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|---|---|
| Title | Development and validation of a novel computer-aided score to predict the risk of in-hospital mortality for acutely ill medical admissions in two acute hospitals using their first electronically recorded blood test results and vital signs: a cross-sectional study |
| Authors | Faisal, Muhammad;Scally, Andrew;Jackson, Natalie;Richardson, Donald;Beatson, Kevin;Howes, Robin;Speed, Kevin;Menon, Madhav;Daws, Jeremey;Dyson, Judith;Marsh, Claire;Mohammed, Mohammed A. |
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# Supplementary Material

The NEWS [https://www.rcplondon.ac.uk/projects/outputs/national-early-warning-score-news] is based on a scoring system in which a score is allocated to vital signs physiological measurements already undertaken when patients present to, or are being monitored in hospital. Six physiological parameters form the basis of the scoring system:

| Physiological Parameters | 3 | 2 | 1 | 0 | 1 | 2 | 3 |
|---|---|---|---|---|---|---|---|
| Respiration Rate | ≤8 | | 9 - 11 | 12 - 20 | | 21 - 24 | ≥25 |
| Oxygen Saturations | ≤91 | 92 - 93 | 94 - 95 | ≥96 | | | |
| Any Supplemental Oxygen | | Yes | | No | | | |
| Temperature | ≤35.0 | | 35.1 - 36.0 | 36.1 - 38.0 | 38.1 - 39.0 | ≥39.1 | |
| Systolic BP | ≤90 | 91 - 100 | 101 - 110 | 111 - 219 | | | ≥220 |
| Heart Rate | ≤40 | | 41 - 50 | 51-90 | 91 - 110 | 111 - 130 | ≥131 |
| Level of Consciousness | | | | Alert | | | Voice, Pain, or Unconscious |

A score is allocated to each as they are measured, the magnitude of the score reflecting how extreme the parameter varies from the norm. This score is then aggregated, and uplifted for people requiring oxygen.

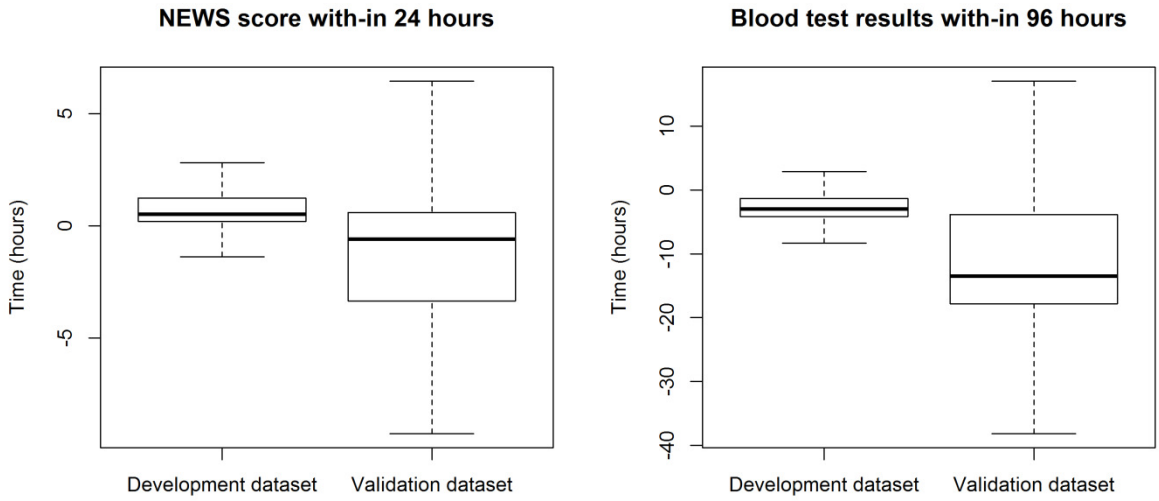



**Figure S1 Distribution of time to first NEWS score and Blood test results for development and validation datasets.**

| Blood tests results recorded | Development dataset N(%) | Validation dataset N(%) |
|---|---|---|
| within 24 hours | 29255 (94.4) | 24341 (92.7) |
| within 48 hours | 894 (2.9) | 1098 (4.2) |
| within 72 hours | 512 (1.6) | 495 (1.9) |
| within 96 hours | 335 (1.1) | 313 (1.2) |

**Table S1 Distribution of time to the first set of Blood test results recorded within 4 days for development and validation datasets.**

| Characteristic | Development dataset | Validation dataset |
|---|---|---|
| N | 6104 | 10504 |
| Male (%) | 3008 (49.3) | 4875 (46.4) |
| Mean Age (SD) | 61.4 (20.2) | 64.7 (21.4) |
| Median Length of Stay (days) (IQR) | 1.1 (4.0) | 1.4 (4.4) |
| In-hospital mortality (%) | 405 (6.6) | 434 (4.1) |

