A Fuzzy Decision Tree Approach to ICU Patient Mortality Prediction

Anonymous Author(s): 3 members
Implementation Track

1 Abstract

Early hospital mortality prediction can optimize medical staff decision making regarding the treatment of a severely ill patient in the intensive care units (ICUs). Due to the high mortality rates and scarcity of human and material resources in ICUs, ICU staff members need to make optimal clinical and administrative decision including the amount of medical attention needed by a patient and triage, determining the priority of treatment. This study aims to determine the performance of a fuzzy decision tree (FDT) method for predicting patients mortality in ICUs. In order to predict the risk, the most significant features from Medical Information Mart for Intensive Care II (MIMIC-II) dataset were extracted and fed into the FDT model, and the results from the model were analyzed in terms of the efficiency for application purposes in comparison with other machine learning (ML) techniques, such as Bayesian Ensemble, Support Vector Machine, Logistic Regression with Markov Model, Linear Bayes, Neural Network, and Time-Series Motifs. The FDT yielded results that have high interpretability compared to other models, improving it's applicability to aid doctors in making decisions in the ICUs. The accuracy of the model was calculated using a weighted combination score of Sensitivity, Positive Predictive Value and Score1 for comparison purposes. While FDT yielded slightly lower classification accuracy than other ML learning methods, it provided valuable visualization guidelines for human-machine integrated decision making.

2 Introduction

2.1 Background and Motivation

The modern intensive care unit (ICU) has the highest mortality compared to any other units in a hospital[1]. There are more than 5 million ICU admissions per year in the United States for diverse reasons, and all of them require higher frequent assessment and/or technological support than non-ICU patients[2]. Medical errors are more likely to occur in the ICU than in other medical scenes due to the complexity of the care required by the patients, who are extremely ill and undergo multiple complex interventions[3]. On top of mortality effects, it is estimated the annual Cost of Critical Care was $108 billion, and the ICU costs per day were estimated to be an average of $4300 per day [4]. ICU staff members make many crucial clinical and administrative decision such as determining the amount of patient acuity, amount of medical attention needed by a patient, and triage. These decisions are often driven by a dichotomy between investing resources to save a patient or not, increasing the importance of making an optimal decision. An example is nurse staffing and acuity. The ICU normally has a high staffing ratio to improve patient acuity leading to better outcomes[5]. However, the nursing occupation is prone to burn-out and under-staffing, which leads to a reduction in the quality of care[6]. These decisions have the potential to be optimized through information in patient's electronic health record (EHR). An initial solution is the APACHE system to provide patient mortality predictions[7]. This model based its prediction on a set of expert determined rules. Additional models for ICU mortality prediction have been developed using data driven models; unfortunately, these models were determined to lack sufficient use on a individual level.[8].

Many prediction models in use are sub-optimal and leave healthcare professional skeptical due to a lack of understanding of the machine learning decision making process[9]. Risk assessment is crucial to optimize triage and patient acuity decisions. An optimal decision will lead to a reduction in cost of healthcare through efficient resource allocation, and an increase in patient outcomes. EHR data is becoming more available, but is non-standardized between hospital systems, and between patients. This leads to a lack of consistent trends for generic machine learning problems compounding with a lack of understanding of the trend identified by healthcare professionals.

3 Problem Statement

The proposed problem is to identify and build a machine learning method that is capable of handling sparse and complex data from an EHR, while making traceable decision rules that healthcare professionals can understand. From the methods learned in class, the decision tree method creates the most understandable classification. Many attempts to use decision tree to predict mortality have lower accuracy than other machine learning methods. This has left a need to find another tree-based method. Yuan et. al. [10] developed a method using fuzzy decision trees (FDT), a variation of decision tree that creates understandable decisions, and maintain accuracy on-par with other machine learning methods. The FDT model is the focus on this project.

