Localized customized mortality prediction modeling for patients with acute kidney injury admitted to the intensive care unit

By

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LOCAL CUSTOMIZED MORTALITY PREDICTION MODELING FOR PATIENTS WITH ACUTE KIDNEY INJURY ADMITTED TO THE INTENSIVE CARE UNIT

By

LEO ANTHONY CELI, M.D.

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ABSTRACT

Introduction. Models for mortality prediction are traditionally developed from prospective multi-center observational studies involving a heterogeneous group of patients to optimize external validity. We hypothesize that local customized modeling using retrospective data from a homogeneous subset of patients will provide a more accurate prediction than this standard approach. We tested this hypothesis on patients admitted to the ICU with acute kidney injury (AKI), and evaluated variables from the first 72 hours of admission. Methods. The Multi-parameter Intelligent Monitoring for Intensive Care II (MIMIC II) is a database of patients admitted to the Beth Israel Deaconess Medical Center ICU. Using the MIMIC II database, we identified patients who developed acute kidney injury and who survived at least 72 hours in the ICU. 118 variables were extracted from each patient. Second and third level customization of the Simplified Organ Failure Score (SAPS) was performed using logistic regression analysis and the best fitted models were compared in terms of Area under the Receiver Operating Characteristic Curve (AUC) and Hosmer-Lemeshow Goodness-of-Fit test (HL). The patient cohort was divided into a training and test data with a 70:30 split. Ten-fold cross-validation was performed on the training set for every combination of variables that were evaluated. The best fitted model from the cross-validation was then evaluated using the test set, and the AUC and the HL p value on the test set were reported. Results. A total of 1400 patients were included in the study. Of these, 970 survived and 430 died in the hospital (30.7% mortality). We observed progressive improvement in the performance of SAPS on this subset of patients (AUC=0.6419, HL p=0) with second level (AUC=0.6639, HL p=0.2056), and third level (AUC=0.7419, HL p=0.6738) customization. The best fitted model incorporated variables from the first 3 days of ICU admission. The variables that were most predictive of hospital mortality in the multivariate analysis are the maximum blood urea nitrogen and the minimum systolic blood pressure from the third day. Conclusion. A logistic regression model built using local data for patients with AKI performed better than SAPS, the current standard mortality prediction scoring system.

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Introduction

There are numerous severity scoring systems that are available in the intensive care unit (ICU), including Acute Physiology and Chronic Health Evaluation (APACHE), Simplified Acute Physiology (SAPS), and Multiple Organ Dysfunction Score (MODS). Although initially designed for mortality prediction, they universally lack clinically acceptable accuracy at an individual patient level [1]. These systems perform relatively well in predicting how many patients will die in an ICU when the individual patient risks are calculated and averaged for that ICU. Thus, these severity scoring systems are currently used primarily for case-mix determination and benchmarking purposes. However, although the prognostic accuracy of the scoring system for an entire ICU population is good, its prognostic accuracy at different levels of risk, or its calibration, is poor. This suggests that within an ICU, there are groups of patients whose risk of death is over-estimated that are “balanced” by the groups of patients whose risk of death is underestimated. It is also important to note that the performance of these predictive models is always better on whole ICU populations than on specific subsets of ICU patients. For example, they have significantly underestimated the risk of death among patients who develop acute kidney injury (AKI) [2, 3].

Another feature of these severity scoring systems is their variable accuracy among ICU populations in different regions of the world [1]. Not surprisingly, the system performs well on ICU population that is similar to the group of patients whose data were used to build the predictive model. For example, SAPS II, which was developed using data from mostly European ICUs[4], performs well in France but not in the US (AUC = 0.67, Hosmer-Lemeshow p value = 0.05) [5]. But even among ICUs in Europe, the performance of the SAPS for case-mix determination wanes over time. This is referred to as model fade, and is the reason why newer versions of scoring systems are released and replace older versions. APACHE was developed from a North American database using logistic regression on patient variables obtained during the first 24 hours in the ICU [6]. APACHE I was built using 34 patient variables while APACHE IV utilized 142 variables [7]. MODS [8] was also built using North American database. Like SAPS, the performance of APACHE and MODS in different geographic regions varies and their calibration is poor even among ICU groups where they perform well [1]. Even when much bigger patient cohorts from more regions of the world are used, there has been no consistent improvement in calibration looking at studies evaluating the performance of the different scoring systems in the last 10 years [3].

ICU patients who develop AKI are one subset of patients where severity scoring systems have consistently performed poorly. AKI develops in approximately 6% of critically ill patients; two-thirds of these patients require renal support therapy [2]. The largest worldwide multi-center prospective study found that the observed mortality among these patients was substantially greater than predicted by SAPS II (60.3% vs. 45.6%, p < 0.001). In another UK-wide study of ICU patients who develop AKI, the APACHE II score under-predicted the number of deaths [3]. In this study, the null hypothesis of perfect calibration was strongly rejected (p < 0.001) by both the Hosmer-Lemeshow and Cox’s calibration regression.

Several methods have been proposed to improve the performance of existing severity scoring systems. Customization is a simple procedure that adapts a model to specific patient populations [9]. In second level customization, a multivariate regression is run on the same variables included in the severity score on the new database. The new coefficients generated by the model are then used to calculate the “new” severity score. In third level customization, additional variables are evaluated either in addition to the severity score or the original variables included in the severity score. These methods of customization have been successfully used in improving accuracy and calibration of existing severity scoring systems on patients from countries not represented in the original database, as well as for specific subgroup of ICU patients [10].
Another approach that has been used to improve mortality prediction is to calculate severity scores over a period of time [11, 12]. Severity scores on admission to the ICU ignore the many factors that can influence patient outcomes during the course of an ICU stay. These factors include, but are not limited to, the quality of care – the accuracy and timeliness of diagnosis and provision of appropriate treatment – and the patient’s inherent ability to heal as reflected by his response to therapy. Being able to evaluate changes in patient status over time thus represents an improvement on severity scores on admission.

Daily calculation of Sequential Organ Failure Assessment (SOFA) and Logistic Organ Dysfunction (LOD) scores has been evaluated in research studies [13]. These studies have demonstrated that models based on temporal patterns outperformed those based on physiologic variables during the first 24 hours of ICU admission. However, these models remain very poorly calibrated, preventing their adoption in clinical practice to guide management decisions for individual patients. Poor calibration of these models has been attributed to the observation that the influence and contribution of the variables on mortality change over time [14].

At present, ICU clinicians focus on and evaluate a subset of physiologic variables and their evolution over time when deciding whether to carry on with an individual patient or whether to recommend switching to comfort measures only. The selection of which variables are important is based on clinical intuition and experience, and likely varies from patient to patient and from one clinician to another.

Over the last few decades, the associated mortality of patients with AKI has remained largely unchanged (even after adjustment for age and severity of illness) despite advances in ICU care, including renal and other organ support therapy [15, 16]. Dialysis and/or filtration in the ICU is not only costly but also consumes a significant fraction of nursing time diverted from tasks that may be more beneficial in terms of patient outcomes. To date, no AKI-specific severity of illness scoring method has exhibited excellent predictive power for mortality [3]. Such a system might assist clinicians in predicting which patients would benefit from renal support therapy.

Rather than developing predictive models with good discrimination and calibration among general ICU populations in different regions of the world, we build a case for "local", customized models for homogeneous patient subsets built on patients from one’s own ICU database.

The specific questions we addressed are as follows:

1. To determine whether customization using local institutional data on patients with AKI will perform better compared to SAPS in predicting mortality
2. To assess whether variables over the first 72 hours in the ICU can predict mortality better than variables obtained during the first 24 hours of admission among this subset of patients
3. To evaluate whether the addition of selected interaction terms into the best fitted logistic regression model would improve the accuracy
4. To compare the logistic regression models using automated and heuristically-driven variable selection
5. To evaluate whether filtering using principal component analysis can improve the accuracy of mortality prediction models built on patients with AKI

6. To compare different machine learning algorithms in predicting mortality among this subset of ICU patients

Methods

The Laboratory of Computational Physiology at Massachusetts Institute of Technology (MIT) developed and maintains the Multi-parameter Intelligent Monitoring for Intensive Care (MIMIC II) database, a high resolution database of ICU patients admitted to the Beth Israel Deaconess Medical Center (BIDMC) since 2003 that has been de-identified by removal of all Protected Health Information [17]. An Institutional Review Board (IRB) approval was obtained from both MIT and BIDMC for the development, maintenance and public use of a de-identified ICU database. The MIMIC II database currently consists of data from more than 18,000 patients that has been de-identified and formatted to facilitate data-mining. The 3 sources of data are waveform data collected from the bedside monitors, hospital information systems and other third party clinical information systems.

Using the MIMIC II database, we identified the patients who had an ICD-9 diagnosis of acute renal failure (584.9) and who survived at least 72 hours in the ICU. We verified whether the patients developed acute kidney injury at around the time of ICU admission by looking at the serum creatinine and urine output during the first 72 hours in the ICU. Patients whose serum creatinine determinations were less than 1.0 mg/dl and who had an average urine output of 0.5 ml/kg/hr during the first three days of their ICU stay were excluded from the cohort, as they are unlikely to have sustained acute kidney injury at around the time of ICU admission.

Variable Selection

The outcome of interest is survival to hospital discharge. The covariates that were evaluated included demographic factors (age and sex), SAPS, Glasgow Coma Score (GCS), and physiologic variables measured during the first three days in the ICU. We obtained the minimum, maximum, standard deviation and average value of the majority of the physiologic variables. For variables where a low value does not have clinical significance during critical illness (e.g. serum creatinine, serum bilirubin, blood urea nitrogen), only the maximum values were extracted from the database. We only included the worst Glasgow Coma Score (GCS) on presentation to the ICU because as soon as a patient is intubated, GCS becomes clinically irrelevant as a patient is typically given medications in order to tolerate the endotracheal tube. At this time, a low GCS is no longer a reflection of central nervous system dysfunction. Finally, some variables were excluded (minimum temperature, minimum respiratory rate) because a significant fraction of the data was deemed inaccurate after manual inspection. This will be explained further in the discussion section of this paper.

Inclusion of the minimum, maximum and average values, and the standard deviation, which are not independent, may represent redundant variables. However, noise reduction and consequently better class separation may be obtained by adding variables that are presumably redundant [18]. Only perfectly correlated variables are truly redundant in the sense that no additional information is gained by adding them. The complete list of variables that were obtained and evaluated is found in Table 1.
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Table 1. List of Features
A univariate logistic regression was performed on each of the variables to determine whether they are correlated with hospital mortality.

We employed two automated feature selection algorithms as well as domain knowledge for variable selection. The algorithms were correlation-based feature subset selection (CFS) and consistency subset evaluation using the best first search method (greedy hill-climbing with backtracking). Correlation-based feature subset selection assesses the predictive ability of each attribute individually and the degree of redundancy among them, preferring sets of attributes that are highly correlated with the outcome but have low inter-correlation [19]. Consistency subset evaluation assesses attribute sets by the degree of consistency in class values when the training instances are projected onto the set. The consistency of any subset of attributes can never improve on that of the full set, so that this evaluator seeks the smallest subset whose consistency is the same as that of the full attribute set.

We also evaluated various combinations of the variables based on domain expertise. Variables with a p value greater than 0.05 in the univariate or in a multivariate analysis were still considered for inclusion or were retained in a model, as they can still contribute to the performance of a model with good discrimination and calibration.

**Pre-Processing**

Instead of replacing the missing values with the mean for variables with Gaussian distribution or the median for all other variables, we applied a set of rules derived from clinical experience. The rules are as follows:

1. If the values for a certain variable are missing for all three days, they are replaced by the middle value of the normal range of that variable. If a variable is not measured in the ICU, e.g. serum bilirubin, there is a good likelihood that there is no concern that this may be abnormal.

2. A missing value on the second ICU day was replaced with the average of the first and third day values. A missing value on the first or third ICU day was replaced with the second day value.

3. If values on two of the first three days in the ICU are missing, they are both replaced with the value that is present.

**Statistical Analysis**

The patient cohort was divided into a training and test data with a 70:30 split. The test set was not used to build any of the models. Ten-fold cross-validation was performed on the training set ten times for every combination of variables that were evaluated. Two sets of AUC and Hosmer-Lemeshow (HL) p value were obtained for each model. The first is the average of the ten values obtained from each of the cross-validation run. The second was obtained by evaluating the model that performed the best on the training set on the test data, in order to eliminate a learning bias. Only the second set of AUC and HL p value is reported.

The SAPS of each patient was converted to predicted mortality using the following formula:

\[ \text{Predicted Death Rate} = \frac{e^{(\logit)}}{1+e^{(\logit)}}, \]  

where \( \logit = -7.7631 + 0.0737 \times \text{SAPS} + 0.9971 \times \text{ln(SAPS+1)} \) [8]. The predicted death rate was compared against the true outcome, and an Area under the Receiver Operating Characteristic Curve (AUC) was calculated. This AUC is used as the benchmark to compare the AUC's of the customized models.
Using the R software (R version 2.7.2, The R Foundation for Statistical Computing, Auckland, New Zealand), second level customization was performed by building a multivariate regression model using the physiologic variable components of SAPS. Ten-fold cross-validation was performed on the training set and the best-fitted model was evaluated on the test set.

Third level customization was performed by evaluating various combinations of variables from the first three days in the ICU to predict mortality among these patients with AKI. We built logistic regression model using the variables selected by the correlation-based feature subset evaluator and the consistency subset evaluator. We did the same for the different combination of variables selected based on domain expertise. We then compared the performance of the best fitted models on the test data.

A number of interaction terms, selected based on clinical knowledge, were evaluated to see whether they improved the performance of the best multivariate logistic regression models. These included:

1. Blood pressure and heart rate – The effect of the heart rate on mortality might differ at different blood pressure levels. Bradycardia is deleterious among patients who are hypotensive, but may be protective for those who are normotensive by reducing the oxygen requirement of the heart.

2. Age and serum creatinine – The effect of serum creatinine on mortality might differ at different age groups.

3. BUN and serum creatinine – Protein catabolism is more marked among patients who are sicker. This results in an increased nitrogen load to the kidneys for excretion. The consequence of protein catabolism, as reflected by the blood urea nitrogen, might differ among patients depending on their kidney function.

4. Sex and serum creatinine - The effect of serum creatinine on mortality might differ between men and women.

5. Glucose standard deviation and GCS – The influence of glucose variability, a result of impairment in neurohormonal mechanisms, on clinical outcome might vary according to the level of CNS dysfunction, as measured by the GCS.

To compare different machine learning algorithms in predicting hospital mortality, Weka version 3.5.7 (University of Waikato, Hamilton, New Zealand) was used. Weka uses the Quasi-Newton method to optimize outcome prediction.

Filtering

Principal component analysis was performed on the training set to filter these data using the first four largest eigenvectors, accounting for 99.75% of the variability. We performed filtering by collapsing the Eigenvectors down and re-projecting the data back into the original space. Logistic regression analysis was then performed on the filtered data using ten-fold cross-validation to determine whether the accuracy of prediction can be improved by using this noise reduction approach.
Results

There were a total of 1400 patients with an ICD-9 diagnosis of acute renal failure who survived at least 72 hours in the ICU. Of these, 970 survived and 430 died in the hospital (30.7% mortality). These were divided into a training set (979 patients) and test set (421 patients). The difference between the mortality rate of the training set (31.9%) and test set (28.2%) is not statistically significant (p > 0.05). The difference in the distributions of the variables in the training and test sets is also not statistically significant (data not shown). The distributions of selected variables in the entire patient cohort among survivors and non-survivors are shown below.

A. SAPS Distribution among Survivors and Non-Survivors

Red:
Mean (Survivors) = 15.6
Standard Deviation (Survivors) = 5.2

Blue:
Mean (Non-Survivors) = 18.3
Standard Deviation (Non-Survivors) = 5.2

B. Age Distribution among Survivors and Non-Survivors

Red:
Mean (Survivors) = 68.0
Standard Deviation (Survivors) = 16.0

Blue:
Mean (Non-Survivors) = 71.9
Standard Deviation (Non-Survivors) = 15.6
C. Sex Distribution among Survivors and Non-Survivors

Survivors:
- 561 Males (57.8%)
- 409 Females (42.2%)

Non-Survivors:
- 244 Males (56.6%)
- 187 Females (43.4%)

D. Maximum Serum Creatinine on Day 1 among Survivors and Non-Survivors

Red:
- Mean (Survivors) = 2.41 mg/dl
- Standard Deviation (Survivors) = 1.96 mg/dl

Blue:
- Mean (Non-Survivors) = 2.29 mg/dl
- Standard Deviation (Non-Survivors) = 1.57 mg/dl

E. Minimum Glasgow Coma Score on Day 1 among Survivors and Non-Survivors

Red:
- Mean (Survivors) = 9.6
- Standard Deviation (Survivors) = 4.7

Blue:
- Mean (Non-Survivors) = 9.1
- Standard Deviation (Non-Survivors) = 4.4
F. Maximum Heart Rate on Day 1 among Survivors and Non-Survivors

Red:
Mean (Survivors) = 106.2
Standard Deviation (Survivors) = 22.1

Blue:
Mean (Non-Survivors) = 109.7
Standard Deviation (Non-Survivors) = 25.3

G. Maximum Heart Rate on Day 2 among Survivors and Non-Survivors

Red:
Mean (Survivors) = 101.9
Standard Deviation (Survivors) = 21.2

Blue:
Mean (Non-Survivors) = 105.7
Standard Deviation (Non-Survivors) = 23.4

H. Maximum Heart Rate on Day 3 among Survivors and Non-Survivors

Red:
Mean (Survivors) = 101.2
Standard Deviation (Survivors) = 20.8

Blue:
Mean (Non-Survivors) = 105.8
Standard Deviation (Non-Survivors) = 24.4
I. Minimum Systolic Blood Pressure on Day 1 among Survivors and Non-Survivors

Red:
Mean (Survivors) = 90.0 mmHg
Standard Deviation (Survivors) = 16.7 mmHg

Blue:
Mean (Non-Survivors) = 84.9 mmHg
Stand. Deviation (Non-Survivors) = 17.0 mmHg

J. Minimum Systolic Blood Pressure on Day 2 among Survivors and Non-Survivors

Red:
Mean (Survivors) = 96.1 mmHg
Standard Deviation (Survivors) = 17.0 mmHg

Blue:
Mean (Non-Survivors) = 90.5 mmHg
Stand. Deviation (Non-Survivors) = 17.6 mmHg

K. Minimum Systolic Blood Pressure on Day 3 among Survivors and Non-Survivors

Red:
Mean (Survivors) = 99.1 mmHg
Standard Deviation (Survivors) = 17.8 mmHg

Blue:
Mean (Non-Survivors) = 91.3 mmHg
Stand. Deviation (Non-Survivors) = 18.9 mmHg
L. Average Serum Hematocrit on Day 1 among Survivors and Non-Survivors

Red:
Mean (Survivors) = 31.0%
Standard Deviation (Survivors) = 4.9%

Blue:
Mean (Non-Survivors) = 30.7%
Standard Deviation (Non-Survivors) = 4.9%

M. Average Serum Hematocrit on Day 2 among Survivors and Non-Survivors

Red:
Mean (Survivors) = 30.4%
Standard Deviation (Survivors) = 4.2%

Blue:
Mean (Non-Survivors) = 30.4%
Standard Deviation (Non-Survivors) = 4.2%

N. Average Serum Hematocrit on Day 3 among Survivors and Non-Survivors

Red:
Mean (Survivors) = 30.4%
Standard Deviation (Survivors) = 4.0%

Blue:
Mean (Non-Survivors) = 30.4%
Standard Deviation (Non-Survivors) = 3.9%
O. Glucose Variability (Standard Deviation) on Day 1 among Survivors and Non-Survivors

