# Vertex Seminar

Predicting Mortality of ICU Patients:

The PhysioNet/Computing in Cardiology Challenge 2012

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# Outline


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# Overview

The goal of this project was to develop a model to predict in-hospital death using the PhysioNet 2012 data

## Motivation

- Prediction of patient-specific outcomes is useful for 1) clinical decision making, 2) improving patient outcomes, and 3) optimizing resource allocation
- Modeling the trajectory of disease or patient outcomes using demographic and/or hospital data is a challenging task, especially for Intensive Care Unit (ICU) patient populations

## Objectives

- Using the 2012 PhysioNet dataset (N=4000), the goal is to predict **if a patient will die in the hospital** using baseline patient characteristics and time series data collected over the span of 48 hours
- Specifically, teams in this challenge were evaluated by their ability to maximize $\boldsymbol{min(Recall, Precision)}$; in other words, we are interested in predicting the positive class but must balance FPs and FNs

# Features

There were 4 baseline and 37 time series features, recorded at various time points across 48 hours

***Baseline***

*Age* (years), *Gender* (0: female, or 1: male), *Height* (cm),
*ICUType* (1: Coronary Care Unit, 2: Cardiac Surgery Recovery Unit, 3: Medical ICU, or 4: Surgical ICU)

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***Dynamic***

*Albumin* (g/dL)
*ALP* [Alkaline phosphatase (IU/L)]
*ALT* [Alanine transaminase (IU/L)]
*AST* [Aspartate transaminase (IU/L)]
*Bilirubin* (mg/dL)
*BUN* [Blood urea nitrogen (mg/dL)]
*Cholesterol* (mg/dL)
*Creatinine* [Serum creatinine (mg/dL)]
*DiasABP* [Invasive diastolic arterial blood pressure (mmHg)]
*FiO2* [Fractional inspired $O_2$ (0-1)]
*GCS* [Glasgow Coma Score (3-15)]
*Glucose* [Serum glucose (mg/dL)]
*HCO3* [Serum bicarbonate (mmol/L)]
*HCT* [Hematocrit (%)]
*HR* [Heart rate (bpm)]
*K* [Serum potassium (mEq/L)]
*Lactate* (mmol/L)
*Mg* [Serum magnesium (mmol/L)]
*MAP* [Invasive mean arterial blood pressure (mmHg)]
*MechVent* [Mechanical ventilation respiration (0:false, or 1:true)]
*Na* [Serum sodium (mEq/L)]
*NIDiasABP* [Non-invasive diastolic arterial blood pressure (mmHg)]
*NIMAP* [Non-invasive mean arterial blood pressure (mmHg)]
*NISysABP* [Non-invasive systolic arterial blood pressure (mmHg)]
*PaCO2* [partial pressure of arterial $CO_2$ (mmHg)]
*PaO2* [Partial pressure of arterial $O_2$ (mmHg)]
*pH* [Arterial pH (0-14)]
*Platelets* (cells/nL)
*RespRate* [Respiration rate (bpm)]
*SaO2* [$O_2$ saturation in hemoglobin (%)]
*SysABP* [Invasive systolic arterial blood pressure (mmHg)]
*Temp* [Temperature (°C)]
*TropI* [Troponin-I (µg/L)]
*TropT* [Troponin-T (µg/L)]
*Urine* [Urine output (mL)]
*WBC* [White blood cell count (cells/nL)]
*Weight* (kg)

# Prevailing modeling strategy

Rather than modeling “long” data, my prevailing hypothesis was that discretizing time and transforming the data into “wide” format would be an optimal strategy primarily due to the sample size and computational constraints

**“Long” data**

| | | $X_1$ | $X_2$ | $X_3$ |
|---|---|---|---|---|
| $P_1$ | $T_1$ | | | |
| | $T_2$ | | | |
| | $T_3$ | | | |
| | $T_4$ | | | |
| $P_2$ | $T_1$ | | | |
| | $T_2$ | | | |
| | $T_3$ | | | |
| | $T_4$ | | | |

Form discrete time “bins”

| | | | $X_1$ | $X_2$ | $X_3$ |
|---|---|---|---|---|---|
| $P_1$ | $\boldsymbol{B_1}$ | $T_1$ | | | |
| | | $T_2$ | | | |
| | $\boldsymbol{B_2}$ | $T_3$ | | | |
| | | $T_4$ | | | |
| $P_2$ | $\boldsymbol{B_1}$ | $T_1$ | | | |
| | | $T_2$ | | | |
| | $\boldsymbol{B_2}$ | $T_3$ | | | |
| | | $T_4$ | | | |

**“Wide” data**, where $X_i$ have been summarized by some function

| | $B_1$ | | | $B_2$ | | |
|---|---|---|---|---|---|---|
| | $X_1$ | $X_2$ | $X_3$ | $X_1$ | $X_2$ | $X_3$ |
| $P_1$ | | | | | | |
| $P_2$ | | | | | | |

$P_i$: the $i$th person
$T_i$: the $i$th continuous time point
$X_i$: the $i$th feature
$B_i$: the $i$th discrete (binned) time point

# Approach

This project was carried out in four distinct steps: explore, wrangle, train, and evaluate

**Phase 1** *(completed in R)*

**Phase 2** *(completed in Python)*

1

## *Explore*

- (A) Patient attributes & outcomes – examine distributions and class imbalance
- (B) Aggregated features – explore distributions, outliers, missingness, correlations
- (C) Longitudinal features – corroborate hypothesis about optimal modeling strategy and define discrete time bins

2

## *Wrangle*

- Remove redundant features
- Discretize time, calculate within-person time series features, pivot to wide
- Partition the train and test sets (80/20 split), stratifying by the imbalanced outcome
- Impute train and test data in an unbiased manner with missForest

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## *Train*

- Engineer ensemble model
- Establish training pipeline that winsorizes, normalizes, and tunes hyperparameters within a k-fold CV framework
- Investigate optimal base learners and meta learners through trial and error
- Generate test set predictions (probability of death)

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## *Evaluate*

- Plot PR curve and identify the optimal threshold
- Convert probability predictions to binary predictions and calculate standard suite of metrics
- Benchmark results against 2012 competition teams
- Conduct high-level feature importance analysis

# Section 1: Explore

# (A) Patient attributes by outcome

As a first step, I started by examining the distributions of patient attributes by the outcome

| | Survived (N=3446) | Died (N=554) | P-value[1] |
|---|---|---|---|
| **Age** | | | <0.01 |
| <50 | 764 (22.2%) | 72 (13.0%) | |
| 50-59 | 549 (15.9%) | 61 (11.0%) | |
| 60-69 | 599 (17.4%) | 83 (15.0%) | |
| 70-79 | 698 (20.3%) | 117 (21.1%) | |
| 80+ | 836 (24.3%) | 221 (39.9%) | |
| **Gender** | | | 0.34 |
| Female | 1498 (43.5%) | 253 (45.7%) | |
| Male | 1946 (56.5%) | 300 (54.2%) | |
| Missing | 2 (0.1%) | 1 (0.2%) | |
| **Height** | | | 0.01 |
| Short (<165 cm) | 569 (16.5%) | 94 (17.0%) | |
| Average (165-180 cm) | 895 (26.0%) | 111 (20.0%) | |
| Tall (180+ cm) | 381 (11.1%) | 56 (10.1%) | |
| Missing | 1601 (46.5%) | 293 (52.9%) | |
| **ICU Type** | | | <0.01 |
| Cardiac Surgery Recovery Unit | 831 (24.1%) | 43 (7.8%) | |
| Coronary Care Unit | 496 (14.4%) | 81 (14.6%) | |
| Medical ICU | 1206 (35.0%) | 275 (49.6%) | |
| Surgical ICU | 913 (26.5%) | 155 (28.0%) | |

[1]Calculated via a chi-squared test for independence

- There is severe class imbalance, with 86% of the patients surviving and 14% of the patients dying in-hospital; this requires special attention during train/test splits and training
- The distributions of patient baseline features vary significantly across the different outcome classes
- A lot of patients are missing height values, which should be considered for imputation

# (B) Aggregating the dynamic features for exploration

Given the prevailing modeling strategy, dynamic features were aggregated by taking the mean (ignoring missing values) for each person; this simplifies exploration of the data, as now we have one row per patient

**"Long" data**

| | | $X_1$ | $X_2$ | $X_3$ |
|---|---|---|---|---|
| $P_1$ | $T_1$ | | | |
| | $T_2$ | | | |
| | $T_3$ | | | |
| | $T_4$ | | | |
| $P_2$ | $T_1$ | | | |
| | $T_2$ | | | |
| | $T_3$ | | | |
| | $T_4$ | | | |

$P_i$: the $i$th person
$T_i$: the $i$th continuous time point
$X_i$: the $i$th feature