The major advantage of using fuzzy rules for classification applications is to maintain transparency as well as a high accuracy rate. There is extensive research on fuzzy set-based machine learning. For example, Rasmani and Shen [11] have proposed a weighted-fuzzy-subsethood-based learning method. Yuan and Shaw [10] have proposed FDTs induction using fuzzy entropy. Fuzzy logic describes truth values on a range from 0 to 1 differing from Boolean logic where a value is true, 1, or false, 0. The variability in truth value is meant to represent the vagueness and uncertainty in human decision making. Decision are then formed by aggregating multiple fuzzy logic terms.

FDTs have a root on the top and several leaf nodes at the bottom. When a new data sample needs to be classified by the FDT, it traverses from the top to the bottom. The prediction class is chosen as the output class of a leaf node in the bottom for which the data sample reaches highest truth value. For the same training dataset, FDT induction may generate different results with a different minimal number of instances per leaf, which is used as a criterion to terminate the tree building process. Fig. 3 shows a simplified tree generated by FDT induction.

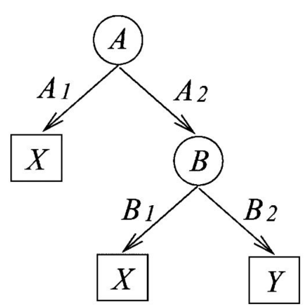

Figure 1: Figure taken from Huang et. al. Fuzzy logic are represented by A and B. Decision tree classes are X and Y

The benefit of using FDT is developing a set of understandable rules similar to decision made by current healthcare professionals. Combining numerical data and logical combinations, the FDT will remain highly accurate while increasing the understandability [12]. FDTs focus on creating structures of data belonging to a particular class as opposed to regular decision trees, which focus on differentiating sample from different classes. The end result of the FDT is readable, and can be verified and studied by clinical experts to ensure the decision is based of a clinical basis.

4 Related Work

Decision trees are a topic covered in class briefly. The decision tree origin comes from the need to create rule extrapolated from past experience(data). The top-down strategy for forming decision trees is based upon recursively dividing subsets of the data until a certain depth or certain accuracy is met. The top-down decision tree classifier consists of an original root node, where each child node is a divide subset based on a inequality of a feature set. Each subset is further divided until a leaf is reached. The leaf represents the predicted class of the data. As simple decision tree algorithm is developed by Hunt include a recursive approach to developing the tree[13]. Each tree has two steps:

1. If a set of S objects belongs to class C_i, then S is a leaf labelled by class C_i
2. Else select a feature, v_i, with a test, T, with the outcomes of $T(v_i) \to O_1, O_2, .., O_n$, where O are possible outcome categories. S_i is now a subset fitting into one of the outcomes, and is then used to recursively build a new tree.

There are many problems with decision trees including the tendency to over fit data, and build over complex trees that are not well equipped to unseen data. Some additional tools are formulated to compensate such as tree pruning. Additional problems with decision trees revolve around the harsh boundary's of each decision. These boundaries and the tree can often be vary with small data perturbations. Decision trees are intuitive and follow human decision making except the decision tree does not model vagueness in human decision making. This is a preface for the development of FDT, where fuzzification of the decision process closely mirrors the uncertainties of a human [10].

4.1 Fuzzy Models for Classification in Medicine

Pota el. al. [14] introduced a technique to Combine Interpretable Fuzzy Models and Probabilistic Inference in Medical Decision Support Systems(DSSs). The approach allows to extract from a training dataset a knowledge base made of interpretable fuzzy sets and fuzzy rules, to calculate probabilities of classes. The method can be split into 3 main steps:

1. Calculation of the priori probability $p(x_v|c_k)$ of each point x_v , given that the class is c_k.
2. Transformation of the priori probability into Interpretable Fuzzy Sets
3. Construction of Base and Inference rule

using one-dimensional models for each one of the H known input variables, it is possible to combine the prioris by assuming independence of input variables and compute the probability of each class by Eq. 1:

$$p(c_k|F_T) = \sum_{t=1}^{T} \lambda_{t-k}\mu_t(x) \tag{1}$$

where λ can be seen as the probability of having the class c_k, given that the fuzzy set F_T, and $\mu_t(x)$ is the orthogonal fuzzy class.