Red:  
Mean (Survivors) = 26.1 mg/dl  
Blue:  
Mean (Non-Survivors) = 24.9 mg/L

P. Glucose Variability (Standard Deviation) on Day 2 among Survivors and Non-Survivors

Red:  
Mean (Survivors) = 13.3 mg/dl  
Blue:  
Mean (Non-Survivors) = 15.3 mg/L

Q. Glucose Variability (Standard Deviation) on Day 3 among Survivors and Non-Survivors

Red:  
Mean (Survivors) = 10.7 mg/dl  
Blue:  
Mean (Non-Survivors) = 12.8 mg/dl
R. Maximum White Blood Count on Day 1 among Survivors and Non-Survivors

Red:
Mean (Survivors) = 14.5 x 10^3/uL
Standard Deviation (Survivors) = 13.5 x 10^3/uL

Blue:
Mean (Non-Survivors) = 15.8 x 10^3/uL
Stand. Deviation (Non-Survivors) = 11.0 x 10^3/uL

S. Maximum White Blood Count on Day 2 among Survivors and Non-Survivors

Red:
Mean (Survivors) = 12.6 x 10^3/uL
Standard Deviation (Survivors) = 7.2 x 10^3/uL

Blue:
Mean (Non-Survivors) = 15.1 x 10^3/uL
Stand. Deviation (Non-Survivors) = 10.9 x 10^3/uL

T. Maximum White Blood Count on Day 3 among Survivors and Non-Survivors

Red:
Mean (Survivors) = 12.0 x 10^3/uL
Standard Deviation (Survivors) = 6.9 x 10^3/uL

Blue:
Mean (Non-Survivors) = 14.6 x 10^3/uL
Stand. Deviation (Non-Survivors) = 10.4 x 10^3/uL
U. Minimum Serum Bicarbonate on Day 1 among Survivors and Non-Survivors

Red:
Mean (Survivors) = 22.1 mEq/L
Standard Deviation (Survivors) = 4.5 mEq/L

Blue:
Mean (Non-Survivors) = 21.8 mEq/L
Standard Deviation (Non-Survivors) = 4.5 mEq/L

V. Minimum Serum Bicarbonate on Day 2 among Survivors and Non-Survivors

Red:
Mean (Survivors) = 22.8 mEq/L
Standard Deviation (Survivors) = 4.4 mEq/L

Blue:
Mean (Non-Survivors) = 22.0 mEq/L
Standard Deviation (Non-Survivors) = 4.7 mEq/L

W. Minimum Serum Bicarbonate on Day 3 among Survivors and Non-Survivors

Red:
Mean (Survivors) = 23.3 mEq/L
Standard Deviation (Survivors) = 4.2 mEq/L

Blue:
Mean (Non-Survivors) = 22.4 mEq/L
Standard Deviation (Non-Survivors) = 4.4 mEq/L
X. Urine Output on Day 1 among Survivors and Non-Survivors

Red:
Mean (Survivors) = 1380.6 ml
Standard Deviation (Survivors) = 1530.4 ml

Blue:
Mean (Non-Survivors) = 919.6 ml
Standard Deviation (Non-Survivors) = 1209.5 ml

Y. Urine Output among on Day 2 among Survivors and Non-Survivors

Red:
Mean (Survivors) = 2116.9 ml
Standard Deviation (Survivors) = 1474.9 ml

Blue:
Mean (Non-Survivors) = 1525.8 ml
Standard Deviation (Non-Survivors) = 1533.1 ml

Z. Urine Output on Day 3 among Survivors and Non-Survivors

Red:
Mean (Survivors) = 1998.0 ml
Standard Deviation (Survivors) = 1428.6 ml

Blue:
Mean (Non-Survivors) = 1525.0 ml
Standard Deviation (Non-Survivors) = 1292.1 ml
<table>
<thead>
<tr>
<th>Variable</th>
<th>Value (P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAPS</td>
<td>3.44e-16</td>
</tr>
<tr>
<td>AGE</td>
<td>0.0122</td>
</tr>
<tr>
<td>SEX</td>
<td>0.822</td>
</tr>
<tr>
<td>MIN GCS 1ST DAY</td>
<td>0.00363</td>
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<tr>
<td>MAX BUN 1ST DAY</td>
<td>0.00195</td>
</tr>
<tr>
<td>MAX BUN 2ND DAY</td>
<td>6.4e-07</td>
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<tr>
<td>MAX BUN 3RD DAY</td>
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<td>MAX TEMP 1ST DAY</td>
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<td>MAX TEMP 2ND DAY</td>
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<tr>
<td>MAX TEMP 3RD DAY</td>
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<td>MAX RESP 1ST DAY</td>
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<td>MAX RESP 2ND DAY</td>
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<td>MAX RESP 3RD DAY</td>
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<td>MIN HR 1ST DAY</td>
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<tr>
<td>STDDEV HR 1ST DAY</td>
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<tr>
<td>AVG HR 1ST DAY</td>
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<tr>
<td>MAX HR 2ND DAY</td>
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<td>MAX HR 3RD DAY</td>
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<td>AVG HR 2ND DAY</td>
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<td>0.00734</td>
</tr>
<tr>
<td>AVG HR 3RD DAY</td>
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</tr>
<tr>
<td>MIN SYSBP 1ST DAY</td>
<td>8.8e-06</td>
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<tr>
<td>MAX SYSBP 1ST DAY</td>
<td>0.00419</td>
</tr>
<tr>
<td>STDDEV SYSBP 1ST DAY</td>
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</tr>
<tr>
<td>AVG SYSBP 1ST DAY</td>
<td>1.12e-06</td>
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<tr>
<td>MIN SYSBP 2ND DAY</td>
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<td>AVG SYSBP 2ND DAY</td>
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<td>2.89e-09</td>
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<td>MAX SYSBP 3RD DAY</td>
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<td>MIN SODIUM 1ST DAY</td>
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<tr>
<td>MIN SODIUM 2ND DAY</td>
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<td>STDDEV SODIUM 2ND DAY</td>
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<td>AVG SODIUM 2ND DAY</td>
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</tr>
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<td>MIN POTASSIUM 1ST DAY</td>
<td>0.16325</td>
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<td>0.9065</td>
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<td>0.775</td>
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<td>STDDEV POTASSIUM 2ND DAY</td>
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<td>AVG POTASSUM 2ND DAY</td>
<td>0.06747</td>
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<td>0.4029</td>
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<td>STDDEV POTASSUM 3RD DAY</td>
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</tr>
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<td>AVG POTASSUM 3RD DAY</td>
<td>0.0392</td>
</tr>
<tr>
<td>MIN GLUCOSE 1ST DAY</td>
<td>0.53679</td>
</tr>
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<td>MAX GLUCOSE 1ST DAY</td>
<td>0.570680</td>
</tr>
<tr>
<td>STDDEV GLUCOSE 1ST DAY</td>
<td>0.973</td>
</tr>
<tr>
<td>AVG GLUCOSE 1ST DAY</td>
<td>0.3212</td>
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<td>0.141</td>
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<td>0.235</td>
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<tr>
<td>MIN GLUCOSE 3RD DAY</td>
<td>0.528</td>
</tr>
<tr>
<td>MAX GLUCOSE 3RD DAY</td>
<td>0.0454</td>
</tr>
<tr>
<td>STDDEV GLUCOSE 3RD DAY</td>
<td>0.0781</td>
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<tr>
<td>AVG GLUCOSE 3RD DAY</td>
<td>0.00231</td>
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<tr>
<td>MIN BICARBONATE 1ST DAY</td>
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<td>MAX BICARBONATE 1ST DAY</td>
<td>0.066</td>
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<td>STDDEV BICARBONATE 1ST DAY</td>
<td>0.637</td>
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<tr>
<td>AVG BICARBONATE 1ST DAY</td>
<td>0.06901</td>
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<td>MIN BICARBONATE 2ND DAY</td>
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<td>AVG BICARBONATE 3RD DAY</td>
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<tr>
<td>MIN WBC 1ST DAY</td>
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<td>MAX WBC 1ST DAY</td>
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</tr>
<tr>
<td>STDDEV WBC 1ST DAY</td>
<td>0.835</td>
</tr>
<tr>
<td>AVG WBC 1ST DAY</td>
<td>0.0222</td>
</tr>
<tr>
<td>MIN WBC 2ND DAY</td>
<td>0.000142</td>
</tr>
<tr>
<td>MAX WBC 2ND DAY</td>
<td>3.8e-05</td>
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<tr>
<td>STDDEV WBC 2ND DAY</td>
<td>0.0167</td>
</tr>
<tr>
<td>AVG WBC 2ND DAY</td>
<td>6.5e-05</td>
</tr>
<tr>
<td>MIN WBC 3RD DAY</td>
<td>5.77e-05</td>
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<tr>
<td>MAX WBC 3RD DAY</td>
<td>5.13e-06</td>
</tr>
<tr>
<td>STDDEV WBC 3RD DAY</td>
<td>0.00217</td>
</tr>
<tr>
<td>AVG WBC 3RD DAY</td>
<td>1.64e-05</td>
</tr>
<tr>
<td>MIN HEMATOCRIT 1ST DAY</td>
<td>0.170</td>
</tr>
<tr>
<td>MAX HEMATOCRIT 1ST DAY</td>
<td>0.638</td>
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<tr>
<td>STDDEV HEMATOCRIT 1ST DAY</td>
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</tr>
<tr>
<td>AVG HEMATOCRIT 1ST DAY</td>
<td>0.273</td>
</tr>
<tr>
<td>MIN HEMATOCRIT 2ND DAY</td>
<td>0.0223</td>
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<tr>
<td>MAX HEMATOCRIT 2ND DAY</td>
<td>0.966</td>
</tr>
<tr>
<td>STDDEV HEMATOCRIT 2ND DAY</td>
<td>0.000994</td>
</tr>
<tr>
<td>AVG HEMATOCRIT 2ND DAY</td>
<td>0.239</td>
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<tr>
<td>MIN HEMATOCRIT 3RD DAY</td>
<td>0.0245</td>
</tr>
<tr>
<td>MAX HEMATOCRIT 3RD DAY</td>
<td>0.935</td>
</tr>
<tr>
<td>STDDEV HEMATOCRIT 3RD DAY</td>
<td>0.00376</td>
</tr>
<tr>
<td>AVG HEMATOCRIT 3RD DAY</td>
<td>0.22</td>
</tr>
</tbody>
</table>
BB. SAPS vs. Second Level Customization

The SAPS physiologic variables are as follows:

<table>
<thead>
<tr>
<th>SAPS Variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE</td>
</tr>
<tr>
<td>MAX_BUN_1ST_DAY</td>
</tr>
<tr>
<td>MIN_GCS_1ST_DAY</td>
</tr>
<tr>
<td>MIN_WBC_1ST_DAY</td>
</tr>
<tr>
<td>MIN_SYSBP_1ST_DAY</td>
</tr>
<tr>
<td>MIN_POTASSIUM_1ST_DAY</td>
</tr>
<tr>
<td>MAX_HR_1ST_DAY</td>
</tr>
<tr>
<td>MAX_SODIUM_1ST_DAY</td>
</tr>
<tr>
<td>MAX_TEMP_1ST_DAY</td>
</tr>
<tr>
<td>MIN_BICARBONATE_1ST_DAY</td>
</tr>
<tr>
<td>OUTPUT_1ST_DAY</td>
</tr>
<tr>
<td>MAX_BILIRUBIN_1ST_DAY</td>
</tr>
</tbody>
</table>

The table below shows the AUC and Hosmer-Lemeshow p value on the test data of SAPS and the best fitted multivariate model of the SAPS physiologic variables using the training data.

<table>
<thead>
<tr>
<th>Model</th>
<th>Area under the ROC Curve</th>
<th>Hosmer-Lemeshow P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAPS Predicted Death Rate = ( \frac{e^{(\text{Logit})}}{1+e^{(\text{Logit})}} )</td>
<td>0.6419</td>
<td>0</td>
</tr>
<tr>
<td>Logit = -7.7631 + 0.0737<em>SAPS + 0.9971</em>ln(SAPS+1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Second Level Customization</td>
<td>0.6639</td>
<td>0.2056</td>
</tr>
<tr>
<td>(Multivariate Regression using SAPS Variables)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The ROC Curves are shown below.

![ROC Curves](image1.png)  
SAPS  
Second Level Customization
CC. SAPS Physiologic Variables on Day 1 vs. Day 2 vs. Day 3

The table below shows the AUC and Hosmer-Lemeshow p value on the test data of the best fitted logistic regression models of the SAPS physiologic variables from Day 1, Day 2 and Day 3 using the training data.

<table>
<thead>
<tr>
<th>Model</th>
<th>Area Under the ROC Curve</th>
<th>Hosmer-Lemeshow p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1 SAPS Variables</td>
<td>0.6539</td>
<td>0.2036</td>
</tr>
<tr>
<td>Day 2 SAPS Variables</td>
<td>0.6578</td>
<td>0.1332</td>
</tr>
<tr>
<td>Day 3 SAPS Variables</td>
<td>0.7030</td>
<td>0.5208</td>
</tr>
</tbody>
</table>

The ROC Curves are shown below.

The p values of the variables in the best fitted logistic regression model using the SAPS physiologic variables from Day 1, Day 2 and Day 3 are shown below. The variables whose p values are less than 0.05 are boxed.

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE</td>
<td>0.0032</td>
<td>AGE</td>
</tr>
<tr>
<td>MIN_SYSBP_1ST_DAY</td>
<td>0.0057</td>
<td>MIN_SYSBP_2ND_DAY</td>
</tr>
<tr>
<td>MAX HR_1ST_DAY</td>
<td>0.0548</td>
<td>MAX HR_2ND_DAY</td>
</tr>
<tr>
<td>MAX TEMP_1ST_DAY</td>
<td>0.2178</td>
<td>MAX TEMP_2ND_DAY</td>
</tr>
<tr>
<td>OUT 1ST_DAY</td>
<td>0.0178</td>
<td>OUT 2ND_DAY</td>
</tr>
<tr>
<td>MAX BUN_1ST_DAY</td>
<td>0.0327</td>
<td>MAX BUN 2ND_DAY</td>
</tr>
<tr>
<td>MIN WBC_1ST_DAY</td>
<td>0.0093</td>
<td>MIN WBC 2ND_DAY</td>
</tr>
<tr>
<td>MIN POTSM_1ST_DAY</td>
<td>0.5553</td>
<td>MIN POTSM 2ND_DAY</td>
</tr>
<tr>
<td>MAX SODM_1ST_DAY</td>
<td>0.2490</td>
<td>MAX SODM 2ND_DAY</td>
</tr>
<tr>
<td>MIN BICARB_1ST_DAY</td>
<td>0.6979</td>
<td>MIN BICARB 2ND_DAY</td>
</tr>
<tr>
<td>MAX BILU_1ST_DAY</td>
<td>3.76e-05</td>
<td>MAX BILU 2ND_DAY</td>
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<tr>
<td>MIN GCS_1ST_DAY</td>
<td>0.0074</td>
<td></td>
</tr>
</tbody>
</table>

P Values of the Variables in the Best Fitted Models
DD. Logistic Regression Models using Combination of Day 1, Day 2 and Day 3 SAPS Physiologic Variables

<table>
<thead>
<tr>
<th>Model</th>
<th>Area Under the ROC Curve</th>
<th>Hosmer-Lemeshow p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 3 SAPS Variables</td>
<td>0.7030</td>
<td>0.5208</td>
</tr>
<tr>
<td>Day 1 SAPS Variables + Day 2 SAPS Variables</td>
<td>0.6964</td>
<td>0.5032</td>
</tr>
<tr>
<td>Day 2 SAPS Variables + Day 3 SAPS Variables</td>
<td>0.7454</td>
<td>0.4640</td>
</tr>
<tr>
<td>Day 1 SAPS Variables + Day 3 SAPS Variables</td>
<td>0.7352</td>
<td>0.3778</td>
</tr>
<tr>
<td>Day 1 SAPS Variables + Day 2 SAPS Variables + Day 3 SAPS Variables</td>
<td>0.7419</td>
<td>0.6738</td>
</tr>
</tbody>
</table>

The ROC Curves are shown below.

- Day 1 and 2 SAPS Variables
- Day 2 and 3 SAPS Variables
- Day 1 and 3 SAPS Variables
- Day 1, 2 and 3 SAPS Variables
The p values of the variables in the best fitted logistic regression model using the SAPS physiologic variables from Day 1, Day 2 and Day 3 are shown below. The variables whose p values are less than 0.05 are boxed.

<table>
<thead>
<tr>
<th>Variable</th>
<th>P Value</th>
<th>Variable</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MIN_SYSBP_1ST_DAY</td>
<td>0.442367</td>
<td>MIN_SYSBP_2ND_DAY</td>
<td>0.895548</td>
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<td>MAX_HR_1ST_DAY</td>
<td>0.403927</td>
<td>MAX_HR_2ND_DAY</td>
<td>0.480650</td>
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<tr>
<td>MAX_TEMP_1ST_DAY</td>
<td>0.709826</td>
<td>MAX_TEMP_2ND_DAY</td>
<td>0.080553</td>
</tr>
<tr>
<td>OUTPUT_1ST_DAY</td>
<td>0.079730</td>
<td>OUTPUT_2ND_DAY</td>
<td>0.208689</td>
</tr>
<tr>
<td>MAX_BUN_1ST_DAY</td>
<td>0.225744</td>
<td>MAX_BUN_2ND_DAY</td>
<td>0.780805</td>
</tr>
<tr>
<td>MIN_WBC_1ST_DAY</td>
<td>0.821370</td>
<td>MIN_WBC_2ND_DAY</td>
<td>0.677556</td>
</tr>
<tr>
<td>MIN_POTSM_1ST_DAY</td>
<td>0.597589</td>
<td>MIN_POTSM_2ND_DAY</td>
<td>0.835240</td>
</tr>
<tr>
<td>MAX_SODIUM_1ST_DAY</td>
<td>0.380777</td>
<td>MAX_SODIUM_2ND_DAY</td>
<td>0.051881</td>
</tr>
<tr>
<td>MIN_BICARB_1ST_DAY</td>
<td>0.579316</td>
<td>MIN_BICARB_2ND_DAY</td>
<td>0.927018</td>
</tr>
<tr>
<td>MAX_BIL_1ST_DAY</td>
<td>0.083459</td>
<td>MAX_BIL_2ND_DAY</td>
<td>0.184281</td>
</tr>
</tbody>
</table>

Comparison of Models using Variables selected by CFS and Consistency Subset Evaluator Algorithms

The table below lists the variables selected by the two feature selection algorithms. Except for a few exceptions (boxed), the two algorithms came up with identical variables.
The AUC and HL $p$ value of the best fitted logistic regression models using combination of Day 1, Day 2 and Day 3 SAPS physiologic variables, and the variables selected by CFS and Consistency Subset Evaluator algorithms are tabulated below.

<table>
<thead>
<tr>
<th>Model</th>
<th>Area Under the ROC Curve</th>
<th>Hosmer-Lemeshow $p$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1 SAPS Variables +</td>
<td>0.7419</td>
<td>0.6738</td>
</tr>
<tr>
<td>Day 2 SAPS Variables +</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 3 SAPS Variables</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Variables selected by CFS Subset Evaluation Algorithm</td>
<td>0.7332</td>
<td>0.5945</td>
</tr>
<tr>
<td>Variables selected by Consistency Subset Evaluation Algorithm</td>
<td>0.7289</td>
<td>0.6279</td>
</tr>
</tbody>
</table>

### FF. Effect of Interaction Terms on the Performance of the Best Fitted Logistic Regression Model

The effect of the addition of heuristically selected interaction terms on the performance of the best fitted logistic regression model using combination of Day 1, Day 2 and Day 3 SAPS physiologic variables is shown below.

