | 1.2 [0.4 - 3.6] |

*CRB-65*: Severity score for community-acquired pneumonia; *CRP*: C-reactive protein; *MR-proADM*: Mid-regional proadrenomedullin; *NEWS*: National Early Warning Score; *PCT*: Procalcitonin; *qSOFA*: quick Sequential Organ Failure Assessment; *SOFA*: Sequential Organ Failure Assessment.

**Figure S4. AUROC analysis for infection-related 28-day mortality upon ED presentation and 72 hours**



**B**

**A**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Biomarkers and clinical scores** | **AUC** | **Cut-off** | **Sensitivity** | **Specificity** | **PPV** | **NPV** | **LR+** | **LR-** | **OR** |
| ED admission | MR-proADM | 0.84 [0.79-0.89] | 1.77 | 0.80 [0.63-0.90] | 0.79 [0.76-0.82] | 0.15 [0.10-0.21] | 0.99 [0.98-0.99] | 3.88 [3.07-4.90] | 0.25 [0.12-0.52] | 15.4 [6.2 - 38.4] |
| PCT | 0.68 [0.59-0.77] | 0.2 | 0.80 [0.63-0.90] | 0.50 [0.46-0.53] | 0.07 [0.05-0.10] | 0.98 [0.96-0.99] | 1.59 [1.31-1.93] | 0.40 [0.20-0.83] | 3.9 [1.6 - 9.7] |
| Lactate | 0.67 [0.57-0.78] | 1.9 | 0.70 [0.52-0.83] | 0.69 [0.65-0.73] | 0.12 [0.08-0.17] | 0.97 [0.95-0.99] | 2.24 [1.72-2.93] | 0.44 [0.25-0.76] | 5.1 [2.3 - 11.5] |
| CRP | 0.51 [0.41-0.60] | 7 | 0.75 [0.57-0.87] | 0.39 [0.36-0.43] | 0.05 [0.04-0.08] | 0.97 [0.94-0.99] | 1.24 [0.99-1.55] | 0.63 [0.33-1.21] | 2.0 [0.8 - 4.7] |
| SOFA | 0.83 [0.77-0.89] | 3 | 0.77 [0.59-0.88] | 0.74 [0.71-0.77] | 0.12 [0.08-0.17] | 0.99 [0.97-0.99] | 2.95 [2.33-3.73] | 0.32 [0.16-0.60] | 9.4 [3.9 - 22.2] |
| qSOFA | 0.77 [0.69-0.85] | 1 | 0.83 [0.66-0.93] | 0.68 [0.65-0.72] | 0.11 [0.07-0.15] | 0.99 [0.97-1.00] | 2.63 [2.16-3.20] | 0.24 [0.11-0.54] | 10.8 [4.1 - 28.6] |
| NEWS | 0.75 [0.68-0.83] | 5 | 0.67 [0.49-0.81] | 0.75 [0.71-0.78] | 0.11 [0.07-0.16] | 0.98 [0.96-0.99] | 2.64 [1.99-3.52] | 0.45 [0.27-0.74] | 5.9 [2.7 - 12.9] |
| CRB-65 | 0.75 [0.68-0.83] | 2 | 0.63 [0.46-0.78] | 0.75 [0.72-0.78] | 0.10 [0.07-0.16] | 0.98 [0.96-0.99] | 2.54 [1.88-3.44] | 0.49 [0.30-0.78] | 5.2 [2.4 - 11.2] |
| SIRS | 0.62 [0.53-0.71] | 2 | 0.63 [0.46-0.78] | 0.56 [0.52-0.59] | 0.06 [0.04-0.09] | 0.97 [0.95-0.98] | 1.43 [1.07-1.90] | 0.66 [0.41-1.06] | 2.2 [1.0 - 4.6] |
| 72 hours | MR-proADM | 0.75 [0.65-0.85] | 1.57 | 0.68 [0.48-0.83] | 0.76 [0.71-0.80] | 0.17 [0.11-0.25] | 0.97 [0.94-0.99] | 2.80 [2.02-3.88] | 0.42 [0.24-0.75] | 6.6 [2.8 - 15.9] |
| PCT | 0.63 [0.51-0.75] | 1.78 | 0.48 [0.30-0.67] | 0.82 [0.78-0.86] | 0.16 [0.10-0.26] | 0.96 [0.93-0.97] | 2.67 [1.68-4.26] | 0.63 [0.43-0.93] | 4.2 [1.8 - 9.7] |
| Lactate | 0.56 [0.46-0.66] | 1.7 | 0.75 [0.55-0.88] | 0.48 [0.41-0.54] | 0.12 [0.08-0.19] | 0.95 [0.90-0.98] | 1.43 [1.10-1.85] | 0.53 [0.26-1.07] | 2.7 [1.0 - 7.1] |
| CRP | 0.57 [0.43-0.71] | 16.4 | 0.30 [0.15-0.52] | 0.73 [0.67-0.78] | 0.08 [0.04-0.16] | 0.93 [0.89-0.96] | 1.09 [0.54-2.20] | 0.96 [0.72-1.30] | 1.1 [0.4 - 3.1] |
| SOFA | 0.75 [0.67-0.84] | 2 | 0.88 [0.70-0.96] | 0.51 [0.46-0.57] | 0.11 [0.08-0.17] | 0.98 [0.95-0.99] | 1.81 [1.51-2.17] | 0.23 [0.08-0.68] | 7.8 [2.3 - 26.4] |
| qSOFA | 0.61 [0.51-0.72] | 1 | 0.52 [0.33-0.70] | 0.70 [0.65-0.74] | 0.11 [0.06-0.18] | 0.95 [0.92-0.97] | 1.72 [1.14-2.59] | 0.69 [0.45-1.04] | 2.5 [1.1 - 5.7] |
| NEWS | 0.68 [0.58-0.79] | 4 | 0.56 [0.37-0.73] | 0.73 [0.68-0.78] | 0.13 [0.08-0.21] | 0.96 [0.93-0.98] | 2.09 [1.42-3.08] | 0.60 [0.38-0.94] | 3.5 [1.5 - 7.9] |
| CRB-65 | 0.65 [0.56-0.74] | 1 | 0.96 [0.80-0.99] | 0.25 [0.21-0.30] | 0.08 [0.06-0.12] | 0.99 [0.94-1.00] | 1.29 [1.16-1.42] | 0.16 [0.02-1.09] | 2.2 [1.0 - 5.0] |
| SIRS | 0.60 [0.49-0.72] | 1 | 0.72 [0.52-0.86] | 0.43 [0.38-0.48] | 0.08 [0.05-0.13] | 0.96 [0.91-0.98] | 1.26 [0.97-1.64] | 0.65 [0.34-1.23] | 1.9 [0.8 - 4.8] |

*CRB-65*: Severity score for community-acquired pneumonia; *CRP*: C-reactive protein; *MR-proADM*: Mid-regional proadrenomedullin; *NEWS*: National Early Warning Score; *PCT*: Procalcitonin; *qSOFA*: quick Sequential Organ Failure Assessment; *SOFA*: Sequential Organ Failure Assessment.