The method implemented in this paper uses similar approach to construct the base and inteference rule. However, The model uses decision tree, instead of priori probabilistic method, to extrapolate the fuzzy logic to return more interpretable results.

4.2 Weighted-Subsethood-Based Method

The Subsethood-Based Method (SBM) consists of three main steps:

- Classifying training data into subgroups, and each subgroup will have the value based on the preferred voting.
- Calculating fuzzy subsethood values of a certain output class to each input fuzzy term. The method of fuzzy subsethood is shown in Eq. 2.

  $$Sub(X, A_i) = (X \cap A_i)/X \tag{2}$$

  where X is a class of data, A_i is fuzzy sets defined on the universe of discourse, $Sub(X, A_i)$ represents the degree to which X is a subset of A1 [11], and $\cap$ is a t-norm operator (MIN) described in Table 1.

- Creating rules based on fuzzy subsethood values.

Table 1: Table of example aggregation

Name	t-norm($\cap$)
MIN/MAX	$\min\{a, b\} = a \wedge b$
Algebraic	ab
Łukasiewicz	$\max\{a + b - 1, 0\}$
EINSTEIN	$\frac{ab}{2-(a+b-ab)}$

The Weighted SBM (WSBM) is a weighted version of the SBM. It uses a certain weighting strategy to represent fuzzy terms rather than choosing the one that has the greatest subsethood value per variable. The weigh for a fuzzy term A_i ($w(X, A_i)$) is defined by Eq. 3.

$$w(X, A_i) = \frac{Sub(X, A_i)}{\underset{j \in A}{argmax}\ \ Sub(X, A_j)} \tag{3}$$

The WSBM then constructs a pattern tree with two depths. On the second depth, all fuzzy terms (with different weights) for each variable aggregate via a t-conorm operator; on the first depth the aggregated values, further aggregate via a t-norm operator. The method applied in this paper incorporated ideas of WSBM to handle the weighting strategy of the model.

5 Methodologies

5.1 Dataset

This study used the datasets provided for the Physionet 2012 challenge [15]. These datasets were originally extracted by the Physionet 2012 challenge coordinators from the openly available Multiparameter Intelligent Monitoring in Intensive Care (MIMIC) II database, developed by the MIT Lab for Computational Physiology to aid patient monitoring research in the critical care environment [16]. The dataset is composed of 4000 patients. All patients are 16 years or older and had ICU stays of at least 48 hours. The data was formatted as time-stamped measurements for 37 distinct variables. Furthermore, measurements for 5 static variables (Age, Gender, Height, ICUType, Weight), which were collected once at the beginning of the patient's ICU stay, are also present in the datasets. However, not all variables are available in all cases and the label is unbalanced. There is a minority class (death) with roughly one-seventh of the total data size, and a majority class (survival).

5.2 Data Pre-processing

All the static variables were converted into scalar features by using their scalar values. Each patient's time-stamped temporal variables were converted to scalar features by extracting the mean and standard deviation. Therefore, for each temporal variable two features were extracted. For static variables, especially height and weight features, a feasibility filter was applied that replaces the implausible values for a more reasonable one. For instance, for a height value below 70cm, it is presumed that the recording unit was erroneous by using inches instead of centimeters. Therefore, a conversion from inches to centimeters was applied. Feature values with missing data were substitute with NaN (Not a Number). Features with the number of missing data higher than a threshold are excluded from the dataset. The threshold was set to be 200 [17]. The Pearson's correlation coefficients matrix were computed for each pair of features. When the coefficient is higher than 0.6, the feature with most NaN was eliminated. After the preprocessing step, the number of features was reduced from 75 to 33. Finally, the remaining NaN entries were replaced by the mean values of their features.

