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Machine Learning For Detection Of Acute Respiratory Distress Syndrome

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Abstract: In some clinical applications, the performance of a machine learning algorithm may be negatively impacted by patient incorrect label uncertainty during training for a supervised learning job. For instance, because of uncertainty in the patient's condition or the unreliability of the diagnostic criteria, even clinical professionals may be less confident when making a medical diagnosis for some patients. Thus, certain examples utilized in algorithm training could have incorrect labels applied to them, which would negatively impact the algorithm's performance. In certain situations, professionals might be able to measure their diagnostic uncertainty, though. In order to account for such clinical diagnostic ambiguity while training an algorithm to predict individuals who develop acute respiratory distress syndrome (ARDS), we provide a robust technique that uses support vector machines (SVM). A condition of the severely sick known as ARDS is identified using clinical criteria that are known to be unreliable. Our method of representing ambiguity in the diagnosis of ARDS involves assigning a graded weight of confidence to every training label. In order to limit overfitting, we also employed a unique time-series sampling technique to address the issue of intercorrelation among the longitudinal clinical data from each patient utilised in model training. Based on preliminary results, we may compare our technique that takes into account the uncertainty of training labels with a traditional SVM algorithm and obtain a significant improvement in the system's ability to diagnose patients with ARDS on a hold-out sample.

Keywords: Machine learning, support vector machine, label uncertainty, acute respiratory distress syndrome, sampling from longitudinal electronic health records (EHR).

I.INTRODUCTION

Severe respiratory failure brought on by extensive lung inflammation is the hallmark of Acute Respiratory Distress Syndrome (ARDS), a potentially fatal illness. Improved patient outcomes and prompt care depend on the early and precise identification of ARDS. The use of machine learning (ML) algorithms in the medical field has shown a lot of promise recently for the identification and diagnosis of a wide range of illnesses. In order to enhance diagnostic precision and enable timely intervention, this research investigates the application of machine learning algorithms for the diagnosis of acute respiratory distress syndrome.

Because of its quick start and propensity for worsening, ARDS presents a serious challenge to medical personnel. Early detection of ARDS allows for timely and effective therapies, which can have a substantial influence on patient outcomes. Even though they are valuable, traditional diagnostic techniques can not always result in early diagnosis.

ML algorithms are a viable way to improve ARDS detection because of their capacity to examine intricate patterns and correlations in data.

The availability of high-quality, carefully-curated datasets is essential for building machine learning models for ARDS identification. ML algorithms may be trained and validated using patient data, such as clinical parameters, vital signs, laboratory findings, and imaging investigations. To guarantee the models' resilience, preprocessing procedures include resolving class imbalances, managing missing data, and normalising features.

Finding pertinent characteristics is essential to creating precise machine learning models. The selection of variables that are clinically significant and aid in the early identification of ARDS requires domain expertise and coordination with healthcare experts. Respiratory rate, oxygen saturation, results from a chest X-ray, and inflammatory markers are examples of features.

II. RELATED WORKS

Every year, 200,000 individuals in the US are afflicted with the severe sickness syndrome known as Acute Respiratory Distress Syndrome (ARDS) [1]. Despite the 30% death rate associated with ARDS, patients can benefit from a variety of evidence-based therapy techniques to enhance their prognosis [2]. Recent data, however, indicates that individuals with ARDS may not be diagnosed at the time of the illness and may not get evidence-based treatments that have been shown to lower mortality [3]. Poor detection of ARDS has been explicitly linked to healthcare personnel' incapacity to handle the enormous volumes of clinical data collected while providing care for these patients [4]. To enhance early ARDS diagnosis, algorithms that evaluate electronic health record (EHR) data and notify clinicians when patients exhibit ARDS symptoms have been suggested [5, 6].

Currently, EHR data is analysed using straightforward rule-based computerised algorithms to screen patients for ARDS [7]. To identify patients, current algorithms look for wording compatible with ARDS throughout radiological reports. However, for these methods to be effective, chest imaging needs to be done as soon as ARDS manifests itself, and a radiologist needs to promptly and properly interpret the radiological image using terminology that may be read as consistent with ARDS. For these dependencies to be successfully implemented in clinical practice, there exist issues. Systems that identify at-risk patients only using routinely gathered clinical data may notify physicians of individuals who require further assessment, especially initiating chest imaging for prompt diagnosis of ARDS.