<table>
<thead>
<tr>
<th>Model</th>
<th>Area Under the ROC Curve</th>
<th>Hosmer-Lemeshow $p$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Best Fitted Model</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Best Fitted Model with Blood Pressure*Heart rate</td>
<td>0.7419</td>
<td>0.6738</td>
</tr>
<tr>
<td>Best Fitted Model with Age*Serum Creatinine</td>
<td>0.7239</td>
<td>0.1296</td>
</tr>
<tr>
<td>Best Fitted Model with BUN*Serum Creatinine</td>
<td>0.7440</td>
<td>0.0624</td>
</tr>
<tr>
<td>Best Fitted Model with Sex*Serum Creatinine</td>
<td>0.7310</td>
<td>0.1745</td>
</tr>
<tr>
<td>Best Fitted Model with Glucose Standard Deviation*GCS</td>
<td>0.7384</td>
<td>0.3866</td>
</tr>
</tbody>
</table>
GG. Principal Component Analysis of the Variables
HH. Best Fitted Logistic Regression Model using Filtered Data

<table>
<thead>
<tr>
<th></th>
<th>Original Data AUC</th>
<th>Filtered Data AUC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1 SAPS + Day 3 SAPS</td>
<td>0.735</td>
<td>0.610</td>
</tr>
<tr>
<td>Day 2 SAPS + Day 3 SAPS</td>
<td>0.745</td>
<td>0.607</td>
</tr>
<tr>
<td>Day 1 SAPS + Day 2 SAPS + Day 3 SAPS</td>
<td>0.742</td>
<td>0.612</td>
</tr>
</tbody>
</table>
II. Best Fitted Logistic Regression Models using Different Machine Learning Algorithms

Below is the performance of five machine-learning algorithms in predicting hospital mortality among patients with AKI using combination of Day 1, Day 2 and Day 3 SAPS physiologic variables.

<table>
<thead>
<tr>
<th>Model</th>
<th>Accuracy</th>
<th>Mean Absolute Error</th>
<th>Area under the ROC Curve</th>
</tr>
</thead>
<tbody>
<tr>
<td>Logistic Regression</td>
<td>70.68%</td>
<td>0.3796</td>
<td>0.685</td>
</tr>
<tr>
<td>Bayes Net</td>
<td>68.13%</td>
<td>0.3587</td>
<td>0.682</td>
</tr>
<tr>
<td>Naive Bayes</td>
<td>71.91%</td>
<td>0.2906</td>
<td>0.691</td>
</tr>
<tr>
<td>Classification and Regression Tree</td>
<td>67.52%</td>
<td>0.4154</td>
<td>0.562</td>
</tr>
<tr>
<td>Artificial Neural Network</td>
<td>65.58%</td>
<td>0.3428</td>
<td>0.633</td>
</tr>
</tbody>
</table>

Below is the performance of five machine-learning algorithms in predicting hospital mortality among patients with AKI using variables selected by the CFS Subset Evaluator algorithm.

<table>
<thead>
<tr>
<th>Model</th>
<th>Accuracy</th>
<th>Mean Absolute Error</th>
<th>Area under the ROC Curve</th>
</tr>
</thead>
<tbody>
<tr>
<td>Logistic Regression</td>
<td>71.20%</td>
<td>0.3762</td>
<td>0.704</td>
</tr>
<tr>
<td>Bayes Net</td>
<td>68.85%</td>
<td>0.3490</td>
<td>0.687</td>
</tr>
<tr>
<td>Naive Bayes</td>
<td>71.20%</td>
<td>0.2910</td>
<td>0.698</td>
</tr>
<tr>
<td>Classification and Regression Tree</td>
<td>68.03%</td>
<td>0.3980</td>
<td>0.619</td>
</tr>
<tr>
<td>Artificial Neural Network</td>
<td>64.45%</td>
<td>0.3615</td>
<td>0.645</td>
</tr>
</tbody>
</table>

Below is the performance of five machine-learning algorithms in predicting hospital mortality among patients with AKI using variables selected by the Consistency Subset Evaluator algorithm.

<table>
<thead>
<tr>
<th>Model</th>
<th>Accuracy</th>
<th>Mean Absolute Error</th>
<th>Area under the ROC Curve</th>
</tr>
</thead>
<tbody>
<tr>
<td>Logistic Regression</td>
<td>71.20%</td>
<td>0.3726</td>
<td>0.706</td>
</tr>
<tr>
<td>Bayes Net</td>
<td>67.93%</td>
<td>0.3497</td>
<td>0.689</td>
</tr>
<tr>
<td>Naive Bayes</td>
<td>70.07%</td>
<td>0.2997</td>
<td>0.692</td>
</tr>
<tr>
<td>Classification and Regression Tree</td>
<td>67.31%</td>
<td>0.4129</td>
<td>0.583</td>
</tr>
<tr>
<td>Artificial Neural Network</td>
<td>66.19%</td>
<td>0.3438</td>
<td>0.651</td>
</tr>
</tbody>
</table>
Discussion

The physiologic response of a patient to stress or disease is the main determinant of the outcome [20]. Bion [21] suggests this response is dependent on three factors; severity of the acute insult, the treatment given, and the patient's degree of physiological reserve.

Severity scoring systems capture the stressor event. Over the last decade, there has been a push to measure quality of therapy, but this has not been incorporated into mortality prediction. Of the three factors, the physiologic reserve is the least characterized.

Physiologic reserve accounts for the difference in clinical outcome that two patients with identical mortality risks and treatment may have. It is defined as the body's response to stress and disease at a cellular level and the variation between individuals is thought to be largely influenced by genetic factors. This reserve dictates how the patient responds to and heals from the acute insult, such as sepsis, trauma, burns or major surgery, regardless of the treatments provided in the ICU, and may be the most significant of the three factors. There is currently no biomarker for physiologic reserve, but age, cardio-pulmonary reserve, immune and nutritional status have been used in various combinations as a surrogate marker.

At present, only the patients at extremely high risk are able to have their outcome predicted with high specificity (i.e. a low number of false negative predictions), and there is still a relatively low sensitivity to pick up patients that will die despite having a less than extremely high risk of death.

The 31% mortality of this subgroup of patients with AKI is higher than the 12% mortality of patients in the MIMIC II database [22], and is consistent with published literature. Chertow and colleagues previously showed that even small changes in serum creatinine while in the hospital were independently associated with an increased risk of dying [23].
Distribution of Variables among Survivors and Non-Survivors

The non-survivors had a higher SAPS and were older than the patients who survived to hospital discharge. Among this subset of ICU patients who developed AKI, there was no significant difference between those who survived and those who died as regards the initial and subsequent serum creatinine levels during the first 72 hours in the ICU. This suggests that although AKI contributes to hospital mortality, the initial degree of renal dysfunction, as measured by the serum creatinine, does not exert a significant influence on whether the patient recovers or not, as reflected by hospital mortality. This is supported further by the finding that there was likewise no significant difference in the serum bicarbonate levels between the survivors and non-survivors over the first three ICU days. The serum bicarbonate is measured primarily to detect the presence of metabolic acidosis. Renal dysfunction is one of the most common etiologies of metabolic acidosis in the ICU.

The minimum GCS score on the first ICU day, a surrogate for the worst level of consciousness at the time of presentation in the ICU, is lower among the non-survivors. The patients who died had a higher maximum heart rate and a lower minimum systolic blood pressure for each of the first three days in the ICU as compared to those who survived to hospital discharge.

The hematocrit did not significantly differ between the survivors and non-survivors during the first 72 hours in the ICU. The WBC, however, was higher among the non-survivors, with the gap widening from the first to the third ICU day, suggesting a more intense initial inflammatory response among the non-survivors.

The patients who died had a lower urine output than those who survived on each of the first three days in the ICU.

Finally, with a few exceptions (systolic blood pressure, serum bicarbonate), for this group of patients who survived more than 72 hours in the ICU, the variance (as measured by the standard deviation) of the physiologic variables decreased over the first three days in the ICU, whether or not the patient survived to hospital discharge. This likely reflects interventions to correct abnormal physiologic parameters as is customary in the ICU in an attempt to influence clinical outcomes, e.g. transfusion to correct anemia, potassium replacement, beta-blockade for tachycardia.

Mortality Prediction by SAPS and Second Level Customization

The first question we wanted to address is whether customization using local institutional data on patients with AKI will perform better compared to SAPS in predicting mortality. The accuracy of mortality prediction models is assessed based on discrimination between survivors and non-survivors and on correspondence between observed and predicted mortality across the entire range of risk (calibration). We reported the AUC and the Hosmer-Lemeshow p value as measures of discrimination and calibration, respectively, for all the logistic regression models. Given that we had a total of 118 variables we extracted from each of the patients in the cohort, an exhaustive search for the combination of variables that would yield the most accurate model in terms of mortality prediction was out of the question. To get some idea whether a variable is correlated with mortality, we performed univariate regression analysis for each the 118 variables. However, we did not select variables based solely on the p value in the univariate analysis. We know that variables with significant p values on univariate analysis may lose their significance once it is adjusted for other variables in a multivariate analysis. We also know that although variables may not be significantly correlated with the outcome of interest in a
multivariate model (as reflected by the p value), they may still contribute to the accuracy of the entire model.

Based on the p value on univariate analysis, SAPS \( (p = 3.44 \times 10^{-6}) \) is the variable that is most correlated with hospital mortality, followed by the maximum blood urea nitrogen \( (p = 3.27 \times 10^{-10}) \) and the minimum systolic blood pressure from the third day \( (p = 2.89 \times 10^{-9}) \). Most variables had increasing significance from the first to the third day based on progressively lower p values. This is most evident with the urine output, maximum heart rate, systolic blood pressure measurements, maximum serum potassium, maximum BUN, minimum serum bicarbonate, serum glucose measurements, and white blood count measurements. Based on univariate analysis, the third ICU day had the most variables correlated with hospital mortality. The exception is the maximum respiratory rate. This is the only variable that reached significance during the first, but not on the second and third day. This is easily explained by the fact that the sickest patients tend to be mechanically ventilated by the second and third day.

Among patients who developed acute renal failure, it appears that the serum creatinine is NOT a determinant of outcome in terms of survival. Neither serum sodium nor glucose also appears to be correlated with mortality among this subset of patients.

The AUC and Hosmer-Lemeshow p value of SAPS among the MIMIC II patients with AKI that we obtained \( (AUC = 0.6419, p = 0) \) are consistent with the performance of SAPS in predicting mortality among ICU patients in the US \( (AUC = 0.67, p = 0.05) \) [5]. In a UK study cited earlier, APACHE II, another severity scoring system looking at physiologic variables during the first 24 hours in the ICU, also had poor calibration \( (\text{Hosmer-Lemeshow } p < 0.001) \) when used to predict death among patients with AKI [3]. This poor performance of current predictive models when applied to (1) regions different from where the model was built and (2) specific subsets of ICU patients is the main impetus for this research.

Second level customization involved performing a multivariate logistic regression using the SAPS physiologic variables. There was improvement in both discrimination and calibration as evaluated by the AUC and Hosmer-Lemeshow p value, respectively. The improvement in the AUC is nicely depicted in the ROC curves.

**Third Level Customization: Choosing Variables using Heuristics**

We chose to evaluate physiologic variables extending past 24 hours and up to 72 hours of ICU admission based on studies suggesting that information from the third ICU day improves mortality prediction. Research conducted by Girou and colleagues [24] demonstrated that whereas severity scores on admission failed to predict mortality, APACHE II and SAPS on the third ICU day of the patients who died were significantly higher than those of the survivors. In another study from Mayo Clinic [25], among the sickest patients admitted to the ICU, only 6% of patients whose APACHE III scores on the third ICU day were higher than the admission scores survived to hospital discharge, as compared to 43% of patients whose third day APACHE II scores were lower or remained the same.

We then developed logistic regression models using the day 1, day 2 and day 3 SAPS physiologic variables separately. Consistent with the findings from the univariate analysis, the model using Day 3 SAPS variables had the best AUC and Hosmer-Lemeshow p value, supporting the hypothesis that the physiologic status of the patient with AKI on the third ICU day is most predictive of the clinical outcome. This finding is also consistent with the conclusions of the Girou study cited above. The same SAPS
physiologic variables were significantly correlated with hospital mortality from each of the three days: minimum systolic blood pressure, urine output, maximum BUN, maximum WBC and maximum serum bilirubin. Of these, as in the univariate analyses, the maximum blood urea nitrogen and the minimum systolic blood pressure from the third ICU day had the lowest p value.

We proceeded with combining SAPS physiologic variables from two (Day 1 + Day 2, Day 2 + Day 3, Day 1 + Day 3) and then all three days in order to see whether this strategy, which reflects the evolution of the patient's physiologic status, might improve the accuracy of mortality prediction. There is improvement in the AUC as we added SAPS physiologic variables from either Day 1 or Day 2 to Day 3 variables. But the model that performed the best when both discrimination and calibration are assessed is the one that incorporated SAPS physiologic variables from all three days. It is quite interesting to note that when multivariate analysis was performed on SAPS physiologic variables from the first 72 hours, there were only four variables that were significantly correlated with the hospital mortality: the age, the Glasgow Coma Score on the 1st day, and once again, the maximum BUN and the minimum systolic blood pressure from the 3rd ICU day.

**Third Level Customization: Choosing Variables using Algorithms**

We employed two algorithms - correlation-based feature subset selection (CFS) and the consistency subset evaluation - to choose variables for logistic regression. The variables selected by the two algorithms are almost identical, and are quite similar to the SAPS variables, which were originally identified by a panel of experts. We then compared the AUC and Hosmer-Lemeshow p value of the resulting models with those of the model using a combination of the Day 1, Day 2 and Day 3 SAPS physiologic variables. The performance of the three models did not differ significantly; they all have good discrimination and calibration. The feature selection algorithms matched the heuristics of expert clinicians in identifying variables that predict patient outcomes.

**Evaluation of Interaction Terms in Logistic Regression**

There are a number of ICU mortality studies suggesting the presence of effect modification. For example, liver failure increased the mortality of cirrhotic patients with AKI but had no effect on cirrhotic patients without AKI [26]. We explored possible effect modification and evaluated a number of interaction terms that were selected based on clinical knowledge.

None of the interaction terms improved the discrimination of the best fitted logistic regression model using Day 1, Day 2 and Day 3 SAPS physiologic variables. The models that included the interaction terms had lower Hosmer-Lemeshow p values, suggesting poorer calibration. Possible explanations for our finding include selection of the wrong interaction terms, effect modification that may not be constant over time, and effect modification involving three or more variables.
Filtering using Principal Component Analysis

We attempted to reduce the noise by filtering. Principal component analysis (PCA) was performed on the training set to filter these data using the first four largest eigenvectors, accounting for 99.75% of the variability. However, when logistic regression analysis was performed on the filtered data, the resulting AUC was much lower than that of the same model performed on the original data.

The goal of PCA is to seek new variables, which are orthogonal linear combinations of the old parameters, to better explain the variation in the data set. Since each new component is found by looking for the projection of maximum variance in the data, the smallest Eigenvalues are often assumed to be due to noise. We performed filtering by collapsing the Eigenvectors down and re-projecting the data back into the original space. However, if the signal-to-noise ratio of the data is low and the noise dominates, then the larger Eigenvalues may correspond to noise, and we might have inadvertently filtered out data, and retained noise.

Another reason PCA may be a poor method for separating noise from signal is that PCA assumes that the underlying variables are Gaussian. Non-Gaussian variables will therefore not be well captured by this method.

Performance of Different Machine Learning Algorithms

Finally, we investigated how other machine learning algorithms perform against logistic regression using the variables from the best fitted regression models, i.e. those using the SAPS physiologic variables from the first 72 hours and the variables chosen by the feature selection algorithms. Naïve Bayes performed as well as logistic regression based on accuracy, mean absolute error and area under the ROC curve. It performed better than Bayesian Network in all three models. This is a bit surprising given that the variables we evaluated are not independent. However, Bayesian Network may overfit more than Naive Bayes which might explain its poorer performance.

Limitations of the Study

Despite a significant improvement in the AUC and Hosmer-Lemeshow p value with third level customization using the SAPS physiologic variables from the first 72 hours in the ICU, a much higher AUC would have been more convincing evidence to support our hypothesis. There are several reasons why a higher AUC was not seen with the logistic regression models that were presented. The first is data noise. During pre-processing, some of the variables that were initially considered had to be dropped because inspection of the values revealed a significant fraction of the data was inaccurately captured. We decided to exclude total fluid input after finding that 30% of patients were administered less than a liter of fluid for the entire day. From clinical experience, patients who are admitted to the ICU are given at least a liter of fluid to replace insensible losses (which are higher in a critically-ill patient) even in the presence of acute kidney injury. We also removed minimum temperature after finding that about a third of the patients had temperature below normal. We suspect that this is likely a result of a displaced rectal probe capturing inaccurate data. Finally, minimum respiratory rate was excluded with respiratory rates below 8. This is unusual in the ICU even when the patient is mechanically ventilated. We suspect that these measurements were taken when the chest wall motion detector was dislodged which happens often (and for the most part ignored by ICU nurses). We can only speculate how much inaccuracy is present with the data that we ended up using to develop the models. We see data noise as
the main disadvantage in developing classification and regression algorithms using retrospective data. The data that were used to build the original models that are the basis of existing severity scoring systems were entered manually from paper records, and were more likely verified at the time of entry by reviewing the progress notes if there is inaccuracy suspected.

Another possible reason why it is difficult to develop a model based on retrospective clinical data with excellent discrimination and calibration is because quality of care, an important determinant of clinical outcome, requires more meticulous data extraction. To illustrate, two hypovolemic patients who have the same severity of illness might both have gotten 2 liters of crystalloid solution. This level of information is captured in the database and is routinely extracted for clinical studies. However, one patient might have received it over 30 minutes, while the other was given this amount over 2 hours. This information might seem trivial but may be the reason why one patient develops an acute kidney injury while the other does not. Another illustration would be two identical patients who develop an acute abdomen requiring a surgical intervention. The extracted data accurately documents that both patients went to surgery. However, one patient might have taken an hour longer before surgery was started, or one patient's surgery took longer because it was a senior surgical resident who performed the operation. The last example to drive the point would be two similar patients presenting with the same infection of identical severity. They are administered the same antibiotic but one patient received it sooner than the other. The interval between the times of administration might be enough to lead to different outcomes.

But this is not to say that none of this information is present in a data set similar to the one that was used for this project. In the first example, the patient who received the fluid over a longer period of time will eventually have a rise in serum creatinine, which will predict a worse clinical outcome. In the second illustration, the patient where surgical intervention was delayed or took longer may develop complications that will be reflected by a different course of blood pressure measurements. And in the last example, the patient who did not get the antibiotics in a more timely fashion may take more days to defervesc. The question is how much detail is required to be incorporated in a data set to adequately capture the contribution of quality of care to clinical outcome.

**Clinical Application**

The optimal mortality prediction model should capture the heuristics employed by expert clinicians as they look at the evolution of physiologic variables over time to assess whether a patient is responding favorably to treatment and is likely to have a good clinical outcome. There is a large variation among ICU clinicians in terms of when end-of-life discussions are initiated among patients who do not survive their hospitalization [27, 28]. Experienced doctors and nurses are more likely to confidently predict a poor outcome and recommend switching to comfort measures sooner than novice clinicians. What we are aiming to build is a patient-subset specific model that captures all the determinants of the patient's clinical outcome - the severity of illness, how the patient is handling the physiologic insult on his own, how well he is responding to the treatments being administered, and the quality of the care he is provided.