**Table S2 Characteristics of emergency admissions with incomplete data in development and validation datasets.**

| | | Example 1 (Discharged alive) | | | Example 2 (Discharged dead) | | |
|---|---|---|---|---|---|---|---|
| Variable Name | Coefficient | Values | Transformed | Log(Odds) | Values | Transformed | Log(Odds) |
| Intercept | -3.22 | 1 | 1 | -3.22 | 1 | 1 | -3.22 |
| Male | 0.14 | 1 | 1 | 0.14 | 0 | 0 | 0 |
| Age | 0.077 | 51 | 51 | 3.927 | 44 | 44 | 3.388 |
| Albumin | -0.104 | 36 | 36 | -3.744 | 11 | 11 | -1.144 |
| 1/sqrt(Creatinine) | 9.883 | 86 | 0.107832773 | 1.065711 | 153 | 0.080845 | 0.798993 |
| Haemoglobin | 0.002 | 148 | 148 | 0.296 | 48 | 48 | 0.096 |
| Log(Potassium) | -0.024 | 3.4 | 1.223775354 | -0.02937 | 6.9 | 1.931521 | -0.04636 |
| Sodium | -0.023 | 111 | 111 | -2.553 | 130 | 130 | -2.99 |
| Log(White Blood Count) | 1.167 | 12 | 2.484906493 | 2.899886 | 34.7 | 3.546739 | 4.139045 |
| Log(Urea) | 1.211 | 7.8 | 2.054123604 | 2.487544 | 28.6 | 3.353407 | 4.060975 |
| **AKI (reference 0)** | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| AKI stage 1 | 0.131 | 0 | 0 | 0 | 0 | 0 | 0 |
| AKI stage 2 | 0.443 | 0 | 0 | 0 | 1 | 1 | 0.443 |
| AKI stage 3 | -0.388 | 0 | 0 | 0 | 0 | 0 | 0 |
| NEWS | 0.093 | 2 | 2 | 0.186 | 9 | 9 | 0.837 |
| Log(Respiratory) | 0.569 | 16 | 2.772588547 | 1.577603 | 22 | 3.091042 | 1.758803 |
| Temperature | -0.145 | 36 | 36 | -5.22 | 36.5 | 36.5 | -5.2925 |
| Log(Systolic) | -0.919 | 133 | 4.89034882 | -4.49423 | 112 | 4.718499 | -4.3363 |
| Log(Diastolic) | 0.777 | 79 | 4.369447577 | 3.395061 | 74 | 4.304065 | 3.344258 |
| Log(Pulse) | 0.511 | 63 | 4.143134465 | 2.117142 | 149 | 5.003946 | 2.557016 |
| Oxygen Saturation | -0.016 | 94 | 94 | -1.504 | 95 | 95 | -1.52 |
| Oxygen supplementation | 0.606 | 0 | 0 | 0 | 0 | 0 | 0 |
| **Alert** | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Pain | 0.716 | 0 | 0 | 0 | 0 | 0 | 0 |
| Voice | 0.395 | 0 | 0 | 0 | 0 | 0 | 0 |
| Unconscious | 1.925 | 0 | 0 | 0 | 1 | 1 | 1.925 |
| Age * Log(White Cell Count) | -0.015 | - | 126.7302311 | -1.90095 | - | 156.0565 | -2.34085 |
| 1/sqrt( Creatinine)* Log(White Cell Count) | 1.481 | - | 0.267954358 | 0.39684 | - | 0.286737 | 0.424657 |
| AKI stage 3 * 1/sqrt( Creatinine) | 15.551 | - | 0 | 0 | - | 0 | 0 |
| **Sum of Log(Odds)** | | - | - | **-4.17677** | - | - | **2.882744** |
| **Probability of dying** | | - | - | **0.015116** | - | - | **0.946987** |

**Table S3 Coefficient of CARM model to predict in-hospital mortality with two examples (one discharged alive and one discharged died).**

We accounted a baseline difference in risk of death in the external validation data by adding 0.52 to the CARM logit model using an iterative procedure described elsewhere[1].

