MedBrain: A Novel Deep Learning Tool for Holistic Patient Data Interpretation and Clinical Event Prediction

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0 Abstract

Approximately 55,000 patients are treated daily in Intensive Care Units (ICUs) within the United States. Clinical decision making for such patients requires rapid yet holistic patient data review. However, with copious patient chart data (vitals, diagnoses, labs, notes, and prescriptions), there is information overload, leading to slower care and poorer outcomes. Current Computer-Aided Diagnostic solutions are used minimally, as they either lack interpretability or are unable to provide meaningful insight into patient data relationships.

MedBrain is an interpretable deep learning framework created to improve clinician decision-making by predicting significant clinical events and identifying relevant patient variables based on chart data. Models were trained on time-series patient data from Beth Israel Hospital (2001-2012) after manual preprocessing via outlier detection, imputation, and quality control. Natural language processing algorithms were constructed to incorporate diagnoses and note embeddings into the dataset. Multiple Long Short Term Memory (LSTM) Recurrent Neural Networks with Attention were engineered to predict future likelihood of critical short-term events of mortality, sepsis, vancomycin antibiotic administration, and myocardial infarction.

These achieved an Area under the Receiver Operating Characteristic (AUROC) curve of 0.94, 0.88, 0.83, and 0.80, respectively (>0.80 signifies robust model). Attention maps allowed the novel discovery of unknown patient-variable interactions, such as diuretic *furosemide* as an early predictor of sepsis. Moreover, analysis of diagnosis embeddings enables physicians to evaluate for possible overlooked diagnoses associated with the patient's past diagnoses.

This innovative prediction model harnesses the power of deep learning while providing unprecedented explainability via attention mechanisms, reducing information overload by distilling vast patient data to show only relevant variables. Consequently, MedBrain's robust clinical decision support could potentially improve care efficacy, speed, and cost.

1 Introduction

Each day, around 55,000 patients are treated in Intensive Care Units (ICUs) within the United States. These patients possess an average length of stay of 3.80 days with a mortality rate between 10-29%; furthermore, the operation of their stays in ICUs costs about 82 billion dollars per year (Halpern NA, Pastores SM 2005). This tremendous number of patients produces a great excess of real-time and historical patient data that may, at times, overload medical staff. This data requires quick analysis as the patient acuity is unknown and may be hazardous. Further, physicians spend an inordinate amount of time comprehending patient history via notes, charts, etc to create an accurate diagnosis and prognosis. This procedure requires holistic analysis of patient history and features; for instance, a patient with abdominal pain may be due to appendicitis, gallstones, gallbladder inflammation, or a

myriad of other causes. Often, personalized patient features assist in properly diagnosing patients. By prioritizing the exhibition of high-value patient features, the amount of available data to sift through diminishes significantly. In turn, decreased information overload occurs, which is connected to quicker patient process times as well as fewer errors (Ahmed 2011).

Prioritization of data may occur in various forms; most commonly, although not uniformly widespread, a scoring system of patient features. These systems, such as the APACHE II (Acute Physiology And Chronic Health Evaluation II) score or the SOFA (Sequential Organ Failure Assessment) score, aid practitioners in determining the acuity of the patient's condition (Suistomaa M, et al 2002). They consist of integer-based scoring operations that account for various patient features. Moreover, machine learning algorithms like logistic regression and single-layer perceptrons are increasingly useful in clinical decision making: these algorithms have proved to be beneficial in predicting survival and hospital stay length. However, many of these models were trained on a specific demographic of data, and thus lack generalizability. In addition, these models do not account for time-varying data, often lack interpretability, and possess a selection of features a priori thereby not allowing usage of the full gambit of collected features (Kaji D, et al. 2019).

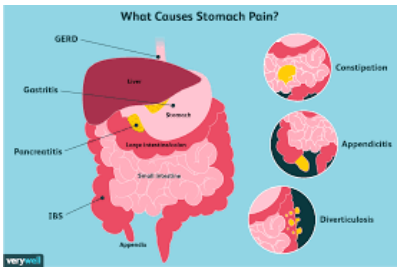

Figure 1: Possible Causes of Abdominal Pain (Fogoros 2019)

These issues may be averted by utilizing sequential deep learning techniques and interrogating them. A real-time interactive prediction of mortality and intervention strategies would provide physicians with an interpretable framework to synthesize patient condition. My research will focus on developing a time-to-event clinical event prediction as well as identifying relevant patient features for diagnosis/prognosis. Recent advances in this field have introduced a variety of deep learning techniques for time-to-event prediction. Notably, the novel self-attentive Attend and Diagnose model improves predictive accuracy for mortality and disease but does not examine interpretability (Song, et al 2017).

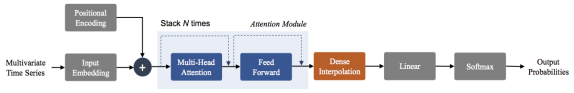

Figure 2: The Attend and Diagnose model hierarchy that utilizes a simple self-attention mechanism to enable sequence formation without recurrence (Song, et al 2017).

2 Methods

This research worked to develop intelligent methods to identify major clinical events and interpret patient charts, vitals, and notes. As such, it was split into a few stages: accumulation of data, data preprocessing and exploration, experimentation of classical techniques, experimentation of deep learning techniques, and thorough analysis. First, a preliminary literature review was conducted to accumulate information about clinical events, current prediction methods, and possible model structures. This stage of the study allowed a full immersion into the present field of research, which better enables feature engineering and analysis when constructing a model.

2.1 Data

To garner data for this project, the Citi Program Human Subjects Biomedical Course was completed. Next, the PhysioNet database was reached out to in order to acquire the MIMIC III dataset (Medical Information Mart for Intensive Care III). This is a "large, database comprising de-identified health-related data associated with over forty thousand patients who stayed in critical care units of the Beth Israel Deaconess Medical Center between 2001 and 2012." (MIMIC III). This dataset possesses distinct 38,597 adult patients and 49,785 hospital admissions. Within this data is demographics, vitals, lab tests, chart events, physician notes, results, procedures, medications, caregiver notes, imaging reports, and mortality among other information; it is widely regarded as the preeminent healthcare patient chart database. Once downloaded, this dataset was integrated into a postgresql database to provide organization, access, and storage.

Current research focuses on mortality prediction. While this research shows promising results, it does not provide physicians with the interpretability necessary to explain these results -- consequently, the output of such "blackbox models" is rendered purposeless due to a variety of bias and training concerns. Furthermore, while mortality prediction yields accurate results, in practice, this score may not be a good indicator of clinical deterioration. That is why this study places special emphasis on clinical events and developing interpretable models (via SHAP and attention mechanisms) that highlight important patient features in clinical decision making; concomitantly, the physician may confirm, correct, or deny model outputs.

2.2 EDA/Preprocessing

Exploratory data analysis was conducted to acquire a familiarity with the dataset and problem. This would enable a far more productive preprocessing step. In this step, histograms were created of salient features such as age, sex, admission location, etc. Any patient that was assigned an age over 300 (done for de-identification) was reassigned an age of 89. Additionally, neonatal patients were excluded from this study. Frequency histograms of microbiology, lab, and chart events were plotted to discern the most relevant events (in an attempt to condense the dataset size without losing pertinent information). Only the most frequently-occuring eight microbiology events, twenty lab events, and twenty chart events were utilized in this study. Further, this

data was linked via the *item_id* variable back to the eponymous value. Certain predictor variables that strongly correlated with the response and were rare in practice were excluded from the dataset (troponin in myocardial infarction modeling, vancomycin administration in vancomycin modeling) to avoid conventional solutions. The data was grouped into chunks of 12-hour, 24-hour, 48-hour, and all data and the mean, max, and min of each variable was calculated. Another one-hot encoded vector corresponding to the hospital location with the diagnosis was appended to this vector. Additionally, the remaining hospital stay length or remaining time until deceasement was computed for the survival analysis model. Features with over 75% of the data missing were removed and values over the 95% percentile were replaced with the median (as there is the presence of erroneous measurements). This exploration and preprocessing occurred using primarily the *pandas*, *numpy*, and *matplotlib* libraries.

For all experiments, 80% of the data was designated to the training set and 20% of the data was designated to the validation set. All models were trained on the training set and hyperparameter tuned by viewing metrics of evaluation on the validation set. To reduce the class imbalance, positive sampling of the positive class occurred.

2.3 Models

Initially, a simple Gradient Boosted Trees Model was employed by the *XGBoost* library employing all solely structured data to predict mortality. This model acted as a baseline from which to compare more advanced models.