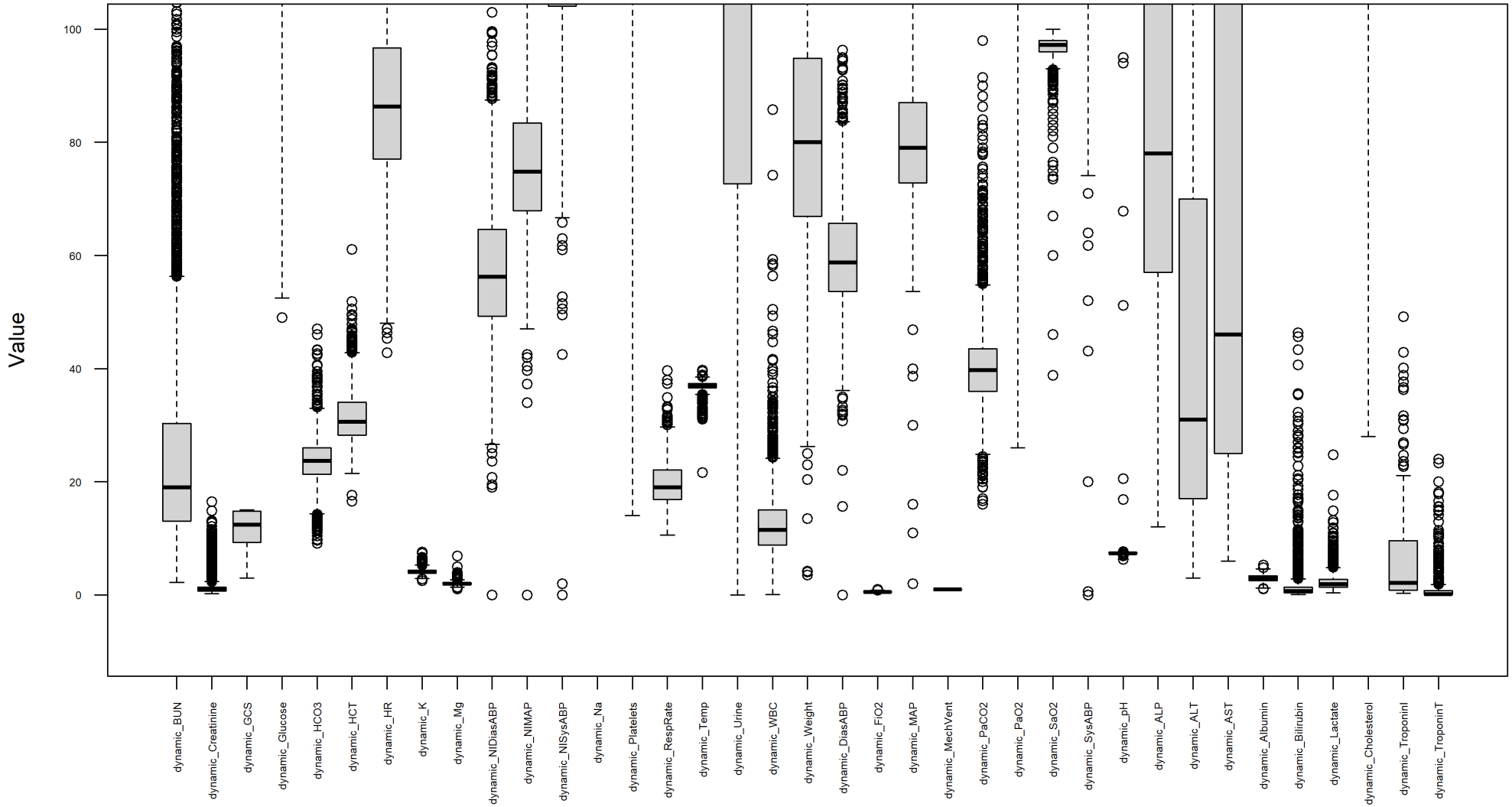
**"Wide" data**, where $X_i$ were obtained by taking the mean

| | $X_1$ | $X_2$ | $X_3$ |
|---|---|---|---|
| $P_1$ | | | |
| $P_2$ | | | |

This simplifies exploration of the dynamic features and allows us to look at things like pairwise correlations, etc.

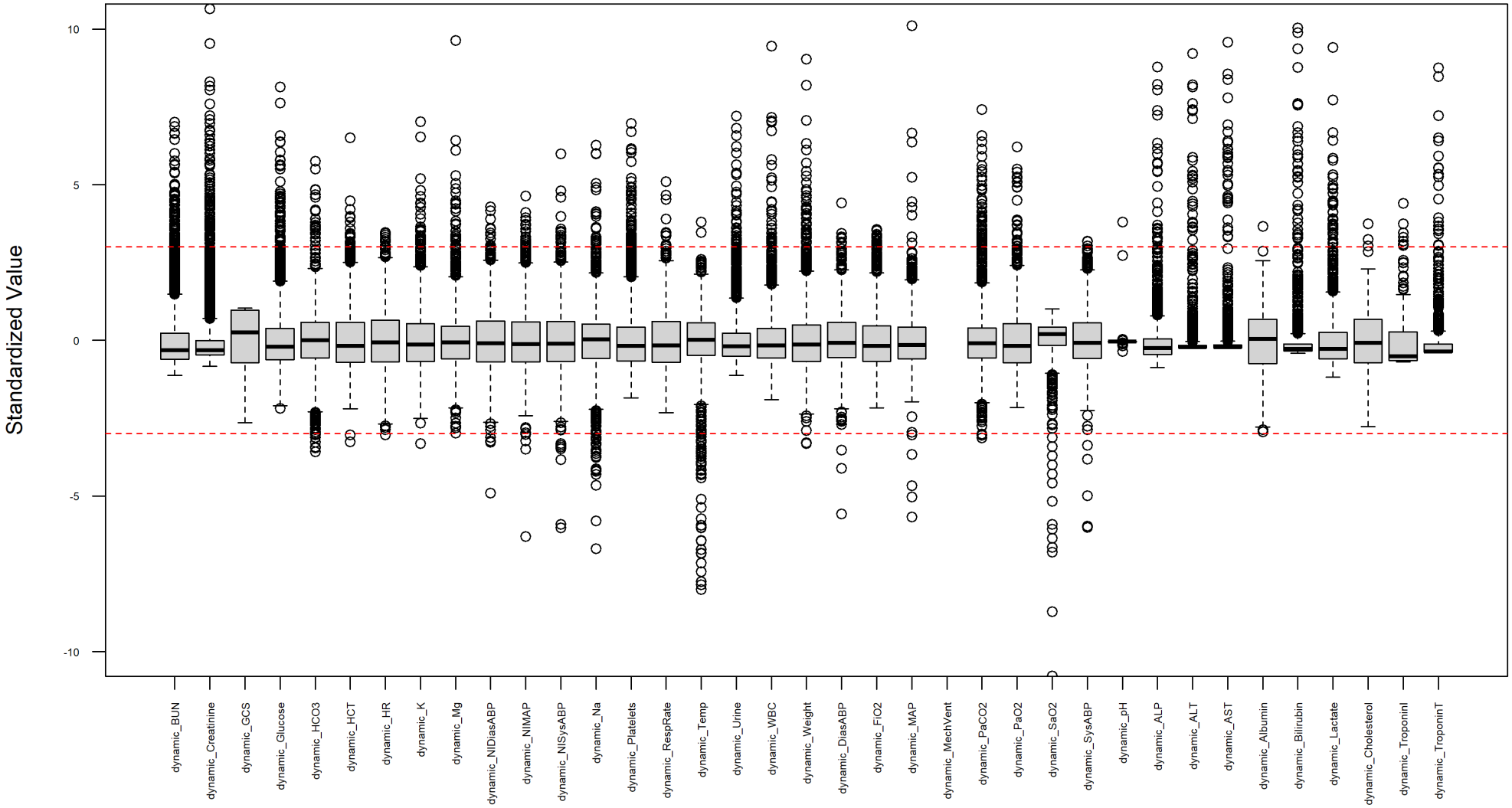
# (B) Distributions of dynamic features *(1 of 2)*

Analyzing the distributions of each feature reveals that they are on completely different scales; normalization during modeling is key, otherwise features with higher variation will dominate



# (B) Distributions of dynamic features *(2 of 2)*

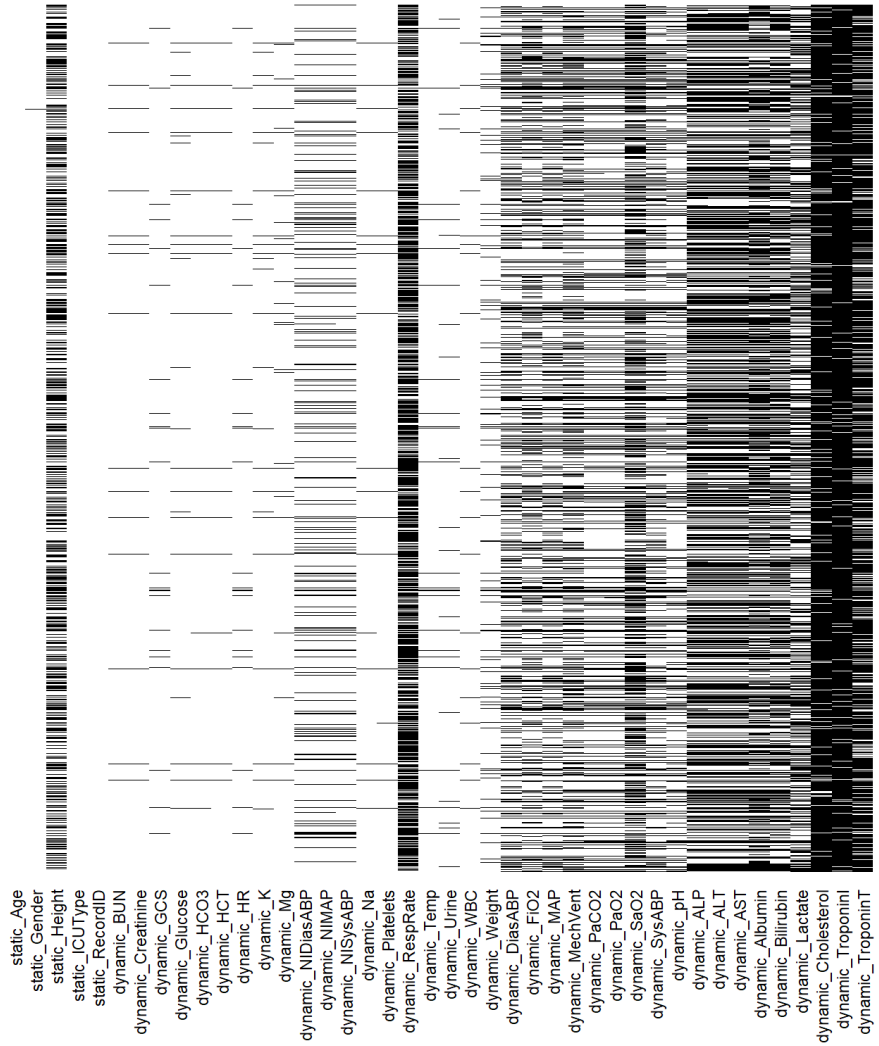
Upon standardizing the features (Z-score), much of the data still appeared to be “outliers” >3 deviations away from the mean; winsorization or clipping of values during modeling should help deal with this issue



# (B) Missingness patterns

An analysis of missingness revealed that some features may be removed and that the data may be MAR

**Heatmap of missingness (in black) by feature**




- Extreme missingness observed in Troponin I/T variables and Cholesterol (≈80%+)
- Some evidence that data may be missing at random (MAR), or in other words, the missingness in one variable is explained by missingness in another (i.e., they are correlated)
- This motivates potentially 1) removing Troponin I/T and Cholesterol, and 2) using imputation methods tailored for MAR data