1 Faisal M, Howes R, Steyerberg EW, *et al.* Using routine blood test results to predict the risk of death for emergency medical admissions to hospital: an external model validation study. *QJM* 2017;**110**:27–31. doi:10.1093/qjmed/hcw110

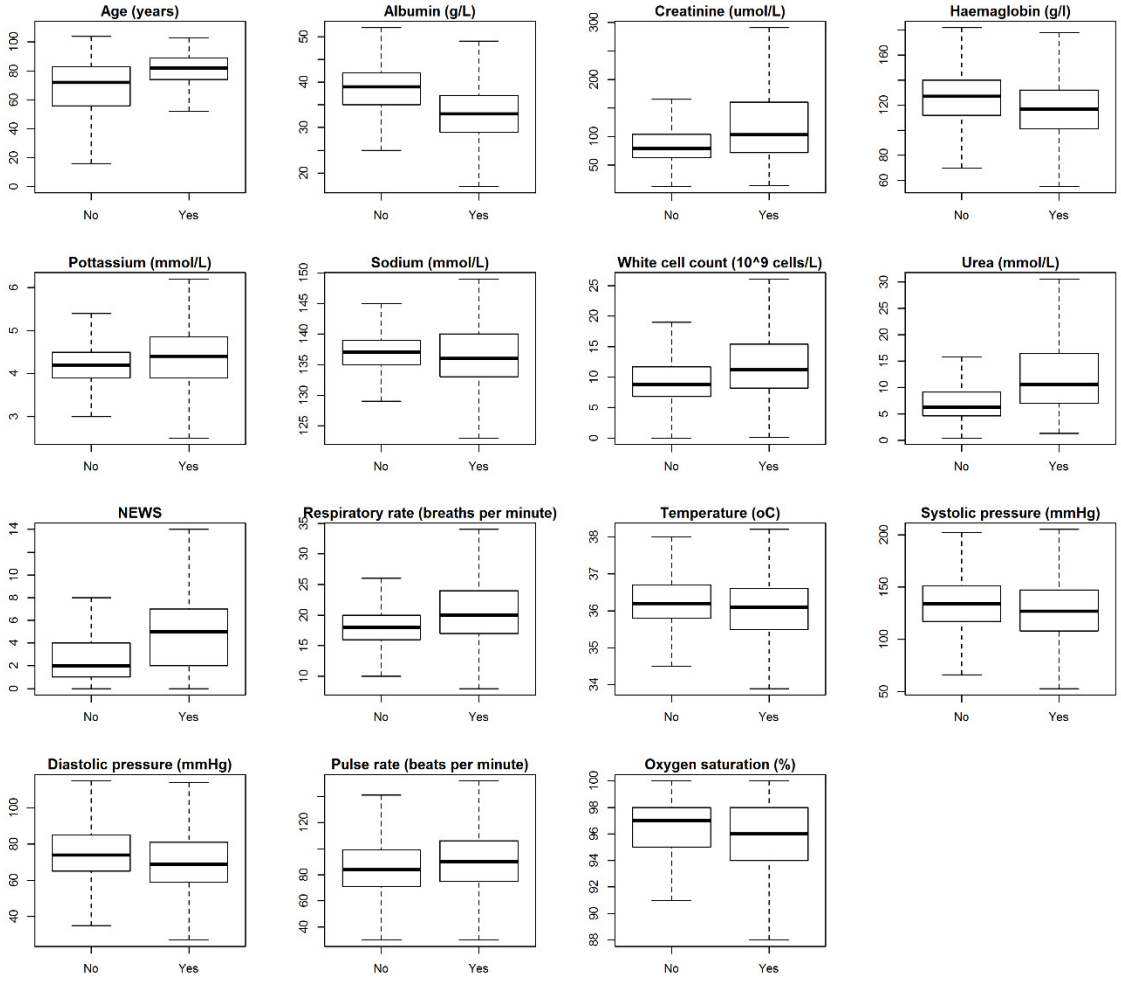



**Figure S2 Boxplot without outliers for continuous covariates with respect to patient's discharge status (Alive/Died) for NLAG hospitals**

