Supplementary Online Content

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**eFigure 1.** Three Clinical Scenarios That Demonstrate the Need for More Sophisticated Analyses of ICU Physiological Data  
**eFigure 2.** Calibration of the 2 Models Validated on Data From All 3 Institutions Using 10-fold Cross Validation  
**eTable 1.** Laboratory Test Results and Vital Signs  
**eTable 2.** Derived Measures of Variability and Clinical Trajectory for Each Laboratory Test Result and Vital Sign  
**eTable 3.** Characteristics of the Study Population by Site  
**eTable 4.** Rates of Missingness Among the Predictive Variables Used in Our Analysis  
**eTable 5.** Results of the Sensitivity Analysis Comparing Validation Using All Patients With Using Only Those Alive at 24 Hours  
**eTable 6.** List of Coefficient Values of Derived Measures of Clinical Trajectory for the Pooled Model (Model 2 in the Text) With 192 Such Variables

This supplementary material has been provided by the authors to give readers additional information about their work.
In Panel a), all three patients—A, B, and C—are recorded as having the same single worst value (SWV) of 3 of the Glasgow Coma Score (GCS) over the 24-hour period following ICU admission. Patient A is admitted with a GCS value of 15, but his neurological status deteriorates rapidly (e.g. as in the case of an epidural hematoma), resulting in a GCS of 3. Patient B follows the opposite course, being admitted with a GCS of 3 before improving to a GCS of 15. Patient C is admitted with

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a GCS of 3, but never improves. In contrast, using the slopes of the linear trends associated with each of these three series of GCS could stratify the mortality risk.

Similarly, Panel b) depicts the time course of heart rate (HR) for two patients admitted to the ICU following myocardial infarction. Patient A experiences atrial fibrillation with rapid ventricular response, which is managed with β-blockers to achieve a target rate of 110 bpm. Patient B, meanwhile, experiences intermittent ventricular tachycardia, marked by periods of elevated HR >160 bpm before returning to a relatively stable baseline. Both patients are recorded as having a SWV of HR roughly in the same range, resulting in similar risk estimates. However, the persistent variability (even though rate control is achieved) of Patient A’s HR, as indicated by the standard deviation of the series, may indicate a poorer prognosis compared to Patient B.

Panel c) depicts serum creatinine (SCr) values over time for two patients. Two measurements of SCr are obtained for each patient. Patient A is initially admitted to the ICU with comorbid chronic kidney disease following surgery. His SCr on admission is 1.9mg/dL, and a repeat measurement 24 hours later is unchanged. However, Patient B experiences an rapid elevation of SCr from 0.7 to 1.9mg/dL in the 24 hours following admission, indicating the onset of acute kidney injury caused by, e.g., renal hypoperfusion associated with septic shock. Both patients attain the same SWV of SCr, even though Patient B has a poorer prognosis, as indicated by using the difference between first and last measurements within this 24-hour window.
eFigure 2. Calibration of the 2 Models Validated on Data From All 3 Institutions Using 10-fold Cross Validation

Includes models 2 and 3 in Methods. The error bars depict the bootstrap 95% confidence intervals. Note that the model with notes tends to underpredict mortality for the lower-risk deciles as compared to the model without notes, and vice versa for patients in the middle deciles of risk, but these differences do not appear significant.
### eTable 1. Laboratory Test Results and Vital Signs

#### Laboratory values

- **Arterial blood gas components**
  - Bicarbonate (mmol/L)
  - PaCO₂ (mm Hg)
  - pH
  - PaO₂ (mm Hg)

- **Blood count components**
  - Hematocrit (%)
  - Platelets (x10⁹/L)
  - White blood cells (x10⁹/L)

- **Other chemistries**
  - Bilirubin (mg/dL)
  - Creatinine (mg/dL)
  - Glucose (mg/dL)
  - Lactate (mmol/L)
  - Potassium (mmol/L)
  - Sodium (mmol/L)
  - Urea (mg/dL)

#### Vital signs

- Temperature (degrees Celsius)
- Heart rate (beats per minute)
- Respiratory rate (breaths per minute)
- Oxygen saturation (%)
- Mean arterial pressure (mm Hg)
- Fraction of inspired oxygen (FiO₂) (%)

#### Glasgow Coma Scale

- Total score (3-15)
- Eye response (1-4)
- Verbal response (1-6)
- Motor response (1-5)

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All observations in the first 24 hours of ICU admission were retrieved from the electronic health record.
eTable 2. Derived Measures of Variability and Clinical Trajectory for Each Laboratory Test Result and Vital Sign

**Measures of the distribution of each laboratory test or vital sign**
- First value observed within the 24 hours following ICU admission
- Last value observed within the 24 hours following ICU admission
- Maximum value observed within the 24 hours following ICU admission
- Minimum value observed within the 24 hours following ICU admission