# (B) Pairwise correlations among dynamic variables

## Correlation analysis supports dropping Troponin I/F and Cholesterol and using regression-based imputation

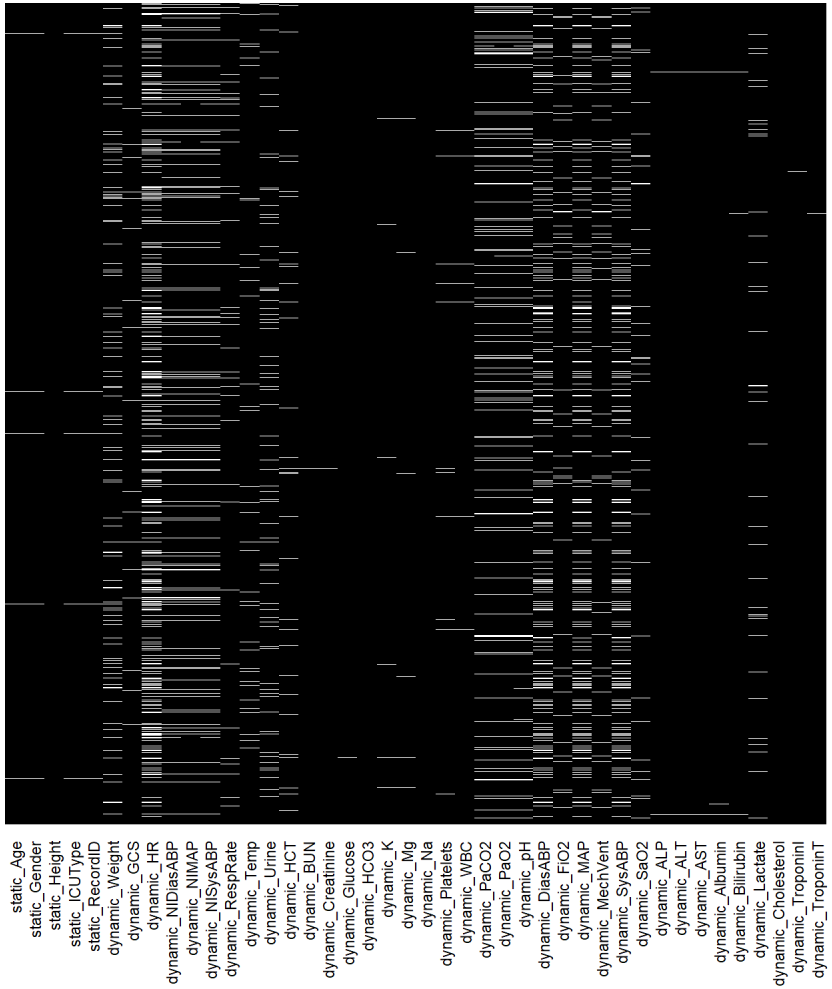
| | Outcome | BUN | Creatinine | GCS | Glucose | HCO3 | HCT | HR | K | Mg | NIDiasABP | NIMAP | NISysABP | Na | Platelets | RespRate | Temp | Urine | WBC | Weight | DiasABP | FiO2 | MAP | PaCO2 | PaO2 | SaO2 | SysABP | pH | ALP | ALT | AST | Albumin | Bilirubin | Lactate | Cholesterol | TroponinI | TroponinT |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Outcome | NA | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| BUN | 0.22 | NA | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Creatinine | 0.12 | 0.68 | NA | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| GCS | (0.26) | (0.03) | (0.02) | NA | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Glucose | 0.11 | 0.12 | 0.04 | (0.11) | NA | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| HCO3 | (0.13) | (0.24) | (0.25) | 0.17 | (0.08) | NA | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| HCT | (0.01) | (0.10) | (0.06) | 0.03 | 0.03 | 0.11 | NA | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| HR | 0.07 | (0.06) | (0.03) | (0.13) | 0.05 | (0.11) | (0.07) | NA | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| K | 0.02 | 0.28 | 0.31 | (0.01) | 0.07 | (0.10) | (0.06) | 0.02 | NA | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mg | 0.06 | 0.30 | 0.16 | (0.05) | 0.03 | (0.02) | (0.01) | (0.09) | 0.25 | NA | | | | | | | | | | | | | | | | | | | | | | | | | | |
| NIDiasABP | (0.09) | (0.14) | (0.03) | 0.01 | (0.01) | 0.06 | 0.27 | 0.17 | (0.14) | (0.04) | NA | | | | | | | | | | | | | | | | | | | | | | | | | |
| NIMAP | (0.08) | (0.12) | (0.01) | 0.03 | 0.01 | 0.10 | 0.24 | 0.04 | (0.15) | (0.09) | 0.89 | NA | | | | | | | | | | | | | | | | | | | | | | | | |
| NISysABP | (0.06) | (0.04) | 0.03 | 0.06 | 0.04 | 0.11 | 0.12 | (0.11) | (0.12) | (0.05) | 0.56 | 0.83 | NA | | | | | | | | | | | | | | | | | | | | | | | |
| Na | 0.02 | 0.03 | (0.05) | (0.15) | (0.02) | 0.09 | 0.11 | (0.01) | (0.23) | (0.00) | 0.10 | 0.12 | 0.10 | NA | | | | | | | | | | | | | | | | | | | | | | |
| Platelets | (0.02) | (0.04) | (0.03) | 0.09 | 0.00 | 0.08 | 0.10 | 0.03 | (0.01) | (0.01) | 0.07 | 0.06 | 0.06 | (0.05) | NA | | | | | | | | | | | | | | | | | | | | | |
| RespRate | 0.11 | (0.00) | (0.03) | (0.10) | 0.05 | (0.04) | (0.02) | 0.33 | (0.07) | 0.03 | 0.02 | (0.02) | (0.05) | 0.02 | 0.10 | NA | | | | | | | | | | | | | | | | | | | | |
| Temp | (0.06) | (0.19) | (0.11) | (0.18) | (0.03) | 0.07 | (0.03) | 0.21 | (0.07) | (0.11) | 0.03 | 0.04 | 0.03 | 0.01 | (0.02) | 0.08 | NA | | | | | | | | | | | | | | | | | | | |
| Urine | (0.12) | (0.20) | (0.17) | 0.16 | (0.02) | 0.11 | 0.10 | (0.03) | (0.12) | (0.10) | 0.17 | 0.16 | 0.06 | 0.02 | 0.05 | (0.07) | 0.02 | NA | | | | | | | | | | | | | | | | | | |
| WBC | 0.09 | 0.10 | 0.03 | (0.11) | 0.05 | (0.13) | 0.04 | 0.12 | 0.07 | 0.06 | (0.09) | (0.09) | (0.06) | 0.00 | 0.25 | 0.15 | 0.04 | (0.11) | NA | | | | | | | | | | | | | | | | | |
| Weight | (0.06) | 0.08 | 0.09 | (0.05) | 0.07 | 0.08 | 0.04 | 0.02 | 0.16 | 0.05 | 0.01 | 0.00 | (0.02) | (0.04) | (0.03) | (0.07) | 0.09 | 0.05 | 0.04 | NA | | | | | | | | | | | | | | | | |
| DiasABP | (0.06) | (0.16) | (0.10) | (0.05) | 0.01 | 0.07 | 0.27 | 0.16 | (0.12) | (0.09) | 0.54 | 0.47 | 0.23 | 0.11 | 0.04 | 0.01 | 0.05 | 0.17 | (0.03) | 0.05 | NA | | | | | | | | | | | | | | | |
| FiO2 | 0.05 | 0.02 | 0.00 | 0.18 | 0.05 | (0.03) | 0.03 | 0.12 | 0.10 | 0.05 | (0.05) | (0.08) | (0.09) | (0.09) | 0.03 | 0.23 | (0.03) | (0.00) | 0.06 | 0.06 | (0.09) | NA | | | | | | | | | | | | | | |
| MAP | (0.03) | (0.10) | (0.06) | (0.00) | 0.00 | 0.11 | 0.23 | 0.01 | (0.20) | (0.11) | 0.42 | 0.46 | 0.35 | 0.15 | 0.07 | 0.00 | 0.03 | 0.12 | (0.06) | 0.02 | 0.50 | (0.14) | NA | | | | | | | | | | | | | |
| PaCO2 | (0.09) | (0.07) | (0.11) | 0.11 | (0.02) | 0.70 | 0.09 | (0.02) | 0.15 | 0.01 | (0.04) | (0.02) | 0.02 | 0.07 | 0.10 | (0.12) | 0.02 | 0.03 | (0.04) | 0.18 | 0.00 | 0.02 | 0.05 | NA | | | | | | | | | | | | |
| PaO2 | (0.09) | (0.18) | (0.11) | (0.05) | (0.04) | (0.02) | (0.15) | (0.09) | 0.01 | (0.00) | (0.02) | (0.02) | (0.01) | (0.03) | (0.15) | (0.21) | (0.00) | 0.07 | (0.08) | (0.10) | (0.05) | (0.13) | (0.06) | (0.13) | NA | | | | | | | | | | | |
| SaO2 | (0.08) | (0.07) | (0.03) | (0.01) | 0.01 | (0.09) | (0.11) | (0.06) | (0.02) | 0.00 | (0.03) | 0.02 | 0.05 | (0.03) | (0.01) | (0.14) | 0.08 | 0.05 | (0.02) | (0.05) | (0.03) | (0.18) | 0.02 | (0.18) | 0.35 | NA | | | | | | | | | | |
| SysABP | (0.06) | (0.05) | (0.04) | 0.01 | 0.05 | 0.14 | 0.10 | (0.19) | (0.14) | (0.06) | 0.26 | 0.43 | 0.49 | 0.11 | 0.00 | (0.10) | 0.02 | 0.10 | (0.10) | (0.03) | 0.61 | (0.16) | 0.38 | 0.03 | (0.05) | 0.03 | NA | | | | | | | | | |
| pH | 0.03 | (0.01) | 0.01 | 0.03 | 0.00 | (0.02) | 0.00 | 0.01 | 0.01 | (0.01) | (0.02) | (0.02) | (0.00) | (0.03) | 0.01 | (0.01) | 0.01 | (0.00) | (0.01) | (0.01) | (0.01) | 0.04 | (0.00) | (0.01) | (0.02) | 0.00 | (0.00) | NA | | | | | | | | |
| ALP | 0.13 | 0.17 | 0.15 | 0.08 | 0.02 | (0.10) | (0.03) | 0.02 | 0.05 | 0.05 | (0.04) | (0.05) | (0.05) | (0.06) | 0.11 | (0.07) | (0.07) | (0.05) | 0.10 | (0.04) | (0.08) | (0.05) | (0.03) | (0.05) | (0.10) | (0.08) | (0.08) | (0.01) | NA | | | | | | | |
| ALT | 0.07 | 0.02 | 0.08 | (0.06) | 0.07 | (0.10) | 0.06 | 0.11 | 0.00 | 0.03 | 0.02 | 0.02 | 0.00 | 0.02 | (0.10) | 0.02 | (0.02) | (0.06) | 0.01 | (0.01) | 0.02 | 0.03 | 0.03 | (0.10) | (0.04) | (0.10) | (0.07) | (0.01) | 0.09 | NA | | | | | | |
| AST | 0.12 | 0.03 | 0.10 | (0.13) | 0.11 | (0.14) | 0.02 | 0.13 | 0.06 | 0.05 | (0.02) | (0.03) | (0.04) | 0.02 | (0.11) | 0.04 | (0.02) | (0.08) | 0.03 | 0.00 | 0.03 | 0.06 | (0.02) | (0.12) | (0.03) | (0.11) | (0.07) | (0.00) | 0.13 | 0.85 | NA | | | | | |
| Albumin | (0.18) | (0.13) | (0.04) | 0.21 | 0.05 | 0.26 | 0.35 | (0.21) | (0.08) | 0.04 | 0.29 | 0.31 | 0.27 | 0.05 | 0.03 | (0.13) | 0.01 | 0.17 | (0.13) | 0.00 | 0.15 | (0.05) | 0.19 | 0.13 | 0.16 | 0.04 | 0.18 | 0.02 | (0.16) | (0.00) | (0.04) | NA | | | | |
| Bilirubin | 0.20 | 0.21 | 0.16 | (0.01) | (0.05) | (0.15) | (0.07) | 0.00 | (0.02) | 0.17 | (0.05) | (0.07) | (0.06) | (0.12) | (0.20) | (0.08) | (0.12) | (0.09) | 0.01 | 0.04 | (0.08) | 0.03 | (0.07) | (0.16) | (0.10) | 0.00 | (0.08) | (0.01) | 0.21 | 0.08 | 0.10 | (0.09) | NA | | | |
| Lactate | 0.21 | 0.06 | 0.08 | (0.26) | 0.20 | (0.21) | (0.01) | 0.17 | 0.09 | 0.04 | (0.05) | (0.07) | (0.09) | 0.03 | (0.18) | 0.06 | (0.08) | (0.04) | 0.07 | 0.02 | 0.01 | 0.12 | (0.08) | (0.19) | 0.02 | (0.09) | (0.13) | 0.00 | 0.07 | 0.33 | 0.47 | (0.10) | 0.22 | NA | | |
| Cholesterol | (0.07) | (0.10) | (0.12) | 0.03 | 0.12 | 0.09 | 0.27 | (0.12) | 0.04 | 0.10 | 0.08 | 0.06 | (0.00) | (0.12) | (0.00) | 0.05 | 0.08 | 0.04 | (0.05) | (0.03) | 0.09 | 0.03 | 0.10 | 0.07 | 0.09 | 0.06 | 0.08 | 0.03 | 0.04 | (0.07) | (0.05) | 0.42 | (0.08) | (0.02) | NA | |
| TroponinI | 0.04 | 0.08 | (0.00) | 0.00 | 0.07 | (0.00) | 0.04 | (0.02) | (0.01) | 0.08 | 0.06 | 0.03 | (0.03) | (0.03) | (0.02) | 0.12 | (0.04) | (0.03) | (0.05) | 0.04 | (0.01) | 0.09 | (0.04) | (0.12) | 0.03 | 0.09 | (0.04) | (0.05) | (0.18) | (0.05) | (0.08) | 0.18 | (0.04) | (0.11) | (0.25) | NA |
| TroponinT | 0.00 | (0.03) | 0.00 | 0.00 | 0.02 | (0.05) | 0.14 | (0.03) | 0.03 | 0.08 | (0.01) | (0.07) | (0.17) | (0.11) | (0.02) | 0.01 | 0.05 | 0.02 | 0.06 | (0.03) | 0.04 | 0.03 | (0.05) | (0.10) | 0.05 | 0.02 | (0.19) | (0.02) | (0.08) | 0.05 | 0.10 | 0.10 | (0.03) | 0.05 | 0.10 | NA |