The construction of reference patient cohorts for the algorithm's training presents another difficulty in the development of an ARDS detection system. Clinical specialists must assess each patient's clinical data in a sophisticated manner in order to diagnose ARDS.

Using this extra information about diagnostic certainty during training could result in more effectively learning and better generalisation to new patient cases when training an algorithm to detect ARDS, as opposed to eliminating patients with diagnostic uncertainty. A new machine learning approach called "learning with uncertainty" [12] would be a good fit for the problem of developing an ARDS detection system. Learning a function $f(x): X \rightarrow Y$, which translates input training data $x \in X$ to class $y \in Y$, is the typical machine-learning classification job. X is a feature space of each patient's covariates, and Y is the classification label. Labelled training examples provide well-defined input data for the model's training. On the other hand, in certain clinical applications, there can be ambiguity in the training labels, which could have a negative impact on model training. In the case of ARDS, for instance, there could be tough situations when clinical ambiguity makes it difficult for the doctor to diagnose a patient. This ambiguity might thus have a negative impact on model training, leading to the mislabeling of training data.

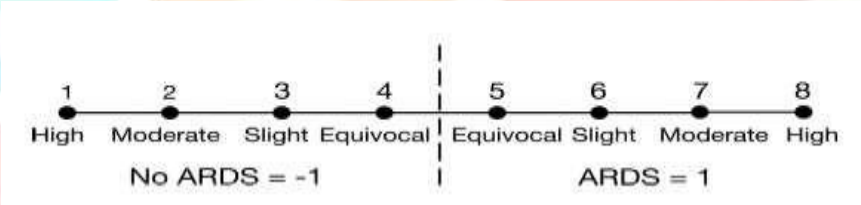
In the current investigation, clinical experts provided their degree of confidence in the diagnosis after reviewing each patient's clinical data to assess whether or not they acquired ARDS. The confidence of the label's annotation served as a representation of this uncertainty grade. The confidence weighting of the label is utilised as extra information in the training process of a support vector machines learning model. This method is a type of instance-weighted SVM, however during SVM training, we employ a clinical expert's confidence in the diagnostic weights rather than learning weights based on the data's attributes [17] or weights based on the class label [18]. This method

balances the impact of such uncertain inputs in the learning process, avoids deleting doubtful data, and adds a more realistic depiction of uncertainty in real-world applications.

III. METHODOLOGY

The patient group consisted of consecutive adult patients who were admitted to the hospital in January 2016 and were diagnosed with moderate hypoxia, which was defined as needing a nasal cannula to provide more than 3 L of extra oxygen for at least two hours. More patients who experienced acute hypoxic respiratory failure (PaO2/FiO2 ratio of less than 300 mm Hg while on invasive mechanical ventilation) in February and March of 2016 and who are at an increased risk of developing ARDS were added to the group. The technique for detecting ARDS was developed using data from 401 patients in total.

Based on the Berlin criteria, a team of knowledgeable medical professionals examined each patient to see if ARDS was developing [32]. Since ARDS lacks a straightforward gold standard, expert performance cannot be benchmarked in this clinical diagnosis. However, these patients were assessed independently by three experts, and their scores were averaged, because it is known that individuals with acute hypoxic respiratory failure have only modest inter-rater reliability for ARDS diagnosis. Apart from ascertaining the presence or absence of the diagnosis and documenting the beginning time of ARDS in individuals that tested positive, the experts were also requested to indicate their degree of confidence in the diagnosis classification (high, moderate, low, or ambiguous). Before being used in this study, the experts thoroughly evaluated this 4-point confidence scale to ensure that it accurately captured the range of uncertainty that they could have while evaluating patient situations. As shown in Fig. 1, their diagnosis label and confidence level may then be translated into a 1–8 scale, where 1 indicates no ARDS with high confidence and 8 indicates ARDS with high confidence.



Those obtained before to the time of onset in patients who developed ARDS were labelled as no ARDS, but those gathered subsequent to the time of onset were labelled as ARDS. Following expert evaluation, 48 out of the cohort's patients received an ARDS diagnosis with a confidence level of 5 or above.