**Mean**

**Measures of variability or clinical trajectory**
- Standard deviation
- First value minus last value collected
- Linear trend as fit by least squares
eTable 3. Characteristics of the Study Population by Site

|                              | MPMC   | UCSF    | BIDMC   |
|------------------------------|--------|---------|---------|
| Patients, number             | 15,666 | 38,624  | 46,906  |
| Deaths, number (%)           | 1,770  | 3,581   | 5,154   |
|                              | (11.3%)| (9.3%)  | (11.0%) |
| Length of first ICU stay, mean (IQR), days | 2.2 (0-2) | 3.3 (1-3) | 4.1 (1-4) |
| Length of hospital stay, mean (IQR), days | 8.5 (3-10) | 14.6 (4-16) | 10.1 (4-12) |
| Age, mean ± SD (IQR), y      | 68.0±16.6 | 57.5±17.1 | 62.1±16.5 |
|                              | (57-81) | (47-69) | (51-76) |
| Male gender, number (%)      | 6,993  | 18,056  | 26,850  |
|                              | (44.6%)| (46.7%) | (57.2%) |
| Age categories, y            |        |         |         |
| <40                          | 978    | 6,291   | 4,928   |
|                              | (6.2%) | (16.3%) | (10.5%) |
| 40-59                        | 3,569  | 13,080  | 13,918  |
|                              | (22.8%)| (33.9%) | (29.7%) |
| 60-79                        | 6,559  | 15,755  | 20,514  |
|                              | (41.9%)| (40.8%) | (43.7%) |
| >79                          | 4,560  | 3,498   | 7,546   |
|                              | (29.1%)| (9.1%)  | (16.1%) |
| Type of ICU at first admission |       |         |         |
| Combined medical/surgical    | 15,666 | 16,552  | 0 (0%)  |
|                              | (100%) | (42.8%) |         |
| Medical                      | 0 (0%) | 558 (1.4%) | 18,552 (39.6%) |
| Surgical                     | 0 (0%) | 0 (0%)  | 21,910 (46.7%) |
| Neurological                 | 0 (0%) | 14,242 (36.9%) | 0 (0%) |
| Coronary care                | 0 (0%) | 7,272 (18.9%) | 6,444 (13.7%) |

Abbreviations: MPMC: Mills-Peninsula Medical Center; UCSF: University of California, San Francisco; BIDMC: Beth Israel Deaconess Medical Center.
eTable 4. Rates of Missingness Among the Predictive Variables Used in Our Analysis

| Variable     | Missingness, % |
|--------------|----------------|
|              | MPMC | UCSF | BIDMC |
| Lactate      | 53.49 | 43.82 | 40.19 |
| Urea         | 0.86  | 3.09  | 0.25  |
| Creatinine   | 1.93  | 1.44  | 0.23  |
| Hematocrit   | 1.29  | 1.00  | 0.12  |
| Sodium       | 1.45  | 0.83  | 0.19  |
| Potassium    | 1.37  | 0.86  | 0.10  |
| PCO2         | 57.99 | 28.50 | 33.70 |
| Bilirubin    | 42.97 | 54.60 | 54.33 |
| Glucose      | 1.04  | 5.85  | 0.20  |
| Platelets    | 1.55  | 3.09  | 0.45  |
| PO2          | 51.33 | 27.63 | 33.70 |
| WBC          | 1.55  | 1.18  | 0.66  |
| pH           | 52.05 | 27.63 | 30.85 |
| Bicarbonate  | 53.95 | 0.76  | 33.70 |
| MAP          | 0.00  | 0.03  | 0.33  |
| Temperature  | 0.00  | 0.02  | 0.41  |
| Respirations | 0.00  | 0.01  | 0.41  |
To assess whether the models were unduly influenced by data from patients who died within the 24-hour period for which we collected data, we conducted a sensitivity analysis by developing models using only patients alive at 24 hours following ICU admission. We re-validated the models in this separate cohort and compared our results to those obtained in the original cohort. For each model, we compared the difference in AUC increases observed for each cohort relative to that of the model validated in the previous step – i.e., the difference in AUC increase for model #2 as compared to model #1 (baseline single worst value model), and similarly, model #3 (model #2 + NLP) was compared to model #2. The incremental gains in AUC as additional data is made available to the predictive algorithms when including patients who died in the first 24 hours were very similar to the incremental gains when excluding such patients.

|                                      | All patients | Only patients alive at 24 hours | Difference |
|--------------------------------------|--------------|---------------------------------|------------|
| Base model, best and worst coded values only | .883         | .866                            | -.017      |
| Add all coded values                 | .898         | .882                            | -.016      |
| Increment in AUC                     | +.015        | +.016                           | +.001      |
| Add notes                            | .913         | .899                            | -.016      |
| Increment in AUC                     | +.015        | +.017                           | +.002      |