- Dropping Troponin I/F and Cholesterol is warranted, as they are barely correlated with the outcome but are correlated with other features (so may be redundant)
  - Pairwise correlations provide further evidence that regression-based imputation approaches may be valid

# (C) Corroborating the modeling strategy

Lastly, to understand if modeling “long” data was viable, I examined the available dynamic features across time

**Heatmap of missingness (in black) by feature, ordered by patient and continuous time**




- There is substantial missingness in this data, with most features having 80%+ missingness
- Due to the sparsity and number of observations, imputing this data would be very challenging
- Evidence supports transforming to wide format and leveraging tabular ML algorithms

# (C) Going from “long” to “wide”

Recall that transforming the data from “long” to “wide” requires careful selection of a discrete time bin

**“Long” data**

| | | $X_1$ | $X_2$ | $X_3$ |
|---|---|---|---|---|
| $P_1$ | $T_1$ | | | |
| | $T_2$ | | | |
| | $T_3$ | | | |
| | $T_4$ | | | |
| $P_2$ | $T_1$ | | | |
| | $T_2$ | | | |
| | $T_3$ | | | |
| | $T_4$ | | | |

Choosing a discrete time bin is critical

| | | | $X_1$ | $X_2$ | $X_3$ |
|---|---|---|---|---|---|
| $P_1$ | $\boldsymbol{B_1}$ | $T_1$ | | | |
| | | $T_2$ | | | |
| | $\boldsymbol{B_2}$ | $T_3$ | | | |
| | | $T_4$ | | | |
| $P_2$ | $\boldsymbol{B_1}$ | $T_1$ | | | |
| | | $T_2$ | | | |
| | $\boldsymbol{B_2}$ | $T_3$ | | | |
| | | $T_4$ | | | |

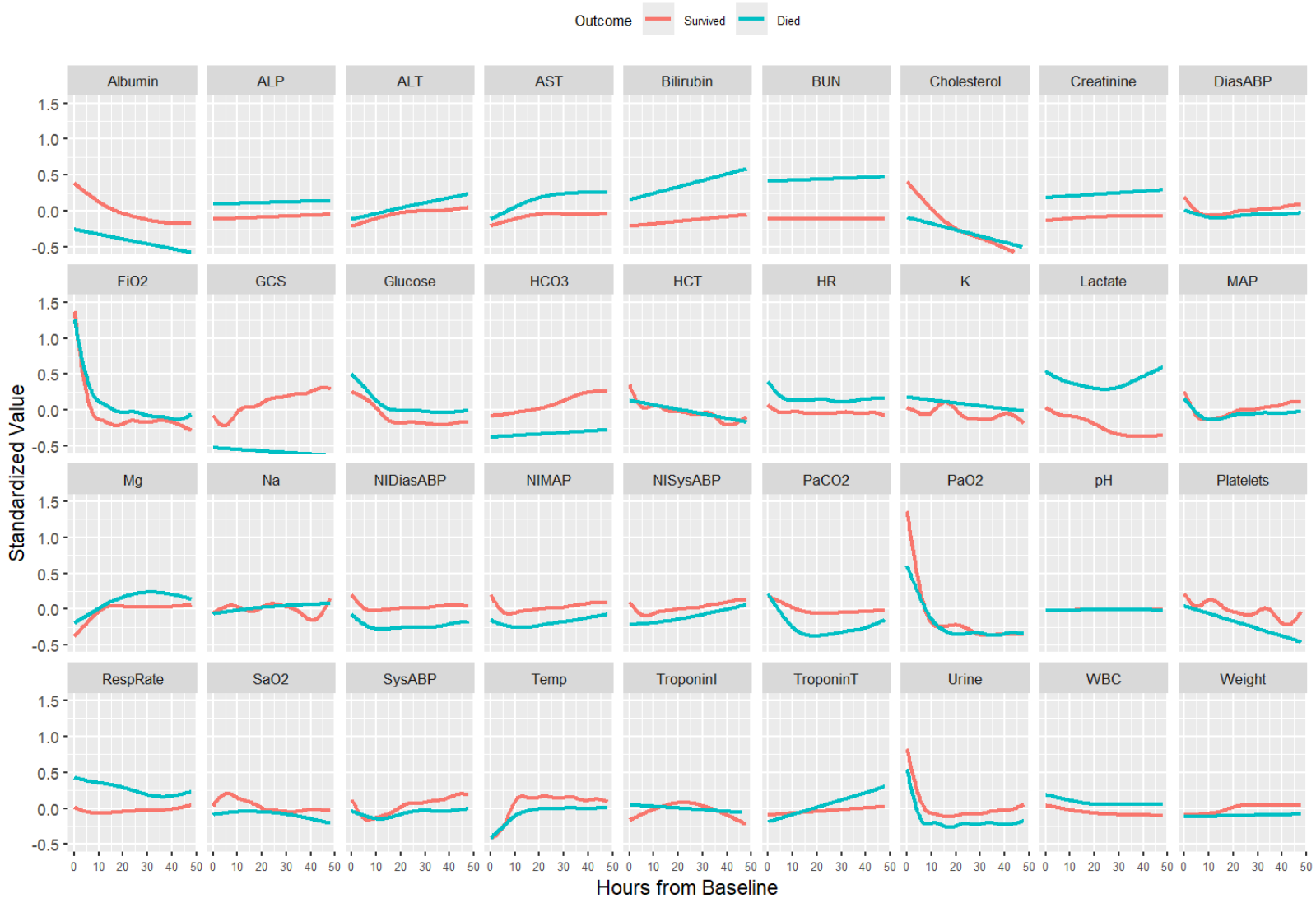
**“Wide” data**, where $X_i$ have been summarized by some function

| | $B_1$ | | | $B_2$ | | |
|---|---|---|---|---|---|---|
| | $X_1$ | $X_2$ | $X_3$ | $X_1$ | $X_2$ | $X_3$ |
| $P_1$ | | | | | | |
| $P_2$ | | | | | | |

$P_i$: the $i$th person
$T_i$: the $i$th continuous time point
$X_i$: the $i$th feature
$B_i$: the $i$th discrete (binned) time point

# (C) Identifying a discrete time window *(1 of 2)*

To inform the optimal discrete time window, I looked for trends in the dynamic features across continuous time