From here, the datasets were split into the 12-hour available data, 24-hour available data, 48-hour available data, and all data. Separate gradient boosted trees were trained to predict mortality of the patients at these different times in the patients stay. Various metrics of evaluation including specificity, sensitivity, the area under the precision-recall curve, the area under the receiver operating characteristic curve were analyzed. Moreover, Shapley Explanatory Values (SHAP) were examined via a mix of Summary Plots, Force Plots, and Dependency Plots to ensure model veracity as well as to view interactions between models. A Generalized Additive Model was constructed and trained on the identical dataset. This model was scrutinization using Microsoft's InterpretML Library and Graphical Interface. Finally, a *cox-proportional hazards* model was then employed (aka a survival analysis model) to predict the time until release or deceasement.

1. Initialize $f_0(x) = \arg\min_\gamma \sum_{i=1}^{N} L(y_i, \gamma)$.
2. For $m = 1$ to M:
   (a) For $i = 1, 2, \ldots, N$ compute
   $$r_{im} = -\left[\frac{\partial L(y_i, f(x_i))}{\partial f(x_i)}\right]_{f=f_{m-1}}.$$
   (b) Fit a regression tree to the targets r_{im} giving terminal regions R_{jm}, $j = 1, 2, \ldots, J_m$.
   (c) For $j = 1, 2, \ldots, J_m$ compute
   $$\gamma_{jm} = \arg\min_\gamma \sum_{x_i \in R_{jm}} L\left(y_i, f_{m-1}(x_i) + \gamma\right).$$
   (d) Update $f_m(x) = f_{m-1}(x) + \sum_{j=1}^{J_m} \gamma_{jm} I(x \in R_{jm})$.
3. Output $\hat{f}(x) = f_M(x)$.

Figure 3: Gradient Trees Algorithm

This model, the most sophisticated of those so far, incorporated the sequential nature of the data into consideration. SHAP values were calculated and analyzed.

Next, more sophisticated techniques were attempted. First, four deep feed-forward

networks were constructed in Keras to predict the mortality at different times within the patient stay. These were modified to predict the onset of Sepsis, Myocardial Infarction, and Vancomycin Antibiotic Administration. Following this alteration, unstructured note event data was vectorized with a Bidirectional Encoder Representations from Transformers (BERT) model to extract sentence vector representations. A skip gram was created to convert each one-hot encoded diagnosis vector into a 36-dimensional embedding. Each sentence's numeric representation in a hospital admission was summed, and this was appended to each patient's vector of structured data. Then, multiple Long Short Term Memory (LSTM) Recurrent Network were optimized with attention mechanisms. The attention vector works to learn weight by utilizing the context of the input vector, where weights corresponding to features are found to focus the next layer of the model on certain features. These features may be extracted to find high activation functions of feature-pairings, leading to a much higher interpretability. After this network was constructed and modified, hyperparameter tuning was conducted. Furthermore, the salient patient characteristics that drive a clinical event prediction were extracted via analysis of the hidden layer activation functions. A myriad of metrics (AUC, AUPRC, Specificity, Sensitivity, F1, etc) were evaluated on these networks.

3 Results

Baseline Gradient Boosted Trees (XGBoost) mortality prediction models were tested for performance at the 12-hour patient stay mark, the 24-hour patient stay mark, the 48-hour patient stay mark, and 1-hour before departure/deceasement. Metrics of evaluation included the area under the Receiver Optimizer Characteristic (ROC) curve, the area under the Precision-Recall Curve, and the accuracy.

The ROC curve plots the false positive rate versus the true positive rate at different decision thresholds, describing how well the model can differentiate between patients who will survive their stay and those who will not. The metric of the area under the ROC curve lies between 0 and 1. Values that are closer to 1 indicate a better predictive value. The Precision-Recall curve plots precision vs. recall at various predictor thresholds, describing the tradeoff between true positive rate and positive predictive power. This curve is more aptly suited to describe imbalanced datasets, such as MIMIC-iii mortality (only ~10% samples are positive).

The 12-hour-mark-predictor XGBoost model achieved an Area under the ROC (AUROC) of 0.803 (applicable models > 0.80). In addition, the Area under the Precision-Recall Curve (AUPRC) was 0.344, presenting a concave up curve with acceptable precision and recall in middle decision boundary ranges. In contrast, the 24-hour-mark-predictor XGBoost model achieved an AUROC of 0.826 and an AUPRC of 0.359. The 48-hour-mark-predictor XGBoost model

achieved an AUROC of 0.841 and an AUPRC of 0.417. Finally, the XGBoost model using all data except the hour before the conclusion of data collection achieved an AUROC of 0.939 and an AUPRC of 0.634. The Precision-Recall curve of this model is notable as it is concave-down, indicating better performance in practice (however, it must be noted that predicting mortality an hour before the event does not empower the clinician to take effective preventative measures). When the SHapley Additive exPlanations (SHAP) values were analyzed among these models, age, anion gap mean, and platelet count min were found to be the preeminent predictors of mortality at the 12-hour mark; age, anion gap mean, and urea nitrogen min were found to be the preeminent predictors of mortality at the 24-hour mark; age, urea nitrogen min, and bicarbonate mean were found to be the preeminent predictors of mortality at the 48-hour mark; at the hour mark, peripheral capillary oxygen saturation min, heart rate min, and systolic blood pressure min were found to be the preeminent predictors of mortality.

The Generalized Additive Model yielded similar results with an AUROC of 0.93 (predicting using all data except for the last hour). This model displayed peripheral capillary oxygen saturation min, heart rate min, age, anion gap mean, and urea nitrogen min as with the highest variable importance.

The constructed cox-proportional hazards model (survival analysis) model, which employs a parametric approach to determine the timing and occurrence of events, performed ably, with a concordance statistic, or C-statistic, of 0.75. This metric of evaluation determines the fraction of concordant pairs, or patient pairs for which the outcome and the order of deceasement/departure is predicted correctly. SHAP value examination exhibited age, oxygen saturation min, and urea nitrogen min to be paramount indicators of the predicted time-to-event.

The deep feed-forward neural network predicting data from the 12-hour mark attained an AUROC of 0.931 on the validation set, the network using 24-hour data reached an AUROC of 0.941 on the validation set, the network using 48-hour data reached an AUROC of 0.951 on the validation set, and the network using all data except the last hour reached an AUROC of 0.971 on the validation set (attesting to the power of deep learning). Among these models, age, mean corpuscular hemoglobin concentration, anion gap minimum, urea nitrogen minimum, chloride minimum, heart rate minimum, and systolic minimum were found to be the most influential patient features.

The skip gram of the diagnosis embeddings cannot be evaluated with traditional techniques as it is an unsupervised tool to visualize diagnosis embeddings. However, based off rudimentary relationship analysis, the vector space exhibits signs of captured semantic meaning (e.g. diagnosis vectors such as diabetes and high blood sugar are closer than diagnosis such as pregnancy and cancer). After the concatenation of embedded note event data to the patient vectors, the trained clinical event Long

Short Term Memory (LSTM) Recurrent Neural Networks possessed next-day predictive AUROC of 0.881 for sepsis, 0.832 for MI, and 0.841 for vancomycin administration. Pulled attention maps were able to highlight individual prediction variable influences.

This pipeline of mortality prediction, clinical event prediction, and then chart/vital/note interpretation is highly effectual, producing a fully-automated model for patient short-term risk and long-term risk prediction.

Overall, the clinical event predictor, with a GBM survey accuracy of 85.13% and an Ensemble CNN accuracy of 87.16% on validation sets, producing a fully-automated model for high-risk lung cancer candidate selection and malignant pulmonary nodule detection/assessment.

4 Discussion

MedBrain's amelioration of detection and management of mortality, sepsis, vancomycin antibiotic administration, and myocardial infarction is crucial to improving ICU outcomes. The engineered LSTM with attention mechanisms was able to achieve AUCs indicative of applicable value (>0.80) in modeling eventual clinical deterioration via the aforestated events. As expected, the models received an advantage from more data; thus the networks utilizing 48-hours worth of data and networks utilizing all data except the last hour performed better than those of 12 and 24 hours worth of data.

Models developed for unstructured data preprocessing possess standalone value. The patient diagnoses embeddings may assist in ensuing physician diagnosing of patients. Given the inherent spatial associations in this medical vector space, physicians may use cosine similarity as a metric to examine possible diagnoses frequently found with the patient's current/past diagnosis. In addition, the note embeddings developed via the fine-tuned BERT model provide insight into critical words and pairings. The highlighting of these critical words and phrases could allow clinicians to process past notes at a much faster rate.