5.3 Fuzzification Logic

The first important step in creating fuzzy trees is to fuzzify the variables. The goal of fuzzification is to map the features set $x \in \mathbb{X}_i$ to a likelihood measurement of a category, $\mathbb{X}_i \rightarrow [0, 1]$. Three major tuning parameters, the number of categories, the functions mapping $f_i : \mathbb{X}_i \rightarrow [0, 1]$, and function parameters, are dependent on the problem statement. The the triangular piece-wise linear, trapezoid piece-wise linear, and the continuous Gaussian function, the most popular fuzzification variable, are implemented with three categories for each, *high*, *medium*,*low*, except for binary variables, where no mapping is required[18]. An example of all three fuzzification function can be seen in the figure 2

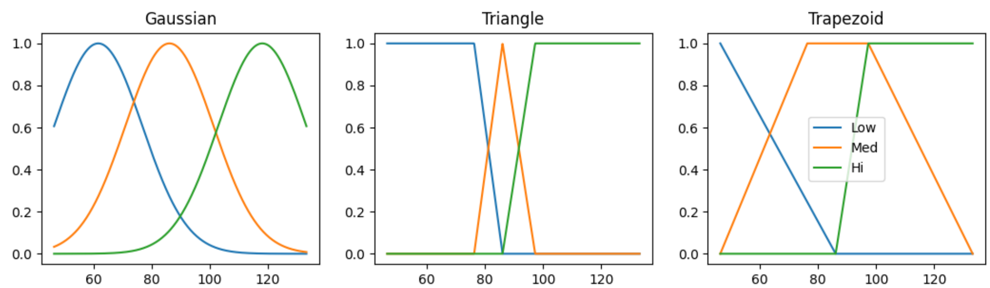

Figure 2: Example fuzzification functions for the Gaussian, triangular, and trapezoidal. Each fuzzification is split into three categories: *low, medium,* and *high*. Key points of the function involve corresponding percentiles

5.4 Fuzzy Decision Tree Induction

The model used follows the FDT induction method proposed by Yuan et al. [10]. Yuan et al have used fuzzy entropy to generate Fuzzy Decision Tree (FDT). It has a root on the top and several leaf nodes at the bottom. In order to classify a data sample, the model traverses from the root to the bottom of the tree and chooses the highest truth value as prediction class. For the same training dataset, FDT induction may generate different results with a different minimal number of instances per leaf due to the vagueness of a fuzzy set.

The vagueness of a fuzzy set ($E_v(A)$) can be express by a fuzzy entropy described in Eq. 4.

$$E_v(A) = -\frac{1}{n}\sum_{i=1}^{n}(\mu_i \ln(\mu_i) + (1-\mu_i)\ln(1-\mu_i)) \tag{4}$$

where A denote a fuzzy set on the universe U with membership function $\mu_a(\mu)$ for all $\mu \in$ U, and n is the size of the discrete set U.

Another factor that causes entropy in a generation process of a FDT is the measure of ambiguity. A fuzzy membership function p(x) of a fuzzy variable Y defined on class X can be interpreted as the possibility of taking value x for Y among all elements in X. The ambiguity is defined in Eq. 5.

$$E_a(Y) = \sum_{i=1}^{n}(\pi_i^* - \pi_{i+1}^*)\ln(i) \tag{5}$$

where $\pi = (\pi(x) \mid x \in X)$ denote a normalized possibility distribution of Y on X, and n is the size of the class set X, π^* is the permutation of the possibility distribution in sorted order.

In this case, $\pi(x) = 1$ means that Y = x is fully possible, $\pi(x) = 0$ means that Y = x is fully impossible. Therefore, the higher $\pi(x)$ is, the more possible that Y = x. Applying the fuzzy logic defined on Table 1, and defining A and B both as subset of X, we have, $\pi(A \cap B) = min(\pi(A), \pi(B))$ and $\pi(A \cup B) = max(\pi(A), \pi(B))$. The possibility distribution π is normalized to $\operatorname{argmax}_{x \in X} \pi(x) = 1$.