During the first six days of a patient's hospital stay, time-stamped vital signs and laboratory results were taken from each patient's Electronic Health Record (EHR) and used as clinical characteristics (covariates) to train the ARDS algorithm. On the advice of clinical specialists, only regularly obtained vital signs and laboratory results that could be associated with ARDS were included. On request, more information on the clinical variables included in the model might be provided. By using this method, the model's total feature count was reduced to 24 variables that are often used in clinical practice. Statistical feature selection approaches were not applied before the model was trained. Every two hours, patients were checked on, and past data was kept on file until a new value was noted. In cases when a patient's vital sign or laboratory tests were not conducted, clinical data was assumed to be normal. When creating clinical prediction models, this is the conventional method that is used, and it assumes that data is not obtained because the treating physician had a low suspicion that it would be aberrant.

IV. PATIENT RECORDS

The patient group consisted of consecutive adult patients who were admitted to the hospital in January 2016 and were diagnosed with moderate hypoxia, which was defined as needing a nasal cannula to provide more than 3 L of extra oxygen for at least two hours. More patients who experienced acute hypoxic respiratory failure (PaO2/FiO2 ratio of less than 300 mm Hg while on invasive mechanical ventilation) in February and March of 2016 and who are at an increased risk of developing ARDS were added to the group. The technique for detecting ARDS was developed using data from 401 patients in total.

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In order to put this sampling technique into practice, we first computed pairwise correlation distance matrices to show reliance across the time series data for each patient. Each observation is represented as a 1-by-n row vector, and the correlation distance between vectors Xa and Xb for a single pair of observations is calculated as follows given an m-by-n matrix for each patient's data, where m is the number of times the patient was seen.

$$d_{ab} = 1 - \frac{(X_a - \bar{X}_a)(X_b - \bar{X}_b)'}{\sqrt{(X_a - \bar{X}_a)(X_a - \bar{X}_a)'}\sqrt{(X_b - \bar{X}_b)(X_b - \bar{X}_b)'}}$$

where:

$$\bar{X}_a = \frac{1}{n}\sum_j X_{aj} \text{ and } \bar{X}_b = \frac{1}{n}\sum_j X_{bj}$$

An m-by-m correlation distance matrix for each paired observation made on the patient may be obtained using this correlation distance formula.

The initial step in the sampling process involves calculating the correlation distances between Xt and {Xt }, where Xt is the time-series data instance at the beginning of a patient's data set and Xt } is the span of all following time-points. Next, a sample threshold denoted by ξ is established, signifying the point at which the interdependency among data becomes increasingly restricted.

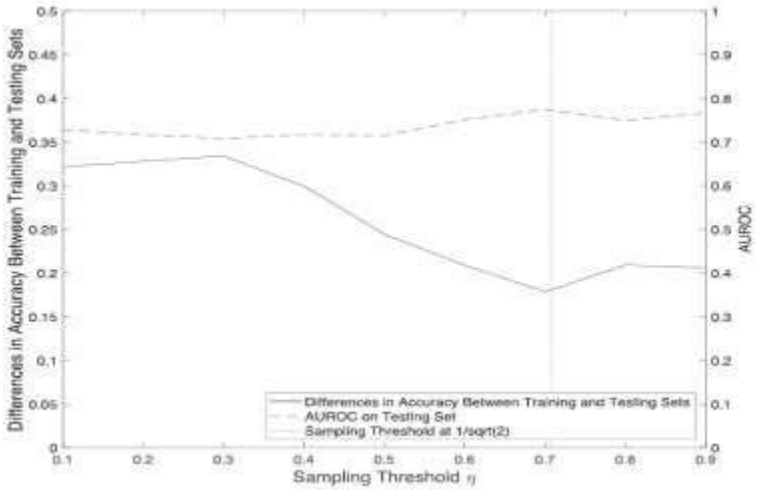


Fig. 2. Effects of different sampling thresholds on prediction generalizability with SVM.