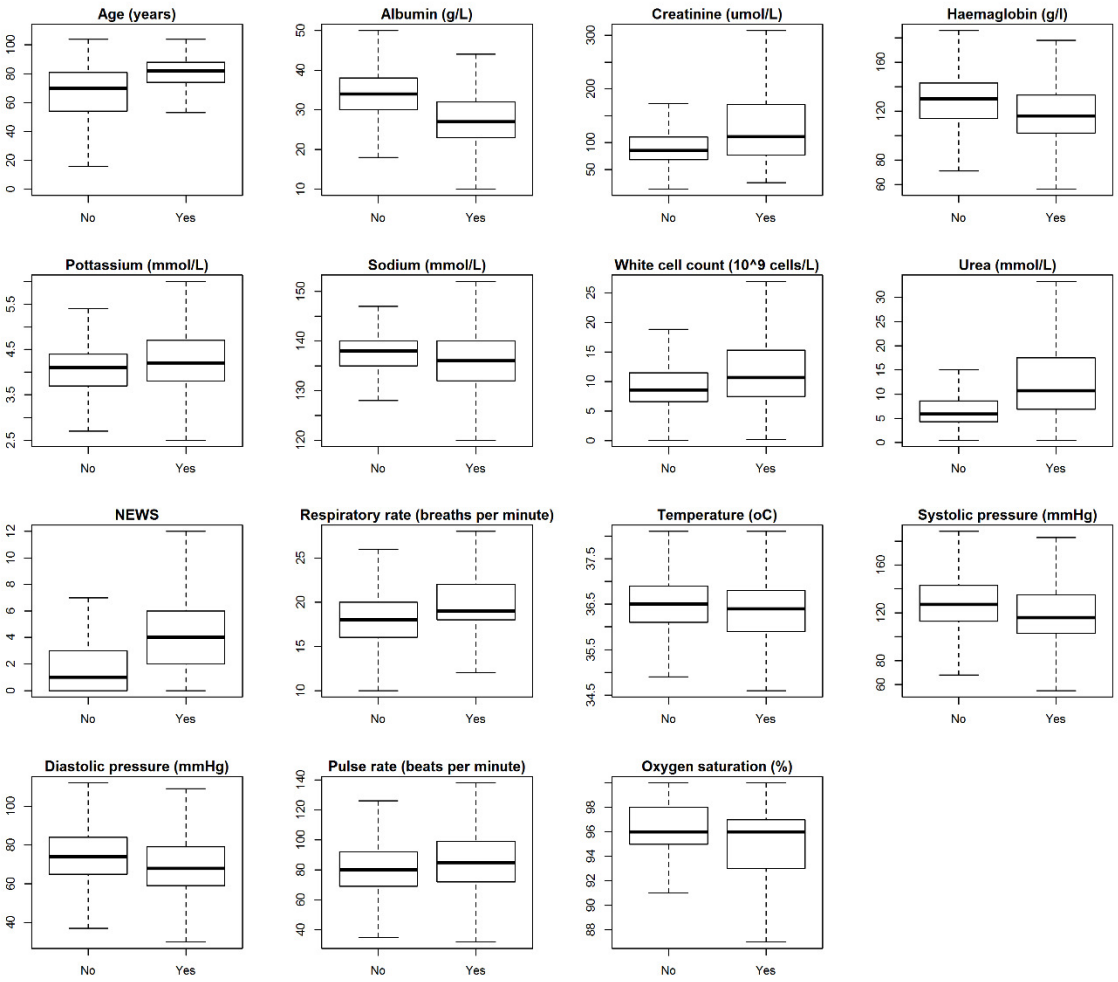



**Figure S3 Boxplot without outliers for continuous covariates with respect to patient's discharge status (Alive/Died) for York hospital**