Two hyperparameters play a significant role in the FDT induction: β and α. If the ambiguity of a branch during the iterative step falls below a certain threshold, $1-\beta$, the branch is terminated as a leaf. Otherwise, the algorithm investigates if an additional attribute will further partition the branch and further reduce classification ambiguity. This process is followed until no further tree growth is possible. An object belongs to a branch only when the corresponding membership is greater than α. While α filters insignificant branches/leaves, β controls the growth of the tree. Selecting these two parameters is paramount for the implementation of FDTs.

6 Evaluation

6.1 Evaluation Metrics

The results between predicted binary outcomes and observed outcomes was assessed by combination of the number of true positives (TP), false positives (FP), true negatives (TN), and false negatives (FN). The formulas for calculating these statistics are shown in Table 1.

Table 1: List of the performance evaluation metrics

Statistic	**Equation**
Sensitivity (Se)	$\frac{TP}{(TP+FN)}$
Positive Predictive Value (PPV)	$\frac{TP}{(TP+FP)}$

In order to assess the performance of the algorithm, the dataset was split into 70% training set and 30% test set. The model output was a binary variable that dictated high or low mortality risk. The high risk was considered as the positive case, while the low risk was considered as the negative case. The triangular fuzzification method was the one used. The variables considered were chosen as discussed in the "Data Preprocessing" section. Table 2 shows the model performance in terms of the defined metrics for both training and validation sets.

Table 2: Model Performance Evaluation Metrics

Statistic	**Training**	**Validation**
Sensitivity (Se)	0.621	0.532
Positive Predictive Value (PPV)	0.604	0.498

A common metric for calculating the model accuracy is taking the smallest value of sensitivity and PPV, which is defined as the Score1. The FDT had a Score1 of 0.49 on the validation set. Table 3 shoes how FDT compares to other algorithms that predicted binary classification of ICU deaths based on the same dataset. As seen, FDT performed better than Linear Bayes, Neural Networks and Time-Series Motifs. It performed slightly worse than Bayesian Ensemble, SVM and Logistic Regression with Markov Model. However, using FDTs provide other advantages, such as increasing human interpretability, which is discussed in the next section. With accuracy comparable to the best models and ability to translate algorithmic decisions to human-machine decision making, FDTs are promising in terms of use in hospital settings.

Table 3: Score1 for Binary Classification of ICU Mortality Across Models

Model	**Score1**
Bayesian Ensemble [19]	0.535
SVM-GLM [20]	0.534
Logistic Regression w/ Markov Model [21]	0.501
FDT (This Study)	0.498
Linear Bayes [22]	0.493
Neural Network [23]	0.492
Time-Series Motifs [24]	0.456

6.2 Interpretability

One of the advantages of using decision trees is the possibility to translate the algorithmic reasoning into a language that can be easily understood by humans. In the medical field, this is specially important as algorithms are used as an assisting tool for doctors to make critical decisions. In order to create the pattern tree for use in ICUs, it's important to consider the tradeoff between tree size and interpretability. There are two major aspects that define the tree size: the accuracy stopping criteria and the number of feature variables considered.

For an increase in accuracy, the algorithm will generate more nodes and branches in order to fit the data into the pattern tree. However, as the number of branches and nodes increases, it becomes harder to interpret the tree outputs. For example, a tree with a depth of dozens of nodes might be the most accurate over the dataset, but it won't be useful for a doctor to make a decision as going over dozens of node levels will take too long in a hospital setting. Further, as the size of the tree increases, so does the risk of overfitting. A large tree will generally not be generalizable as the branches and nodes will be specific to the observed training data, compromising accuracy over the test set. Thus, it's important to limit the tree growth while ensuring accuracy for the purposes of applying FDTs to estimating mortality rates in ICUs. In general, the tree size is determined by the two previously mentioned hyperparameters, α and β. For the purposes of this section on interpretability, this study considered α and β value that limit the number of node levels to 5.