The strong performance in mortality prediction may be attributed to the LSTM's ability to model time-series data and form deep contextual relationships facilitated by attention. As such, MedBrain's AUROC of 0.94 greatly exceeds the most widely used ICU mortality prediction score, APACHE II, which achieves an AUROC of 0.77 (from retrospective cohort study conducted by Polita et al.). Upon analysis of the model on the validation dataset, there were discernible differentiators between the LSTM when predicting on the patients 12-hour data, 24-hour data, 48-hour data, and all data except the last hour. Notably, while age possessed the highest variable importance in the first three of these models, in the last model the best predictor of ultimate mortality was the minimum oxygen saturation percentage (SpO2). Nevertheless, this is likely as clinical deterioration has already begun in patients by the last hour; thus, the minimum SpO2 percentage of these patients may fall dramatically, suggesting that the patient is close to expiration. The developed system better detects high-risk patients and better captures

obscure/unfamiliar variable relationships, especially beneficial in unusual cases.

Sepsis prediction obtained high predictive value, likely because variables in the Systemic Inflammatory Response Syndrome (SIRS) criteria that were a component of the calculation for presence of Sepsis were located in the dataset. Additionally, a variety of antibiotics signalled infection; the attention maps identified powerful antibiotics like vancomycin and ceftriaxone as indicators of sepsis. Prediction of future vancomycin antibiotic administration also achieved robust success. This may be due in part as vancomycin is often administered to treat sepsis. Moreover, from activations extracted from the attention maps and SHAP values, it may be theorized that antibiotics such as cefazolin and diuretics such as furosemide that were given beforehand are proxies for vancomycin administration. Finally, myocardial infarction models performed well, but with less precision, as there were far fewer strong predictors (no EKG, chest pain analysis, etc) and far fewer patients with a positive condition. The model's ability to predict a new heart attack was also hindered as medications utilized in MI treatment are also utilized to treat long-term heart disease. Nonetheless, this model retains value in application as the sensitivity was reasonable and attended variables were confirmed as pertinent in literature.

MedBrain effectively aids in providing urgent decision-making support by predicting clinical events and distilling holistic patient data to those germane to present care. Variable-level attention maps and SHapley Additive exPlanations (SHAP) values unveil the once "blackbox" of this deep learning model. Without this layer of transparency, these predictions would be unusable; as physicians would have no way of identifying the driving patient variables to stage interventions and there would be no proper method to ensure that there are no biases/warps in the model.

Overall, this prediction could allow more accurate and expeditious detection of patients at high-risk for mortality, sepsis, myocardial infarction or in need of vancomycin administration, engendering better intervention. Such models may also aid in identifying potentially unfamiliar, yet important, predictive variables from eclectic patient inputs. By diminishing information overload, clinicians may better parse patient data relationships; consequently, care efficacy would increase and use of gunshot testing may be reduced, thereby improving cost. The combined MedBrain is a formative system for intelligent clinical decision-making support.

4.1 Future Research

Future research is necessary. As the onset of significant clinical events (e.g. Sepsis) may occur rapidly, it would be beneficial to predict clinical events on an granular of real-time basis. Furthermore, contextual decomposition should be explored in healthcare to show physicians whether a variable increases or decreases risk. Finally, other visualization options could provide a more succinct summary of salient patient feature.

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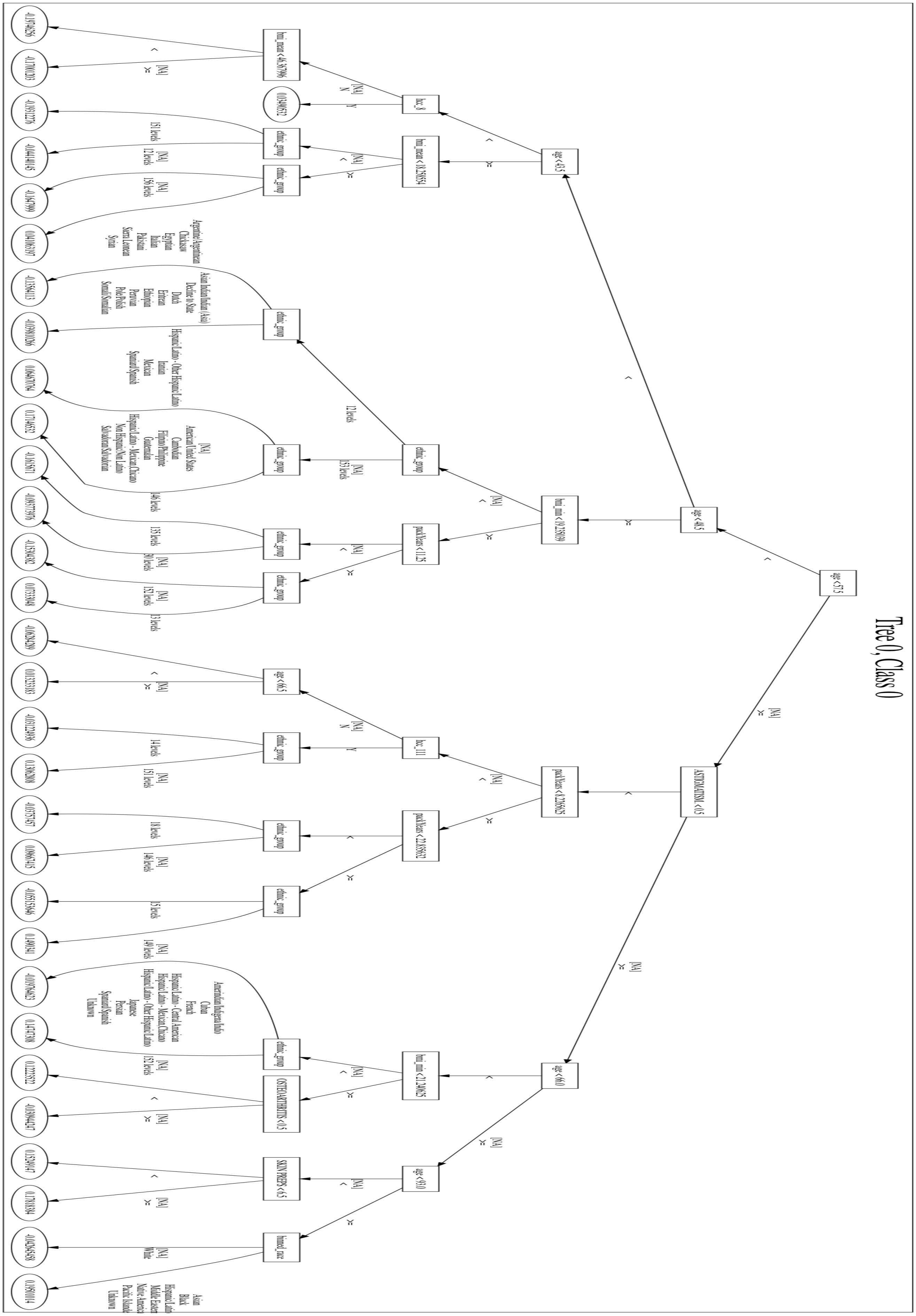
Appendix