V. SUPPORT VECTOR MACHINE

To take label uncertainty in the classification model into account, we apply the Support Vector Machine formulation found in [40] as follows. This formulation incorporates the slack variable ξi to permit some misclassification and also includes the penalty parameter C to establish soft-margin decision boundaries because ARDS and non-ARDS examples are not linearly separable. In this implementation, support vectors that are based on patients' data with high label confidence are given more weight and influence in the SVM decision boundary.

$$\min_{w,\xi} \frac{1}{2} \parallel w \parallel^2 + C \sum_{i=1}^{N} z_i \xi_i$$

subject to:

$$\begin{cases} y_i(w^T x_i + b) \geq 1 - \xi_i, & i = 1, \ldots, N \\ \xi_i \geq 0 \end{cases}$$

where:

$$z_i = (|l_i - \alpha| - \beta) * \gamma + \delta$$

As seen in Fig. 1, uncertainty in the label (li) is integrated inside (zi) to directly affect the box constraint (C). The formula for zi creates a scalable weight for that particular observation by combining two linear adjustments for the label annotation's uncertainty (li).

Algorithm 1: Pseudocode for our algorithm to sample time-series data and reduce inter-dependency.

Input : All available time-series data $\langle X_t \rangle$ from each patient.
for *each patient* **do**
  partition data into separate bins according to the classification label;
  if *size of either bins is* ≤ 4 **then**
    sample all available data;
  else
    1) select X_t at the start of the time-series data and sample this instance;
    2) calculate the pairwise correlation distance from X_t to $\langle X_t \rangle$;
    3) sample the first row in $\langle X_t \rangle$ with a correlation distance $< \eta$ and set as the new X_t;
    repeat
      1) set $\langle X_t \rangle$ as all points subsequent to X_t;
      2) calculate the pairwise correlation distance matrix from X_t to $\langle X_t \rangle$;
      3) sample the first row where the correlation distance is $< \eta$ and set as the new X_t;
    until *pairwise distance of* X_t *to* $\langle X_t \rangle > \eta$;
  end
end
Output: Partial data $\{X_t, X_{t1}, X_{t2}, \ldots, X_{tn}\}$ with reduced inter-correlation from each patient.

In this application, we scale li, with a range of 1–8, into the weighting zi, having a range of 40–100 in increments of 20, by setting α = 4.5, β = 3.0, γ = 20, and δ = 90. Consequently, ambiguous labels (such as li = 4 or 5) receive the weight zi = 40, but labels with great confidence (such as li = 1 or 8) receive the weight zi = 100. After that, zi is set to 1.

In order to make the classifier place greater focus on points with high confidence, this formula for zi modifies sample weighting based on li and rescales the C parameter as Ci for each observation in a patient's data structure.

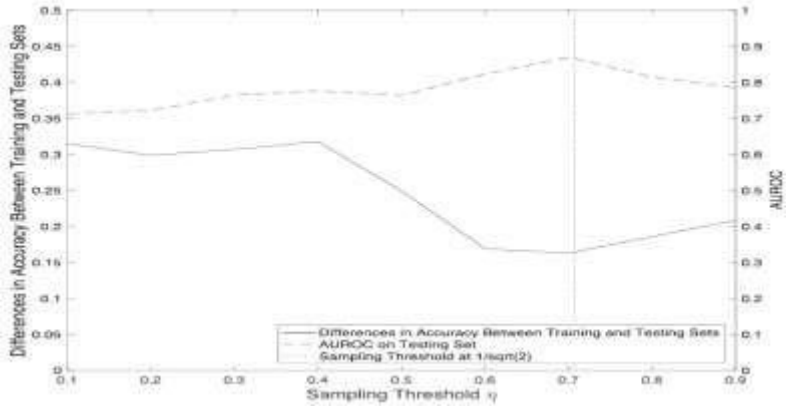


Fig. 3. Effects of different sampling thresholds on prediction generalizability with SVM and label uncertainty.

To ensure that our proposed sampling strategy and threshold still maintains for SVM with label uncertainty, we repeat the previous analysis to show the effect of different sampling thresholds on prediction generalizability. Fig. 3 confirms that optimal results are achieved when the sampling threshold is approximately 0.7, which supports the previous analysis and the literature suggested value of $\sqrt{1/2}$.

The main learning methods that we compare in this study are linear SVM with and without label uncertainty. The data was initially normalised in order to keep features with wide dynamic ranges from dominating the separating hyperplane before these models were constructed.The training data was then sampled in order to reduce correlation between data points on the same patient, using the previously mentioned recommended sampling procedure. The training set had 13,722 total incidences before sampling, with 736 of those being positive. Following sampling, a total of 1,893 cases were found, of which 736 were positive.