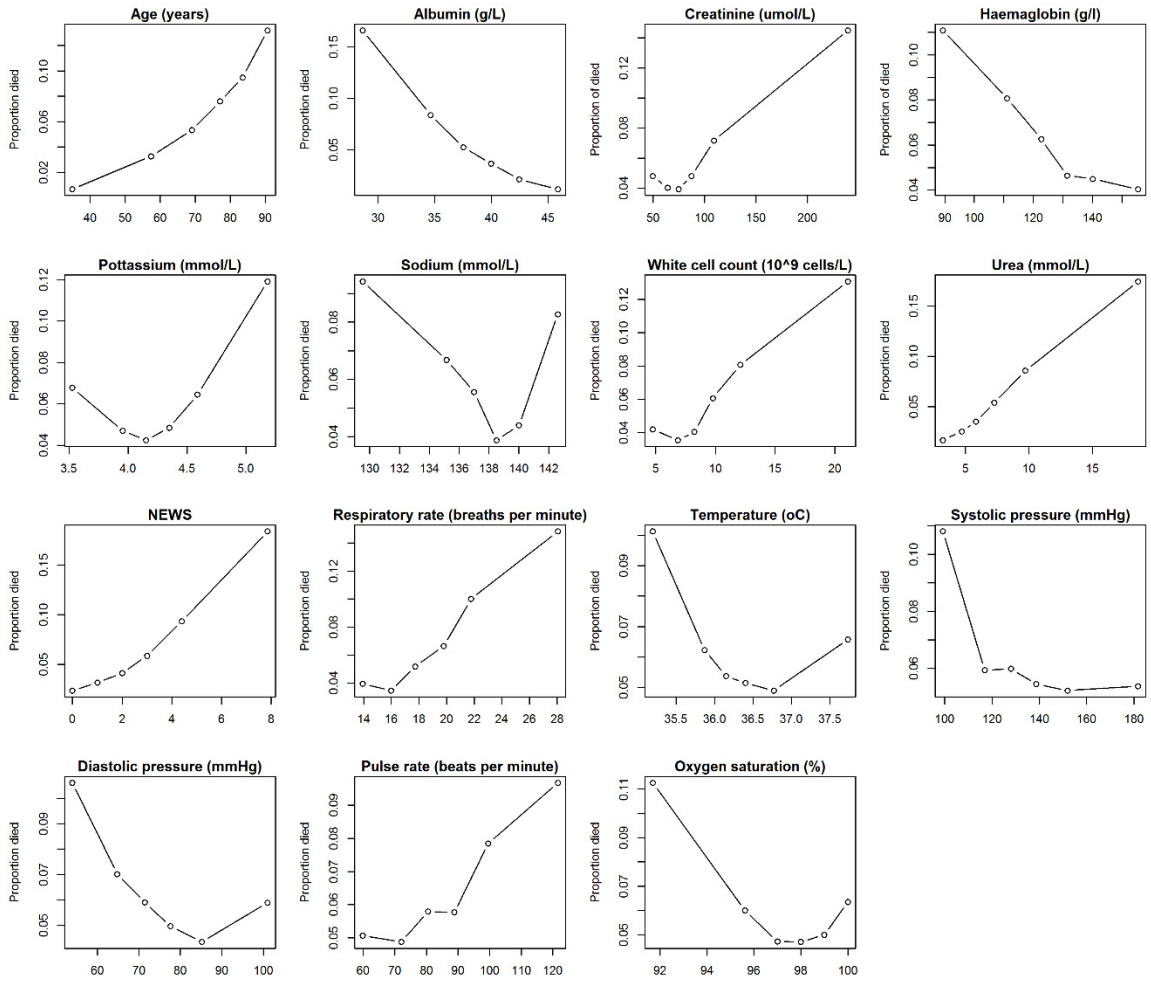



**Figure S4 Line plots showing the observed risk of death with continuous covariates for NLAG hospitals**

NB: y-axis range changes in each plot.