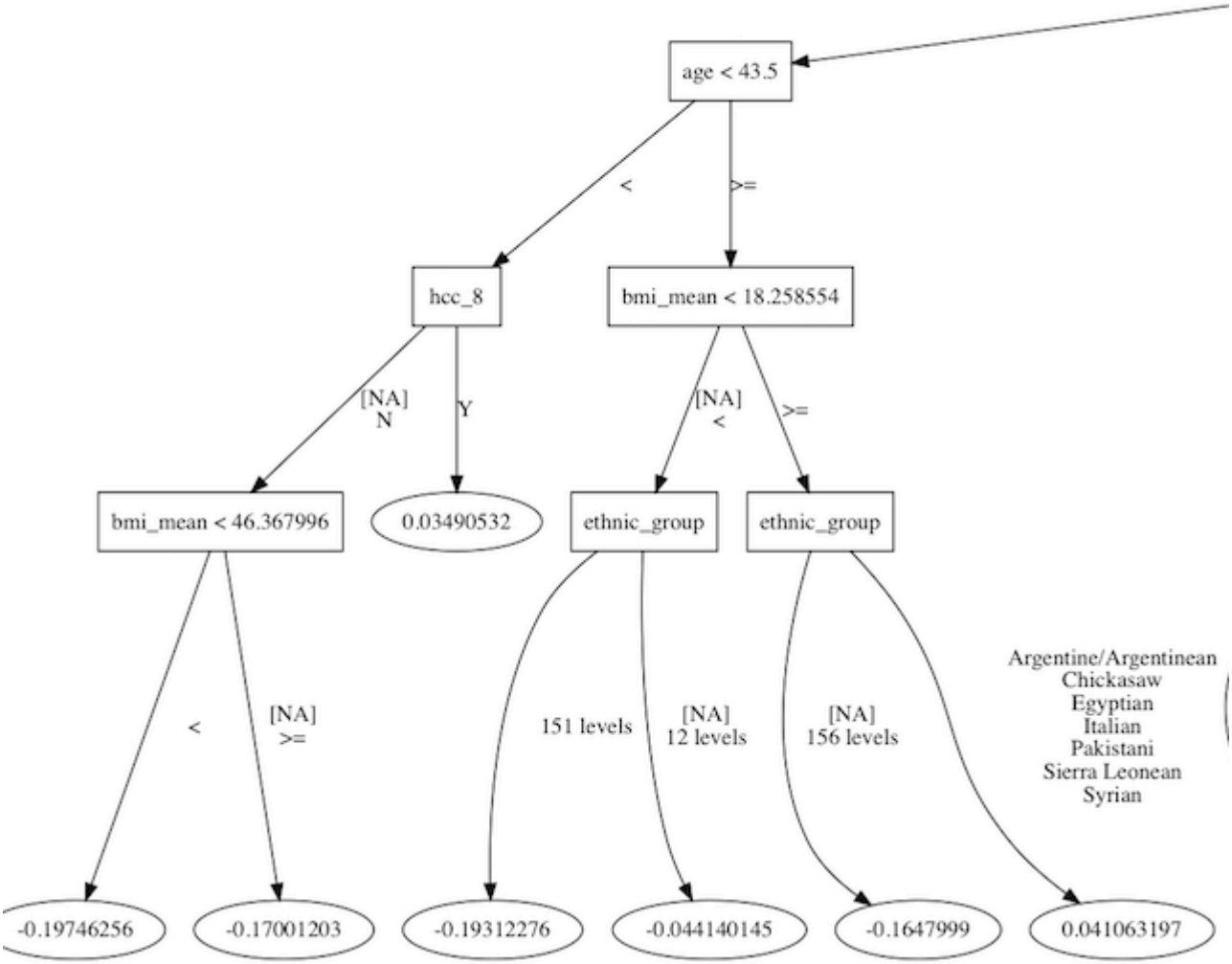
Variables	Scores	Variables	Scores
Heart Rate		Ht (%)	
≤ 54	5	< 0	9
55-69	1	20-29.9	2
70-109	0	30-45.9	0
110-139	1	46-59.9	2
≥ 140	5	> 60	9
Respiratory Rate		WBC(× $10^3/mm^3$)	
≤ 5	10	< 2.9	3
11-Jun	2	3-19.9	0
24-Dec	0	≥ 20	3
25-34	2	GCS	
35-49	6	3	12
≥ 50	10	4	11
If $FIO_2 \geq 0.5$:(A-a)O_2 (mmHg)		5	10
< 00	0	6	9
200-349	2	7	8
≥ 350	3	8	7
If $FIO_2 < 0.5$:(A-a)O_2 (mmHg)		9	6
<60	7	10	5
≥ 61	0	11	4
PH		12	3
< 7.24	4	13	2
7.25-7.32	0	14	1
7.33-7.59	2	15	0
≥ 7.6	4	Chronic Organ Insufficiency immune-compromised and:	
Age			
≤ 44	0	Non-Operative	3
45-74	2	Emergency-postoperative	3
≥ 75	6	Elective-Postoperative	2
Total Score Sum of scores			

*Ht: Hematocrit, WBC: White blood cells count, GCS: Glasgow coma score

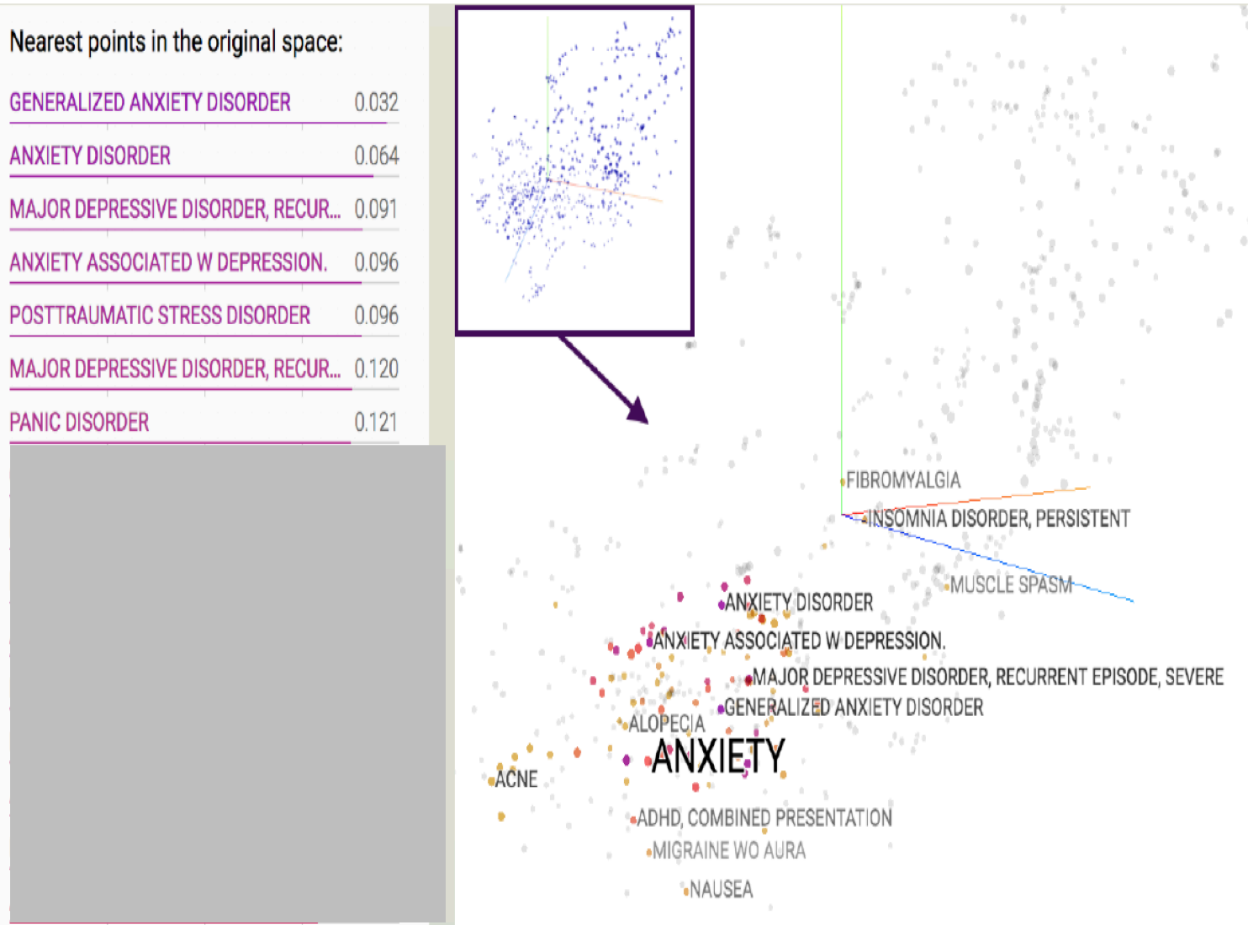
LIMITED

Appendix Figure 1: APACHE II System Used


Tree 0, Class 0



Appendix Figure 2: Gradient Boosted Tree Extracted (1 out of 50)



Appendix Figure 3: Diagnoses Embeddings Visualized

He states he was in his usual state of health until 10:30 last evening when he woke up feeling cold; 1 hour later he developed moderate to severe sharp chest pain radiating across his chest associated with nausea, diaphoresis, and dypsnea. The pain was fairly constant and did not resolve until he was given sL NTG at 6 am by EMS. He has been pain free since. Presenting vitals BP 109/66, HR 71, O2 sat 88% on RA. CXR showed congestive heart failure; initial troponin-I was mildly elevated at 0.4, CK 70. He given aspirin and furosemide 80 mg IV (with ~600cc diuresis), Nitropaste [**1-3**]", and Lovenox 80 mg SQ. During the ambulance transfer to the [**Hospital1 18**], he also received ~500 cc IVF for ? low BP). On further questioning, Mr. [**Known lastname 1858**] has very poor exercise tolerance due to knee pain that he attributes to osteoarthritis. But he says that he gets chest pain (similar to pain he had last night) with fairly minimal exertion (picking up his 11 lb cat, carrying 1 gallon jug of water, first getting up from sitting to walk outside or to walk to the bedroom). The pain is associated with dyspnea and is relieved with few minutes rest. His symptoms occur about every day to every other day and have been stable over the past year