To identify the ideal value of the hyper-parameter C using grid search across $C \in \{0.001, 0.01, 0.1, 1, 10, 100, 1000\}$, 5-fold cross validation was used to the training data. Afterwards, we used this ideal C value to retrain the model on the complete training set. The patients in the hold-out dataset were subsequently classified using this revised model and all of their data (i.e., no sampling was done on the holdout data).

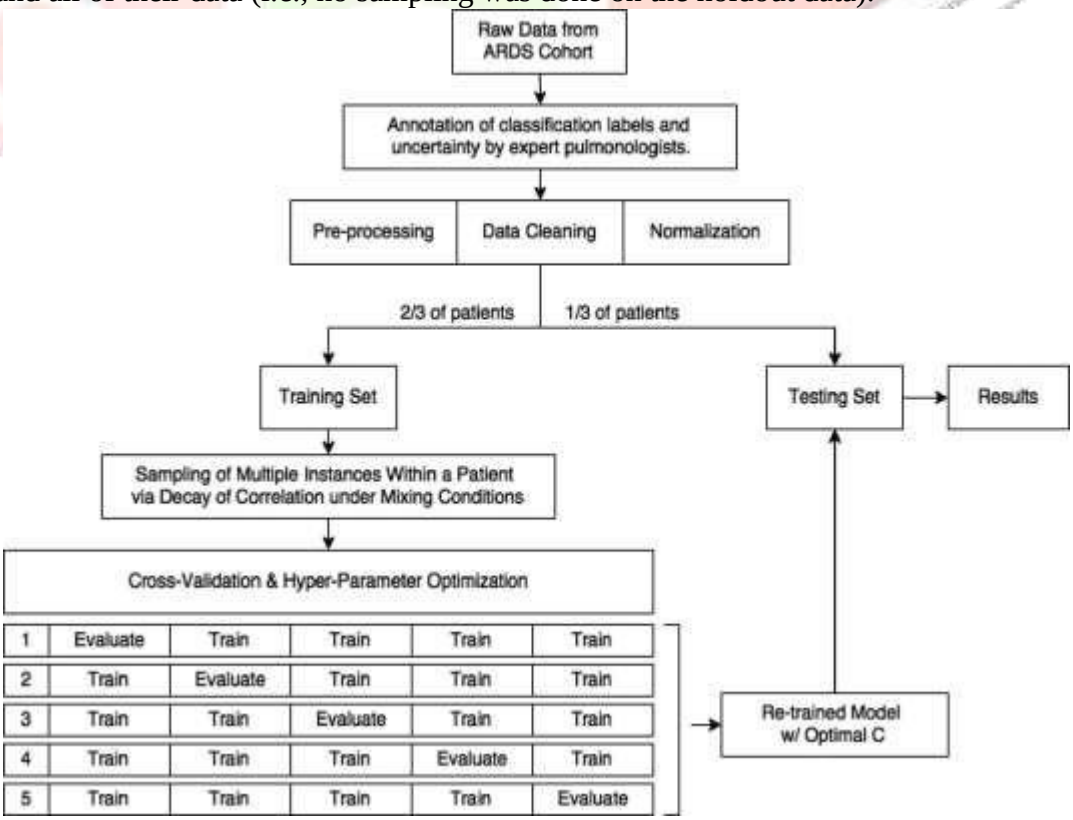


Fig. 4. Flowchart of this study's protocol with 5-fold cross-validation and hyper-parameter optimization using grid search.

The majority of specialists examining the patient assigns a label, which is compared to the model predictions for each patient in the holdout sample, i.e., ARDS = 1 or −1. Using the same subsampled training/testing bins and 5-fold cross validation partitions, we also evaluate the performance of our suggested SVM approach with Random Forest and Logistic Regression to see if the obtained results are on par with or better than other cutting-edge techniques.

VI. RESULTS AND DISCUSSION

From the research cohort, 401 patient cases in total were available. Of the samples in this collection, 353 were negative and 48 were positive for ARDS. A hold-out group of one third of the patients was retained for testing, while the remaining two thirds were employed in the model training procedure. To prevent bias in the data, all samples from the same patients are retained only in the testing or training sets not both.