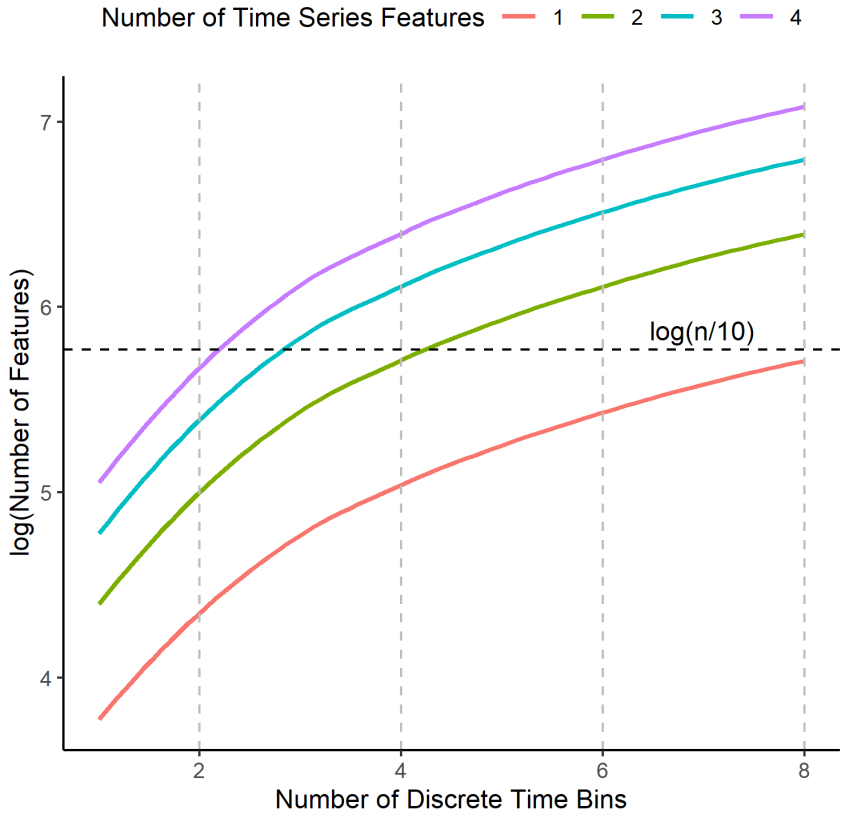



- I plotted the average standardized values for patients in both classes across continuous time, using splines
- There was some evidence of oscillatory or cyclic patterns in some variables (e.g., K, Platelets)
- Can make an argument that discretizing time by two 24-hour bins would capture these cycles

# (C) Identifying a discrete time window *(2 of 2)*

Given the explosion in cardinality and diminishing completeness that is observed when increasing the number of discrete time bins, I elected to go with two 24-hour bins

***As you increase the number of discrete time bins, the number of features in the training data (cardinality) explodes…***




***As you increase the number of discrete time bins, the proportion of dynamic features with at least one complete observation decreases…***

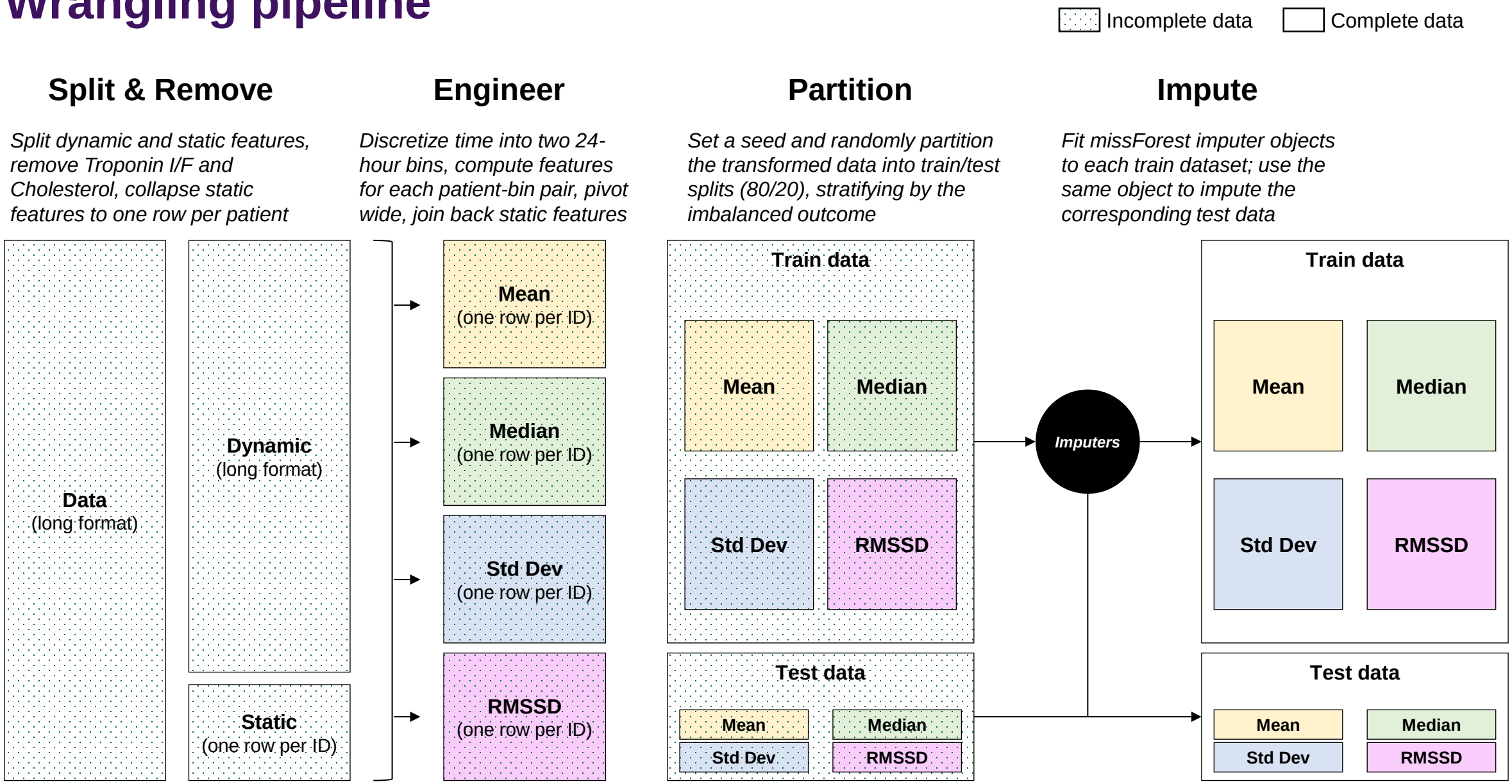
| | One 48-hr bin | Two 24-hr bins | Four 12-hr bins | Six 8-hr bins | Eight 6-hr bins |
|---|---|---|---|---|---|
| Bin 1 | 0.70 | 0.69 | 0.62 | 0.57 | 0.53 |
| Bin 2 | | 0.62 | 0.52 | 0.49 | 0.45 |
| Bin 3 | | | 0.49 | 0.44 | 0.44 |
| Bin 4 | | | 0.48 | 0.42 | 0.38 |
| Bin 5 | | | | 0.44 | 0.38 |
| Bin 6 | | | | 0.40 | 0.40 |
| Bin 7 | | | | | 0.40 |
| Bin 8 | | | | | 0.35 |
| **Avg** | **0.70** | **0.65** | **0.53** | **0.46** | **0.42** |

# Summary of exploration

| Data type | Visualization(s) | Question(s) | Implications & decisions |
|---|---|---|---|
| **(A) Patient attributes & outcomes** | Table 1 | ▪ Is there outcome imbalance?<br>▪ Are patient attributes balanced across the outcome?<br>▪ Are there missing patient attributes? | ▪ Need to deal with outcome imbalance in train/test split and modeling<br>▪ Distribution of attributes vary<br>▪ Height is often missing – consider imputing |
| **(B) Aggregated features** | Boxplots | ▪ Are the features on the same scale?<br>▪ Are there any outliers that need to be dealt with? | ▪ Need to normalize during modeling<br>▪ Need to winsorize during modeling |
| | Heatmap | ▪ Are there missing features?<br>▪ If so, are there any missingness patterns to be gleaned? | ▪ Tropinin I/F and Cholesterol have substantial missingness – consider removing<br>▪ Data looks MAR – consider regression-based imputation |
| | Correlation matrix | ▪ Are the continuous variables correlated with the outcome and amongst each other? | ▪ Tropinin I/F and Cholesterol are barely correlated with outcome, so okay to remove<br>▪ Others are correlated, which supports regression-based imputation |
| **(C) Longitudinal features** | Heatmap | ▪ How much missingness is there across time?<br>▪ Can this inform the optimal modeling strategy? | ▪ Substantial missingness, which would be difficult to impute<br>▪ Best approach is to discretize time, pivot wide, and use tabular machine learning methods |
| | Spaghetti plots | ▪ Are there meaningful trends across time that may inform the discretization strategy? | ▪ Can make an argument that two 24-hour bins captures adequate signal in the data |
| | Line plot, frequency table | ▪ Are there other things we should consider to inform the discretization strategy?<br>▪ Can we confirm an optimal time bin? | ▪ As a function of the number of bins, consider cardinality and the proportion of columns with at least one observation<br>▪ Confirmed that two 24-hour bins is optimal for this problem |

# Section 2: Wrangle

# Wrangling pipeline



# Feature engineering *(1 of 2)*

The “engineer” phase involved 1) discretizing time into two 24-hour bins, 2) calculating four time series features for each patient-bin pair, and then 3) pivoting the data into wide format

***Discretize time into two 24-hour bins***

| ID | Time | **Time Bin** | Predictor |
|---|---|---|---|
| A | 1.3 | **1** | $x_1$ |
| A | 4.5 | **1** | $x_2$ |
| A | 7.8 | **1** | $x_3$ |
| A | 12.0 | **1** | $x_4$ |
| A | 21.0 | **1** | $x_5$ |
| A | 24.6 | **2** | $x_{6,}$ |
| A | 29.0 | **2** | $x_7$ |
| A | 40.0 | **2** | $x_8$ |
| A | 42.1 | **2** | $x_9$ |

***Calculate time series features for each patient-bin pair***

| ID | Time Bin | Predictor – Mean | Predictor – Median | Predictor – Std Dev | Predictor – RMSSD |
|---|---|---|---|---|---|
| A | 1 | $x_{1,1}$ | $x_{1,2}$ | $x_{1,3}$ | $x_{1,4}$ |
| A | 2 | $x_{2,1}$ | $x_{2,2}$ | $x_{2,3}$ | $x_{2,4}$ |