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Appendix Figure 4: Highlighting of Critical Words/Phrases Via Attention

Chief Complaint: Transferred s/p vertebroplasty s/p respiratory\n failure\n HPI:\n 64 year old man with ESRD on hemodialysis (from FSGS) last yesterday.\n HCV, CAD w/stent, HTN and newly diagnosed metastatic poorly\n differentiated cancer (likely NSCLC) presenting from PACU after\n re-intubation post vertebroplasty for respiratory distress. Briefly, pt\n presented [**1-19**] with shortness of breath, which has resolved over the\n course of admission. On recent CT scan (to rule out PE), his disease\n was noted to be "substantially progressed" since his last CT less than\n one month prior. In addition, he had a pathologic fracture of T4 noted\n on the same CT, and he was noted to have DVT on LE ultrasound and that\n time placed on a heparin drip. [**1-31**] transferred to the OMED for\n chemotherapy targeted toward his progressive cancer. Scheduled for\n vertebroplasty of T4 once INR <1.5, therefore for vertebroplasty today.\n \n During vertebroplasty, BP, VS stable on ventilation. Minimal blood\n loss. Received 1350 cc crystalloid, no urine output as expected.\n Extubed, and at 16:30 rolled into PACU with o2 sats 90%10 L with\n reported difficulty moving air. Nasal trumpet inserted, pt suctioned\n scant amount. RR 16. Ten minutes later no improvement in status, 80% on\n 10L, HR 110\'s-120\'s, face mask placed and pt reintubated. Propofol\n restarted. CXR with worsening pulmonary edema, no focal opacities.\n Discussed with renal team, to be staffed in AM.\n Patient admitted from: PACU\n History obtained from Medical records\n Patient unable to provide history: Sedated\n Allergies:\n Penicillins\n Rash;\n Adhesive Tape (Topical)\n Rash;\n Last dose of Antibiotics:\n Infusions:\n Propofol - 25 mcg/Kg/min\n Heparin Sodium - 1,100 units/hour\n Other ICU medications:\n Other medications:\n Metronidazole 500mg PO BID (last day [**2198-2-4**])\n Lisinopril 20mg PO daily\n Nifedipine CR 30mg PO daily\n Metoprolol 100mg PO BID\n ASA 325mg PO daily\n Plavix (held)\n Isosorbide Mononitrate 30mg PO daily\n Acetylcysteine Neb Q6H PRN\n Albuterol Neb Q6H PRN\n Ipratropium Neb Q6H PRN\n Acetaminophen 1000mg PO Q8H\n Nephrocaps\n Calcium Acetate 667mg TID with meals\n Pantoprazole 40mg PO BID\n Oxycodone SR 40mg PO Q8H\n Oxycodone 5-10mg PO Q4H: PRN\n Docusate 100mg PO BID\n Senna\n Epoietin Alfa at dialysis\n Guaifenesin\n Past medical history:\n Family history:\n Social History:\n PMHX:\n #. Onc HX: [**12-11**] pre-renal transplant CT scan chest noted enlarged RML\n nodule, w/ subcentimeter FDG avid scattered lymph nodes. Developed neck\n pain and found to have C2 pathological fracture, [**11-22**] cytology\n demonstrated poorly differentiated carcinoma. Likely non-small cell\n lung carcinoma, with RML mass and metastasis to the cervical and sacral\n spine. The only manifestation of his disease currently is cervical neck\n pain, s/p pathologic fracture and posterior cervical arthrodesis C1-C3\n and palliative XRT. Holding on chemo as access issues.\n #. CAD s/p angioplasty D1 [**7-10**] and stents to OM2/3 in [**3-11**]\n #. ESRD secondary to FSGS on HD (MWF)\n #. Hypertension\n #. LLE peroneal nerve palsy [**1-6**] GSW to L leg\n #. Thalassemia trait\n #. h/o Substance abuse (heroin/cocaine); reports none since [**2163**]\n #. CHF w/ EF 35% in [**11-11**], EF 25-30% on [**Date Range **] [**2198-1-23**]\n #. MR - 2+ on [**Month/Day/Year **] in [**11-11**]; now found to be 3+ MR [**First Name (Titles) **] [**Last Name (Titles) **]\n #. Pathological C2 Fx s/p C1-3 Fusion\n #. Parotiditis - [**12-12**] (levo/flagyl)\n #. CDiff - [**12-12**]\n #. HCV - grade 1 inflammation and stage 0 fibrosis on bx [**2-9**]\n NC\n Occupation:\n Drugs:\n Tobacco:\n Alcohol:\n Other: lives with girlfriend, has 2 sons, used to work in construction,\n + smoker 1 PPD for many years quit recently, rare ETOH, no drugs.\n Review of systems:\n Flowsheet Data as of [**2198-2-2**] 07:39 AM\n Vital Signs\n Hemodynamic monitoring\n Fluid Balance\n 24 hours\n Since 12 AM\n Tmax: 36.4\nC (97.5\n Tcurrent: 35.9\nC (96.6\n HR: 60 (57 - 63) bpm\n BP: 103/54(66) {93/49(60) - 103/54(66)} mmHg\n RR: 13 (11 - 15) insp/min\n SpO2: 100%\n Heart rhythm: SR (Sinus Rhythm)\n Height: 67 Inch\n Total In:\n 1,465 mL\n PO:\n TF:\n IVF:\n 115 mL\n Blood products:\n 1,350 mL\n Total out:\n 0 mL\n 0 mL\n Urine:\n NG:\n Stool:\n Drains:\n Balance:\n 0 mL\n 1,465 mL\n Respiratory\n Ventilator mode: CMV/ASSIST\n Vt (Set): 550 (550 - 550) mL\n RR (Set): 14\n RR (Spontaneous): 0\n PEEP: 5 cmH2O\n FiO2: 50%\n RSBI: 21\n PIP: 20 cmH2O\n Plateau: 18 cmH2O\n SpO2: 100%\n ABG: ///25/\n Ve: 6.8 L/min\n Physical Examination\n General Appearance: Well nourished\n Eyes / Conjunctiva: constricted pupils bilaterally\n Head, Ears, Nose, Throat: Normocephalic, Endotracheal tube\n Cardiovascular: (S1: Normal), (S2: Normal), (Murmur: Systolic)\n Peripheral Vascular: (Right radial pulse: Present), (Left radial pulse:\n Present), (Right DP pulse: Not assessed), (Left DP pulse: Not assessed)\n Respiratory / Chest: (Expansion: Symmetric), (Breath Sounds: Crackles :\n), anterior, scant crackles\n Abdominal: Soft, Bowel sounds present\n Extremities: Right: Absent, Left: Absent\n Skin: Not assessed, No(t) Rash: , No(t) Jaundice\n Neurologic: Responds to: Unresponsive, Movement: Not assessed, Sedated,\n Tone: Not assessed\n Labs / Radiology\n 275 K/uL\n 7.2 g/dL\n 80 mg/dL\n 5.9 mg/dL\n 32 mg/dL\n 25 mEq/L\n 99 mEq/L\n 4.8 mEq/L\n 136 mEq/L\n 23.7 %\n 7.5 K/uL\n [image002.jpg]\n [**2195-12-7**]\n 2:33 A2/29/[**2197**] 03:12 AM\n [**2195-12-11**]\n 10:20 P\n [**2195-12-12**]\n 1:20 P\n [**2195-12-13**]\n 11:50 P\n [**2195-12-14**]\n 1:20 A\n [**2195-12-15**]\n 7:20 P\n 1//11/006\n 1:23 P\n [**2196-1-7**]\n 1:20 P\n [**2196-1-7**]\n 11:20 P\n [**2196-1-7**]\n 4:20 P\n WBC\n 7.5\n Hct\n 23.7\n Plt\n 275\n Cr\n 5.9\n TropT\n 0.10\n Glucose\n 80\n Other labs: PT / PTT / INR:14.1/29.3/1.2, CK / CKMB /\n Troponin-T:15/2/0.10, ALT / AST:[**5-20**], Alk Phos / T Bili:39/0.2,\n Albumin:2.6 g/dL, LDH:185 IU/L, Ca++:9.3 mg/dL, Mg++:2.0 mg/dL, PO4:5.9\n mg/dL\n Assessment and Plan\n 64 year-old M with ESRD on HD CAD, metastatic poorly differentiated\n cancer (likely NSCLC)s/p vertebroplasty with respiratory failure.\n .\n # Acute respiratory failure: post extubation after 1300 cc fluids in\n anuric patient with depressed EF. Also consider aspiration, pt also\n lethargic therefore sedation also could be contributing. No clear\n evidence for PE, though patient with LE DVT on IV heparin until 6AM. Pt\n also with severe lung disease given CA.\n -continue on vent, with last gas can likely decrease Fi02.\n -discussed with renal HD tomorrow AM to remove fluid as overloaded\n -CXR in AM\n -CX data\n -Extubate once pulmonary edema improved, propofol weaned.\n .\n #Pump: CHF, systolic dysfunction EF 25-30%. Anuric with 1+ liter fluid.\n No LE edema, sparse crackles, cannot assess JVP given neck collar.\n Evidence of worsening pulmonary edema on radiology.\n -continue cardiac meds\n -HD today as per renal.\n .\n # Metastatic NSCLC. plan was to receive navelbine [**1-30**], but could not\n receive [**1-6**] no access.\n - discussion with oncology regarding time of continued treatment\n - discussion of access for chemo, PICC placement.\n .\n # vertebral fractures: s/p C1-C3 fusion, new T4 compression fracture\n without neurologic compromise. S/P vertebroplasty\n - NPO\n - heparin gtt was held 6am prior to procedure, will now restart as per\n IR.\n - continue to wear back and neck collar.\n -C spine collar to continue, can hold when patient eating.\n -Pain control with morphine. To resume PO regimen once extubated.\n .\n # DVT: continue heparin as above, hold coumadin until s/p\n vertebroplasty. Discussion with IP in AM in terms of time to restart\n coumadin\n .\n # ESRD: HD M/W/F. Discussed with renal team regarding volume overload.\n Pt to likely undergo dialysis in AM.\n .\n # C-diff +: Continue flagyl. Last day [**2-4**]\n .\n # HTN: Holding parameters. Hold nifedipine, to be restarted by team. In\n chart noted patient becomes hypotensive during dialysis. SBP 95-100 on\n propofol drip.\n .\n # Anemia: stable.\n -Guaiac all stools\n -on Heparin drip for DVT\n -epo with dialysis.\n .\n # CAD: ROMI negative on admission but MR [**First Name (Titles) **] [**Last Name (Titles) 300**] worse on new [**Last Name (Titles) **]\n compared to 2 months ago. EF was 35-40% and is now 25-30% and MR is 3+\n increased from 2+.\n - medically managed on ASA, Plavix, statin, BB, ACE, nitrates\n -Consider restarting plavix in AM, as vertebroplasty complete.\n .\n # Parotiditis - stone of stentson\'s duct initially seen on [**2197-12-7**],\n patient has passed stone. Levoflox/vanco stopped.\n .\n # Hep C: stable, not on treatment.\n .\n # Prophylaxis: Heparin drip/ bowel regimen, cont PPI\n # FEN: NPO, avoiding IV fluids,\n # comm: wife [**Name (NI) **] [**Telephone/Fax (1) 1284**]\n # Dispo: Pending extubation to be called out to OMED\n # Code: Full\n ICU Care\n Nutrition:\n Glycemic Control:\n Lines:\n 20 Gauge - [**2198-2-2**] 02:03 AM\n Prophylaxis:\n DVT: LMW Heparin\n Stress ulcer:\n VAP: HOB elevation\n Comments:\n Communication: Comments:\n Code status: Full code\n Disposition:\n'