Fig. 5 displays the average correlation decay for the data of each subject. At a distance of about 22 hours, the correlation between Xt and Xt averagely falls below η. When the data was analysed individually based on the categorization label, Fig. 6 demonstrates that the decay of correlation was different: decay of correlation is detected when ARDS = -1 but not when ARDS = 1. As a result, the data for the sample under the η technique was processed when ARDS = -1, hence lowering the quantity of negative instances needed for model training. Sampling was not done because of the smaller sample size and absence of correlation decay at ARDS=1, which would have made the class imbalance worse.

When evaluating in the holdout sample, we saw an improvement of more than 10% in AUROC (0.8548 versus 0.7542) when the SVM was trained to take uncertainty in the label into account (Fig. 7).The SVM model that took into account label uncertainty also showed better specificity and beats the standard model when the algorithms were benchmarked at sensitivity of 95% and 90% (to guarantee few ARDS patients are missed) (Table I). Because it is crucial clinically for a model to have a high sensitivity and not overlook instances of ARDS, these sensitivity thresholds were set to high values.

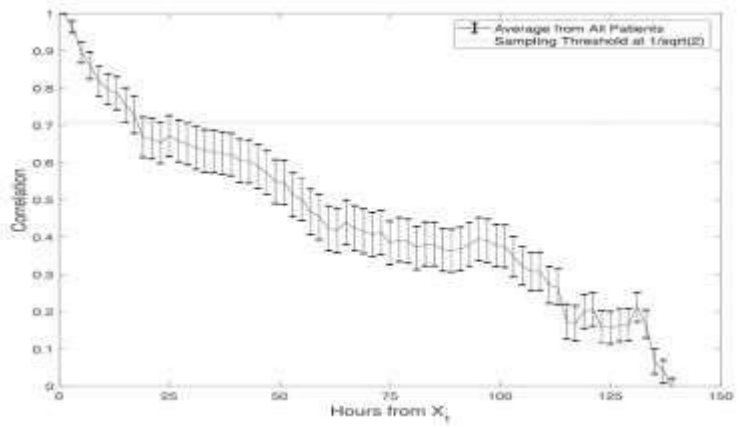
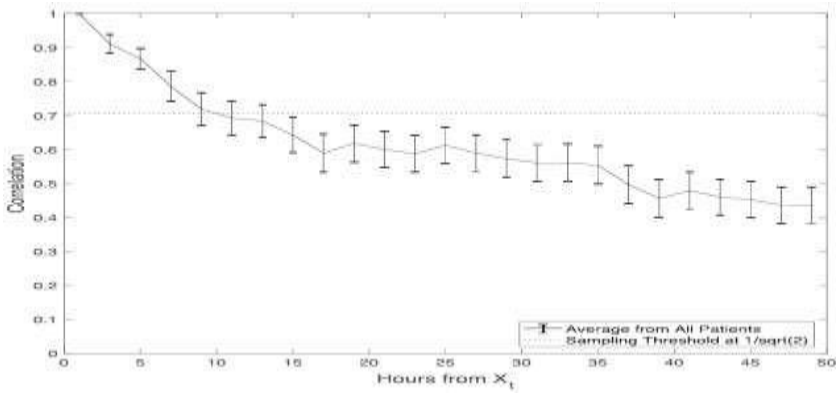


Fig. 5. Average decay of correlation from all patients.

Using regularly gathered electronic health record data, we demonstrate a powerful machine learning system to identify Acute Respiratory Distress Syndrome in hospitalised patients. Compared to a traditional SVM learning model, we find a 10% improvement in AUROC in a hold-out data set when label uncertainty is included as a weight on classification penalty throughout the learning process.

As a restricting weight of confidence on the SVM's box constraint, the clinical expert's uncertainty in each patient's categorization label was incorporated into the training process of our suggested SVM model.



This method makes use of clinical specialists' information on the level of uncertainty associated with each label, as opposed to treating it as simple stochastic noise, in order to increase the effectiveness of model training. Our label weighting implementation (zi) rescales the cost of misclassification based on the uncertainty associated with each label (li), hence directly influencing the C parameter. In the SVM decision boundary, support vectors derived from patient data with high label certainty are given greater weight, whereas examples Figure 6.