Further, increasing the number of variables considered in the pattern tree might improve classification accuracy, but could also be detrimental for interpretability. A tree that considers dozens of variables might provide the most accurate results, but often some variables have minor impact on the output and might only make tree interpretation more convoluted. For the purposes of improving interpretability in this section, this study considered only 5 out of the 75 available variables. These variables were chosen based on metrics that have been previously used by doctors in ICUs, such as the SAPS score[25] and the SOFA score[26].

Fig. 3 shows a tree that includes the 5 chosen variables, selected for representability purposes. GCS stands for Glasgow Coma Scale. A high value for mechanical ventilator score indicates that the patient is on a mechanical ventilator, while a low value mean he/she is not. The output nodes indicate mortality risk as a binary variable. Table 4 shows confidence for the classification branches of the tree.

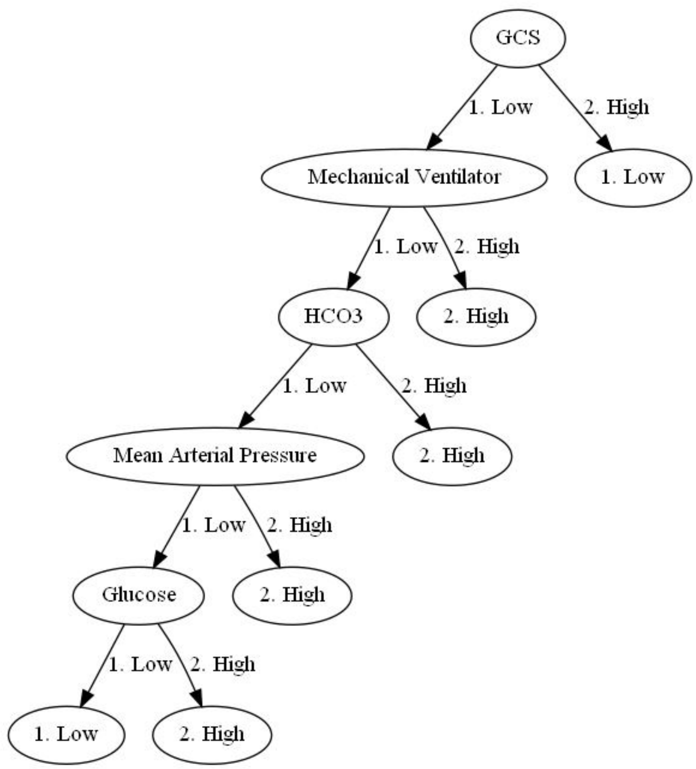

Figure 3: Simplified FDT showing some of the most significant attributes for determining mortality rate in ICUs.

Table 4: Classification Probability Confidence Levels

GCS	Mech Ventilator	HCO_3	MAP	Glucose	Risk	Confidence
High	None	None	None	None	Low	0.58
Low	High	None	None	None	High	0.62
Low	Low	High	None	None	High	0.71
Low	Low	Low	High	None	High	0.67
Low	Low	Low	Low	High	High	0.80
Low	Low	Low	Low	Low	Low	0.83

As seen in Fig. 3, the tree can provide guidelines for doctors to determine if a patient is at high risk or not. For instance, a high value of GSC indicates that the patient has little brain injury and is, therefore, at low risk. High glucose levels can serve as an indicator that the patient is subject to kidney complications[27] and is, therefore, at high risk. Further, each one of these classifications is assigned a confidence level, shown in Table 4. In general, the branches downstream of the tree have higher classification accuracy as they consider more variables in the decision. Overall, the FDT provides reliable indicators that a patient is at risk, having the potential to graphically assist doctors in making decisions. However, this method provides lower accuracy compared to other machine learning methods, such as Bayesian Ensemble and SVM.