The gold standard in evidence-based medicine is a well-designed, well-executed multi-center prospective randomized controlled trial. Even when such trials are performed and subsequently published, they very rarely, if ever, provide clear evidence upon which to base the management of an individual patient. Patient prognostication is no exception. There is an abundance of literature on risk assessment performed prospectively. However, patients enrolled in prospective randomized controlled
trials are heterogeneous, and conclusions are valid for the "average" patient. In addition, these trials are executed in very strictly monitored, and thus artificial, conditions, and often, findings in these studies do not translate to the real world ICU. It is difficult to predict whether an individual patient is likely to behave like the "average" patient in the multi-center prospective randomized trial. Hence, day-to-day clinical decisions are still based mostly on personal experience, experiences shared with colleagues, and consideration of reported data if they exist.

Data mining may provide an additional tool for decision support [17]. The main objective of this project is to determine whether customization of predictive models for specific subgroup of patients yields more accurate predictions. As more ICUs switch to a paperless system, large regional or even local ICU database become available for building models. Rather than developing models with good external validity by including a heterogeneous patient population from various continents as has been traditionally done, an alternative approach would be to build models for specific patient subsets using one's own local or regional database.

We suspect that we will not be able to capture fully the heuristics of an experienced clinician. For that reason, we will not be able to build a model that can replace years of ICU experience. We see the value of decision support systems, including predictive models, based on data mining of empiric data in assisting novice attending physicians, fellows and residents in the ICU. Learning the right amount of fluid to administer, for example, or developing the intuition of whether a patient will benefit from a specific intervention or not, usually requires years of practice. By being able to extract information about similar patients from a database, specifically how they responded to certain treatments, learning may be accelerated and may allow junior doctors to make decisions with more precision and confidence.

All machine learning algorithms assume that real world situations are similar to the training data. This exposes them to the problem of induction in logic. The classic example is the Black Swan phenomenon which argues that rare events are more common than has been traditionally assumed [29]. Nassim Taleb, who popularized the phenomenon, divides real world events into Mediocristan, which fit the bell curve model, and Extremistan, which don't. He suggests that most real-world phenomena actually inhabit Extramistan rather than Mediocristan. We suspect these phenomena co-exist. Nevertheless, this is the reason why it is crucial that we prospectively evaluate whether the use of data mining to assist clinical decision making will lead to better clinical outcomes.

But even if we come up with a mortality prediction model based on local institutional empiric data that has excellent sensitivity and specificity, the question remains whether clinicians will embrace this approach. Will we be able to convince them that information from a very large cohort of patients whose clinical course is stored in an electronic database might be more reliable than a composite of the patients they have encountered in the past whose clinical course may be imperfectly stored in their memory? Will we be able to convince them that their clinical intuition on an individual patient might be enhanced by the experience of numerous clinicians who have taken care of clinically similar patients? Qualitative studies addressing these issues will be the subject of my thesis project at the Harvard School of Public Health.

References:


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Appendix A. SQL Query to Extract Patient Cohort from MIMIC II

CREATE OR REPLACE VIEW LEO EVOLUTION (subject_id, expire_flg, age, sex, intime, outtime, los, max_bili_1st_day, max_bili_2nd_day, max_bili_3rd_day, max_creat_1st_day, max_creat_2nd_day, max_creat_3rd_day, min_hr_1st_day, max_hr_1st_day, stddev_hr_1st_day, avg_hr_1st_day, min_hr_2nd_day, max_hr_2nd_day, stddev_hr_2nd_day, avg_hr_2nd_day, min_hr_3rd_day, max_hr_3rd_day, stddev_hr_3rd_day, avg_hr_3rd_day, min_sodium_1st_day, max_sodium_1st_day, stddev_sodium_1st_day, avg_sodium_1st_day, min_sodium_2nd_day, max_sodium_2nd_day, stddev_sodium_2nd_day, avg_sodium_2nd_day, min_sodium_3rd_day, max_sodium_3rd_day, stddev_sodium_3rd_day, avg_sodium_3rd_day, min_sysbp_1st_day, max_sysbp_1st_day, stddev_sysbp_1st_day, avg_sysbp_1st_day, min_sysbp_2nd_day, max_sysbp_2nd_day, stddev_sysbp_2nd_day, avg_sysbp_2nd_day, min_sysbp_3rd_day, max_sysbp_3rd_day, stddev_sysbp_3rd_day, avg_sysbp_3rd_day, max_resp_1st_day, max_resp_2nd_day, max RESP_3rd_day, min_hematocrit_1st_day, max_hematocrit_1st_day, stddev_hematocrit_1st_day, avg_hematocrit_1st_day, min_hematocrit_2nd_day, max_hematocrit_2nd_day, stddev_hematocrit_2nd_day, avg_hematocrit_2nd_day, min_hematocrit_3rd_day, max_hematocrit_3rd_day, stddev_hematocrit_3rd_day, avg_hematocrit_3rd_day, min_glucose_1st_day, max_glucose_1st_day, stddev_glucose_1st_day, avg_glucose_1st_day, min_glucose_2nd_day, max_glucose_2nd_day, stddev_glucose_2nd_day, avg_glucose_2nd_day, min_glucose_3rd_day, max_glucose_3rd_day, stddev_glucose_3rd_day, avg_glucose_3rd_day, min_wbc_1st_day, max_wbc_1st_day, stddev_wbc_1st_day, avg_wbc_1st_day, min_wbc_2nd_day, max_wbc_2nd_day, stddev_wbc_2nd_day, avg_wbc_2nd_day, min_wbc_3rd_day, max_wbc_3rd_day, stddev_wbc_3rd_day, avg_wbc_3rd_day, min_potassium_1st_day, max_potassium_1st_day, stddev_potassium_1st_day, avg_potassium_1st_day, min_potassium_2nd_day, max_potassium_2nd_day, stddev_potassium_2nd_day, avg_potassium_2nd_day, min_potassium_3rd_day, max_potassium_3rd_day, stddev_potassium_3rd_day, avg_potassium_3rd_day, max_bun_1st_day, max_bun_2nd_day, max_bun_3rd_day, min_gcs_1st_day, max_gcs_1st_day, stddev_gcs_1st_day, avg_gcs_1st_day, min_temp_1st_day, max_temp_1st_day, stddev_temp_1st_day, avg_temp_1st_day, min_temp_2nd_day, max_temp_2nd_day, stddev_temp_2nd_day, avg_temp_2nd_day, min_temp_3rd_day, max_temp_3rd_day, stddev_temp_3rd_day, avg_temp_3rd_day,
WITH lastStay AS (
    select distinct subject_id,
        first_value(intime)
            over ( partition by subject_id
                    order by subject_id, intime DESC) as intime,
        first_value(outtime)
            over ( partition by subject_id
                    order by subject_id, intime DESC) as outtime,
        first_value(expire_flg)
            over ( partition by subject_id
                    order by subject_id, intime DESC) as expire_flg,
        first_value(age)
            over ( partition by subject_id
                    order by subject_id, intime DESC) as age,
        first_value(sex)
            over ( partition by subject_id
                    order by subject_id, intime DESC) as sex
    from ( -- Returns any ICU stay that falls between the
              -- hospitalization period
        select had.subject_id, icu.icustay_id, icu.intime, icu.outtime,
            had.expire_flg, icu.age, icu.sex
        from ( -- Returns the last hospital admissions for patients
                    -- with the required ICD9 code,
            select distinct subject_id,
                first_value(adm_dt)
                    over(partition by subject_id
                            order by subject_id, adm_dt DESC) as adm_dt,
                first_value(disch_dt)
                    over(partition by subject_id
                            order by subject_id, adm_dt DESC) as disch_dt,
                first_value(expire_flg)
                    over(partition by subject_id
                            order by subject_id, adm_dt DESC) as expire_flg
            from ( -- Returns all the hospital admissions for people
                        -- who had the ICD9 code: Subarachnoid Hemorrhage
                select a.hadm_id, a.subject_id, a.adm_dt,
                    a.disch_dt, a.expire_flg
                from mimic2v2l.admissions a,
                    mimic2v2l.icd9 icd

where icd.hadm_id = a.hadm_id
    and icd.code in ('584.9')
)
order by subject_id
)
)^had,

-- Returns all the adult ICU stays where the patient was least 3 days in the ICU
select icustay_id, subject_id, intime, outtime,
    (months_between(intime, dob) /12) age, sex
from
    -- Returns all ICU stays
    SELECT s.icustay_id, cen.subject_id, dob,
        p.sex, min(cen.intime) as intime,
        max(cen.outtime) as outtime
    FROM mimic2v21.icustay s,
        mimic2v2l.censusevents cen,
        mimic2v2l.d_patients p
    WHERE cen.census_id = s.census_id
        and p.subject_id = cen.subject_id
        and p.dob is not null
    GROUP BY s.icustay_id, cen.subject_id, dob, p.sex
)
where (months_between(intime, dob) /12) >= 15
    and (outtime - intime) >= 3
) icu
where icu.subject_id = had.subject_id
    and icu.intime >= had.adm_dt
    and icu.intime <= had.disch_dt
)--where subject_id in (117, 145, 250, 252)
order by subject_id
),
-- Returns the max, min, stddev, average values for each category
-- and each of the 3 days of the last ICU stay
RawData as ( select distinct subject_id, expire_flg, round(age) age, sex,
    intime, outtime, round(outtime - intime, 1) los,
    max(bili_1st_day) 
        over (partition by subject_id) as max_bili_1st_day,
    max(bili_2nd_day) 
        over (partition by subject_id) as max_bili_2nd_day,
    max(bili_3rd_day) 
        over (partition by subject_id) as max_bili_3rd_day,
    max(creat_1st_day) 
        over (partition by subject_id) as max_creat_1st_day,
    max(creat_2nd_day) 
        over (partition by subject_id) as max_creat_2nd_day,
    max(creat_3rd_day) 
        over (partition by subject_id) as max_creat_3rd_day,
    min(hr_1st_day) 
        over (partition by subject_id) as min_hr_1st_day,
    max(hr_1st_day) 
        over (partition by subject_id) as max_hr_1st_day,
    round(stddev(hr_1st_day)
over (partition by subject_id), 1) as stddev_hr_1st_day,
round(avg(hr_1st_day)
over (partition by subject_id), 1) as avg_hr_1st_day,
min(hr_2nd_day)
over (partition by subject_id) as min_hr_2nd_day,
max(hr_2nd_day)
over (partition by subject_id) as max_hr_2nd_day,
round(stddev(hr_2nd_day)
over (partition by subject_id), 1) as stddev_hr_2nd_day,
round(avg(hr_2nd_day)
over (partition by subject_id), 1) as avg_hr_2nd_day,
min(hr_3rd_day)
over (partition by subject_id) as min_hr_3rd_day,
max(hr_3rd_day)
over (partition by subject_id) as max_hr_3rd_day,
round(stddev(hr_3rd_day)
over (partition by subject_id), 1) as stddev_hr_3rd_day,
round(avg(hr_3rd_day)
over (partition by subject_id), 1) as avg_hr_3rd_day,
min(sodium_1st_day)
over (partition by subject_id) as min_sodium_1st_day,
max(sodium_1st_day)
over (partition by subject_id) as max_sodium_1st_day,
round(stddev(sodium_1st_day)
over (partition by subject_id), 1) as stddev_sodium_1st_day,
round(avg(sodium_1st_day)
over (partition by subject_id), 1) as avg_sodium_1st_day,
min(sodium_2nd_day)
over (partition by subject_id) as min_sodium_2nd_day,
max(sodium_2nd_day)
over (partition by subject_id) as max_sodium_2nd_day,
round(stddev(sodium_2nd_day)
over (partition by subject_id), 1) as stddev_sodium_2nd_day,
round(avg(sodium_2nd_day)
over (partition by subject_id), 1) as avg_sodium_2nd_day,
min(sodium_3rd_day)
over (partition by subject_id) as min_sodium_3rd_day,
max(sodium_3rd_day)
over (partition by subject_id) as max_sodium_3rd_day,
round(stddev(sodium_3rd_day)
over (partition by subject_id), 1) as stddev_sodium_3rd_day,
round(avg(sodium_3rd_day)
over (partition by subject_id), 1) as avg_sodium_3rd_day,
min(sysbp_1st_day)
over (partition by subject_id) as min_sysbp_1st_day,
max(sysbp_1st_day)
over (partition by subject_id) as max_sysbp_1st_day,
round(stddev(sysbp_1st_day)
over (partition by subject_id), 1) as stddev_sysbp_1st_day,
round(avg(sysbp_1st_day)
over (partition by subject_id), 1) as avg_sysbp_1st_day,
min(sysbp_2nd_day)
over (partition by subject_id) as min_sysbp_2nd_day,
max(sysbp_2nd_day)
over (partition by subject_id) as max_sysbp_2nd_day,
round(stddev(sysbp_2nd_day)
over (partition by subject_id), 1) as stddev_sysbp_2nd_day,
round(avg(sysbp_2nd_day)
    over (partition by subject_id), 1) as avg_sysbp_2nd_day,
min(sysbp_3rd_day)
    over (partition by subject_id) as min_sysbp_3rd_day,
max(sysbp_3rd_day)
    over (partition by subject_id) as max_sysbp_3rd_day,
round(stddev(sysbp_3rd_day)
    over (partition by subject_id), 1) as stddev_sysbp_3rd_day,
round(avg(sysbp_3rd_day)
    over (partition by subject_id), 1) as avg_sysbp_3rd_day,
min(resp_lst_day)
    over (partition by subject_id) as minresp_lst_day,
max(resp_lst_day)
    over (partition by subject_id) as maxresp_lst_day,
round(stddev(resp_lst_day)
    over (partition by subject_id), 1) as stddevresp_lst_day,
round(avg(resp_lst_day)
    over (partition by subject_id), 1) as avg_resp_lst_day,
min(resp2nd_day)
    over (partition by subject_id) as minresp2nd_day,
max(resp2nd_day)
    over (partition by subject_id) as maxresp2nd_day,
round(stddev(resp2nd_day)
    over (partition by subject_id), 1) as stddevresp_2nd_day,
round(avg(resp2nd_day)
    over (partition by subject_id), 1) as avg_resp_2nd_day,
min(resp3rd_day)
    over (partition by subject_id) as minresp3rdday,
max(resp3rd_day)
    over (partition by subject_id) as maxresp_3rd_day,
round(stddev(resp3rd_day)
    over (partition by subject_id), 1) as stddevresp_3rdday,
round(avg(resp3rd_day)
    over (partition by subject_id), 1) as avg_resp_3rd_day,
round(min(hematocrit_1st_day)
    over (partition by subject_id), 1) as min_hematocrit_1st_day,
round(max(hematocrit_1st_day)
    over (partition by subject_id), 1) as max_hematocrit_1st_day,
round(stddev(hematocrit_1st_day)
    over (partition by subject_id), 1) as stddev_hematocrit_1st_day,
round(avg(hematocrit_1st_day)
    over (partition by subject_id), 1) as avg_hematocrit_1st_day,
round(min(hematocrit_2nd_day)
    over (partition by subject_id), 1) as min_hematocrit_2nd_day,
round(max(hematocrit_2nd_day)
    over (partition by subject_id), 1) as max_hematocrit_2nd_day,
round(stddev(hematocrit_2nd_day)
    over (partition by subject_id), 1) as stddev_hematocrit_2nd_day,
round(avg(hematocrit_2nd_day)
    over (partition by subject_id), 1) as avg_hematocrit_2nd_day,
round(min(hematocrit_3rd_day)
    over (partition by subject_id), 1) as min_hematocrit_3rd_day,
round(max(hematocrit_3rd_day)
    over (partition by subject_id), 1) as max_hematocrit_3rd_day,
round(stddev(hematocrit_3rd_day)
    over (partition by subject_id), 1) as stddev_hematocrit_3rd_day,
round(avg(hematocrit_3rd_day)
    over (partition by subject_id), 1) as avg_hematocrit_3rd_day,
round(avg(hematocrit_3rd_day)
    over (partition by subject_id), 1) as avg_hematocrit_3rd_day,
over (partition by subject_id), 1) as avg_hematocrit_3rd_day,
   min(glucose_1st_day)
over (partition by subject_id) as min_glucose_1st_day,
max(glucose_1st_day)
over (partition by subject_id) as max_glucose_1st_day,
round(stddev(glucose_1st_day)
over (partition by subject_id), 1) as stddev_glucose_1st_day,
round(avg(glucose_1st_day)
over (partition by subject_id), 1) as avg_glucose_1st_day,
min(glucose_2nd_day)
over (partition by subject_id) as min_glucose_2nd_day,
max(glucose_2nd_day)
over (partition by subject_id) as max_glucose_2nd_day,
round(stddev(glucose_2nd_day)
over (partition by subject_id), 1) as stddev_glucose_2nd_day,
round(avg(glucose_2nd_day)
over (partition by subject_id), 1) as avg_glucose_2nd_day,
min(glucose_3rd_day)
over (partition by subject_id) as min_glucose_3rd_day,
max(glucose_3rd_day)
over (partition by subject_id) as max_glucose_3rd_day,
round(stddev(glucose_3rd_day)
over (partition by subject_id), 1) as stddev_glucose_3rd_day,
round(avg(glucose_3rd_day)
over (partition by subject_id), 1) as avg_glucose_3rd_day,
min(wbc_1st_day)
over (partition by subject_id) as min_wbc_1st_day,
max(wbc_1st_day)
over (partition by subject_id) as max_wbc_1st_day,
round(stddev(wbc_1st_day)
over (partition by subject_id), 1) as stddev_wbc_1st_day,
round(avg(wbc_1st_day)
over (partition by subject_id), 1) as avg_wbc_1st_day,
min(wbc_2nd_day)
over (partition by subject_id) as min_wbc_2nd_day,
max(wbc_2nd_day)
over (partition by subject_id) as max_wbc_2nd_day,
round(stddev(wbc_2nd_day)
over (partition by subject_id), 1) as stddev_wbc_2nd_day,
round(avg(wbc_2nd_day)
over (partition by subject_id), 1) as avg_wbc_2nd_day,
min(wbc_3rd_day)
over (partition by subject_id) as min_wbc_3rd_day,
max(wbc_3rd_day)
over (partition by subject_id) as max_wbc_3rd_day,
round(stddev(wbc_3rd_day)
over (partition by subject_id), 1) as stddev_wbc_3rd_day,
round(avg(wbc_3rd_day)
over (partition by subject_id), 1) as avg_wbc_3rd_day,
min(potassium_1st_day)
over (partition by subject_id) as min_potassium_1st_day,
max(potassium_1st_day)
over (partition by subject_id) as max_potassium_1st_day,
round(stddev(potassium_1st_day)
over (partition by subject_id), 1) as stddev_potassium_1st_day,
round(avg(potassium_1st_day)
over (partition by subject_id), 1) as avg_potassium_1st_day,
min(potassium_2nd_day) over (partition by subject_id) as min_potassium_2nd_day,
max(potassium_2nd_day) over (partition by subject_id) as max_potassium_2nd_day,
round(stddev(potassium_2nd_day) over (partition by subject_id), 1) as stddev_potassium_2nd_day,
round(avg(potassium_2nd_day) over (partition by subject_id), 1) as avg_potassium_2nd_day,
min(potassium_3rd_day) over (partition by subject_id) as min_potassium_3rd_day,
max(potassium_3rd_day) over (partition by subject_id) as max_potassium_3rd_day,
round(stddev(potassium_3rd_day) over (partition by subject_id), 1) as stddev_potassium_3rd_day,
round(avg(potassium_3rd_day) over (partition by subject_id), 1) as avg_potassium_3rd_day,
max(bun_1st_day) over (partition by subject_id) as max_bun_1st_day,
max(bun_2nd_day) over (partition by subject_id) as max_bun_2nd_day,
max(bun_3rd_day) over (partition by subject_id) as max_bun_3rd_day,
min(gcs_1st_day) over (partition by subject_id) as min_gcs_1st_day,
round(min(temp_1st_day) over (partition by subject_id), 1) as min_temp_1st_day,
round(max(temp_1st_day) over (partition by subject_id), 1) as max_temp_1st_day,
round(stddev(temp_1st_day) over (partition by subject_id), 1) as stddev_temp_1st_day,
round(avg(temp_1st_day) over (partition by subject_id), 1) as avg_temp_1st_day,
round(min(temp_2nd_day) over (partition by subject_id), 1) as min_temp_2nd_day,
round(max(temp_2nd_day) over (partition by subject_id), 1) as max_temp_2nd_day,
round(stddev(temp_2nd_day) over (partition by subject_id), 1) as stddev_temp_2nd_day,
round(avg(temp_2nd_day) over (partition by subject_id), 1) as avg_temp_2nd_day,
round(min(temp_3rd_day) over (partition by subject_id), 1) as min_temp_3rd_day,
round(max(temp_3rd_day) over (partition by subject_id), 1) as max_temp_3rd_day,
round(stddev(temp_3rd_day) over (partition by subject_id), 1) as stddev_temp_3rd_day,
round(avg(temp_3rd_day) over (partition by subject_id), 1) as avg_temp_3rd_day,
min(bicarbonate_1st_day) over (partition by subject_id) as min_bicarbonate_1st_day,
max(bicarbonate_1st_day) over (partition by subject_id) as max_bicarbonate_1st_day,
round(stddev(bicarbonate_1st_day) over (partition by subject_id), 1) as stddev_bicarbonate_1st_day,
round(avg(bicarbonate_1st_day) over (partition by subject_id), 1) as avg_bicarbonate_1st_day,
min(bicarbonate_2nd_day)
  over (partition by subject_id)  as min_bicarbonate_2nd_day,
max(bicarbonate_2nd_day)
  over (partition by subject_id)  as max_bicarbonate_2nd_day,
round(stddev(bicarbonate_2nd_day)
  over (partition by subject_id), 1) as
stddev_bicarbonate_2nd_day,
round(avg(bicarbonate_2nd_day)
  over (partition by subject_id), 1) as avg_bicarbonate_2nd_day,
min(bicarbonate_3rd_day)
  over (partition by subject_id)  as min_bicarbonate_3rd_day,
max(bicarbonate_3rd_day)
  over (partition by subject_id)  as max_bicarbonate_3rd_day,
round(stddev(bicarbonate_3rd_day)
  over (partition by subject_id), 1) as
stddev_bicarbonate_3rd_day,
round(avg(bicarbonate_3rd_day)
  over (partition by subject_id), 1) as avg_bicarbonate_3rd_day,
round(first_value(in_1st_day)
  over (partition by subject_id
    order by subject_id, intime), 1) as in_1st_day,
round(first_value(out_1st_day)
  over (partition by subject_id
    order by subject_id, intime), 1) as out_1st_day,
round(first_value(in_2nd_day)
  over (partition by subject_id
    order by subject_id, intime), 1) as in_2nd_day,
round(first_value(out_2nd_day)
  over (partition by subject_id
    order by subject_id, intime), 1) as out_2nd_day,
round(first_value(in_3rd_day)
  over (partition by subject_id
    order by subject_id, intime), 1) as in_3rd_day,
round(first_value(out_3rd_day)
  over (partition by subject_id
    order by subject_id, intime), 1) as out_3rd_day
from (  
  -- Tags each value in each category as coming from the first,
  -- second or third day in the ICU
  select subject_id, expire_flg, age, sex, intime, outtime,
  case
    when parameter = 'BILIRUBIN' and day_in_icu = 1
      then valuelnum
    else
      null
    end as bili_1st_day,
  case
    when parameter = 'BILIRUBIN' and day_in_icu = 2
      then valuelnum
    else
      null
    end as bili_2nd_day,
  case
    when parameter = 'BILIRUBIN' and day_in_icu = 3
      then valuelnum
    else
      null
  end)
end as bili_3rd_day,
case
  when parameter = 'CREATININE' and day_in_icu = 1 then valuelnum
  else null
end as creat_1st_day,
case
  when parameter = 'CREATININE' and day_in_icu = 2 then valuelnum
  else null
end as creat_2nd_day,
case
  when parameter = 'CREATININE' and day_in_icu = 3 then valuelnum
  else null
end as creat_3rd_day,
case
  when parameter = 'HR' and day_in_icu = 1 then valuelnum
  else null
end as hr_1st_day,
case
  when parameter = 'HR' and day_in_icu = 2 then valuelnum
  else null
end as hr_2nd_day,
case
  when parameter = 'HR' and day_in_icu = 3 then valuelnum
  else null
end as hr_3rd_day,
case
  when parameter = 'SODIUM' and day_in_icu = 1 then valuelnum
  else null
end as sodium_1st_day,
case
  when parameter = 'SODIUM' and day_in_icu = 2 then valuelnum
  else null
end as sodium_2nd_day,
case
  when parameter = 'SODIUM' and day_in_icu = 3 then valuelnum
  else null
end as sodium_3rd_day,
then valuelnum
else
null
end as sysbp_1st_day,
case
when parameter = 'SYS_BP' and day_in_icu = 2
then valuelnum
else
null
end as sysbp_2nd_day,
case
when parameter = 'SYS_BP' and day_in_icu = 3
then valuelnum
else
null
end as sysbp_3rd_day,
case
when parameter = 'RESPIRATION' and day_in_icu = 1
then valuelnum
else
null
end as resp_1st_day,
case
when parameter = 'RESPIRATION' and day_in_icu = 2
then valuelnum
else
null
end as resp_2nd_day,
case
when parameter = 'RESPIRATION' and day_in_icu = 3
then valuelnum
else
null
end as resp_3rd_day,
case
when parameter = 'HEMATOCRIT' and day_in_icu = 1
then valuelnum
else
null
end as hematocrit_1st_day,
case
when parameter = 'HEMATOCRIT' and day_in_icu = 2
then valuelnum
else
null
end as hematocrit_2nd_day,
case
when parameter = 'HEMATOCRIT' and day_in_icu = 3
then valuelnum
else
null
end as hematocrit_3rd_day,
case
when parameter = 'GLUCOSE' and day_in_icu = 1
then valuelnum
else
null
end as glucose_1st_day,
case
  when parameter = 'GLUCOSE' and day_in_icu = 2
    then valuelnum
  else
    null
end as glucose_2nd_day,
case
  when parameter = 'GLUCOSE' and day_in_icu = 3
    then valuelnum
  else
    null
end as glucose_3rd_day,
case
  when parameter = 'WBC' and day_in_icu = 1
    then valuelnum
  else
    null
end as wbc_1st_day,
case
  when parameter = 'WBC' and day_in_icu = 2
    then valuelnum
  else
    null
end as wbc_2nd_day,
case
  when parameter = 'WBC' and day_in_icu = 3
    then valuelnum
  else
    null
end as wbc_3rd_day,
case
  when parameter = 'POTASSIUM' and day_in_icu = 1
    then valuelnum
  else
    null
end as potassium_1st_day,
case
  when parameter = 'POTASSIUM' and day_in_icu = 2
    then valuelnum
  else
    null
end as potassium_2nd_day,
case
  when parameter = 'POTASSIUM' and day_in_icu = 3
    then valuelnum
  else
    null
end as potassium_3rd_day,
case
  when parameter = 'BUN' and day_in_icu = 1
    then valuelnum
  else
    null
end as bun_1st_day,
case
  when parameter = 'BUN' and day_in_icu = 2
    then valuelnum
  else
    null
end as bun_2nd_day,
then valuelnum
else
  null
end as bun_2nd_day,
case
  when parameter = 'BUN' and day_in_icu = 3
    then valuelnum
  else
    null
end as bun_3rd_day,
case
  when parameter = 'GCS' and day_in_icu = 1
    then valuelnum
  else
    null
end as gcs_1st_day,
case
  when parameter = 'TEMP' and day_in_icu = 1
    then valuelnum
  else
    null
end as temp_1st_day,
case
  when parameter = 'TEMP' and day_in_icu = 2
    then valuelnum
  else
    null
end as temp_2nd_day,
case
  when parameter = 'TEMP' and day_in_icu = 3
    then valuelnum
  else
    null
end as temp_3rd_day,
case
  when parameter = 'BICARBONATE' and day_in_icu = 1
    then valuelnum
  else
    null
end as bicarbonate_1st_day,
case
  when parameter = 'BICARBONATE' and day_in_icu = 2
    then valuelnum
  else
    null
end as bicarbonate_2nd_day,
case
  when parameter = 'BICARBONATE' and day_in_icu = 3
    then valuelnum
  else
    null
end as bicarbonate_3rd_day,
case
  when parameter = 'TOTAL_IN' and day_in_icu = 1
    then valuelnum
  else
    null
end as bicarbonate_3rd_day,
case
  when parameter = 'TOTAL_IN' and day_in_icu = 2
    then valuelnum
  else
    null
end as bicarbonate_3rd_day,
case
  when parameter = 'TOTAL_IN' and day_in_icu = 3
    then valuelnum
  else
    null
end as bicarbonate_3rd_day,
end as in_1st_day,
case
  when parameter = 'TOTAL_IN' and day_in_icu = 2
    then valuelnum
  else
    null
end as in_2nd_day,
case
  when parameter = 'TOTAL_IN' and day_in_icu = 3
    then valuelnum
  else
    null
end as in_3rd_day,
case
  when parameter = 'TOTAL_OUT' and day_in_icu = 1
    then valuelnum
  else
    null
end as out_1st_day,
case
  when parameter = 'TOTAL_OUT' and day_in_icu = 2
    then valuelnum
  else
    null
end as out_2nd_day,
case
  when parameter = 'TOTAL_OUT' and day_in_icu = 3
    then valuelnum
  else
    null
end as out_3rd_day