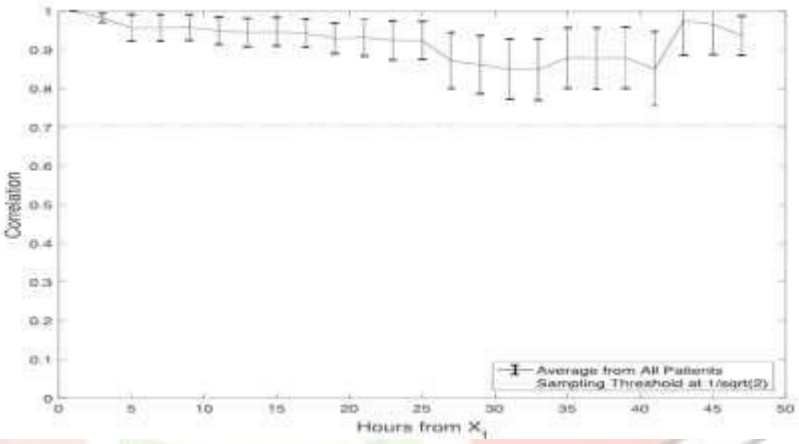


Fig. 6. Average decay of correlation from all patients during (a) negative diagnosis of ARDS and (b) positive diagnosis of ARDS.

Average correlation decay across all patients during (a) an ARDS negative diagnosis and (b) an ARDS positive diagnosis. The standard error of the mean is shown by error bars, and the correlation between the first observation taken on each patient and the time (hours) is represented by each point are given less weight when calculating the SVM hyperplane if there is greater uncertainty. Future research should investigate other mappings between the label uncertainty (li) supplied by clinical specialists and the label weighting (zi) that is employed to determine the SVM decision border.

In order to reduce inter-correlation between data points in the training set, we employed a unique sampling technique and investigated whether the data could be represented under mixing circumstances. In order to represent the data under mixing circumstances, it is necessary for the correlation between data from the same patient to diminish with time, with CF,G(n) → 0 as n→∞. Overall, this assumption was validated by a plot of the correlation function of the data in Fig. 6, but not for the data that had the categorization label ARDS = 1.

	Sampling Based on the Proposed Correlation Decay Method				Random Sampling for Balanced (2:1) Training Data		No Sampling	
	Accuracy	AUROC	Specificity at 95% Sensitivity	Specificity at 90% Sensitivity	Accuracy	AUROC	Accuracy	AUROC
Logistic Regression	0.7263	0.7265	0.3007	0.4267	0.6982	0.6979	0.6621	0.6454
Random Forest	0.7434	0.7488	0.3392	0.4751	0.7111	0.7254	0.6873	0.6903
SVM	0.7492	0.7542	0.3797	0.5114	0.7253	0.7361	0.6920	0.7152
SVM w/ Class-Weighted Cost Function	0.7804	0.8113	0.4571	0.5918	0.7478	0.7703	0.7094	0.7122
SVM w/ Uncertain Labels	0.8157	0.8548	0.5285	0.6450	0.7698	0.7989	0.7188	0.7431

Because it might not be fair to assume that all data types can be represented under mixing conditions, it is necessary to plot the data's correlation function before using the sampling technique. Patients' data showed very high inter-correlation with minimal discernible degradation when they were diagnosed with acute respiratory distress syndrome (ARDS), suggesting a robust mixing mechanism. Consequently, the suggested sampling strategy would have produced relatively few data instances that could be used for training and would not have been successful in decreasing inter-correlation. When considering this finding from a clinical perspective, it made sense. A patient's condition rapidly changes as a result of clinical intervention or a decline in health when they are admitted to the emergency room for pulmonary injury (e.g., sepsis) and have not yet reached the critical stage of ARDS. This causes less stability and inter-correlation in the recorded data. Less quickly would the data alter if the patient had ARDS because that condition is known to be the last stage of lung injury.