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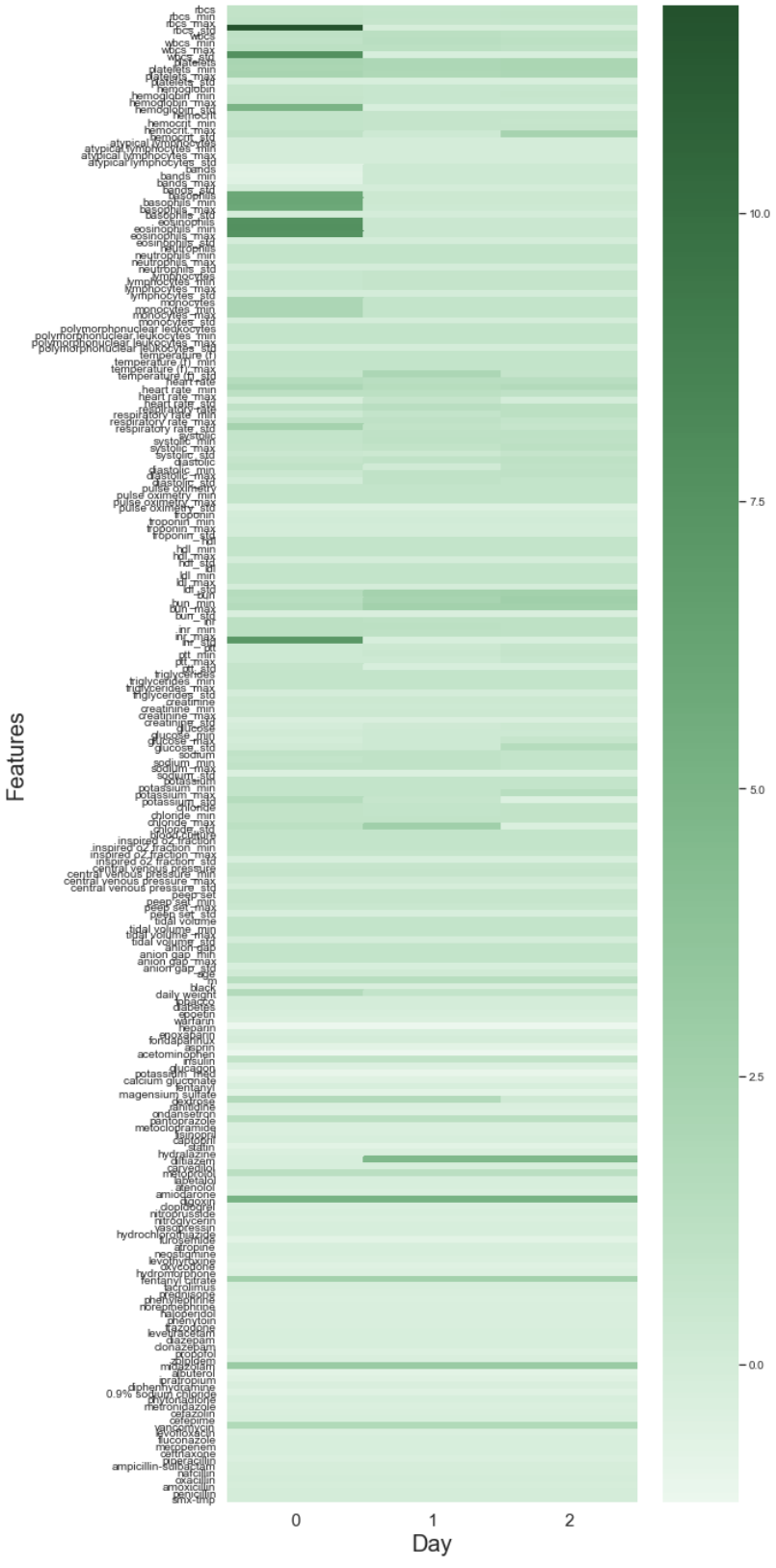
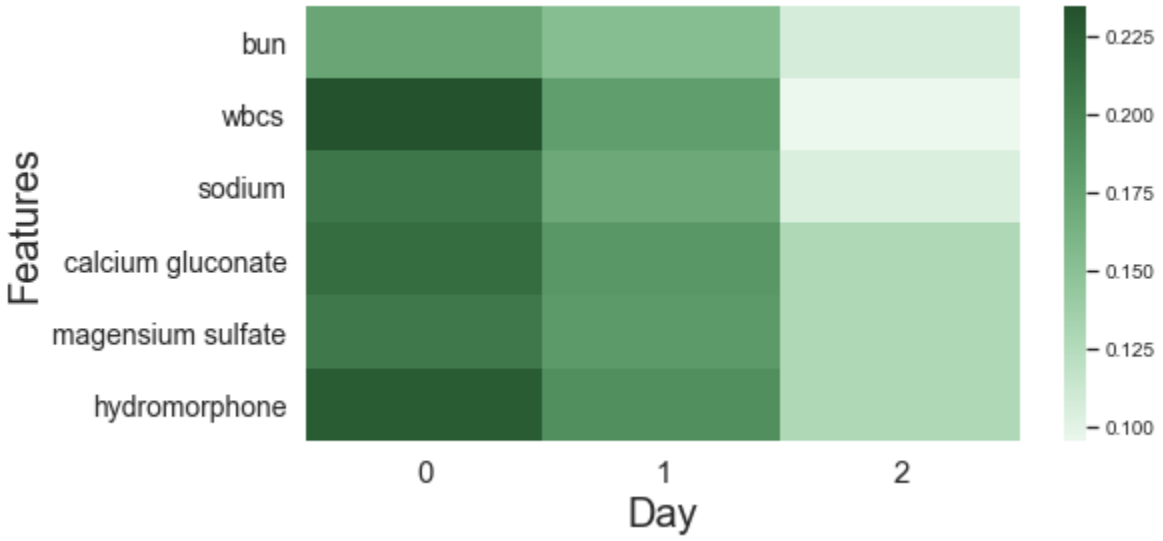
```
BUN                                  0.256195
HDL                                  0.835474
INR                                  0.805314
Inspired O2 Fraction                 0.828730
LDL                                  0.835318
PEEP Set                             0.658234
PTT                                  0.677682
RBCs                                 0.298982
WBCs                                 2.015649
anion gap                            0.813903
atypical lymphocytes                -0.046694
bands                                0.330616
basophils                            0.381396
blood culture                        0.836014
central venous pressure              0.721667
chloride                             0.911587
creatinine                           1.785755
daily weight                         0.825247
diabetes                            -0.002113
diastolic                            1.001999
eosinophils                          0.479636
glucose                              1.383458
heart rate                           1.065947
hemocrit                             0.338775
hemoglobin                           0.303979
lymphocytes                          0.762092
monocytes                            0.794781
neutrophils                          0.840921
platelets                            2.439885
polymorphonuclear leukocytes         0.839994
potassium_x                          0.816422
pulse oximetry                       0.839479
respiratory rate                     0.322793
sodium                               0.855431
systolic                             1.266889
temperature (F)                      0.860105
tidal volume                         0.810452
tobacco                             -0.015838
triglycerides                        0.818678
troponin                             0.067443
BUN_std                             -0.261103
HDL_std                              0.000000
INR_std                             -0.147566
Inspired O2 Fraction_std            -0.134712
LDL_std                              0.000000
PEEP Set_std                        -0.174930
PTT_std                             -0.181870
RBCs_std                            -0.103518
WBCs_std                            -0.192761
anion gap_std                       -0.174407
atypical lymphocytes_std             0.000000
bands_std                            0.000000
basophils_std                        0.000000
central venous pressure_std         -0.128294
chloride_std                         1.216767
creatinine_std                      -0.246752
diastolic_std                        1.026489
eosinophils_std                      0.000000
glucose_std                          0.703436
heart rate_std                       0.395317
hemocrit_std                         3.287776
hemoglobin_std                       6.779672
lymphocytes_std                      0.000000
monocytes_std                        0.000000
neutrophils_std                      0.000000
platelets_std                       -0.215736
polymorphonuclear leukocytes_std     0.000000
potassium_std                        3.350031
pulse oximetry_std                  -0.411423
respiratory rate_std                 0.631375
sodium_std                          -0.322568
systolic_std                         0.685980
temperature (F)_std                  0.170085
tidal volume_std                     0.000000
triglycerides_std                    0.000000
troponin_std                         0.000000
BUN_min                              0.282512
HDL_min                              0.835474
INR_min                              0.811202
Inspired O2 Fraction_min             0.798681
LDL_min                              0.835244
PEEP Set_min                         0.719606
PTT_min                              0.727627
RBCs_min                             0.210973
WBCs_min                             1.812298
anion gap_min                        0.828858
atypical lymphocytes_min            -0.045170
bands_min                            0.338744
basophils_min                        0.386510
central venous pressure_min          0.779019
chloride_min                         0.912461
creatinine_min                       1.839656
diastolic_min                        0.845130
eosinophils_min                      0.482936
glucose_min                          1.449878
heart rate_min                       1.345402
hemocrit_min                         0.263572
hemoglobin_min                       0.226829
lymphocytes_min                      0.763543
monocytes_min                        0.797664
neutrophils_min                      0.840977
platelets_min                        2.010044
polymorphonuclear leukocytes_min     0.840201
potassium_min                        1.348165
pulse oximetry_min                   0.841153
respiratory rate_min                 0.456714
sodium_min                           0.861531
systolic_min                         1.350522
temperature (F)_min                  0.874941
tidal volume_min                     0.818523
triglycerides_min                    0.818546