***Pivot the data into wide format, where there is one row per patient and 8 columns per predictor***

| ID | Predictor – mean (bin 1) | Predictor – median (bin 1) | Predictor – sd (bin 1) | Predictor – rmssd (bin 1) | Predictor – mean (bin 2) | Predictor – median (bin 2) | Predictor – sd (bin 2) | Predictor – rmssd (bin 2) |
|---|---|---|---|---|---|---|---|---|
| A | $x_{1,1}$ | $x_{1,2}$ | $x_{1,3}$ | $x_{1,4}$ | $x_{1,5}$ | $x_{1,6}$ | $x_{1,7}$ | $x_{1,8}$ |

- The static features are joined back to this data prior to imputing
- Some patients may not have observations in both periods, which induces missingness

# Imputation strategy

I used missForest to impute train and test data, as it is a robust state-of-the-art method for MAR data

Requires:

$X$, our $n \times p$ matrix for imputation

$\gamma$, the stopping criterion (it works in iterations, stopping when the difference between iteration `i` and `i + 1` of the imputed dataframes begins to increase for categorical and numeric variables, or after 10 iterations with the default `maxiter` parameter)

Algorithm:

1. Make an initial guess for all missing categorical/numeric values (e.g. mean, mode)
2. $k \leftarrow$ vector of column indices in $X$, sorted in ascending order of % missing
3. while not $\gamma$ do:
4. $\quad X_{old}^{imp} \leftarrow$ store previous imputed matrix
5. $\quad$ for $s$ in $k$ do:
6. $\quad\quad$ Fit a random forest predicting the non-missing values of $X_s$: $y_{obs}^{(s)} \sim x_{obs}^{(s)}$
7. $\quad\quad$ Use this to predict the missing values of $X_s$: predict $y_{mis}^{(s)}$ using $x_{mis}^{(s)}$
8. $\quad\quad X_{new}^{imp} \leftarrow$ update imputed matrix, using the predicted $y_{mis}^{(s)}$
9. $\quad$ end for
10. $\quad$ update $\gamma$
11. end while
12. return the final imputed matrix $X^{imp}$

## *In words…*

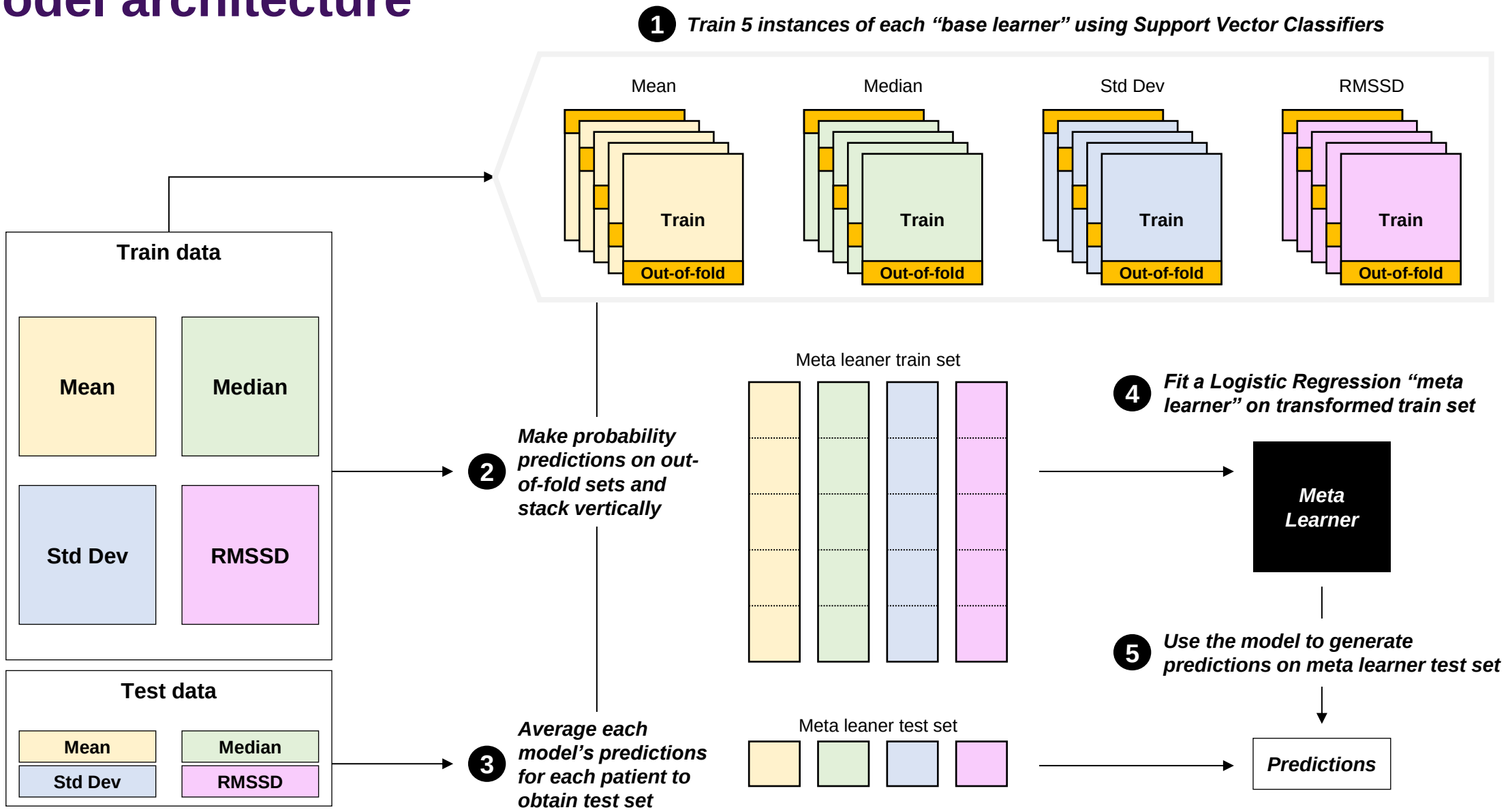
- *Impute all missing data using the mean/mode*
- *For each variable with missing values, fit a random forest on the observed part and then predict the missing part*
- *Repeat iteratively until a stopping criterion is met, or a maximum number of user-specified iterations is reached*
- *After the object is fit, apply it to the test data to preclude any "data leakage" (applies the same process using the same mean/modes and models)*



Stekhoven, D.J. and Bühlmann, P., 2012. MissForest—non-parametric missing value imputation for mixed-type data. *Bioinformatics*, 28(1), pp.112-118.

# Section 3: Train

# Model architecture



# Training considerations

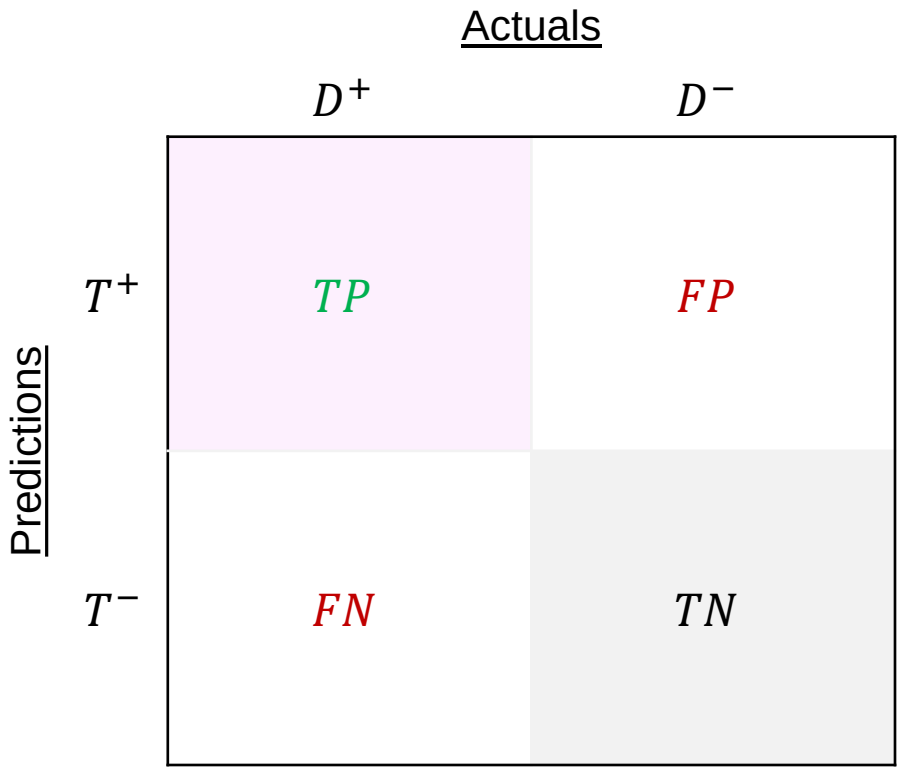
I considered the following components when training machine learning models

| | Transformations[1] | Model choice | Tuned parameters | Tuning strategy | Metric optimized |
|---|---|---|---|---|---|
| ***Base learners*** | Winsorization, Z-score normalization | Support Vector Classifier (SVC) | Tuned: C<br>Preset: kernel (rbf), class weight (balanced) | Grid search, within 5-fold CV framework | Average precision |
| ***Meta learner*** | Min-max normalization | Logistic Regression (LR) | Preset: class weight (balanced) | N/A – preset parameters | N/A – preset parameters |
| ***Reasons*** | ▪ Winsorization used to clip outliers<br>▪ Z-score is a common choice for continuous data on different scales<br>▪ Min-max is a common choice for probabilities | ▪ SVC: outperformed the standard suite of models upon experimentation<br>▪ LR: linear model is typically chosen for meta learner, as the base learners are already flexible | ▪ SVC: C controls regularization, which is commonly tuned; other parameters preset based on domain knowledge<br>▪ LR: class weight set to balanced based on the outcome imbalance | ▪ Hyperparameter space was small enough to utilize a grid search on a local computer | ▪ Average precision accounts for the trade-off between FPs and FNs when trying to predict TPs amidst class imbalance |

[1]The same transformations were made to train and test data to prevent “data leakage”

# Optimizing for average precision

I trained my models to optimize for average precision, as this metric focuses on predicting TPs while minimizing both FNs and FPs in cases of class imbalance



