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MIMIC III and its contribution to critical care prediction models

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Abstract:

Purpose - *The present paper attempts to present the research that has been made on prediction models using deep learning methods with data retrieved from mimic III database and to identify challenges and possible areas for future research.*

Methodology - *A literature research was conducted for articles related to MIMIC III and prediction models related to the database published from 2016 to 2021. Also, reviews and papers related to neural networks, machine learning, data mining and implementation and usage of electronic health records (EHR) in ICU were investigated to support findings from mimic III papers.*

Findings - *Prediction algorithms can be very useful in ICU units. Although some algorithms, such as InSight are specialized in specific diseases, others such as XGBOOST and recurrent neural networks can be used in a broader area, presenting quite accurate results.*

Originality - *Usually, reviews categorize research on MIMIC database per disease or per the desired outcome, such as the prediction of length of stay and the final outcome. The current study categorizes the research based on the tools, prediction models, and algorithms used. This way, it is possible to understand better how each method performs to various conditions and desired outcomes.*

Index Terms — MIMIC III, neural networks, random forests, prediction models, Intensive Care Units, big data

I. INTRODUCTION

Intensive medicine is a multidisciplinary area of medical sciences which is focused on the prevention, diagnosis and treatment of severe diseases and conditions **[1].** The recent crisis of covid-19 resulted in an overwhelming demand for beds, especially in critical care **[2]**. Therefore, nowadays, there is a necessity for the development of tools that will support the even more difficult task of doctors and support staff to address new challenges that the pandemic brings. It is generally accepted that ICUs produce a large amount of data. Properly using these data could be useful for patients' outcome prediction or the possibility of readmission **[3]**. However, a significant barrier in medical studies is the lack of reproducibility, which incommodes the creation of reliable clinical decision-making tools **[4]**. Towards this

direction, a very useful tool for the scientific community is the MIMIC III database. Mimic III is a large database of 26 tables containing data from around 60.000 patients' admissions to the Beth Israel Deaconess Medical Center intensive care unit in Boston, Massachusetts, between 2001 and 2012.

The main categories of data include patient demographics, medications, vital signs, lab results, survival data, length of stay, imaging reports, ICD-9 codes, fluid balance, observation and free text notes from care providers **[5]**. The dataset is freely available, but researchers who wish to use it must complete a recognized course for protecting human research participants and signing a data user agreement. Code is available in MySQL, PostgreSQL and MonetDB. In addition, there are scripts and libraries in Python and R. to facilitate the creation of views from raw data.

II. METHOD

A. Review Stage

This research paper focuses on publications related to MIMIC III database and techniques whose purpose is the prediction of patients' treatment outcomes or their length of stay in ICU. To use the latest available data, the papers have been filtered by year of publication greater than 2016. After that, they have been categorized by the model they use so that performance measurement of every method is possible when applied to various conditions.

III. PREDICTION TOOLS

A. Neural Networks

Neural Networks can be divided into five major categories, artificial neural networks (ANN), Back propagation ANN, Recurrent Neural Networks, convolution neural network and Long Short-Term Memory Recurrent Neural Network. From the healthcare perspective, all the categories above are implemented to create prediction models. Researchers argue that better performance of new machine learning methods exists because clinical data and outcomes are non-linear, and technologies such as random forests (RF), support vector machine and ANN are more capable than regression models **[6]**.

Artificial Neural Networks can be used for early prediction of in-hospital mortality for specific conditions. For example, back propagation A.N.N. can be useful in predicting the mortality of patients with acute pancreatitis. Its significant

advantage is that it can detect the disease earlier than other methods (logistic regression, Ranson score, SOFA score), allowing early interventions that could significantly improve clinical outcomes [7]. In another study, ANN also shows better mortality prediction concerning acute kidney injury (AKI) over Bayesian networks and logistic regression [8]. However, there are differences in machine learning methods applied: For the same disease (AKI), newer studies indicate that random forest has better AUROC and Brier Score than ANN [9].

B. Recurrent and Convolution Neural Networks

Recurrent Neural Networks (RNN) have been proven effective in predicting various outcomes during a patients' treatment in a health care unit. For example, a RNN is being used to predict hospital readmission for lupus patients [10] or for the prediction of a medical event (change in patient's health status) by using data from medical notes [11][12].