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**eTable 6. List of Coefficient Values of Derived Measures of Clinical Trajectory for the Pooled Model (Model 2 in the Text) With 192 Such Variables**

| Derived measure of clinical trajectory | Coefficient value |
|---------------------------------------|-------------------|
| Lactate, maximum value                | 3.76              |
| Lactate, minimum value                | 5.78              |
| Lactate, mean                         | 3.54              |
| Lactate, standard deviation           | 2.22              |
| Lactate, coefficient for linear trend | 0.66              |
| Lactate, first value collected        | 2.39              |
| Lactate, last value collected         | 8.41              |
| Lactate, last minus first value       | 4.33              |
| Urea, maximum value                  | 4.67              |
| Urea, minimum value                  | 5.34              |
| Urea, mean                            | 5.06              |
| Urea, standard deviation              | 1.07              |
| Urea, coefficient for linear trend    | 1.06              |
| Urea, first value collected           | 4.34              |
| Urea, last value collected            | 6.07              |
| Urea, last minus first value          | 2.92              |
| Creatinine, maximum value             | -0.57             |
| Creatinine, minimum value             | 0.05              |
| Creatinine, mean                      | -0.20             |
| Creatinine, standard deviation        | -2.07             |
| Creatinine, coefficient for linear trend | 1.85         |
| Creatinine, first value collected     | -0.69             |
| Creatinine, last value collected      | 0.48              |
| Creatinine, last minus first value    | 3.17              |
| Hematocrit, maximum value             | -1.86             |
| Hematocrit, minimum value             | -0.53             |
| Hematocrit, mean                      | -1.22             |
| Hematocrit, standard deviation        | -1.34             |
| Hematocrit, coefficient for linear trend | -0.34         |
| Hematocrit, first value collected     | -1.58             |
| Hematocrit, last value collected      | -0.37             |
| Hematocrit, last minus first value    | 2.02              |
| Sodium, maximum value                 | -1.11             |
| Sodium, minimum value                 | -2.45             |
| Parameter                  | Value   |
|---------------------------|---------|
| Sodium, mean              | -3.02   |
| Sodium, standard deviation| 4.56    |
| Sodium, coefficient for linear trend | 0.55 |
| Sodium, first value collected | -3.07 |
| Sodium, last value collected | -0.24 |
| Sodium, last minus first value | 3.55 |
| Potassium, maximum value  | -0.04   |
| Potassium, minimum value  | 0.93    |
| Potassium, mean           | 0.51    |
| Potassium, standard deviation | 0.31 |
| Potassium, coefficient for linear trend | 2.30 |
| Potassium, first value collected | 0.39 |
| Potassium, last value collected | 0.80 |
| Potassium, last minus first value | 0.18 |
| PaO2, maximum value       | -4.08   |
| PaO2, minimum value       | -3.46   |
| PaO2, mean                | -4.64   |
| PaO2, standard deviation  | 0.40    |
| PaO2, coefficient for linear trend | 0.64 |
| PaO2, first value collected | -4.08 |
| PaO2, last value collected | -2.24 |
| PaO2, last minus first value | 1.79 |
| Bilirubin, maximum value  | 3.72    |
| Bilirubin, minimum value  | 4.29    |
| Bilirubin, mean           | 4.09    |
| Bilirubin, standard deviation | 0.76 |
| Bilirubin, coefficient for linear trend | 1.49 |
| Bilirubin, first value collected | 3.46 |
| Bilirubin, last value collected | 4.52 |
| Bilirubin, last minus first value | 3.55 |
| Glucose, maximum value    | -1.21   |
| Glucose, minimum value    | 0.82    |
| Glucose, mean             | -0.22   |
| Glucose, standard deviation | 1.19 |
| Glucose, coefficient for linear trend | -0.55 |
| Glucose, first value collected | 1.02 |
| Glucose, last value collected | 1.89 |
| Glucose, last minus first value | 0.07 |
| PaCO2, maximum value      | 1.77    |
| Blood Parameter | Minimum Value | Mean | Standard Deviation | Linear Trend Coefficient | First Value Collected | Last Value Collected | Last Minus First Value |
|-----------------|---------------|------|--------------------|--------------------------|-----------------------|---------------------|------------------------|
| PaCO2           | -1.37         | -1.31| 0.04               | -1.05                    | -0.20                 | -5.25               | -5.95                  |
| Platelets       | -0.60         | -0.91| 1.34               | -0.02                    | -2.65                 | 0.78                | 7.41                   |
| White blood cells | 0.18         | 2.10 | -2.74              | -1.32                    | 1.08                  | 1.08                | -0.21                  |
| pH              | 1.43          | 1.70 | 0.73               | 0.19                     | 1.56                  | -4.29               | -4.46                  |
| Bicarbonate     | 0.69          | 0.72 | -0.24              | -0.41                    | 0.87                  | -2.26               | -5.28                  |