from ( -- The whole raw data, grouping itemids in categories and -- the day in the ICU the measurement occurs.
select subject_id, expire_flg, age, sex,
  intime, outtime,
case
  when itemid in (848, 1538)
    then 'BILIRUBIN'
  when itemid in (791, 3750, 1525)
    then 'CREATININE'
  when itemid in (211)
    then 'HR'
  when itemid in (837, 1536, 3803)
    then 'SODIUM'
  when itemid in (51, 455)
    then 'SYS_BP'
  when itemid in (813)
    then 'HEMATOCRIT'
  when itemid in (811, 1529)
    then 'GLUCOSE'
  when itemid in (1542, 1127, 861, 4200)
    then 'WBC'
  when itemid in (829, 1535, 3792)
    then 'POTASSIUM'
when itemid in (781) then 'BUN'
when itemid in (198) then 'GCS'
when itemid in (676, 677, 678, 679) then 'TEMP'
when itemid in (787) then 'BICARBONATE'
when itemid in (1) then 'TOTAL_IN'
when itemid in (2) then 'TOTAL_OUT'
else 'unknown'
end as parameter,
case
  when charttime <= intime + 1 then 1
  when (charttime > intime + 1) and (charttime <= intime + 2) then 2
  when (charttime > intime + 2) and (charttime <= intime + 3) then 3
else -1
end as day_in_icu,
case
  -- convert farenheit to celsius
  when itemid in (678, 679) and (valuel is not null)
    then ((valuel - 32) * 5/9)
  else valuel
end as valuelnum
from ( -- Get the charted events for the required itemids
  -- from patients in "lastStay"
  select pts.subject_id, pts.expire_flg, pts.age, pts.sex, pts.intime, pts.outtime, c.itemid, c.charttime, c.valuelnum as valuel,
  c.value2num as value2
  from lastStay pts,
  mimic2v21.chartevents c
  where c.subject_id = pts.subject_id
  and c.itemid in (848, 1538, 791, 3750, 1525, 211, 837, 1536, 3803, 51, 455, 618, 813, 811, 1529, 1542, 1127, 861, 4200, 829, 1535, 3792, 781,
and c.charttime >= pts.intime
and c.charttime <= (pts.intime + 3)
UNION
-- Get the total INPUT/OUTPUT from patients
-- in "lastStay"
select pts.subject_id, pts.expire_flg, pts.age,
pts.sex, pts.intime, pts.outtime,
te.itemid, te.charttime, te.cumvolume as
value1,
0 as value2
from lastStay pts,
mimic2v21.totalbalevents te
where te.subject_id = pts.subject_id
and te.itemid in (1, 2)
and te.charttime >= pts.intime
and te.charttime <= (pts.intime + 3)
ORDER BY subject_id
ORDER BY subject_id, intime
);

-- 2. Bilirubin (max)
-- a. If all 3 values are missing, put 0.7. Reason: This is the middle
-- of the normal range.
-- b. If 2 values are missing, replace them with the level that is
-- present.
-- c. If the middle value is missing, replace it with the average of
-- the other 2 values. Otherwise, replace it with the value that's
-- closer time-wise.
Rule2Billi as (
select subject_id,
case
when (max_bili_1st_day is null) and (max_bili_2nd_day is
null) and (max_bili_3rd_day is null) then
0.7
when (max_bili_1st_day is null) and (max_bili_2nd_day is
null) and (max_bili_3rd_day is not null) then
max_bili_3rd_day
when (max_bili_1st_day is null) and (max_bili_2nd_day is
null) and (max_bili_3rd_day is null) then
max_bili_2nd_day
else
max_bili_1st_day
end max_bili_1st_day,
case
when (max_bili_1st_day is null) and (max_bili_2nd_day is
null) and (max_bili_3rd_day is null) then
0.7
when (max_bili_1st_day is null) and (max_bili_2nd_day is
null) and (max_bili_3rd_day is not null) then
max_bili_3rd_day
when (max_bili_1st_day is null) and (max_bili_2nd_day is
null) and (max_bili_3rd_day is null) then
max_bili_2nd_day
else
max_bili_1st_day
end max_bili_1st_day,
max_bili_1st_day
when (max_bili_1st_day is not null) and (max_bili_3rd_day is null) and (max_bili_2nd_day is null)

and (max_bili_3rd_day is not null) then
(max_bili_1st_day + max_bili_3rd_day) / 2
else
max_bili_2nd_day
end max_bili_2nd_day,
case
when (max_bili_1st_day is null) and (max_bili_2nd_day is
null) and (max_bili_3rd_day is null) then
0.7
when (max_bili_1st_day is not null) and (max_bili_2nd_day is
null) and (max_bili_3rd_day is null) then
max_bili_1st_day
when (max_bili_1st_day is null) and (max_bili_2nd_day is
not null) and (max_bili_3rd_day is null) then
max_bili_2nd_day
else
max_bili_3rd_day
end max_bili_3rd_day
from RawData

-- 3Creatinine (max)
-- a.If 2 values are missing, replace them with the level that is present.
-- b.If the middle value is missing, replace it with the average of the
-- other 2 values. Otherwise, replace it with the value that's
closer time-wise.
Rule3Creat as (
select subject_id,
case
when (max_creat_1st_day is null) and (max_creat_2nd_day is
null) and (max_creat_3rd_day is not null) then
max_creat_3rd_day
when (max_creat_1st_day is null) and (max_creat_2nd_day is
not null) and (max_creat_3rd_day is null) then
max_creat_2nd_day
else
max_creat_1st_day
end max_creat_1st_day,
case
when (max_creat_1st_day is null) and (max_creat_2nd_day is
null) and (max_creat_3rd_day is not null) then
max_creat_3rd_day
when (max_creat_1st_day is null) and (max_creat_2nd_day is
null) and (max_creat_3rd_day is null) then
max_creat_2nd_day
else
max_creat_1st_day
end max_creat_1st_day,
case
when (max_creat_1st_day is null) and (max_creat_2nd_day is
null) and (max_creat_3rd_day is not null) then
(max_creat_1st_day + max_creat_3rd_day) / 2
else
max_creat_2nd_day
end max_creat_2nd_day,
case
when (max_creat_1st_day is null) and (max_creat_2nd_day is
null) and (max_creat_3rd_day is null) then
max_creat_1st_day
when (max_creat_1st_day is null) and (max_creat_2nd_day is not null) and (max_creat_3rd_day is null)
then max_creat_2nd_day
else max_creat_3rd_day
end max_creat_3rd_day
from RawData

-- 4. Heart Rate (min/max/average/SD)
-- a. If the first or third day values are missing, use the second day values.
-- b. If the second day values are missing, use the average of the first--
-- and third day values.
Rule4HR as ( select subject_id,
case
  when (min_hr_1st_day is null) then
    min_hr_2nd_day
  else
    min_hr_1st_day
  end min_hr_1st_day,
case
  when (min_hr_1st_day is not null) and (min_hr_2nd_day is null)
and (min_hr_3rd_day is not null) then
    (min_hr_1st_day + min_hr_3rd_day) / 2
  else
    min_hr_2nd_day
  end min_hr_2nd_day,
case
  when (min_hr_3rd_day is null) then
    min_hr_2nd_day
  else
    min_hr_3rd_day
  end min_hr_3rd_day,
case
  when (max_hr_1st_day is null) then
    max_hr_2nd_day
  else
    max_hr_1st_day
  end max_hr_1st_day,
case
  when (max_hr_1st_day is not null) and (max_hr_2nd_day is null)
and (max_hr_3rd_day is not null) then
    (max_hr_1st_day + max_hr_3rd_day) / 2
  else
    max_hr_2nd_day
  end max_hr_2nd_day,
case
  when (max_hr_3rd_day is null) then
    max_hr_2nd_day
  else
    max_hr_3rd_day
  end max_hr_3rd_day,
case
  when (stddev_hr_1st_day is null) then
    stddev_hr_2nd_day
  else

stddev_hr_1st_day
end stddev_hr_1st_day,
case
  when (stddev_hr_1st_day is not null) and (stddev_hr_2nd_day is null) 
    and (stddev_hr_3rd_day is not null) then 
      (stddev_hr_1st_day + stddev_hr_3rd_day) / 2 
    else 
      stddev_hr_2nd_day
end stddev_hr_2nd_day,
case
  when (stddev_hr_3rd_day is null) then 
    stddev_hr_2nd_day
  else 
    stddev_hr_3rd_day
end stddev_hr_3rd_day,
case
  when (avg_hr_1st_day is null) then 
    avg_hr_2nd_day
  else 
    avg_hr_1st_day
end avg_hr_1st_day,
case
  when (avg_hr_1st_day is not null) and (avg_hr_2nd_day is null) 
    and (avg_hr_3rd_day is not null) then 
      (avg_hr_1st_day + avg_hr_3rd_day) / 2 
    else 
      avg_hr_2nd_day
end avg_hr_2nd_day,
case
  when (avg_hr_3rd_day is null) then 
    avg_hr_2nd_day
  else 
    avg_hr_3rd_day
end avg_hr_3rd_day
from RawData