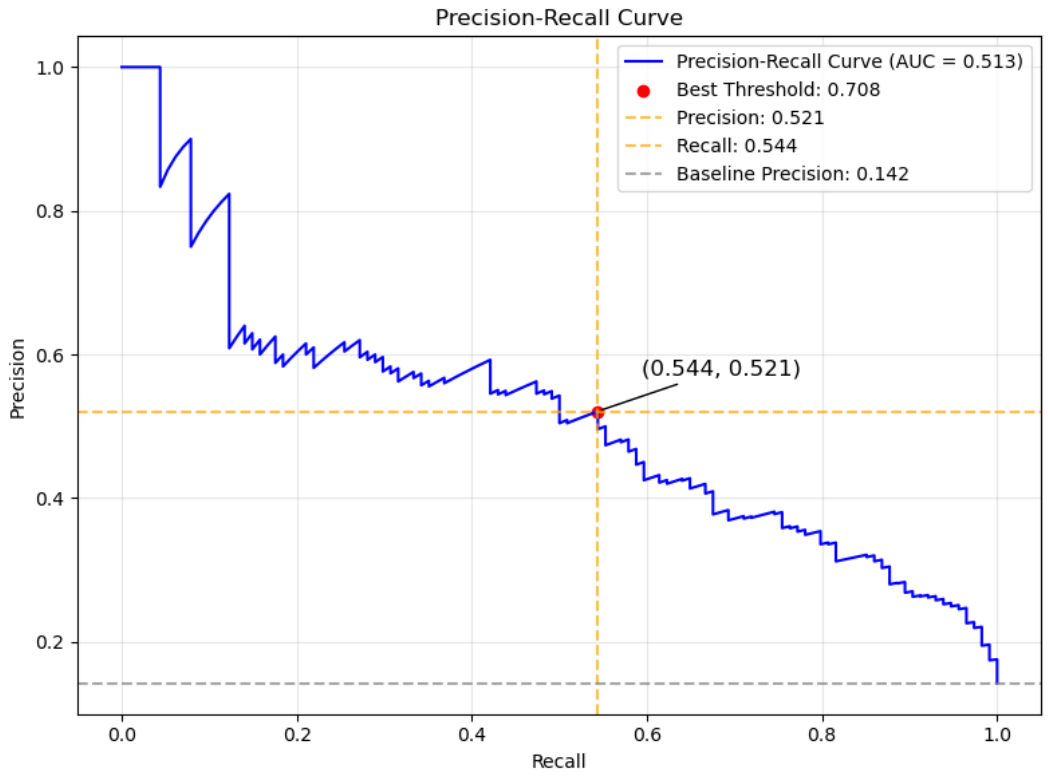

| Metric | Formula |
|---|---|
| $Recall$ | $P(T^+\|D^+) = TP/(TP + FN)$ |
| $Precision$ | $P(D^+\|T^+) = TP/(TP + FP)$ |
| $Avg\ Precision$ | $\sum_n (Recall_n - Recall_{n-1}) \times Precision_n$ <br> where $n$ corresponds to a threshold |

As average precision is **threshold-agnostic**, I maximize it during training and then identify the threshold that maximizes $min(Recall, Precision)$ in the test set

# Section 4: Evaluate

# Results

***The average precision in the test set was 0.513 and the optimal threshold was 0.708, corresponding to a $min(Recall, Precision)$ of 0.521***




***Given the optimal threshold, the probabilities can be discretized and a confusion matrix + all metrics of interest can be analyzed***

| Predictions \ Actuals | $D^+$ | $D^-$ |
|---|---|---|
| $T^+$ | 62 | 52 |
| $T^-$ | 57 | 629 |

$Precision = 0.521$ $\quad Specificity = 0.924$

$Recall = 0.544$ $\quad NPV = 0.917$

$F1 = 0.532$ $\quad Accuracy = 0.864$

# Benchmarks

Despite a different test set, our results are ballpark to those of the top performers

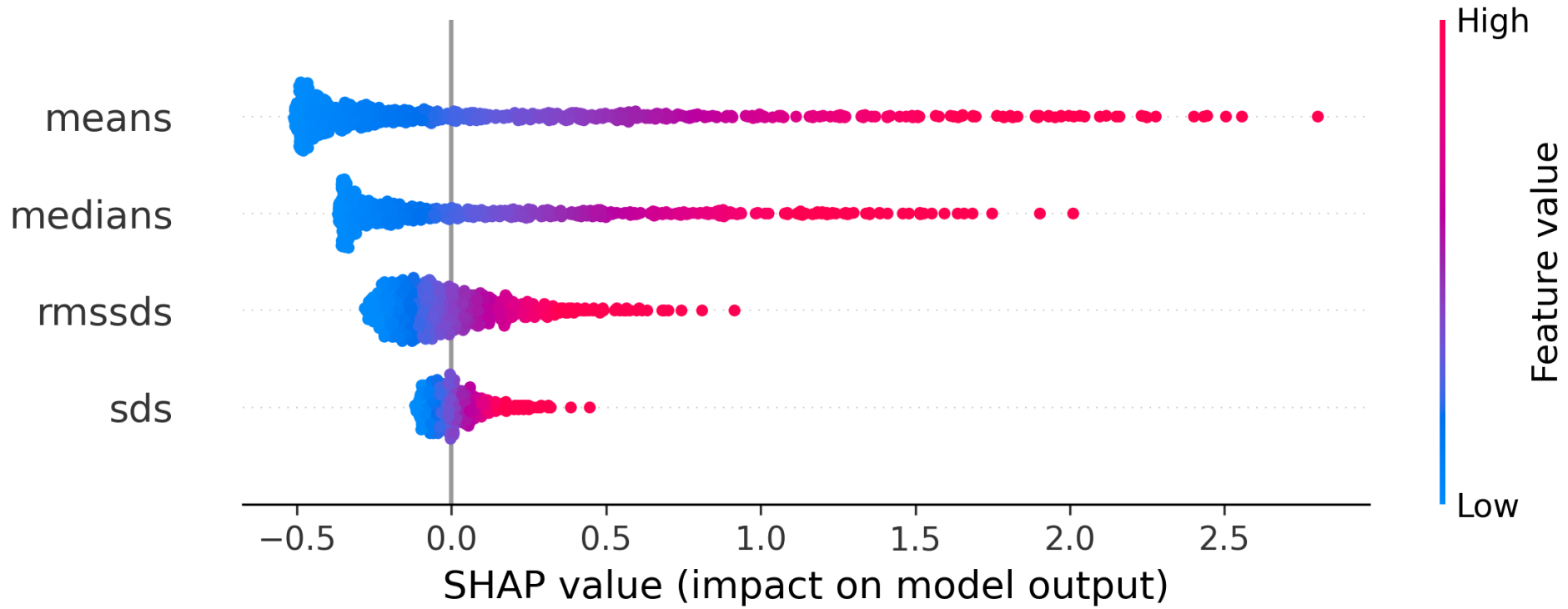
| Team | $min(Recall, Precision)$ |
|---|---|
| Alistair Johnson, Nic Dunkley, Louis Mayaud, Athanasios Tsanas, Andrew Kramer, Gari Clifford | 0.5353 |
| Luca Citi, Riccardo Barbieri | 0.5345 |
| Srinivasan Vairavan, Larry Eshelman, Syed Haider, Abigail Flower, Adam Seiver | 0.5009 |
| Martin Macas, Michal Huptych, Jakub Kuzilek | 0.4928 |
| Henian Xia, Brian Daley, Adam Petrie, Xiaopeng Zhao | 0.4923 |
| Steven L Hamilton, James R Hamilton | 0.4872 |
| Natalia M Arzeno, Joyce C Ho, Cheng H Lee | 0.4821 |
| Chih-Chun Chia, Gyemin Lee, Zahi Karam, Alexander Van Esbroeck, Sean McMillan, Ilan Rubinfeld, Zeeshan Syed | 0.4564 |
| Alexandros Pantelopoulos | 0.4544 |
| Deep Bera, Mithun Manjnath Nayak | 0.4513 |
| *Sample and random predictors* | |
| SAPS-I (in m-code) | 0.3125 |
| SAPS-I (in C) | 0.3097 |
| 86% randomly predicted to survive | 0.1386 |

A $min(Recall, Precision)$ score of **0.521**, ranks **3rd** out of the original teams who participated in the challenge

# Feature importance *(1 of 2)*

While the ensemble is a black box, the meta learner's coefficients can be used to understand which time series features were most influential

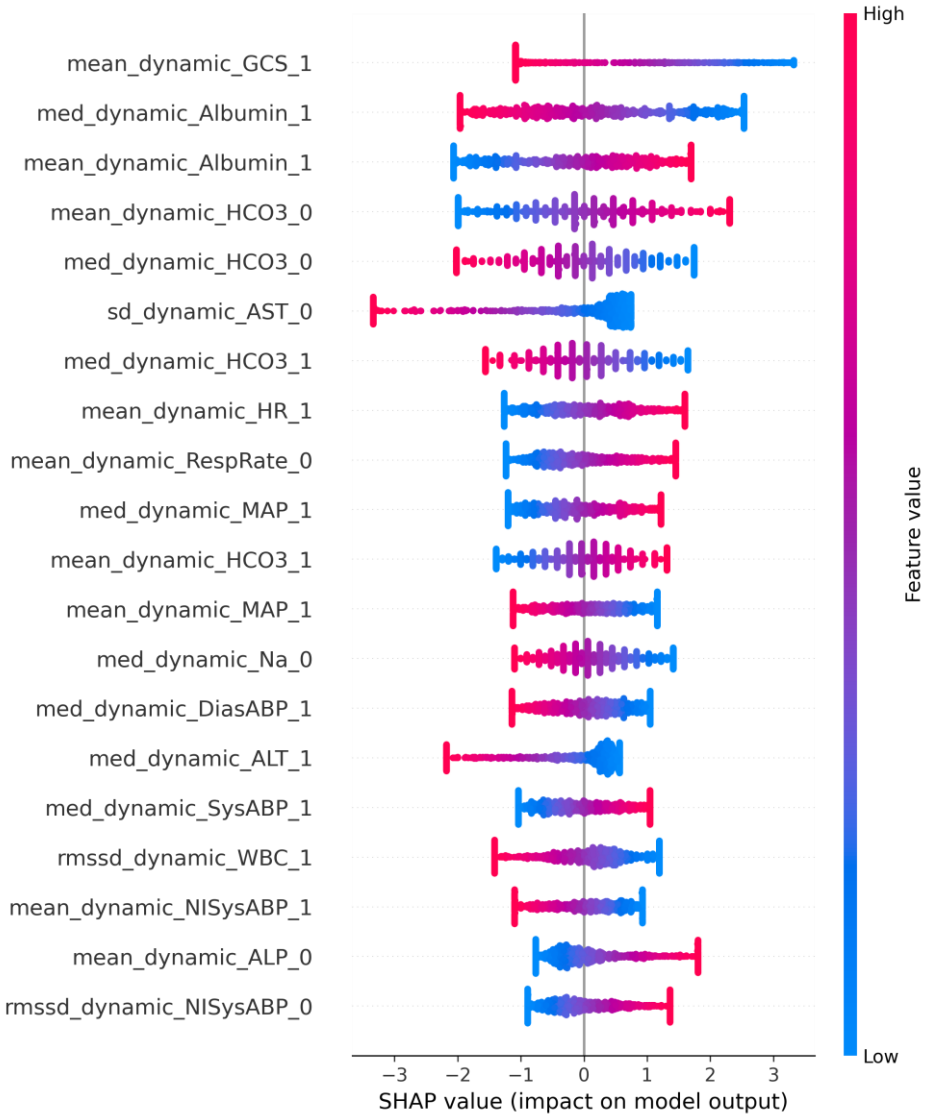
***Higher values of the time series features positively influence the model to make an in-hospital death prediction, while lower values have the opposite influence***