troponin_min                         0.082278
BUN_max                              0.236825
HDL_max                              0.835470
INR_max                              0.799710
Inspired O2 Fraction_max             0.716096
LDL_max                              0.835284
PEEP Set_max                         0.546066
PTT_max                              0.628405
RBCs_max                             0.420564
WBCs_max                             2.357782
anion gap_max                        0.792226
atypical lymphocytes_max            -0.046708
bands_max                            0.310692
basophils_max                        0.374720
central venous pressure_max          0.277546
chloride_max                         0.914430
creatinine_max                       1.694140
diastolic_max                        0.815244
eosinophils_max                      0.473199
glucose_max                          1.159525
heart rate_max                       0.880719
hemocrit_max                         0.442768
hemoglobin_max                       0.411552
lymphocytes_max                      0.759415
monocytes_max                        0.786099
neutrophils_max                      0.840721
platelets_max                        2.924893
polymorphonuclear leukocytes_max     0.839764
potassium_max                        0.837730
pulse oximetry_max                   0.842169
respiratory rate_max                 0.418644
sodium_max                           0.851164
systolic_max                         1.094195
temperature (F)_max                  0.849977
tidal volume_max                     0.801705
triglycerides_max                    0.818206
troponin_max                         0.058347
BLACK                                4.143464
AGE                                  0.605534
M                                   -0.700603
0.9% Sodium Chloride                -0.509534
SMX-TMP                             -0.017297
acetominophen                       -1.194747
albuterol                            1.541824
amiodarone                          -0.293648
amoxicillin                         -0.084684
ampicillin-sulbactam                -0.106259
aspirin                              1.375312
atenolol                            -0.168326
atropine                            -0.204264
calcium gluconate                    1.895451
captopril                           -0.196582
carvedilol                          -0.160390
cefazolin                           -0.263253
cefepime                            -0.206430
ceftriaxone                         -0.227986
clonazepam                          -0.146442
clopidogrel                         -0.300981
dextrose                             0.253282
diazepam                            -0.174283
digoxin(?!.*fab)                    -0.196570
diltiazem                            4.572023
diphenhydramine                     -0.267834
enoxaparin                          -0.177901
epoetin                             -0.135121
fentanyl                            -0.149825
fentanyl citrate                    -0.391069
fluconazole                         -0.183031
fondaparinux                        -0.046316
furosemide                           1.570308
glucagon                            -0.415408
haloperidol                         -0.236200
heparin                              0.858553
hydralazine                         -0.344190
hydrochlorothiazide                 -0.162623
hydromorphone                        2.402936
insulin                              0.917195
ipratropium                         -0.496100
labetalol                           -0.196723
levetiracetam                       -0.214156
levofloxacin                        -0.359177
levothyroxine                       -0.346336
lisinopril                          -0.330519
magensium sulfate                    1.423270
meropenem                           -0.172686
metoclopramide                      -0.342260
metoprolol                          -0.795553
metronidazole                        2.884339
midazolam                           -0.320627
nafcillin                           -0.083038
neostigmine                         -0.174589
nitroglycerin                       -0.331162
nitroprusside                       -0.163129
norepinephrine                      -0.256707
ondansetron                          2.088988
oxacillin                           -0.070552
oxycodone                           -0.560896
pantoprazole                         1.285861
penicillin                          -0.056468
phenylephrine                       -0.320703
phenytoin                           -0.251299
phytonadione                        -0.196153
piperacillin                        -0.295791
potassium_y                          1.032929
prednisone                           3.561686
propofol                            -0.385592
ranitidine                          -0.344811
statin                              -0.710375
tacrolimus                          -0.129095
trazodone                           -0.236095
vancomycin                           1.755627
vasopressin                         -0.136875
warfarin                            -0.308817
zolpidem                            -0.258922
Name: 10903, dtype: float64___
```