Towards this direction, researchers try to implement and improve their RNN by applying them in MIMIC III database for a specific disease outcome or in a more generalized way. Furthermore, recurrent neural networks can also be used in real-time to predict severe complications during a patient's stay in critical care. Meyer et al. applied RNN to patients older than 18 years old that underwent major cardiothoracic surgery to predict possible complications after surgeries. Using routinely collected clinical data from MIMIC III without needing manual data processing, the deep learning methods showed accurate predictions immediately after patient admission to the intensive care unit. More specifically, for mortality, the PPV is 0.90 and the sensitivity 0.85; for renal failure 0.87 and 0.94 and for bleeding 0.84 and 0.74, respectively, outperforming standard clinical reference tools.

A similar approach concerning the data gathered can be used to monitor patients' mortality risk. With the use of long short-term memory Recurrent Neural Network and recent general health data of laboratory tests, vital signs and medications from LABEVENTS, CHARTEVENTS and INPUTEVENTS_MV tables as well as from ADMISSIONS and DEATHTIME tables, it is possible to achieve better AUROC and AUPRC scores compared to SAPS II [13].

Another case of RNN usage is its implementation in predicting sepsis. The purpose was to conduct a retrospective analysis of adult patients admitted to the intensive care unit who did not fall under the definition of sepsis at the time of admission but developed it afterwards. Despite the fact that the length of the look-back significantly impacts the classifier's performance, the result shows that a recurrent neural network is superior to InSight –another method of predicting sepsis- in terms of performance. However, further research is necessary to detect sepsis onset for retrospective analysis [14] correctly.

Recurrent Neural Networks can also be used in conjunction with random forests to create prediction models for patients with various diagnoses. In such cases, the data must include general characteristics such as admissions, CPT Events, ICU Stays Patients, Procedures ICD, Diagnoses ICD9. The resulting predictive model performs with an accuracy of approximately 80% for long and short stays. However,

removing ICU length of stay from the inputs and predicting it for both ICU and hospital in combination with categorized disease conditions would be more beneficial in real life [15]. At this point, it is important to note that most prediction models do not fully utilize the information available to locate the parameters that would be useful [16]. A resource of valuable information that is often not considered is physicians' clinical text notes [5]. With the implementation of deep learning methods (both Recurrent Neural Networks and Convolution Neural Networks) it is possible to achieve high predictive ability in ICD-9 code assignment based on clinical notes [17]. With the use of clinical text, it is also possible to predict Medical Codes (ICD) during a patient's stay in ICU. CNN can aggregate information and select the most relevant parts for each possible code [18]. Both authors indicate that better manipulation of non-standard writing and a better understanding of the relation between symptoms and diagnosis could improve deep learning models or even the ability to predict diagnosis and treatment codes of patients' future admissions.

C. XGBoost

Extreme Gradient Boosting (XGBoost) is a scalable end-to-end tree-boosting system used by data scientists to address various machine learning challenges by using fewer resources to achieve desired results [19]. Compared to other methods, XGBoost shows some interesting findings. Zhu Yibing et al. implemented XGBoost to establish prediction scores on mechanically ventilated patients with the classical severity scores and other features available on the first day of admission of ventilated patients. The model outperformed *K*-nearest neighbors (KNN), logistic regression, bagging, decision tree and random forest methods.

In another study, XGBoost combined with the least absolute shrinkage selection operator (LASSO) and a large variety of clinical data resulted in a good prediction or mortality rate in ICU for patients with heart failure which potentially could contribute to clinical decision-making for patients that belong to this specific category [20]. XGBoost can also be used for specific diagnosis mortality prediction. It performs better than logistic regression and SAPS II in predicting sepsis-3 mortality for a period of 30 days. As in the previous case, the author claims that more accurate prediction models may be clinically helpful and assist clinicians in tailoring made and precision treatment for patients with sepsis-3 [21].

D. Random forests

Random Forest is an efficient technique that can operate in a fast way over large datasets [22]. As presented in chapter B, it has been used in many real-world applications in various fields, including healthcare in combination with the RNN model. However, random forests can be combined with other methods and stand-alone.

Comparisons made with the same predictor variable among the random forest, ANN, support vector machine (SVM) model and customized SAPS II model in predicting in-hospital mortality for ICU patients with Acute Kidney Injuries (AKI) indicate that there is great potential for

implementation of RF model thus allowing rapid clinical intervention **[18]**.

Random forest method can also be useful in detecting patients eligible for discharge by utilizing routinely collected vital signs and lab results of the last 4 hours that meet specific criteria. The prerequisite for this success is to base discharge decisions on historical data of patients that were ready and not ready for discharge. Using this method, machine learning classifiers outperformed the nurse-led discharge (NLD) criteria **[23]**.