5. Sodium (min/max/average/SD)
-- a. If 2 days of min/max/average/SD values are missing, replace them 
-- with min/max/average/SD value that is present.
-- b. If the second day min/max/average/SD values are missing, replace 
-- them with the average of the other 2 days' min/max/average/SD 
-- values.
-- Otherwise, replace them with the min/max/average/SD values that are 
-- closer time-wise.
Rule5Sodium as ( 
  select subject_id,
  case
    when (min_sodium_1st_day is null) 
      and (min_sodium_2nd_day is null) 
      and (min_sodium_3rd_day is not null) then 
        min_sodium_3rd_day 
    when (min_sodium_1st_day is null) 
      and (min_sodium_2nd_day is not null) 
      and (min_sodium_3rd_day is null) then 
        min_sodium_2nd_day 
    else 
      min_sodium_1st_day
  end)
end min_sodium_1st_day, 
case
when (min_sodium_1st_day is null) and (min_sodium_2nd_day is null) and (min_sodium_3rd_day is not null) then
  min_sodium_3rd_day
when (min_sodium_1st_day is not null) and (min_sodium_2nd_day is null) and (min_sodium_3rd_day is not null) then
  min_sodium_1st_day
when (min_sodium_1st_day is null) and (min_sodium_2nd_day is not null) and (min_sodium_3rd_day is null) then
  min_sodium_2nd_day
    case
    when (min_sodium_2nd_day is null) and (min_sodium_3rd_day is not null) then
      min_sodium_3rd_day
    when (min_sodium_2nd_day is not null) and (min_sodium_3rd_day is null) then
      min_sodium_2nd_day
    else
      null
    end
end case

when (max_sodium_1st_day is null) and (max_sodium_2nd_day is null) and (max_sodium_3rd_day is not null) then
  max_sodium_3rd_day
when (max_sodium_1st_day is not null) and (max_sodium_2nd_day is null) and (max_sodium_3rd_day is not null) then
  max_sodium_1st_day
when (max_sodium_1st_day is null) and (max_sodium_2nd_day is not null) and (max_sodium_3rd_day is null) then
  max_sodium_2nd_day
    case
    when (max_sodium_2nd_day is null) and (max_sodium_3rd_day is not null) then
      max_sodium_3rd_day
    when (max_sodium_2nd_day is not null) and (max_sodium_3rd_day is null) then
      max_sodium_2nd_day
    else
      null
    end
end case

when (max_sodium_1st_day is null) and (max_sodium_2nd_day is null) and (max_sodium_3rd_day is not null) then
  max_sodium_3rd_day
when (max_sodium_1st_day is not null) and (max_sodium_2nd_day is null) and (max_sodium_3rd_day is not null) then
  max_sodium_1st_day
when (max_sodium_1st_day is null) and (max_sodium_2nd_day is not null) and (max_sodium_3rd_day is null) then
  max_sodium_2nd_day
    case
    when (max_sodium_2nd_day is null) and (max_sodium_3rd_day is not null) then
      max_sodium_3rd_day
    when (max_sodium_2nd_day is not null) and (max_sodium_3rd_day is null) then
      max_sodium_2nd_day
    else
      null
    end
end case

end case

54
when (stddev_sodium_1st_day is null) and (stddev_sodium_2nd_day is null) and (stddev_sodium_3rd_day is not null) then
    stddev_sodium_3rd_day
when (stddev_sodium_1st_day is null) and (stddev_sodium_2nd_day is not null) and (stddev_sodium_3rd_day is null) then
    stddev_sodium_2nd_day
else
    stddev_sodium_1st_day
end stddev_sodium_1st_day,

when (stddev_sodium_1st_day is null) and (stddev_sodium_2nd_day is null) and (stddev_sodium_3rd_day is not null) then
    stddev_sodium_3rd_day
when (stddev_sodium_1st_day is not null) and (stddev_sodium_2nd_day is not null) and (stddev_sodium_3rd_day is null) then
    (stddev_sodium_1st_day + stddev_sodium_3rd_day) / 2
else
    stddev_sodium_2nd_day
end stddev_sodium_2nd_day,

when (avg_sodium_1st_day is null) and (avg_sodium_2nd_day is null) and (avg_sodium_3rd_day is not null) then
    avg_sodium_3rd_day
when (avg_sodium_1st_day is null) and (avg_sodium_2nd_day is not null) and (avg_sodium_3rd_day is null) then
    avg_sodium_2nd_day
else
    avg_sodium_1st_day
end avg_sodium_1st_day,

when (avg_sodium_1st_day is null) and (avg_sodium_2nd_day is null) and (avg_sodium_3rd_day is not null) then
    avg_sodium_3rd_day
when (avg_sodium_1st_day is not null) and (avg_sodium_2nd_day is not null) and (avg_sodium_3rd_day is null) then
    avg_sodium_2nd_day
else
    avg_sodium_1st_day
end avg_sodium_1st_day,

when (avg_sodium_1st_day is null) and (avg_sodium_2nd_day is null) and (avg_sodium_3rd_day is not null) then
    avg_sodium_3rd_day
when (avg_sodium_1st_day is not null) and (avg_sodium_2nd_day is not null) and (avg_sodium_3rd_day is null) then
    avg_sodium_2nd_day
else
    avg_sodium_1st_day
end avg_sodium_1st_day,

when (avg_sodium_1st_day is null) and (avg_sodium_2nd_day is null) and (avg_sodium_3rd_day is not null) then
    avg_sodium_3rd_day
when (avg_sodium_1st_day is not null) and (avg_sodium_2nd_day is not null) and (avg_sodium_3rd_day is null) then
    avg_sodium_2nd_day
else
    avg_sodium_1st_day
end avg_sodium_1st_day,
when (avg_sodium_1st_day is not null) and (avg_sodium_2nd_day is null) and (avg_sodium_3rd_day is not null) then
    (avg_sodium_1st_day + avg_sodium_3rd_day) / 2
else
    avg_sodium_2nd_day
end avg_sodium_2nd_day,

when (avg_sodium_1st_day is not null) and (avg_sodium_2nd_day is null) and (avg_sodium_3rd_day is null) then
    avg_sodium_1st_day
else
    avg_sodium_3rd_day
end avg_sodium_3rd_day

from RawData
)

-- 6. Respiratory Rate (max)
-- a. Use only maximum respiratory rate as a variable. Reason: There are too many patients with 0 as the minimum respiratory rate.
-- b. Maximum respiratory rate is the important variable anyway.
-- b. If all 3 maximum RR are missing, put 20. Reason: This is the default number that nurses write (even though it is wrong).
-- c. If 2 maximum RR are missing, replace them with the level that is present.
-- d. If the middle maximum RR is missing, replace it with the average of the other 2 maximum RR. Otherwise, replace it with the maximum RR that comes closer time-wise.

Rule6Resp as (
    select subject_id,
    case
        when (max_resp_1st_day is null) and (max_resp_2nd_day is null) and (max_resp_3rd_day is null) then
            20
        when (max_resp_1st_day is null) and (max_resp_2nd_day is null) and (max_resp_3rd_day is not null) then
            max_resp_3rd_day
        when (max_resp_1st_day is null) and (max_resp_2nd_day is not null) and (max_resp_3rd_day is null) then
            max_resp_2nd_day
        else
            max_resp_1st_day
        end max_resp_1st_day,
    case
        when (max_resp_1st_day is null) and (max_resp_2nd_day is null) and (max_resp_3rd_day is null) then
            20
        when (max_resp_1st_day is null) and (max_resp_2nd_day is null) and (max_resp_3rd_day is not null) then
            max_resp_3rd_day
        when (max_resp_1st_day is null) and (max_resp_2nd_day is not null) and (max_resp_3rd_day is null) then
            max_resp_2nd_day
        else
            max_resp_1st_day
        end max_resp_1st_day,
when (maxResp_lst_day is not null) and (maxResp_2nd_day is null) and (maxResp_3rd_day is not null) then
    (maxResp_lst_day + maxResp_3rd_day) / 2
else
    maxResp_2nd_day
end maxResp_2nd_day,

when (maxResp_lst_day is null) and (maxResp_2nd_day is null) and (maxResp_3rd_day is not null) then
    maxResp_3rd_day
else
    maxResp_3rd_day
end maxResp_3rd_day

from RawData

-- 7. Hematocrit (min/max/average/SD)
-- a. If 2 days of min/max/average/SD values are missing, replace them with
-- the min/max/average/SD value that is present.
-- b. If the second day min/max/average/SD values are missing, replace them
-- with the average of the other 2 days' min/max/average/SD values.
-- Otherwise, replace them with the min/max/average/SD values that are
-- closer time-wise.

Rule7Hemat as (}
    select subjectid,
    case
    when (min_hematocrit_lst_day is null) and (min_hematocrit_2nd_day is null) and (min_hematocrit_3rd_day is not null) then
        min_hematocrit_3rd_day
    when (min_hematocrit_lst_day is null) and (min_hematocrit_2nd_day is not null) and (min_hematocrit_3rd_day is null) then
        min_hematocrit_2nd_day
    else
        min_hematocrit_lst_day
    end min_hematocrit_lst_day,
    case
    when (min_hematocrit_lst_day is null) and (min_hematocrit_2nd_day is null) and (min_hematocrit_3rd_day is not null) then
        min_hematocrit_3rd_day
    when (min_hematocrit_lst_day is null) and (min_hematocrit_2nd_day is null) and (min_hematocrit_3rd_day is null) then
        min_hematocrit_lst_day
    when (min_hematocrit_lst_day is not null) and (min_hematocrit_2nd_day is null) and (min_hematocrit_3rd_day is not null) then
        (min_hematocrit_lst_day + min_hematocrit_3rd_day) / 2
    else
        min_hematocrit_lst_day
    end min_hematocrit_lst_day,
    case
    when (min_hematocrit_lst_day is null) and (min_hematocrit_2nd_day is null) and (min_hematocrit_3rd_day is not null) then
        min_hematocrit_3rd_day
    when (min_hematocrit_lst_day is null) and (min_hematocrit_2nd_day is null) and (min_hematocrit_3rd_day is null) then
        min_hematocrit_lst_day
    when (min_hematocrit_lst_day is not null) and (min_hematocrit_2nd_day is null) and (min_hematocrit_3rd_day is not null) then
        (min_hematocrit_lst_day + min_hematocrit_3rd_day) / 2
    else
        min_hematocrit_lst_day
    end min_hematocrit_lst_day
);
else
  min_hematocrit_2nd_day
end min_hematocrit_2nd_day,
case
  when (min_hematocrit_1st_day is not null) and
  (min_hematocrit_2nd_day is null) and (min_hematocrit_3rd_day is null)
  then
    min_hematocrit_1st_day
  when (min_hematocrit_2nd_day is not null) and (min_hematocrit_3rd_day is null)
  then
    min_hematocrit_2nd_day
  else
    min_hematocrit_3rd_day
end min_hematocrit_3rd_day,
case
  when (max_hematocrit_1st_day is not null) and
  (max_hematocrit_2nd_day is null) and (max_hematocrit_3rd_day is null)
  then
    max_hematocrit_3rd_day
  when (max_hematocrit_1st_day is not null) and
  (max_hematocrit_2nd_day is not null) and (max_hematocrit_3rd_day is null)
  then
    max_hematocrit_2nd_day
  else
    max_hematocrit_1st_day
end max_hematocrit_1st_day,
case
  when (max_hematocrit_1st_day is not null) and
  (max_hematocrit_2nd_day is null) and (max_hematocrit_3rd_day is not null)
  then
    max_hematocrit_3rd_day
  when (max_hematocrit_1st_day is not null) and
  (max_hematocrit_2nd_day is not null) and (max_hematocrit_3rd_day is null)
  then
    max_hematocrit_2nd_day
  else
    max_hematocrit_1st_day
end max_hematocrit_2nd_day,
case
  when (max_hematocrit_1st_day is not null) and
  (max_hematocrit_2nd_day is null) and (max_hematocrit_3rd_day is null)
  then
    max_hematocrit_3rd_day
  when (max_hematocrit_1st_day is not null) and
  (max_hematocrit_2nd_day is not null) and (max_hematocrit_3rd_day is null)
  then
    (max_hematocrit_1st_day + max_hematocrit_3rd_day) / 2
  else
    max_hematocrit_2nd_day
end max_hematocrit_2nd_day,
when (stddev_hematocrit_1st_day is null) and
(stddev_hematocrit_2nd_day is null) and (stddev_hematocrit_3rd_day is not null) then
    stddev_hematocrit_3rd_day
when (stddev_hematocrit_1st_day is null) and
(stddev_hematocrit_2nd_day is not null) and (stddev_hematocrit_3rd_day is null) then
    stddev_hematocrit_2nd_day
else
    stddev_hematocrit_1st_day
end stddev_hematocrit_1st_day,

when (stddev_hematocrit_1st_day is null) and
(stddev_hematocrit_2nd_day is null) and (stddev_hematocrit_3rd_day is not null) then
    stddev_hematocrit_3rd_day
when (stddev_hematocrit_1st_day is not null) and
(stddev_hematocrit_2nd_day is null) and (stddev_hematocrit_3rd_day is null) then
    stddev_hematocrit_1st_day
else
    stddev_hematocrit_2nd_day
end stddev_hematocrit_2nd_day,

when (avg_hematocrit_1st_day is null) and
(avg_hematocrit_2nd_day is null) and (avg_hematocrit_3rd_day is not null) then
    avg_hematocrit_3rd_day
when (avg_hematocrit_1st_day is null) and
(avg_hematocrit_2nd_day is not null) and (avg_hematocrit_3rd_day is null) then
    avg_hematocrit_1st_day
else
    avg_hematocrit_2nd_day
end avg_hematocrit_1st_day,
when (avg_hematocrit_1st_day is not null) and
(avg_hematocrit_2nd_day is null) and (avg_hematocrit_3rd_day is null)
then
  avg_hematocrit_1st_day
when (avg_hematocrit_1st_day is not null) and
(avg_hematocrit_2nd_day is null) and (avg_hematocrit_3rd_day is not null)
then
  (avg_hematocrit_1st_day + avg_hematocrit_3rd_day) / 2
else
  avg_hematocrit_2nd_day
end avg_hematocrit_2nd_day,

from RawData

-- 8. Glucose (min/max/average/SD)
-- a. If 2 days of min/max/average/SD values are missing, replace them with
--    min/max/average/SD value that is present.
-- b. If the second day min/max/average/SD values are missing, replace them
--    with the average of the other 2 days' min/max/average/SD values.
--    Otherwise, replace them with the min/max/average/SD values that are
--    closer time-wise.
--
Rule8Glucose as (}
  select subjectid,
  case
    when (min_glucose_1st_day is null) and (min_glucose_3rd_day is not null)
        and (min_glucose_2nd_day
      is null) and (min_glucose_3rd_day is not null)
        min_glucose_3rd_day
    when (min_glucose_1st_day is null) and (min_glucose_3rd_day is not null)
        and (min_glucose_2nd_day
      is not null) and (min_glucose_3rd_day is null)
        min_glucose_2nd_day
    else
        min_glucose_1st_day
  end min_glucose_1st_day,
  case
    when (min_glucose_1st_day is null) and (min_glucose_3rd_day is not null)
        and (min_glucose_2nd_day
      is null) and (min_glucose_3rd_day is not null)
        min_glucose_3rd_day
    when (min_glucose_1st_day is null) and (min_glucose_3rd_day is not null)
        and (min_glucose_2nd_day
      is null) and (min_glucose_3rd_day is not null)
        (min_glucose_1st_day + min_glucose_3rd_day) / 2
    else
        min_glucose_2nd_day
  end min_glucose_2nd_day
from RawData

)}
min_glucose_2nd_day
end min_glucose_2nd_day,
case
  when (min_glucose_1st_day is not null) and (min_glucose_3rd_day is not null) then
    min_glucose_1st_day
  when (min_glucose_1st_day is null) and (min_glucose_3rd_day is not null) then
    min_glucose_2nd_day
  else
    min_glucose_3rd_day
end min_glucose_3rd_day,
case
  when (max_glucose_1st_day is null) and (max_glucose_3rd_day is not null) then
    max_glucose_3rd_day
  when (max_glucose_1st_day is not null) and (max_glucose_3rd_day is not null) then
    (max_glucose_1st_day + max_glucose_3rd_day) / 2
  else
    max_glucose_2nd_day
end max_glucose_2nd_day,
case
  when (stddev_glucose_1st_day is null) and (stddev_glucose_2nd_day is not null) and (stddev_glucose_3rd_day is not null) then
    stddev_glucose_3rd_day
  else
    stddev_glucose_1st_day
end stddev_glucose_1st_day,
case
    when (stddev_glucose_1st_day is null)  and
         (stddev_glucose_2nd_day is null)  and
         (stddev_glucose_3rd_day is not null)  and
         (stddev_glucose_3rd_day is not null)  and
         (stddev_glucose_3rd_day is not null)  and
         (stddev_glucose_3rd_day is not null)  and
         (stddev_glucose_3rd_day is not null)  then
        (stddev_glucose_1st_day + stddev_glucose_3rd_day) / 2
    else
        stddev_glucose_2nd_day
    end stddev_glucose_2nd_day,
end stddev_glucose_2nd_day,
    case
        when (stddev_glucose_1st_day is not null)  and
         (stddev_glucose_2nd_day is null)  and
         (stddev_glucose_3rd_day is not null)  and
         (stddev_glucose_3rd_day is not null)  and
         (stddev_glucose_3rd_day is not null)  and
         (stddev_glucose_3rd_day is not null)  then
        stddev_glucose_3rd_day
    else
        stddev_glucose_3rd_day
    end stddev_glucose_3rd_day,
end stddev_glucose_3rd_day,
    case
        when (avg_glucose_1st_day is null)  and
         (avg_glucose_2nd_day is null)  and
         (avg_glucose_3rd_day is not null)  then
        avg_glucose_3rd_day
    when (avg_glucose_1st_day is null)  and
         (avg_glucose_2nd_day is not null)  and
         (avg_glucose_3rd_day is null)  then
        avg_glucose_2nd_day
    else
        avg_glucose_1st_day
    end avg_glucose_1st_day,
end avg_glucose_1st_day,
    case
        when (avg_glucose_1st_day is null)  and
         (avg_glucose_2nd_day is null)  and
         (avg_glucose_3rd_day is not null)  then
        avg_glucose_3rd_day
    when (avg_glucose_1st_day is null)  and
         (avg_glucose_2nd_day is null)  and
         (avg_glucose_3rd_day is not null)  then
        avg_glucose_3rd_day
    else
        avg_glucose_2nd_day
    end avg_glucose_2nd_day,
end avg_glucose_2nd_day,
    case
        when (avg_glucose_1st_day is null)  and
         (avg_glucose_2nd_day is null)  and
         (avg_glucose_3rd_day is not null)  then
        avg_glucose_3rd_day
    when (avg_glucose_1st_day is null)  and
         (avg_glucose_2nd_day is null)  and
         (avg_glucose_3rd_day is not null)  then
        avg_glucose_3rd_day
    else
        avg_glucose_2nd_day
    end avg_glucose_2nd_day,
avg_glucose_2nd_day
else
avg_glucose_3rd_day
end avg_glucose_3rd_day
from RawData
),

--9.WBC (min/max/average/SD)
--a. If 2 days of min/max/average/SD values are missing, replace them with
--min/max/average/SD value that is present.
--b. If the second day min/max/average/SD values are missing, replace them
--with the average of the other 2 days' min/max/average/SD values.
--Otherwise, replace them with the min/max/average/SD values that are
--closer time-wise.