7 Conclusion

In summary the fuzzy decision tree (FDT) attempts to replicate decision making process of humans while maintaining accuracy similar to other machine learning classifiers. The healthcare setting, particularly in the ICU, requires many fast and important decisions to be made be a limited number of qualified professionals whose outcomes can drastically change a patients life. This paper focused on categorizing the risk of a patient death when admitted to the ICU in order to eliminate help clinicians make optimal decisions when staff patients and triage. The collected data is the data collected by clinicians during a patients time at the ICU and include both time-varying and feature varying data. These two data processing challenges were overcome by using the mean and standard deviation of the variables over time and eliminating variables sparsely measured. The newly compressed data is then fuzzified to create classification similar to human classification. The fuzzy data is used to drive the creation of an FDT. The FDT classification is compared against other common approaches to this problem including SVM, neural network, and linear Bayes for accuracy of the minimum positive predictive value and interpretabiltiy. Overall, the classification accuracy of the FDT remained in the middle range of other classifiers. This outcome is expected as the FDT is chosen for its interpretability to experts outside the field of machine learning and data science. The interpretability of the FDT is much better than the other models due to its lack of exact numeric boundaries, and logic sequence similar to human thinking. The readability is similar to a flow chart, and its results can be verified relatively quickly by an experts intuition about each individual variable. The FDT is not without drawbacks. The FDT can have a tendency to become much more complex and large that is reasonably acceptable to be readable. This happens with the more features, and less correlated features are used. The larger and more complex trees maintain accuracy, but often over fit the training data or are unreadable.

References

[1] Joseph Antonio D. Molina, Eillyne Seow, Bee Hoon Heng, Wai Fung Chong, and Benjamin Ho. Outcomes of direct and indirect medical intensive care unit admissions from the emergency department of an acute care hospital: a retrospective cohort study. *BMJ open*, 4(11):e005553, November 2014.

[2] Society of Critical Care Medicine. *SCCM Critical Care Statistics*. `https://sccm.org/Communications/Critical-Care-Statistics`.

[3] Philip R. Lee Institute for Health Policy Studies. *ICU Outcomes*. `https://healthpolicy.ucsf.edu/icu-outcomes`.

[4] Joseph Dasta, Trent Mclaughlin, Samir Mody, and Catherine Piech. Daily cost of an intensive care unit day: The contribution of mechanical ventilation. *Critical care medicine*, 33:1266–71, 07 2005.

[5] Robert L Kane, Tatyana A Shamliyan, Christine Mueller, Sue Duval, and Timothy J Wilt. The association of registered nurse staffing levels and patient outcomes: systematic review and meta-analysis. *Med Care*, 2007.

[6] Lusine Poghosyan, Sean P. Clarke, Mary Finlayson, and Linda H. Aiken. Nurse burnout and quality of care: cross-national investigation in six countries. *Research in nursing & health*, 33(4):288–298, Aug 2010.

[7] William A. Knaus, Jack E. Zimmerman, Douglas P. Wagner, Elizabeth A. Draper, and Diane E. Lawrence. APACHE—acute physiology and chronic health evaluation: a physiologically based classification system. *Critical Care Medicine*, 9(8):591–597, August 1981.

[8] Alistair E. W. Johnson and Roger G. Mark. Real-time mortality prediction in the intensive care unit. *AMIA ... Annual Symposium proceedings. AMIA Symposium*, 2017:994–1003, Apr 2018.

[9] Lawrence Liao and Daniel B. Mark. Clinical prediction models. *Journal of the American College of Cardiology*, 42(5):851–853, September 2003.

[10] Yufei Yuan and Michael J. Shaw. Induction of fuzzy decision trees. *Fuzzy Sets and Systems*, 69(2):125–139, January 1995.

[11] K. A. Rasmani and Q. Shen. Subsethood-based fuzzy rule models and their application to student performance classification. In *The 14th IEEE International Conference on Fuzzy Systems, 2005. FUZZ '05.*, pages 755–760, 2005.