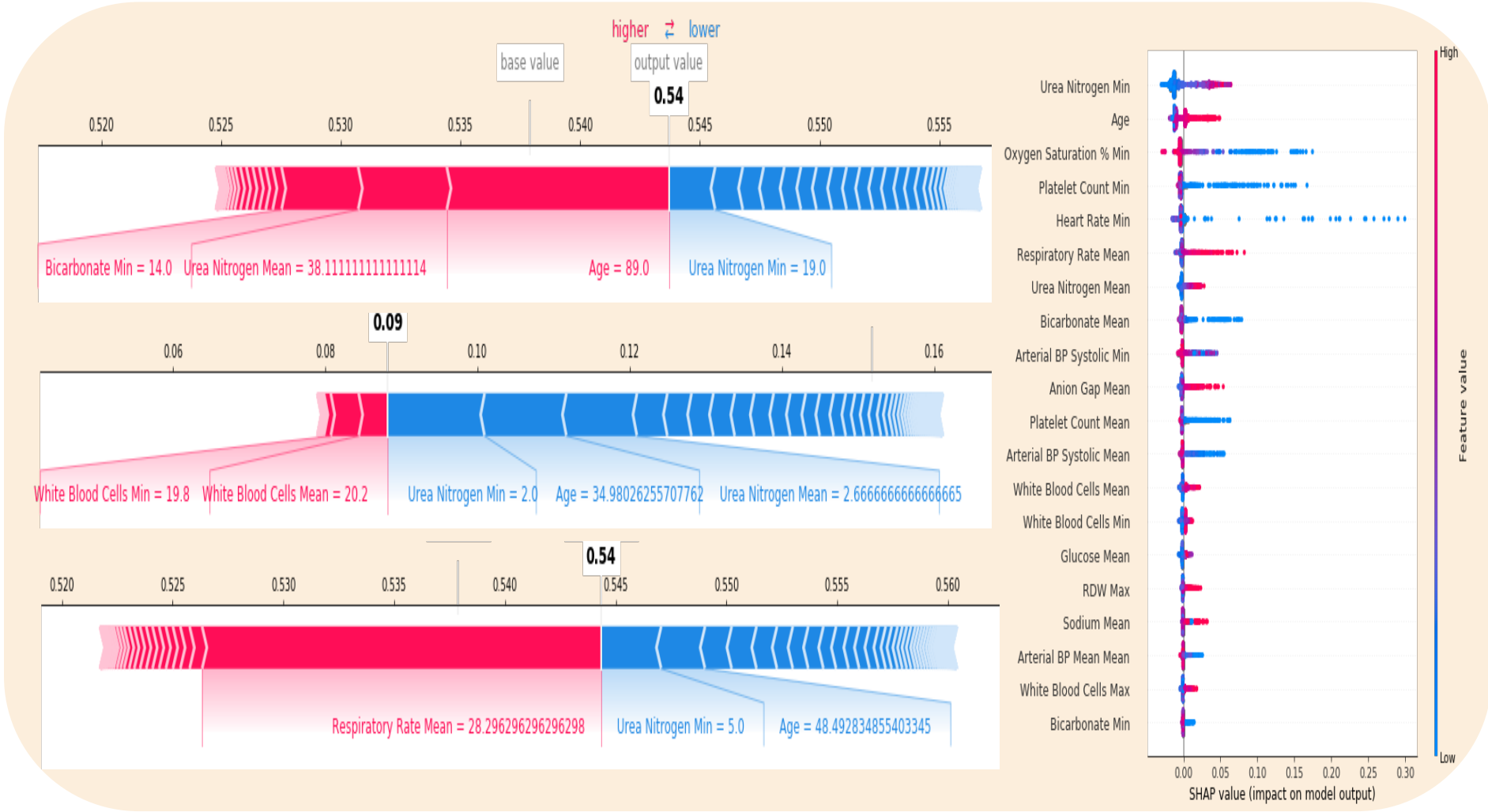
Appendix Figure 5: Example Patient Note


Features
Day
0
1
2
10.0
7.5
5.0
2.5
0.0

Appendix Figure 6: Example Attention Map Patient with Sepsis



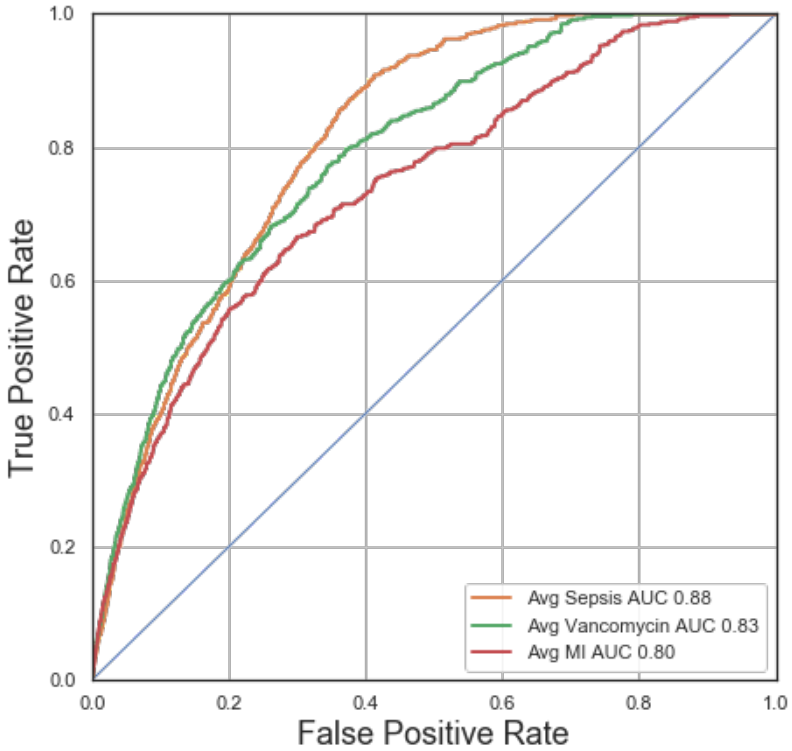
Appendix Figure 7: Thresholded Attention Values for Patient with Pyelonephritis

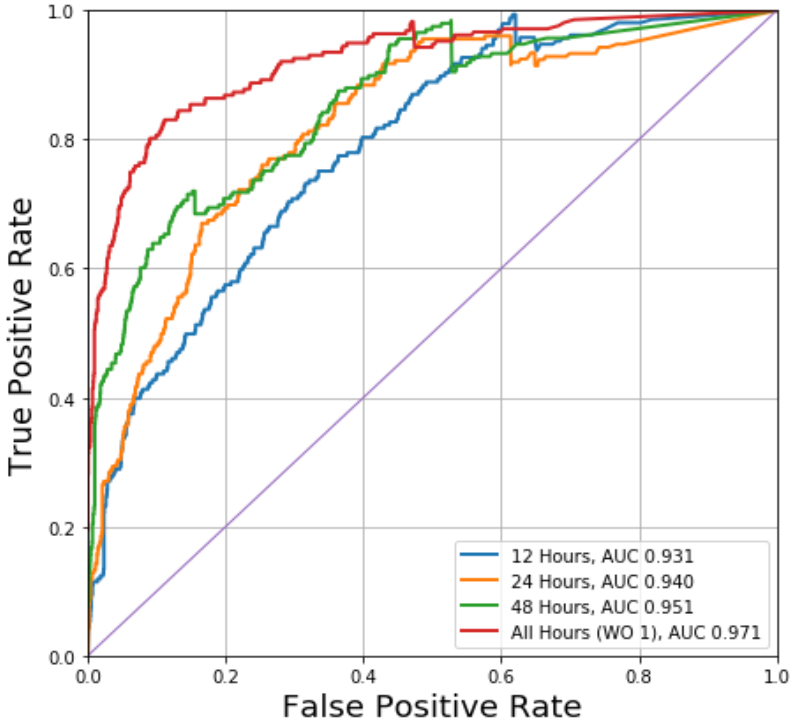


Appendix 8: (a) Examples of SHAP-generated patient variables driving mortality predictions; (b) top 20 highest importance directional patient variables

Evaluation Metric	Mortality	Sepsis	Vancomycin	Myocardial Infarction
AUROC	**0.94**	**0.88**	**0.83**	**0.80**
F1 Score	**86.61**	**69.98**	**66.41**	**37.18**
Precision/Positive Predictive Value	**82.86**	**72.23**	**69.92**	**25.45**
Recall (Sensitivity)/ True Positive Rate	**88.55**	**67.87**	**63.23**	**68.96**

Table 1: Metrics of Evaluation for Deep LSTMs modeling risk of Mortality, Sepsis, Vancomycin, and Myocardial Infarction





Appendix Figure 9: Receiver Operating Characteristic Curves of Mortality at varying times (top) and of sepsis, vancomycin admin, and MI averages among time