Rule9WBC as (
  select subject_id, case
    when (min_wbc_1st_day is null) and (min_wbc_2nd_day is null) then
      min_wbc_3rd_day
    when (min_wbc_1st_day is null) and (min_wbc_3rd_day is null) then
      min_wbc_2nd_day
    else
      min_wbc_1st_day
    end min_wbc_1st_day,
  case
    when (min_wbc_1st_day is null) and (min_wbc_2nd_day is null) then
      min_wbc_3rd_day
    when (min_wbc_1st_day is null) and (min_wbc_3rd_day is not null) then
      min_wbc_3rd_day
    else
      min_wbc_1st_day
    end min_wbc_2nd_day,
  case
    when (min_wbc_1st_day is null) and (min_wbc_2nd_day is null) then
      min_wbc_3rd_day
    when (min_wbc_1st_day is null) and (min_wbc_3rd_day is not null) then
      min_wbc_3rd_day
    else
      min_wbc_1st_day
    end min_wbc_3rd_day,
  case
    when (max_wbc_1st_day is null) and (max_wbc_2nd_day is null) then
      max_wbc_3rd_day
    when (max_wbc_1st_day is null) and (max_wbc_3rd_day is not null) then
      max_wbc_3rd_day
    else
      max_wbc_1st_day
    end max_wbc_1st_day,
  case
    when (max_wbc_1st_day is null) and (max_wbc_2nd_day is null) then
      max_wbc_3rd_day
    when (max_wbc_1st_day is null) and (max_wbc_3rd_day is not null) then
      max_wbc_3rd_day
    else
      max_wbc_1st_day
    end max_wbc_2nd_day,
  case
    when (max_wbc_1st_day is null) and (max_wbc_2nd_day is null) then
      max_wbc_3rd_day
    when (max_wbc_1st_day is null) and (max_wbc_3rd_day is not null) then
      max_wbc_3rd_day
    else
      max_wbc_1st_day
    end max_wbc_3rd_day
)
else
    max_wbc_1st_day
end max_wbc_1st_day,
case
    when (max_wbc_1st_day is null) and (max_wbc_3rd_day is not null) then
        max_wbc_3rd_day
    when (max_wbc_1st_day is not null) and (max_wbc_3rd_day is null) then
        max_wbc_1st_day
    when (max_wbc_1st_day is not null) and (max_wbc_2nd_day is null) then
        (max_wbc_1st_day + max_wbc_3rd_day) / 2
else
    max_wbc_2nd_day
end max_wbc_2nd_day,
case
    when (max_wbc_1st_day is not null) and (max_wbc_3rd_day is null) then
        max_wbc_3rd_day
    when (max_wbc_1st_day is null) and (max_wbc_3rd_day is not null) then
        stddev_wbc_3rd_day
else
    stddev_wbc_1st_day
end stddev_wbc_1st_day,
case
    when (stddev_wbc_1st_day is null) and (stddev_wbc_2nd_day is null) then
        stddev_wbc_2nd_day
    when (stddev_wbc_1st_day is not null) and (stddev_wbc_2nd_day is null) then
        stddev_wbc_1st_day
else
    stddev_wbc_2nd_day
end stddev_wbc_2nd_day,
stddev_wbc_3rd_day
end stddev_wbc_3rd_day,
case
  when (avg_wbc_1st_day is null) and (avg_wbc_2nd_day is null) and (avg_wbc_3rd_day is not null) then
    avg_wbc_3rd_day
  when (avg_wbc_1st_day is null) and (avg_wbc_2nd_day is null) then
    avg_wbc_3rd_day
  when (avg_wbc_1st_day is null) and (avg_wbc_3rd_day is not null) then
    avg_wbc_2nd_day
  else
    avg_wbc_1st_day
end avg_wbc_1st_day,
case
  when (avg_wbc_1st_day is null) and (avg_wbc_2nd_day is null) and (avg_wbc_3rd_day is not null) then
    avg_wbc_3rd_day
  when (avg_wbc_1st_day is null) and (avg_wbc_2nd_day is null) then
    avg_wbc_3rd_day
  when (avg_wbc_1st_day is not null) and (avg_wbc_2nd_day is null) then
    (avg_wbc_1st_day + avg_wbc_3rd_day) / 2
  else
    avg_wbc_2nd_day
end avg_wbc_2nd_day,
case
  when (avg_wbc_1st_day is null) and (avg_wbc_2nd_day is null) and (avg_wbc_3rd_day is not null) then
    avg_wbc_3rd_day
  when (avg_wbc_1st_day is null) and (avg_wbc_2nd_day is null) then
    avg_wbc_3rd_day
  when (avg_wbc_1st_day is not null) and (avg_wbc_2nd_day is null) then
    avg_wbc_3rd_day
  else
    avg_wbc_3rd_day
end avg_wbc_3rd_day
from RawData
)

-- 10. Potassium (min/max/average/SD)
-- a. If 2 days of min/max/average/SD values are missing, replace them with
--    min/max/average/SD value that is present.
-- b. If the second day min/max/average/SD values are missing, replace them
--    with the average of the other 2 days' min/max/average/SD values.
--    Otherwise, replace them with the min/max/average/SD values that are
--    closer time-wise.

Rule10Potassium as (
  select subject_id,
  case
    when (min_potassium_1st_day is null) and (min_potassium_2nd_day is null) and (min_potassium_3rd_day is not null) then
      min_potassium_3rd_day
    when (min_potassium_1st_day is null) and (min_potassium_2nd_day is not null) and (min_potassium_3rd_day is null) then
      min_potassium_2nd_day
    when (min_potassium_1st_day is null) and (min_potassium_2nd_day is null) and (min_potassium_3rd_day is null) then
      min_potassium_2nd_day
    else
      avg_wbc_2nd_day
    end avg_wbc_2nd_day,
  case
    when (min_potassium_1st_day is null) and (min_potassium_2nd_day is null) and (min_potassium_3rd_day is not null) then
      min_potassium_3rd_day
    when (min_potassium_1st_day is null) and (min_potassium_2nd_day is not null) and (min_potassium_3rd_day is null) then
      min_potassium_2nd_day
    when (min_potassium_1st_day is null) and (min_potassium_2nd_day is null) and (min_potassium_3rd_day is null) then
      min_potassium_2nd_day
    else
      avg_wbc_3rd_day
    end avg_wbc_3rd_day
  from RawData
)
else
    min_potassium_1st_day
end min_potassium_1st_day,
case
  when (min_potassium_1st_day is null) and (min_potassium_2nd_day is null) and (min_potassium_3rd_day is not null) then
    min_potassium_3rd_day
  when (min_potassium_1st_day is not null) and (min_potassium_2nd_day is null) and (min_potassium_3rd_day is null) then
    min_potassium_1st_day
  when (min_potassium_1st_day is null) and (min_potassium_2nd_day is not null) and (min_potassium_3rd_day is null) then
    (min_potassium_1st_day + min_potassium_3rd_day) / 2
else
    min_potassium_2nd_day
end min_potassium_2nd_day,
case
  when (min_potassium_1st_day is not null) and (min_potassium_2nd_day is null) and (min_potassium_3rd_day is null) then
    min_potassium_1st_day
  when (max_potassium_1st_day is null) and (maxpotassium_2nd_day is null) and (max_potassium_3rd_day is not null) then
    max_potassium_3rd_day
  when (max_potassium_1st_day is null) and (maxpotassium_2nd_day is not null) and (max_potassium_3rd_day is null) then
    max_potassium_2nd_day
  when (max_potassium_1st_day is not null) and (maxpotassium_2nd_day is null) and (max_potassium_3rd_day is null) then
    max_potassium_l1st_day
else
    max_potassium_3rd_day
end max_potassium_3rd_day,
case
  when (max_potassium_1st_day is null) and (max_potassium_2nd_day is null) and (max_potassium_3rd_day is not null) then
    max_potassium_3rd_day
  when (max_potassium_1st_day is not null) and (maxpotassium_2nd_day is null) and (max_potassium_3rd_day is null) then
    max_potassium_l1st_day
  when (max_potassium_1st_day is not null) and (maxpotassium_2nd_day is null) and (max_potassium_3rd_day is not null) then
    (max_potassium_1st_day + max_potassium_3rd_day) / 2
else
\[
\text{max_potassium\_2nd\_day} \\
\text{end max_potassium\_2nd\_day,} \\
\text{case} \\
\text{when (max_potassium\_1st\_day is not null) and} \\
(\text{max_potassium\_2nd\_day is null}) \quad \text{and (max_potassium\_3rd\_day is null)} \quad \text{then} \\
\text{max_potassium\_1st\_day} \\
\text{when (max_potassium\_1st\_day is null) and} \\
(\text{max_potassium\_2nd\_day is not null}) \quad \text{and (max_potassium\_3rd\_day is null)} \quad \text{then} \\
\text{max_potassium\_2nd\_day} \\
\text{else} \\
\text{max_potassium\_3rd\_day} \\
\text{end max_potassium\_3rd\_day,} \\
\text{case} \\
\text{when (stddev\_potassium\_1st\_day is null) and} \\
(\text{stddev\_potassium\_2nd\_day is null}) \quad \text{and (stddev\_potassium\_3rd\_day is not null)} \quad \text{then} \\
\text{stddev\_potassium\_3rd\_day} \\
\text{when (stddev\_potassium\_1st\_day is null) and} \\
(\text{stddev\_potassium\_2nd\_day is not null}) \quad \text{and (stddev\_potassium\_3rd\_day is null)} \quad \text{then} \\
\text{stddev\_potassium\_2nd\_day} \\
\text{else} \\
\text{stddev\_potassium\_1st\_day} \\
\text{end stddev\_potassium\_1st\_day,} \\
\text{case} \\
\text{when (stddev\_potassium\_1st\_day is null) and} \\
(\text{stddev\_potassium\_2nd\_day is null}) \quad \text{and (stddev\_potassium\_3rd\_day is not null)} \quad \text{then} \\
\text{stddev\_potassium\_3rd\_day} \\
\text{when (stddev\_potassium\_1st\_day is null) and} \\
(\text{stddev\_potassium\_2nd\_day is not null}) \quad \text{and (stddev\_potassium\_3rd\_day is null)} \quad \text{then} \\
\text{stddev\_potassium\_2nd\_day} \\
\text{else} \\
\text{stddev\_potassium\_1st\_day} \\
\text{end stddev\_potassium\_1st\_day,} \\
\text{case} \\
\text{when (stddev\_potassium\_1st\_day is null) and} \\
(\text{stddev\_potassium\_2nd\_day is null}) \quad \text{and (stddev\_potassium\_3rd\_day is not null)} \quad \text{then} \\
\text{stddev\_potassium\_3rd\_day} \\
\text{when (stddev\_potassium\_1st\_day is null) and} \\
(\text{stddev\_potassium\_2nd\_day is not null}) \quad \text{and (stddev\_potassium\_3rd\_day is null)} \quad \text{then} \\
\text{(stddev\_potassium\_1st\_day + stddev\_potassium\_3rd\_day) / 2} \\
\text{else} \\
\text{stddev\_potassium\_2nd\_day} \\
\text{end stddev\_potassium\_2nd\_day,} \\
\text{case} \\
\text{when (stddev\_potassium\_1st\_day is null) and} \\
(\text{stddev\_potassium\_2nd\_day is null}) \quad \text{and (stddev\_potassium\_3rd\_day is null)} \quad \text{then} \\
\text{stddev\_potassium\_1st\_day} \\
\text{when (stddev\_potassium\_1st\_day is null) and} \\
(\text{stddev\_potassium\_2nd\_day is not null}) \quad \text{and (stddev\_potassium\_3rd\_day is null)} \quad \text{then} \\
\text{stddev\_potassium\_2nd\_day} \\
\text{else} \\
\text{stddev\_potassium\_3rd\_day} \\
\text{end stddev\_potassium\_3rd\_day,} \\
\text{case}
\]
when (avg_potassium_1st_day is null) and (avg_potassium_2nd_day is null) and (avg_potassium_3rd_day is not null) then
    avg_potassium_3rd_day
when (avg_potassium_1st_day is null) and (avg_potassium_2nd_day is not null) and (avg_potassium_3rd_day is null) then
    avg_potassium_2nd_day
else
    avg_potassium_1st_day
end avg_potassium_1st_day,

when (avg_potassium_1st_day is null) and (avg_potassium_2nd_day is null) and (avg_potassium_3rd_day is not null) then
    avg_potassium_3rd_day
when (avg_potassium_1st_day is not null) and (avg_potassium_2nd_day is null) and (avg_potassium_3rd_day is null) then
    (avg_potassium_1st_day + avg_potassium_3rd_day) / 2
else
    avg_potassium_2nd_day
end avg_potassium_2nd_day,

when (avg_potassium_1st_day is not null) and (avg_potassium_2nd_day is null) and (avg_potassium_3rd_day is not null) then
    avg_potassium_1st_day
when (avg_potassium_1st_day is not null) and (avg_potassium_2nd_day is not null) and (avg_potassium_3rd_day is null) then
    avg_potassium_2nd_day
else
    avg_potassium_3rd_day
end avg_potassium_3rd_day

from RawData

-- 11.BUN (max)
-- a.If 2 values are missing, replace them with the level that is present.
-- b.If the middle value is missing, replace it with the average of the other
-- 2 values. Otherwise, replace it with the value that's closer time-wise.

Rule11BUN as ( select subject_id, case
    when (max_bun_1st_day is null) and (max_bun_2nd_day is null) and (max_bun_3rd_day is null) then
        max_bun_3rd_day
    when (max_bun_1st_day is null) and (max_bun_2nd_day is not null) and (max_bun_3rd_day is null) then
        max_bun_3rd_day
    when (max_bun_1st_day is not null) and (max_bun_2nd_day is null) and (max_bun_3rd_day is null) then
        max_bun_3rd_day
    when (max_bun_1st_day is null) and (max_bun_2nd_day is null) and (max_bun_3rd_day is not null) then
        max_bun_3rd_day
    when (max_bun_1st_day is not null) and (max_bun_2nd_day is null) and (max_bun_3rd_day is not null) then
        max_bun_3rd_day
    when (max_bun_1st_day is null) and (max_bun_2nd_day is not null) and (max_bun_3rd_day is not null) then
        max_bun_3rd_day
    else
        max_bun_1st_day
end max_bun_3rd_day,

...)
max_bun_2nd_day
else
  max_bun_1st_day
end max_bun_1st_day,
case
  when (max_bun_1st_day is null) and (max_bun_2nd_day is null) and (max_bun_3rd_day is not null) then
    max_bun_3rd_day
  when (max_bun_1st_day is not null) and (max_bun_2nd_day is null) and (max_bun_3rd_day is null) then
    max_bun_1st_day
  when (max_bun_1st_day is not null) and (max_bun_2nd_day is not null) and (max_bun_3rd_day is not null) then
    (max_bun_1st_day + max_bun_3rd_day) / 2
else
  max_bun_2nd_day
end max_bun_2nd_day,
case
  when (max_bun_1st_day is not null) and (max_bun_2nd_day is null) and (max_bun_3rd_day is null) then
    max_bun_1st_day
else
  max_bun_3rd_day
end max_bun_3rd_day

from RawData
}

-- 12. Temperature (min/max/average/SD):
--
-- If the second day min/max/average/SD values are missing, replace them with
-- the average of the other 2 days' min/max/average/SD values.
Otherwise,
-- replace them with the min/max/average/SD values that are closer time-wise.
--
Rule12Temp as (  
  select subject_id,  
  min_temp_1st_day,  
  case
    when (min_temp_1st_day is not null) and (min_temp_2nd_day is null) and (min_temp_3rd_day is not null) then
      (min_temp_1st_day + min_temp_3rd_day) / 2
    else
      min_temp_2nd_day
  end min_temp_2nd_day,
  min_temp_3rd_day,
  max_temp_1st_day,  
  case
    when (max_temp_1st_day is not null) and (max_temp_2nd_day is null) and (max_temp_3rd_day is not null) then
      (max_temp_1st_day + max_temp_3rd_day) / 2
    else
      max_temp_2nd_day
from RawData

end max_temp_2nd_day,
max_temp_3rd_day,
stddev_temp_1st_day,
case
  when (stddev_temp_1st_day is not null) and (stddev_temp_2nd_day
is null) and (stddev_temp_3rd_day is not null) then
     (stddev_temp_1st_day + stddev_temp_3rd_day) / 2
  else
     stddev_temp_2nd_day
  end stddev_temp_2nd_day,
stddev_temp_3rd_day,
avg_temp_1st_day,
case
  when (avg_temp_1st_day is not null) and (avg_temp_2nd_day is
null) and (avg_temp_3rd_day is not null) then
     (avg_temp_1st_day + avg_temp_3rd_day) / 2
  else
     avg_temp_2nd_day
  end avg_temp_2nd_day,
avg_temp_3rd_day
from RawData
)

-- 13. GCS (min), Day 1 only: Replace missing value with 15.
--
Rule13GCS as {
  select subject_id,
    nvl(min_gcs_1st_day, 15)min_gcs_1st_day
  from RawData
}