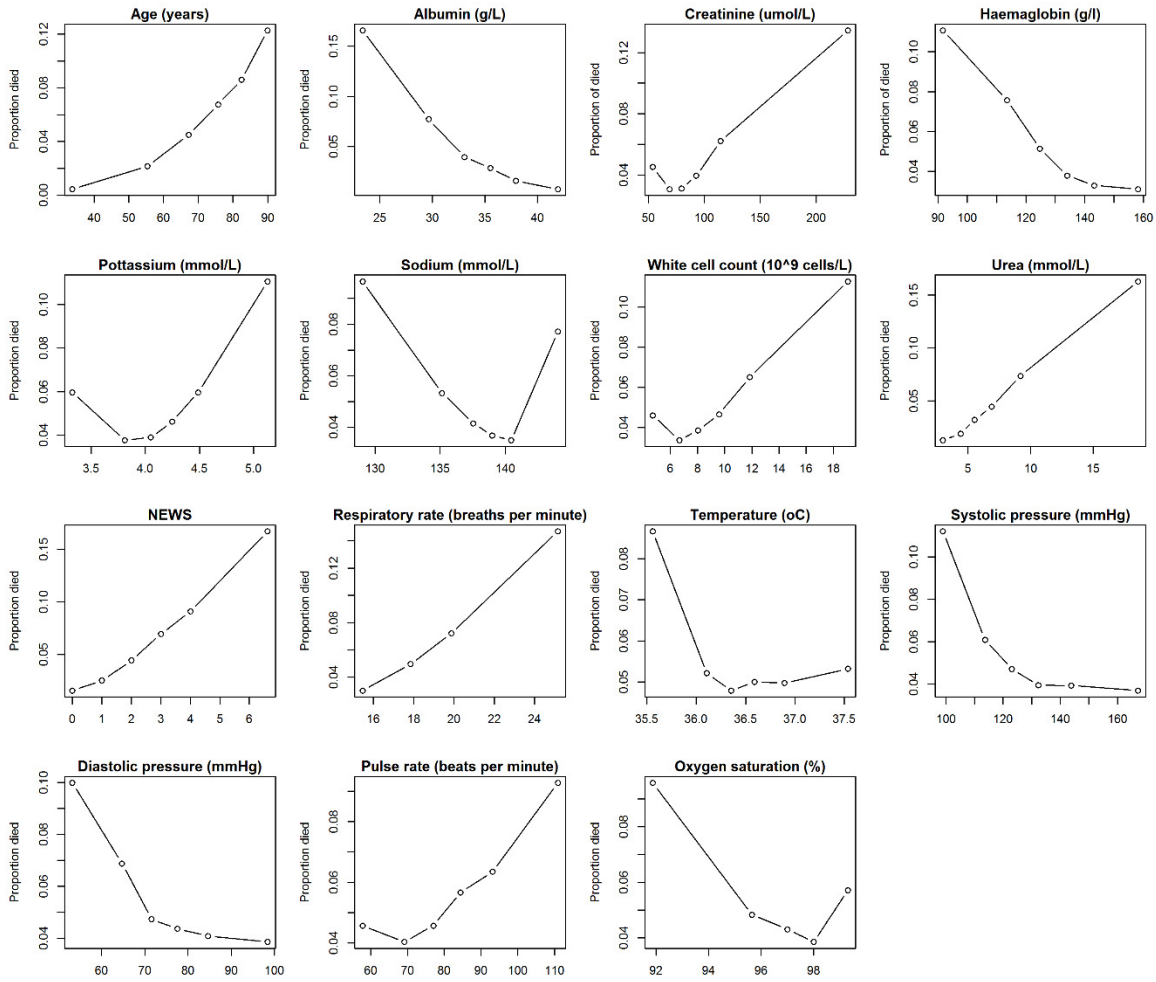



**Figure S5 Line plots showing the observed risk of death with continuous covariates for York hospital.**

NB: y-axis range changes in each plot.

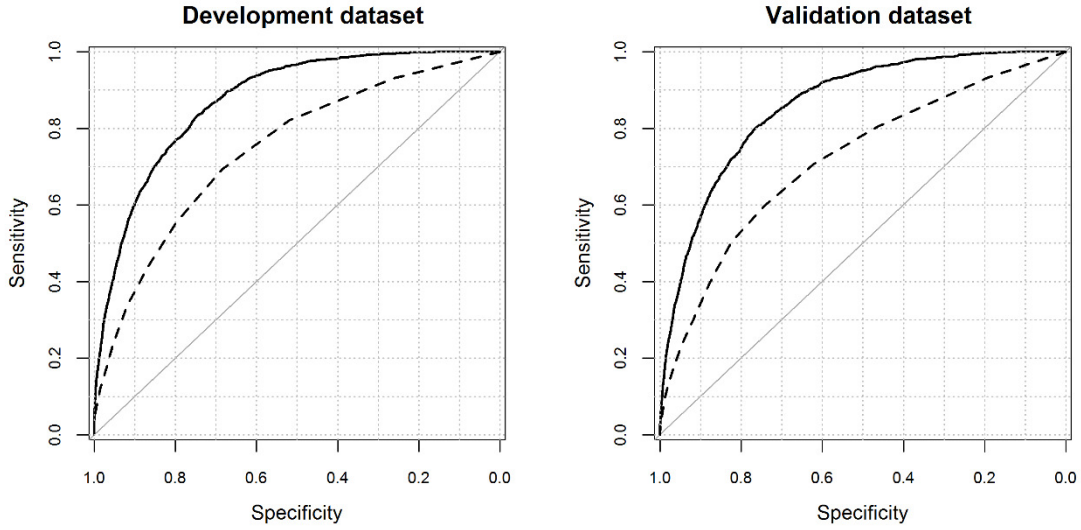



**Figure S6 Area under the Receiver Operating Characteristic curve for development dataset (NEWS =0.75, CARM=0.87) and validation dataset (NEWS=0.72, CARM=0.86).**

Black dashed line for NEWS and black solid line for CARM

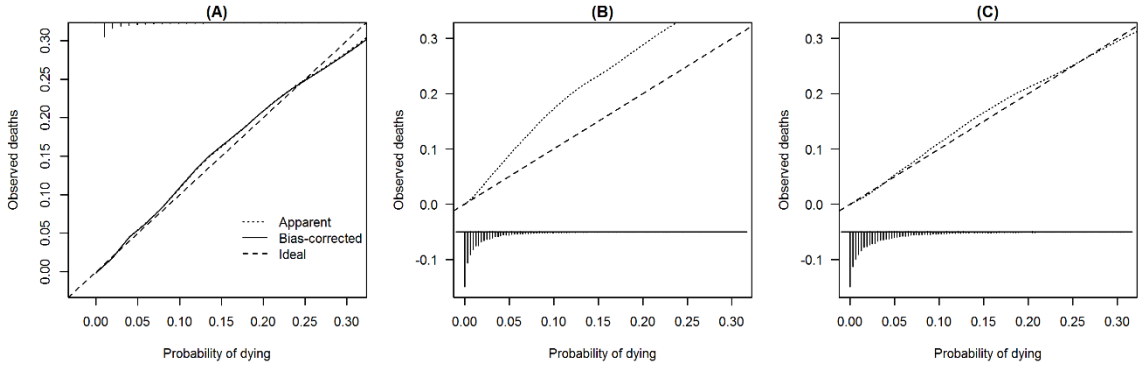



**Figure S7 Internal and external validation with and without re-calibration of CARM model**

(A) Internal validation of development dataset only using bootstrap method (B) performance of CARM model on external validation dataset without any re-calibration (C) performance of CARM model on external validation dataset after correcting for baseline mortality difference (5.7% vs 6.5%).