We chose not to use the sampling approach when ARDS = 1, which would have guaranteed a more equal amount of positive and negative instances in the training data, because there were noticeably more negative than positive examples. Using the sample method for the data instances where ARDS = 1 was observed would have further exacerbated the imbalance between positive and negative examples and hindered the model's capacity to learn an appropriate decision boundary. A pairwise correlation distance matrix was employed in our sampling strategy to measure dependency inside the data structure. Quantifying the assessment of reliance between Xt and {Xt { can be done in a variety of ways. A thorough set of mathematical definitions for dependence coefficients, which describe these mixing requirements and quantify correlation decay, is provided by Bradley et al. We want to conduct a more thorough analysis of the data structure in subsequent work by employing formalised definitions of mixing, including α-mixing coefficient quantification of dependence.

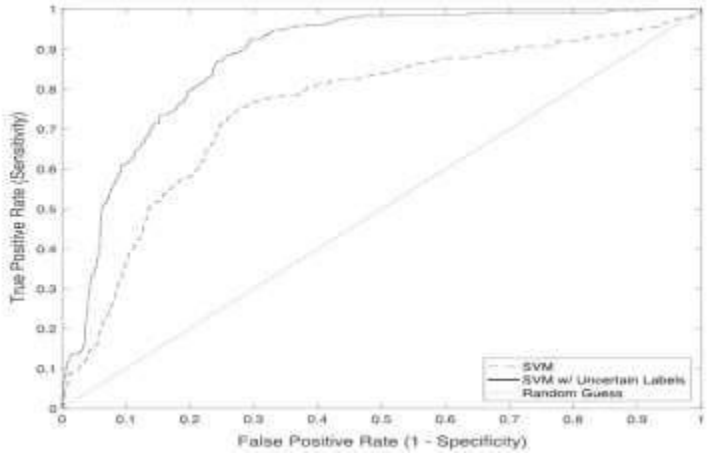


Fig. 7. ROC curve comparing SVM with and without label uncertainty.

By creating a considerably more balanced training dataset and reducing dependencies in each patient's time series data, our sampling approach performs better than utilising all available data (no sampling) from the EHR, bringing the data closer to the state of being i.i.d. For each patient, we also compared our sample technique against random sampling on negative cases in order to get a 2:1 negative to positive ratio.

The ARDS model in this study was fitted with a linear SVM. We discovered that an SVM with a nonlinear kernel (RBF) produced less consistent results in preliminary work not presented. The RBF kernel SVM fared worse (in

terms of accuracy and AUROC) on the hold-out set, although typically outperforming linear SVM on the training dataset. We discovered that the performance of the SVM with RBF kernel was lower on the test set even with 5-fold cross-validation and grid-search hyper-parameter optimisation (of C and gamma). Additionally, the standard deviation of the results (after multiple random train-test splits) was 2-3 times larger than the linear SVM.We hypothesise that the amount of variables utilised as machine learning features and the smaller sample size may have contributed to overfitting. We decided to concentrate on utilising label uncertainty in the modelling process utilising solely linear SVM as it was more reliable.

When creating machine learning algorithms for healthcare applications, privileged information—information that is accessible during training but not during real-time model deployment—may also be commonly available. It may also be pertinent for the diagnosis of acute respiratory distress syndrome.

We demonstrate how the level of trust a skilled physician has in a diagnostic label may be used as critical data to guide the model training procedure. A generalizable strategy that might be used to several medical applications is to take advantage of the recognised diagnostic ambiguity within a medical area. For instance, sepsis is a clinical illness for which prompt diagnosis is essential to provide the best possible therapy. Nonetheless, there is sometimes diagnostic ambiguity, which hinders the development of reliable algorithms for sepsis identification. Similar to ARDS, an algorithm for sepsis diagnosis may perform better when label ambiguity is included during training.

VI. CONCLUSION

This work presents and evaluates a machine learning approach for ARDS identification that incorporates uncertainty in the classification label. In order to avoid the development of a biassed model, it also outlines a unique sampling technique that lowers inter-correlation among longitudinal clinical data. We successfully trained an ARDS classification system using these innovative methods, which performed noticeably better than a typical method. Our suggested SVM technique, which makes use of label uncertainty, was compared to other common classification models, such Random Forest and Logistic Regression, in Table I. The misclassification cost function was proportionate to the weight of imbalance in the datasets. In order to produce a more balanced dataset, we also contrasted our sampling approach with an other technique that uses random sampling on negative cases to get a 2:1 negative to positive ratio from each patient. We also looked at performance utilising all of the available data without sampling.

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