[12] Zhiheng Huang, T.D. Gedeon, and M. Nikravesh. Pattern trees induction: A new machine learning method. *IEEE Transactions on Fuzzy Systems*, 16(4):958–970, August 2008.

[13] J. R. Quinlan. Decision trees and decision-making. *IEEE Transactions on Systems, Man, and Cybernetics*, 20(2):339–346, 1990.

[14] Marco Pota, Massimo Esposito, and Giuseppe De Pietro. Combination of interpretable fuzzy models and probabilistic inference in medical dsss. 11 2013.

[15] Ikaro Silva, George Moody, Daniel J Scott, Leo A Celi, and Roger G Mark. Predicting in-hospital mortality of icu patients: The physionet/computing in cardiology challenge 2012. *Computing in Cardiology*, 39:245–248, 2012.

[16] Mohammed Saeed, Mauricio Villarroel, Andrew T. Reisner, Gari Clifford, Li-Wei Lehman, George Moody, Thomas Heldt, Tin H. Kyaw, Benjamin Moody, and Roger G. Mark. Multiparameter intelligent monitoring in intensive care ii: A public-access intensive care unit database*. *Critical Care Medicine*, 39(5), 2011.

[17] M. Macaš, J. Kuzilek, T. Odstrčilík, and M. Huptych. Linear bayes classification for mortality prediction. In *2012 Computing in Cardiology*, pages 473–476, 2012.

[18] R. Senge and E. Hüllermeier. Top-down induction of fuzzy pattern trees. *IEEE Transactions on Fuzzy Systems*, 19(2):241–252, 2011.

[19] Louis Mayaud Athanasios Tsanas Andrew A Kramer Gari D Clifford Alistair EW Johnson, Nic Dunkley. Patient specific predictions in the intensive care unit using a bayesian ensemble. *Computing in Cardiology*, 2012.

[20] A. Bosnjak and G. Montilla. Predicting mortality of icu patients using statistics of physiological variables and support vector machines. *Computing in Cardiology*, pages 481–484, 2012.

[21] Syed Haider Abigail Flowers Adam Seiver Srinivasan Vairavan, Larry Eshelman. Prediction of mortality in an intensive care unit using logistic regression and a hidden markov model. *Computing in Cardiology*, 2012.

[22] Martin Macas, Jakub Kuzilek, T. Odstrcilik, and Michal Huptych. Linear bayes classification for mortality prediction. *Computing in Cardiology*, pages 473–476, 2012.

[23] Adam Petrie Xiaopeng Zhao Henian Xia, Brian J Daley. A neural network model for mortality prediction in icu. *Computing in Cardiology*, 2012.

[24] Alexander Van Esbroeck Ilan Rubinfeld Zeeshan Syed Sean McMillan, Chih-Chun Chia. Icu mortality prediction using time series motifs. *Computing in Cardiology*, 2012.

[25] Flavio Lopes Ferreira, Daliana Peres Bota, Annette Bross, Christian Mélot, and Jean-Louis Vincent. Serial Evaluation of the SOFA Score to Predict Outcome in Critically Ill Patients. *JAMA*, 286(14):1754–1758, 10 2001.

[26] Flavio Lopes Ferreira, Daliana Peres Bota, Annette Bross, Christian Mélot, and Jean-Louis Vincent. Serial Evaluation of the SOFA Score to Predict Outcome in Critically Ill Patients. *JAMA*, 286(14):1754–1758, 10 2001.

[27] Laetitia Koppe, Elsa Nyam, Kevin Vivot, Jocelyn E. Manning Fox, Xiao-Qing Dai, Bich N. Nguyen, Dominique Trudel, Camille Attané, Valentine S. Moullé, Patrick E. Macdonald, and et al. Urea impairs β cell glycolysis and insulin secretion in chronic kidney disease. *Journal of Clinical Investigation*, 126(9):3598–3612, 2016.