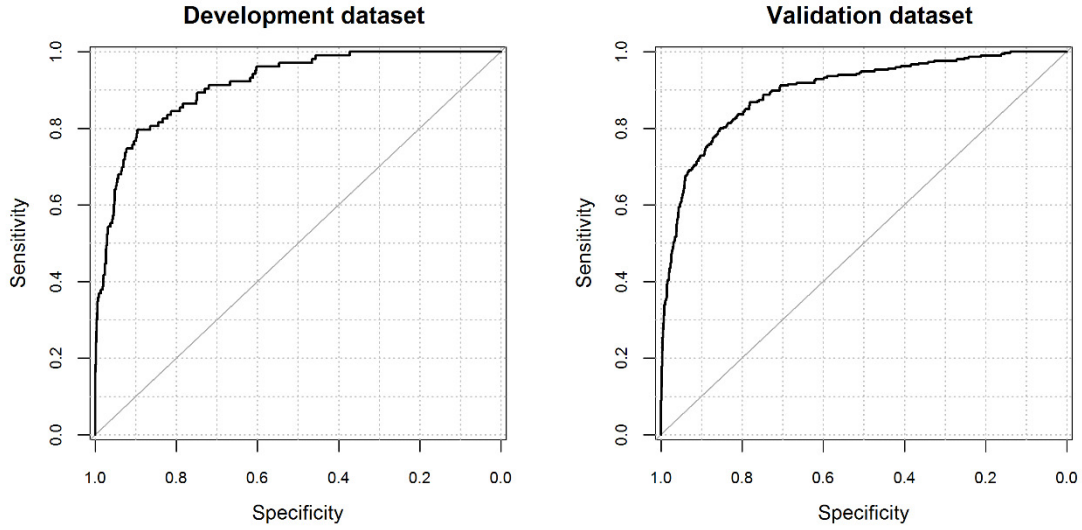



**Figure S8 Receiver Operating Characteristic curve of (median) imputed blood tests results on development dataset and validation dataset.**

NB: patients with imputed values were omitted during model development and validation.

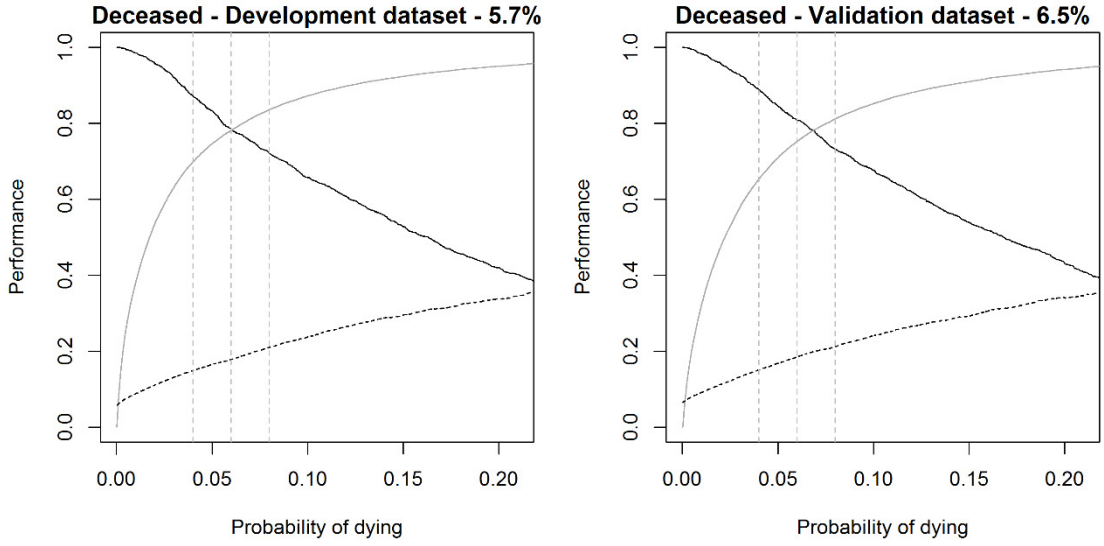



**Figure S9: Sensitivity analysis of CARM model at various thresholds of probability of dying (0.0, 0.01, …, 0.20) on development dataset and validation dataset.**

Black solid line is for sensitivity and black dashed line is for positive predictive value (PPV). Grey solid line is specificity and grey dashed vertical lines are at thresholds (0.04, 0.06, and 0.08).