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| Parameter                                      | Value    |
|-----------------------------------------------|----------|
| Mean arterial pressure, maximum value         | -0.70    |
| Mean arterial pressure, minimum value         | -2.45    |
| Mean arterial pressure, mean                  | -3.85    |
| Mean arterial pressure, standard deviation    | -2.63    |
| Mean arterial pressure, coefficient for linear trend | 0.03    |
| Mean arterial pressure, first value collected | -0.16    |
| Mean arterial pressure, last value collected  | -5.93    |
| Mean arterial pressure, last minus first value| -4.25    |
| Temperature, maximum value                   | -0.93    |
| Temperature, minimum value                   | -1.64    |
| Temperature, mean                            | -3.80    |
| Temperature, standard deviation              | 1.14     |
| Temperature, coefficient for linear trend    | 1.07     |
| Temperature, first value collected           | -1.89    |
| Temperature, last value collected            | -1.84    |
| Temperature, last minus first value          | 0.23     |
| FiO2, maximum value                          | -1.25    |
| FiO2, minimum value                          | 7.05     |
| FiO2, mean                                   | 7.81     |
| FiO2, standard deviation                     | 1.43     |
| FiO2, coefficient for linear trend           | -0.81    |
| FiO2, first value collected                  | -1.73    |
| FiO2, last value collected                   | 6.46     |
| FiO2, last minus first value                 | -0.12    |
| RESP, maximum value                          | 2.37     |
| RESP, minimum value                          | 5.54     |
| RESP, mean                                   | 3.15     |
| RESP, standard deviation                     | -1.51    |
| RESP, coefficient for linear trend           | -0.84    |
| RESP, first value collected                  | 3.49     |
| RESP, last value collected                   | 1.73     |
| RESP, last minus first value                 | -1.62    |
| Glasgow Coma Scale (GCS), maximum value      | -6.38    |
| Glasgow Coma Scale (GCS), minimum value      | -2.51    |
| Glasgow Coma Scale (GCS), mean               | -5.06    |
| Glasgow Coma Scale (GCS), standard deviation | -2.50    |
| Glasgow Coma Scale (GCS), coefficient for linear trend | -0.83    |
| Glasgow Coma Scale (GCS), first value collected | -1.82    |
| Glasgow Coma Scale (GCS), last value collected | -7.09    |
| Glasgow Coma Scale (GCS), last minus first value | -4.49 |
| GCS eye response, maximum value | -6.61 |
| GCS eye response, minimum value | -1.24 |
| GCS eye response, mean | -5.07 |
| GCS eye response, standard deviation | -2.71 |
| GCS eye response, coefficient for linear trend | -1.65 |
| GCS eye response, first value collected | -1.47 |
| GCS eye response, last value collected | -7.18 |
| GCS eye response, last minus first value | -4.43 |
| Pulse, maximum value | 6.02 |
| Pulse, minimum value | 2.94 |
| Pulse, mean | 8.16 |
| Pulse, standard deviation | 2.50 |
| Pulse, coefficient for linear trend | 2.02 |
| Pulse, first value collected | 2.49 |
| Pulse, last value collected | 3.68 |
| Pulse, last minus first value | 0.92 |
| GCS motor response, maximum value | -4.93 |
| GCS motor response, minimum value | -3.11 |
| GCS motor response, mean | -4.89 |
| GCS motor response, standard deviation | -0.95 |
| GCS motor response, coefficient for linear trend | 1.27 |
| GCS motor response, first value collected | -2.22 |
| GCS motor response, last value collected | -5.72 |
| GCS motor response, last minus first value | -2.07 |
| GCS verbal response, maximum value | -5.41 |
| GCS verbal response, minimum value | -2.02 |
| GCS verbal response, mean | -4.23 |
| GCS verbal response, standard deviation | -2.18 |
| GCS verbal response, coefficient for linear trend | -2.49 |
| GCS verbal response, first value collected | -1.08 |
| GCS verbal response, last value collected | -6.42 |
| GCS verbal response, last minus first value | -5.35 |
| Oxygen saturation, maximum value | 0.06 |
| Oxygen saturation, minimum value | -1.91 |
| Oxygen saturation, mean | -5.39 |
| Oxygen saturation, standard deviation | 4.00 |
| Oxygen saturation, coefficient for linear trend | -4.03 |
| Oxygen saturation, first value collected | -1.10 |
| Oxygen saturation, last value collected | -6.75 |
| Oxygen saturation, last minus first value | -4.64 |