-- 14. Systolic Blood Pressure (min/max/average/SD):
--
-- If the second day min/max/ average/SD values are missing, replace them
-- with the average of the other 2 daysâ€™ min/max/ average/SD values.
-- Otherwise, replace them with the min/max/ average/SD values that are
-- closer time-wise.
--
Rule14SysBP as {
  select subject_id,
    min_sysbp_1st_day,
case
  when (min_sysbp_1st_day is not null) and (min_sysbp_2nd_day is
null) and (min_sysbp_3rd_day is not null) then
     (min_sysbp_1st_day + min_sysbp_3rd_day) / 2
  else
     min_sysbp_2nd_day
  end min_sysbp_2nd_day,
min_sysbp_3rd_day,
max_sysbp_1st_day,
case
  when (max_sysbp_1st_day is not null) and (max_sysbp_2nd_day is
null) and (max_sysbp_3rd_day is not null) then
     (max_sysbp_1st_day + max_sysbp_3rd_day) / 2
  else
     max_sysbp_2nd_day
  end max_sysbp_2nd_day,
max_sysbp_3rd_day,
stddev_sysbp_1st_day,
case
  when (stddev_sysbp_1st_day is not null) and (stddev_sysbp_2nd_day is null) and (stddev_sysbp_3rd_day is not null) then
    (stddev_sysbp_1st_day + stddev_sysbp_3rd_day) / 2
  else
    stddev_sysbp_2nd_day
end stddev_sysbp_2nd_day,
stddev_sysbp_3rd_day,
avg_sysbp_1st_day,
case
  when (avg_sysbp_1st_day is not null) and (avg_sysbp_2nd_day is null) and (avg_sysbp_3rd_day is not null) then
    (avg_sysbp_1st_day + avg_sysbp_3rd_day) / 2
  else
    avg_sysbp_2nd_day
end avg_sysbp_2nd_day,
avg_sysbp_3rd_day
from RawData
).
--
-- 15. Bicarbonate (min/max/average/SD)
-- a. Delete 2 patients without min/max/average/SD values for all the three days.
-- b. If 2 days of min/max/average/SD values are missing, replace them with 24/24/24/0.
-- c. If the second day min/max/average/SD values are missing, replace them with the average of the other 2 days’ min/max/average/SD values.
-- Otherwise, replace them 24/24/24/0.
--
Rule15Bicarbonate as (  
  select subject_id,  
case
    when (min_bicarbonate_1st_day is not null) then
      min_bicarbonate_1st_day  
    else
      24
end min_bicarbonate_1st_day,
  case
    when (min_bicarbonate_2nd_day is not null) then
      min_bicarbonate_2nd_day
    when (min_bicarbonate_1st_day is not null) and (min_bicarbonate_2nd_day is null) then
      (min_bicarbonate_1st_day + min_bicarbonate_3rd_day) / 2
    else
      24
end min_bicarbonate_2nd_day,
  case
    when (min_bicarbonate_3rd_day is not null) then
      min_bicarbonate_3rd_day  
    else
      24
end min_bicarbonate_3rd_day,
  case
    when (max_bicarbonate_1st_day is not null) then
      max_bicarbonate_1st_day
    else
      24
end max_bicarbonate_1st_day,
max_bicarbonate_1st_day
else
  24
end max_bicarbonate_1st_day,
case
  when (max_bicarbonate_2nd_day is not null) then
    max_bicarbonate_2nd_day
  when (max_bicarbonate_1st_day is not null) and
    (max_bicarbonate_2nd_day is null) and
    (max_bicarbonate_3rd_day is not null) then
    (max_bicarbonate_1st_day + max_bicarbonate_3rd_day) / 2
  else
    24
end max_bicarbonate_2nd_day,
case
  when (max_bicarbonate_3rd_day is not null) then
    max_bicarbonate_3rd_day
  else
    24
end max_bicarbonate_3rd_day,
case
  when (stddev_bicarbonate_1st_day is not null) then
    stddev_bicarbonate_1st_day
  else
    0
end stddev_bicarbonate_1st_day,
case
  when (stddev_bicarbonate_2nd_day is not null) then
    stddev_bicarbonate_2nd_day
  when (stddev_bicarbonate_1st_day is not null) and
    (stddev_bicarbonate_2nd_day is null) and
    (stddev_bicarbonate_3rd_day is not null) then
    (stddev_bicarbonate_1st_day + stddev_bicarbonate_3rd_day) / 2
  else
    0
end stddev_bicarbonate_2nd_day,
case
  when (stddev_bicarbonate_3rd_day is not null) then
    stddev_bicarbonate_3rd_day
  else
    0
end stddev_bicarbonate_3rd_day,
case
  when (avg_bicarbonate_1st_day is not null) then
    avg_bicarbonate_1st_day
  else
    24
end avg_bicarbonate_1st_day,
case
  when (avg_bicarbonate_2nd_day is not null) then
    avg_bicarbonate_2nd_day
  when (avg_bicarbonate_1st_day is not null) and
    (avg_bicarbonate_2nd_day is null) and
    (avg_bicarbonate_3rd_day is not null) then
    (avg_bicarbonate_1st_day + avg_bicarbonate_3rd_day) / 2
  else
    24
end avg_bicarbonate_2nd_day,
end avg_bicarbonate_2nd_day,
case
  when (avg_bicarbonate_3rd_day is not null) then
    avg_bicarbonate_3rd_day
  else
    24
end avg_bicarbonate_3rd_day
from RawData
)
select d.subject_id, d.expire_flg, d.age, d.sex, 
d.intime, d.outtime, d.los,
r2.max bili_1st_day, r2.max bili_2nd_day, r2.max bili_3rd_day, 
r3.max creat_1st_day, r3.max creat_2nd_day, r3.max creat_3rd_day, 
r4.min hr_1st_day, r4.max hr_1st_day, r4.stddev hr_1st_day, 
r4.avg hr_1st_day, 
r4.min hr_2nd_day, r4.max hr_2nd_day, r4.stddev hr_2nd_day, 
r4.avg hr_2nd_day, 
r4.min hr_3rd_day, r4.max hr_3rd_day, r4.stddev hr_3rd_day, 
r4.avg hr_3rd_day, 
r5.min sodium_1st_day, r5.max sodium_1st_day, r5.stddev sodium_1st_day, 
r5.avg sodium_1st_day, 
r5.min sodium_2nd_day, r5.max sodium_2nd_day, r5.stddev sodium_2nd_day, 
r5.avg sodium_2nd_day, 
r5.min sodium_3rd_day, r5.max sodium_3rd_day, r5.stddev sodium_3rd_day, 
r5.avg sodium_3rd_day, 
r14.min sysbp_1st_day, r14.max sysbp_1st_day, r14.stddev sysbp_1st_day, 
r14.avg sysbp_1st_day, 
r14.min sysbp_2nd_day, r14.max sysbp_2nd_day, r14.stddev sysbp_2nd_day, 
r14.avg sysbp_2nd_day, 
r14.min sysbp_3rd_day, r14.max sysbp_3rd_day, r14.stddev sysbp_3rd_day, 
r14.avg sysbp_3rd_day, 
r6.max resp_1st_day, r6.max resp_2nd_day, r6.max resp_3rd_day, 
r7.min hematocrit_1st_day, r7.max hematocrit_1st_day, 
r7.stddev hematocrit_1st_day, r7.avg hematocrit_1st_day, 
r7.min hematocrit_2nd_day, r7.max hematocrit_2nd_day, 
r7.stddev hematocrit_2nd_day, r7.avg hematocrit_2nd_day, 
r7.min hematocrit_3rd_day, r7.max hematocrit_3rd_day, 
r7.stddev hematocrit_3rd_day, r7.avg hematocrit_3rd_day, 
r8.min glucose_1st_day, r8.max glucose_1st_day, 
r8.stddev glucose_1st_day, r8.avg glucose_1st_day, 
r8.min glucose_2nd_day, r8.max glucose_2nd_day, 
r8.stddev glucose_2nd_day, r8.avg glucose_2nd_day, 
r8.min glucose_3rd_day, r8.max glucose_3rd_day, 
r8.stddev glucose_3rd_day, r8.avg glucose_3rd_day, 
r9.min wbc_1st_day, r9.max wbc_1st_day, r9.stddev wbc_1st_day, 
r9.avg wbc_1st_day, 
r9.min wbc_2nd_day, r9.max wbc_2nd_day, r9.stddev wbc_2nd_day, 
r9.avg wbc_2nd_day, 
r9.min wbc_3rd_day, r9.max wbc_3rd_day, r9.stddev wbc_3rd_day, 
r9.avg wbc_3rd_day, 
r10.min potassium_1st_day, r10.max potassium_1st_day, 
r10.stddev potassium_1st_day, r10.avg potassium_1st_day, 
r10.min potassium_2nd_day, r10.max potassium_2nd_day, 
r10.stddev potassium_2nd_day, r10.avg potassium_2nd_day, 
r10.min potassium_3rd_day, r10.max potassium_3rd_day, 
r10.stddev potassium_3rd_day, r10.avg potassium_3rd_day, 
r11.max bun_1st_day, r11.max bun_2nd_day, r11.max bun_3rd_day,
r13.min_gcs_1st_day, 
 r12.min_temp_1st_day,  r12.max_temp_1st_day, 
 r12.stddev_temp_1st_day,  r12.avg_temp_1st_day,  
 r12.min_temp_2nd_day, r12.max_temp_2nd_day, 
 r12.stddev_temp_2nd_day, r12.avg_temp_2nd_day,  
 r12.min_temp_3rd_day, r12.max_temp_3rd_day, 
 r12.stddev_temp_3rd_day, r12.avg_temp_3rd_day,  
 r15.min_bicarbonate_1st_day, r15.max_bicarbonate_1st_day, 
 r15.stddev_bicarbonate_1st_day, r15.avg_bicarbonate_1st_day, 
 r15.min_bicarbonate_2nd_day, r15.max_bicarbonate_2nd_day, 
 r15.stddev_bicarbonate_2nd_day, r15.avg_bicarbonate_2nd_day, 
 r15.min_bicarbonate_3rd_day, r15.max_bicarbonate_3rd_day, 
 r15.stddev_bicarbonate_3rd_day, r15.avg_bicarbonate_3rd_day,  
 d.in_1st_day, d.out_1st_day,  
 d.in_2nd_day, d.out_2nd_day,  
 d.in_3rd_day, d.out_3rd_day  
from RawData d, 
 Rule2Bili r2,  
 Rule3Creat r3,  
 Rule4HR r4,  
 Rule5Sodium r5,  
 Rule6Resp r6,  
 Rule7Hemat r7,  
 Rule8Glucose r8,  
 Rule9WBC r9,  
 Rule10Potassium r10,  
 Rule11BUN r11,  
 Rule12Temp r12,  
 Rule13GCS r13,  
 Rule14SysBP r14,  
 Rule15Bicarbonate r15  
where r2.subject_id = d.subject_id  
and r3.subject_id = d.subject_id  
and r4.subject_id = d.subject_id  
and r5.subject_id = d.subject_id  
and r6.subject_id = d.subject_id  
and r7.subject_id = d.subject_id  
and r8.subject_id = d.subject_id  
and r9.subject_id = d.subject_id  
and r10.subject_id = d.subject_id  
and r11.subject_id = d.subject_id  
and r12.subject_id = d.subject_id  
and r13.subject_id = d.subject_id  
and r14.subject_id = d.subject_id  
and r15.subject_id = d.subject_id;
Appendix B. Bayesian Network Model to Predict Hospital Mortality using Tenfold Cross-Validation (Weka 3.5.7)

Network structure (nodes followed by parents)
EXPIRE_FLG(2):
  AGE(1): EXPIRE_FLG
  MAX_BILI_1ST_DAY(2): EXPIRE_FLG
  MAX_BILI_2ND_DAY(2): EXPIRE_FLG
  MAX_BILI_3RD_DAY(2): EXPIRE_FLG
  MAX_HR_1ST_DAY(1): EXPIRE_FLG
  MAX_HR_2ND_DAY(1): EXPIRE_FLG
  MAX_HR_3RD_DAY(1): EXPIRE_FLG
  MAX_SODIUM_1ST_DAY(1): EXPIRE_FLG
  MAX_SODIUM_2ND_DAY(1): EXPIRE_FLG
  MAX_SODIUM_3RD_DAY(1): EXPIRE_FLG
  MIN_SYSBP_1ST_DAY(1): EXPIRE_FLG
  MIN_SYSBP_2ND_DAY(2): EXPIRE_FLG
  MIN_SYSBP_3RD_DAY(2): EXPIRE_FLG
  MIN_WBC_1ST_DAY(2): EXPIRE_FLG
  MIN_WBC_2ND_DAY(2): EXPIRE_FLG
  MIN_WBC_3RD_DAY(3): EXPIRE_FLG
  MIN_POTASSIUM_1ST_DAY(1): EXPIRE_FLG
  MIN_POTASSIUM_2ND_DAY(1): EXPIRE_FLG
  MIN_POTASSIUM_3RD_DAY(1): EXPIRE_FLG
  MAX_BUN_1ST_DAY(1): EXPIRE_FLG
  MAX_BUN_2ND_DAY(2): EXPIRE_FLG
  MAX_BUN_3RD_DAY(2): EXPIRE_FLG
  MIN_GCS_1ST_DAY(2): EXPIRE_FLG
  MAX_TEMP_1ST_DAY(1): EXPIRE_FLG
  MAX_TEMP_2ND_DAY(1): EXPIRE_FLG
  MAX_TEMP_3RD_DAY(1): EXPIRE_FLG
  MIN_BICARBONATE_1ST_DAY(1): EXPIRE_FLG
  MIN_BICARBONATE_2ND_DAY(1): EXPIRE_FLG
  MIN_BICARBONATE_3RD_DAY(1): EXPIRE_FLG
  OUT_1ST_DAY(1): EXPIRE_FLG
  OUT_2ND_DAY(2): EXPIRE_FLG
  OUT_3RD_DAY(2): EXPIRE_FLG

LogScore Bayes: -6340.86525861412
LogScore BDeu: -6366.959980500857
LogScore MDL: -6379.0470996560925
LogScore ENTROPY: -6279.192390839399
LogScore AIC: -6308.192390839399

Correctly Classified Instances 667 68.1307 %
Incorrectly Classified Instances 312 31.8693 %
Kappa statistic 0.2192
Mean absolute error 0.3587
Root mean squared error 0.4729
Relative absolute error 82.7199%
Root relative squared error 101.5712%
Total Number of Instances 979

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**Appendix C. Naïve Bayes Model to Predict Hospital Mortality using Tenfold Cross-Validation (Weka 3.5.7)**

**Class N: Prior probability = 0.75**
Day1_In: Normal Distribution. Mean = 3476.8456 StandardDev = 3990.0661 WeightSum = 1121 Precision = 26.3618304387292
Day1_Out: Normal Distribution. Mean = 1380.4209 StandardDev = 1529.7834 WeightSum = 1121 Precision = 18.041666666666668
Day2_In: Normal Distribution. Mean = 3402.7439 StandardDev = 2685.4955 WeightSum = 1121 Precision = 27.937100850978187
Day3_In: Normal Distribution. Mean = 2316.6936 StandardDev = 2160.9165 WeightSum = 1121 Precision = 23.395042858243453
Age: Normal Distribution. Mean = 67.9885 StandardDev = 15.9864 WeightSum = 1121 Precision = 0.06696414950419527
Sex: Normal Distribution. Mean = 0.5593 StandardDev = 0.4965 WeightSum = 1121 Precision = 1.0
SAPS: Normal Distribution. Mean = 15.645 StandardDev = 5.2134 WeightSum = 1121 Precision = 1.0

**Class Y: Prior probability = 0.25**
Day1_In: Normal Distribution. Mean = 3353.4386 StandardDev = 4357.0549 WeightSum = 370 Precision = 26.3618304387292
Day1_Out: Normal Distribution. Mean = 919.2473 StandardDev = 1207.536 WeightSum = 370 Precision = 18.041666666666668
Day2_In: Normal Distribution. Mean = 4551.4823 StandardDev = 3985.3966 WeightSum = 370 Precision = 27.937100850978187
Day2_Out: Normal Distribution. Mean = 1525.689 StandardDev = 1530.8948 WeightSum = 370 Precision = 14.913083257090577
Day3_In: Normal Distribution. Mean = 3178.4379 StandardDev = 2629.7816 WeightSum = 370 Precision = 23.395042858243453
Day3_Out: Normal Distribution. Mean = 1524.8335 StandardDev = 1289.8183 WeightSum = 370 Precision = 19.74827245804541
Age: Normal Distribution. Mean = 71.8786 StandardDev = 15.5724 WeightSum = 370 Precision = 0.06696414950419527
Sex: Normal Distribution. Mean = 0.5459 StandardDev = 0.4979 WeightSum = 370 Precision = 1.0
SAPS: Normal Distribution. Mean = 18.3135 StandardDev = 5.1574 WeightSum = 370 Precision = 1.0
Class N: Prior probability = 0.68
AGE: Normal Distribution. Mean = 73.1266 StandardDev = 29.8511 WeightSum = 668 Precision = 2.7761194029850746
MAX_BILI_1ST_DAY: Normal Distribution. Mean = 1.2636 StandardDev = 3.6117 WeightSum = 668 Precision = 0.7314606741573033
MAX_BILI_2ND_DAY: Normal Distribution. Mean = 1.1886 StandardDev = 3.5429 WeightSum = 668 Precision = 0.80930235813953
MAX_BILI_3RD_DAY: Normal Distribution. Mean = 1.2842 StandardDev = 3.7578 WeightSum = 668 Precision = 0.8093023255813953
MAX_HR_1ST_DAY: Normal Distribution. Mean = 104.8686 StandardDev = 21.9376 WeightSum = 668 Precision = 1.4375
MAX_HR_2ND_DAY: Normal Distribution. Mean = 101.3868 StandardDev = 21.7548 WeightSum = 668 Precision = 1.4375
MAX_HR_3RD_DAY: Normal Distribution. Mean = 101.1086 StandardDev = 20.7177 WeightSum = 668 Precision = 1.3831775700934579
MAX_SODIUM_1ST_DAY: Normal Distribution. Mean = 139.5247 StandardDev = 5.0459 WeightSum = 668 Precision = 1.34375
MAX_SODIUM_2ND_DAY: Normal Distribution. Mean = 139.6047 StandardDev = 4.6469 WeightSum = 668 Precision = 0.6578947368421053
MAX_SODIUM_3RD_DAY: Normal Distribution. Mean = 139.8189 StandardDev = 4.8872 WeightSum = 668 Precision = 1.0
Precision = 0.10384615384615382
MAX_TEMP_2ND_DAY: Normal Distribution. Mean = 37.4802 StandardDev = 0.7806 WeightSum = 668
Precision = 0.11086956521739133
MAX_TEMP_3RD_DAY: Normal Distribution. Mean = 37.3857 StandardDev = 0.745 WeightSum = 668
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Precision = 14.707057256990678

Class Y: Prior probability = 0.32
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79
Appendix D. Artificial Neural Network Model to Predict Hospital Mortality using Tenfold Cross-Validation (Weka 3.5.7)

Sigmoid Node 0

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Sigmoid Node 1

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Attrib: AGE 3.011444954048342
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Attrib MAX_BILI_2ND_DAY 1.5464510940634086
Attrib MAX_BILI_3RD_DAY 0.7355814781056973
Attrib MAX_HR_1ST_DAY -0.09986320578469327
Attrib MAX_HR_2ND_DAY 3.06998489870333
Attrib MAX_HR_3RD_DAY -4.68952739683681
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Attrib MAX_SODIUM_3RDDAY -4.540032243689924
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Attrib MIN_POTASSIUM_1ST_DAY -3.99229519117954
Attrib MIN_POTASSIUM_2ND_DAY 1.678206335946652
Attrib MIN_POTASSIUM_3RDDAY -3.400032423689924
Attrib MAX_BUN_1STDAY -5.749564980570519
Attrib MAX_BUN_2NDDAY -0.9189037118801223
Attrib MAX_BUN_3RD_DAY 0.9967074071536108
Attrib MIN_GCS_1ST_DAY -5.576630579698842
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Attrib MAX_TEMP_2ND_DAY -0.46950015911189685
Attrib MAX_TEMP_3RD_DAY -3.449938689673831
Attrib MIN_BICARBONATE_1ST_DAY 5.261278142374352
Attrib MIN_BICARBONATE_2ND_DAY -3.3240066307473173
Attrib MIN_BICARBONATE_3RD_DAY 8.246792526456543
Attrib OUT_1STDAY -0.9375725192816013
Attrib OUT_2ND_DAY -8.681170140382594
Attrib OUT_3RD_DAY -2.2276958809920324

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Threshold -2.2143117232441596
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Attrib MAX_BILI_1ST_DAY 3.616139552696913
Attrib MAX_BILI_2ND_DAY 0.9327706577032954
Attrib MAX_BILI_3RD_DAY 0.7646661188849441
Attrib MAX_HR_1ST_DAY 4.2499753537208935
Attrib MAX_HR_2ND_DAY -1.6041387445809268
Attrib MAX_HR_3RD_DAY 0.6140432779823328
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Attrib MAX_SODIUM_3RD_DAY 2.150889216771916
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81
Attrib MIN_WBC_1ST_DAY -0.632396786728002
Attrib MIN_WBC_2ND_DAY 1.8280508394191268
Attrib MIN_WBC_3RD_DAY 6.1067253819110485
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Attrib MIN_POTASSIUM_2ND_DAY 7.4953191963343249
Attrib MIN_POTASSIUM_3RD_DAY 3.142674381602027
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Attrib MAX_TEMP_2ND_DAY 0.34389071970147367
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Attrib MIN_BICARBONATE_3RD_DAY -4.260108530984933
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Inputs Weights
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Attrib MAX_BILI_2ND_DAY 4.956216709597813
Attrib MAX_BILI_3RD_DAY 4.506473870821703
Attrib MAX_HR_1ST_DAY -12.113275422055144
Attrib MAX_HR_2ND_DAY -2.627960221939177
Attrib MAX_HR_3RD_DAY 4.184439595327411
Attrib MAX_SODIUM_1ST_DAY 7.171182198992128
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Attrib MAX_BILI_3RD_DAY  1.099024011158244
Attrib MAX_HR_1ST_DAY  3.101912481231386
Attrib MAX_HR_2ND_DAY  3.350620573675467
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Attrib MIN_POTASSIUM_3RD_DAY  -0.99779778327183316
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Attrib MAX_BUN_2ND_DAY  -0.37385377552140237
Attrib MAX_BUN_3RD_DAY  0.491343471885564
Attrib MIN_GCS_1ST_DAY  -4.574150353346714
Attrib MAX_TEMP_1ST_DAY  5.502345914927062
Attrib MAX_TEMP_2ND_DAY  -0.6101232112300015
Attrib MAX_TEMP_3RD_DAY  -3.4176015133968556
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Attrib MIN_BICARBONATE_2ND_DAY  -1.234377189112169
Attrib MIN_BICARBONATE_3RD_DAY  -2.019857456648258
Attrib OUT_1ST_DAY  0.32612887126923973
Attrib OUT_2ND_DAY  -0.08258903653350672
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Inputs  Weights
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Attrib MAX_HR_2ND_DAY -4.4693024764659155
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Attrib OUT_3RD_DAY 4.053708133912279

Sigmoid Node 17
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Sigmoid Node 18
Inputs  Weights

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Correctly Classified Instances 642  65.5771%
Incorrectly Classified Instances 337  34.4229%
Kappa statistic 0.1928
Mean absolute error 0.3428
Root mean squared error 0.5512
Relative absolute error 79.0545%
Root relative squared error 118.3819%
Total Number of Instances 979

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Appendix E. Simple CART to Predict Hospital Mortality using Tenfold Cross-Validation (Weka 3.5.7)

CART Decision Tree: N(668.0/311.0)
Number of Leaf Nodes: 1
Size of the Tree: 1

Correctly Classified Instances 661 67.5179 %
Incorrectly Classified Instances 318 32.4821 %
Kappa statistic 0.0915
Mean absolute error 0.4154
Root mean squared error 0.4753
Relative absolute error 95.7864 %
Root relative squared error 102.0876 %
Total Number of Instances 979

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