NB: We selected thresholds exclusively based on development dataset.

| Characteristics | NLAG AUC (95% CI) | York AUC (95% CI) |
|---|---|---|
| **Overall** | 0.87 (0.87 to 0.88) | 0.86 (0.85 to 0.87) |
| **Sex** | | |
| Male | 0.87 (0.86 to 0.88) | 0.85 (0.84 to 0.86) |
| Female | 0.88 (0.87 to 0.89) | 0.87 (0.86 to 0.88) |
| **Age** | | |
| Age>=75 | 0.81 (0.80 to 0.82) | 0.81 (0.79 to 0.82) |
| Age<75 | 0.91 (0.90 to 0.92) | 0.89 (0.88 to 0.91) |
| **Seasons** | | |
| Spring | 0.87 (0.86 to 0.89) | 0.86 (0.84 to 0.88) |
| Summer | 0.88 (0.87 to 0.90) | 0.85 (0.83 to 0.87) |
| Autumn | 0.87 (0.86 to 0.89) | 0.87 (0.86 to 0.89) |
| Winter | 0.87 (0.85 to 0.88) | 0.86 (0.84 to 0.87) |
| **Length of Stay (LoS)** | | |
| LoS>=5 days | 0.77 (0.76 to 0.79) | 0.75 (0.73 to 0.76) |
| Los<5 days | 0.95 (0.94 to 0.96) | 0.94 (0.93 to 0.95) |
| **Day of the Week** | | |
| Sunday | 0.93 (0.91 to 0.94) | 0.93 (0.92 to 0.95) |
| Monday | 0.87 (0.85 to 0.89) | 0.87 (0.84 to 0.89) |
| Tuesday | 0.87 (0.85 to 0.89) | 0.83 (0.81 to 0.85) |
| Wednesday | 0.86 (0.84 to 0.88) | 0.84 (0.82 to 0.86) |
| Thursday | 0.86 (0.84 to 0.88) | 0.86 (0.84 to 0.88) |
| Friday | 0.88 (0.86 to 0.90) | 0.87 (0.85 to 0.89) |
| Saturday | 0.90 (0.88 to 0.92) | 0.91 (0.89 to 0.92) |
| **Charlson Comorbidity Index** | | |
| Acute Myocardial | 0.84 (0.82 to 0.86) | 0.81 (0.78 to 0.84) |
| Congestive Heart | 0.77 (0.75 to 0.79) | 0.75 (0.73 to 0.78) |
| Peripheral Vascular | 0.78 (0.74 to 0.82) | 0.82 (0.79 to 0.86) |
| Cerebrovascular | 0.78 (0.73 to 0.83) | 0.78 (0.75 to 0.81) |
| Dementia | 0.78 (0.75 to 0.81) | 0.77 (0.73 to 0.80) |
| COPD | 0.85 (0.84 to 0.87) | 0.85 (0.83 to 0.86) |
| Rheumatoid Disease | 0.87 (0.84 to 0.90) | 0.83 (0.79 to 0.88) |
| Peptic Ulcer | 0.88 (0.83 to 0.93) | 0.83 (0.74 to 0.91) |
| Mild LD (Liver) | 0.86 (0.82 to 0.90) | 0.83 (0.76 to 0.90) |
| Diabetes | 0.85 (0.83 to 0.87) | 0.84 (0.82 to 0.86) |
| Diabetes+Complications | 0.79 (0.69 to 0.89) | 0.90 (0.85 to 0.95) |
| Hemiplegia/Paraplegia | 0.80 (0.75 to 0.85) | 0.74 (0.67 to 0.81) |
| RD (Renal) | 0.80 (0.78 to 0.82) | 0.81 (0.78 to 0.83) |
| Cancer | 0.80 (0.78 to 0.83) | 0.81 (0.78 to 0.84) |
| Moderate/Severe LD (Liver) | 0.80 (0.73 to 0.87) | 0.78 (0.71 to 0.84) |
| Metastatic Cancer | 0.77 (0.74 to 0.80) | 0.77 (0.74 to 0.81) |

**Table S4: The c-statistics (95% CI) is showing for CARM model in each hospital by Sex, Age, Seasons, Longer vs. shorter length of stay subjects, Day of the week, and 16 CCI disease groups.**