# Feature importance *(2 of 2)*

Alternatively, the features fed into the individual base learners can be concatenated + explored together using a simple Logistic Regression model (SVC is expensive)

- **Transformations:** mean and median transformations are the most influential, which reflects the prior slide
- **Discrete time bins:** 13/20 of these features span the 24-48 hour period
- **Individual predictors:** Predictors related to Albumin and HCO3 (serum bicarbonate) appear to be very “important”
  - For both predictors, low medians but high means influence the model’s decision to make an in-hospital death prediction
  - This reveals that sharp spikes in these features may be indicative of severe underlying health issues



# Limitations

There are some limitations that should be recognized

- Discretizing time into bins distorts longitudinal signal that may be valuable
- May be missing important time series features that account for unexplained variation in the outcome
- The selected model is not super interpretable, but rather more of a “black box”
- Results are evaluated on one held out test set; in practice, it would be better to have multiple held out sets and perhaps even an external test set
- Unable to do an apples-to-apples comparison to the 2012 teams

# Future directions

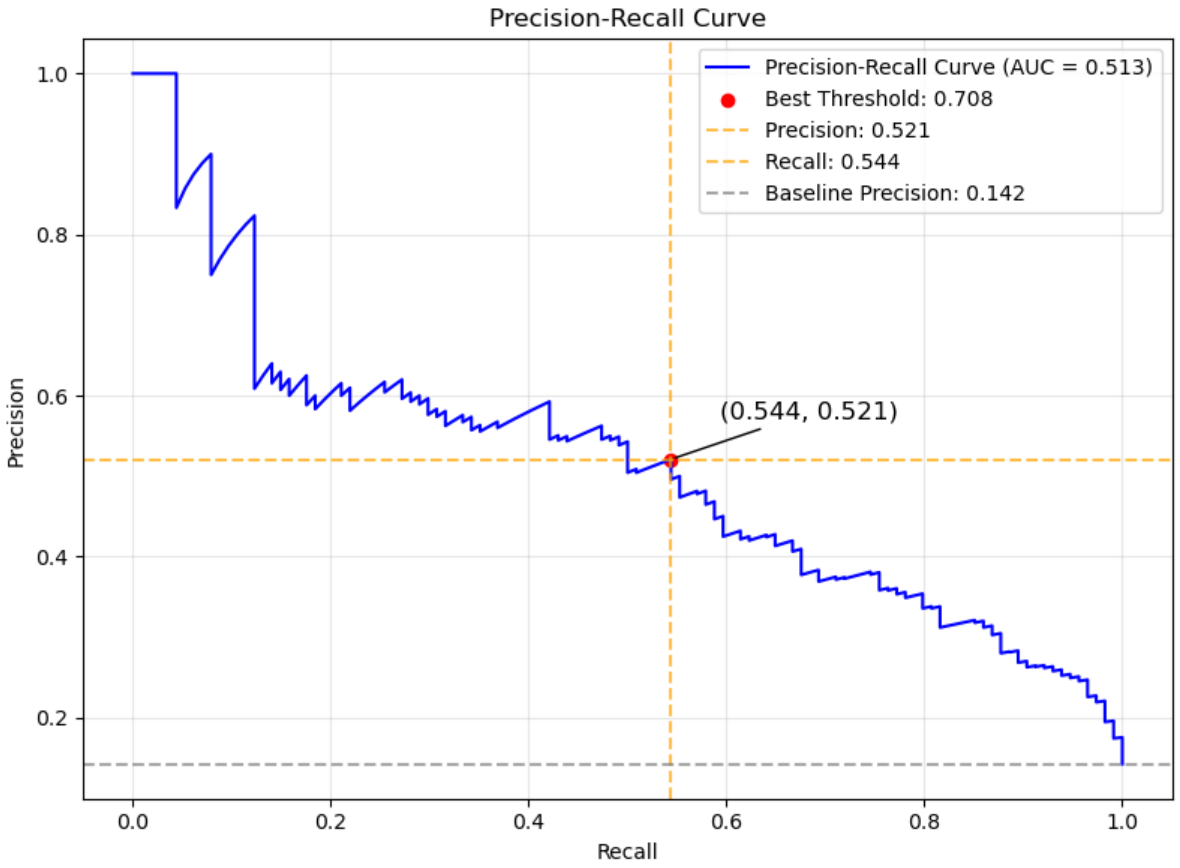
If I had more time, I would do the following…

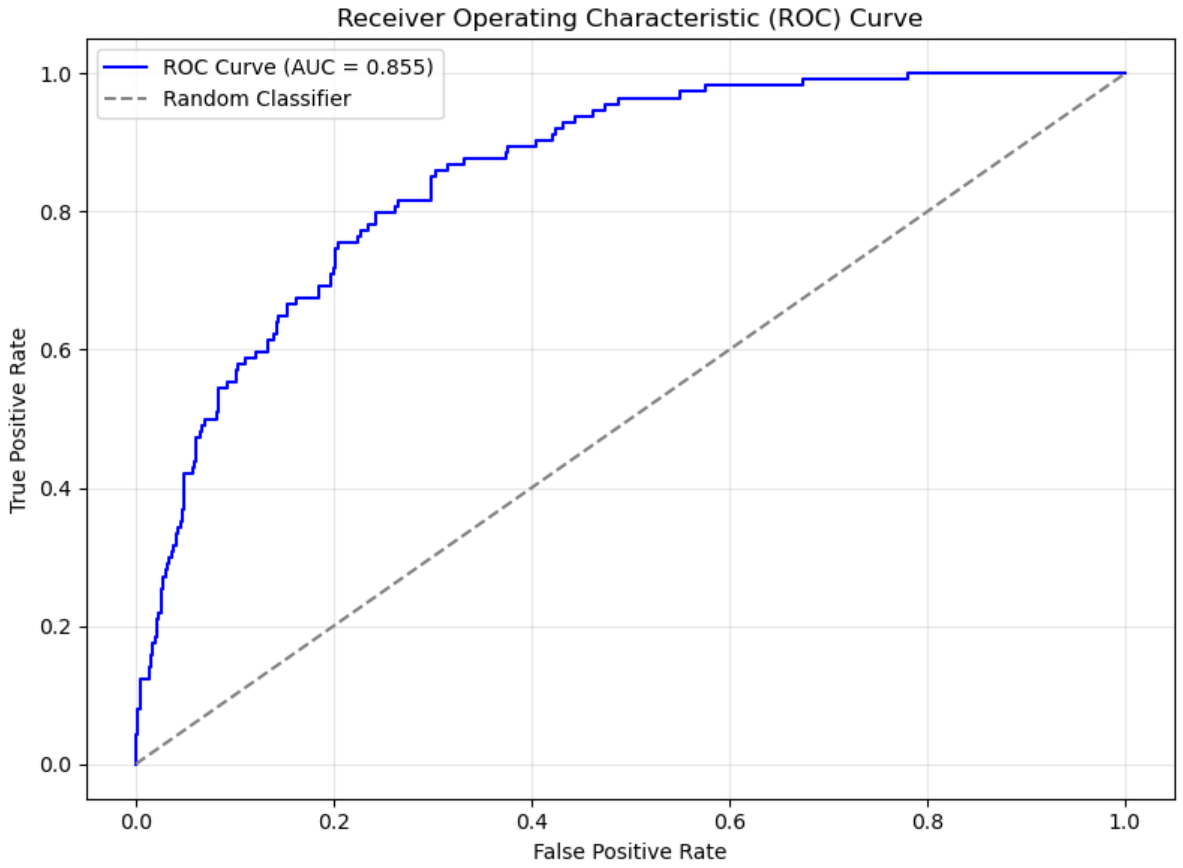
- Explore other discrete time bins + more diverse set of time series features
- Spend more time on model selection (including deep learning models) and hyperparameter tuning
- Experiment with upsampling the minority class or downsampling the majority class during training
- Evaluate pipeline within a nested cross-validation or bootstrapped framework
- Develop deployment code to produce predictions on new unseen data

# Appendix

# PR vs. ROC curves

The PR curve tells a far different story than the ROC curve, as the PR curve prioritizes TPs while the ROC curve considers both TPs and TNs



# Pros & cons of modeling “long” vs. “wide” data

The primary reasons for this hypothesis were due to the relatively small sample size (N=4000) and availability of computational resources; I approached my exploratory data analysis with this strategy in mind

| Strategy | Example | Pros | Cons |
|---|---|---|---|
| Use ML approaches that can accommodate “long” data (i.e. repeated observations per patient) | Recurrent neural networks (e.g., LSTM) | ✓ Leverages longitudinal data<br>✓ No feature engineering<br>✓ Lower bias | × Computationally expensive to train<br>× Requires many samples<br>× Higher variance |
| Transform the data into “wide” format (i.e. one observation per patient) and use tabular approaches | Standard suite of ML classifiers (e.g., Logistic Regression) | ✓ Computationally less expensive<br>✓ More robust to smaller sample size<br>✓ Lower variance | × Potential for increased cardinality<br>× Must engineer features carefully<br>× Higher bias |