E. Auto Triage and InSight

InSight is a machine learning algorithm that detects and predicts sepsis, severe sepsis and septic shock. The algorithm uses fundamental patient data (basic vital signs, peripheral capillary oxygen saturation, Glasgow Coma Score, and age) that can be retrieved from EHR, making it a method that can be integrated into almost every system.

According to several researches, InSight performs well even when there are randomly missing data **[24]**. More than that, InSight outperforms existing sepsis scoring systems in identifying and predicting sepsis-only vital signs data when applied not only to one but to various EHR datasets **[25]**. These results are also confirmed by studies that use data different than MIMIC III, demonstrating a sensitivity of 0.90 (95% CI: 0.89–0.91) and a specificity of 0.81 (95% CI: 0.80–0.82), outperforming existing biomarker detection methods **[26].**

The collection of widely available clinical variables has also been proven useful in other prediction types. An algorithm called AutoTriage uses eight common variables retrieved from EHR to result in patient mortality scores. With the use of 8 common clinical variables (heart rate, pH, pulse pressure, respiration rate, blood oxygen saturation, systolic blood pressure, temperature, and white blood cell count), AutoTriage creates subscores for each one of them alone and in combinations which finally results in a final score **[3]**. Apart from this, AutoTriage can also be used for specific condition mortality prediction model. In similar research for patients with alcohol disorder, AutoTriage generates accurate predictions through multi-dimensional analysis outperforming existing systems (MEWS, SOFA, SAPS II) with an Area Under Receiver Operating Characteristic (AUROC) value of 0.934 for 12-h mortality prediction **[27]**. In both cases, AutoTriage improves the accuracy of mortality prediction in the ICU compared to other severity scoring systems in use.

IV. DATA SELECTION

A major issue in implementing prediction models in the health sector and especially in ICU is data selection. Despite the richness of data, concrete knowledge about data that should be used and for what purpose is still missing. The majority of the prediction models are not fully utilizing the information available to locate the parameters that would be usable. In general, researchers try to indicate useful data for their outcomes. As expected, the depth of data selection varies depending on the method used. A significant advantage of InSight and AutoTriage algorithms is using a few common clinical variables such as demographics, heart rate, pH, pulse pressure, and respiration rate that can be easily obtained from EHR **[3] [24][28]**.

On the contrary, in cases that RNN or Boosting Trees are used, more detailed data are required. The selection of data in these cases is dependent on the disease outcome. For example, in prediction models for mechanically ventilated patients, besides demographics and many vital signs, comorbidities and a large set of laboratory variables are needed **[29]**. A similar approach is also used for predicting mortality for patients with acute kidney injury (AKI) in ICU with the help of random forest. For this case, twelve physiological variables, age, type of admission and three underlying disease variables are retrieved from patient data **[9]**. In cases of hospital length of stay prediction, a combination of various diagnoses based on selected general characteristics data from admissions, CPT Events, ICU Stays, Services, Patients Procedures and Diagnoses ICD data are needed **[15]**. However, the time of the data creation may vary. Among other data such as length of stay and demographics **[21]**, data created in the first 24 hours of a patient's admission to the hospital are of extreme usage.

In cases where text notes (unstructured format) from clinical staff are needed, data that exist mainly on the note events table of the MIMIC III database are mined. This data is useful for ICD-9 code assignment from clinical notes using CNN **[18]** and RNN **[17]**.

Finally, in any case of structural data, it is important to mention that MIMIC III holds data from two systems: that of Philips CareVue and the one of MDSoft MetaVision systems. Each requires a different approach **[30]**.

Table 1: Categorization of final purpose and data types per prediction method

Method Used	Purpose	Data used
Convolution Neural Network	ICD assignment based on clinical test, ICD prediction during ICU stay	medical notes, discharge summaries, laboratory tests, vital signs and medications
Recurrent Neural Network	hospital readmission, change of patient's health status, mortality risk, sepsis prediction	Demographics, medical notes, laboratory tests, vital signs and medications, ICD procedures, ICD diagnoses, discharge summaries
Random Forest	mortality for Acute Kidney Injuries (AKI) patients, discharge eligibility	physiological variables, age, type of admission, underlying disease variables, routinely collected vital signs and laboratory results
AutoTriage	patient mortality scores, specific condition mortality prediction	Common clinical variables such as demographics, heart rate, pH, pulse pressure, respiration rate
XGBoost	prediction scores on mechanically ventilated patients, prediction or mortality rate for patients with heart failure and sepsis, specific diagnosis outcome prediction	Demographic data, length of stay in clinic, vital signs, laboratory results, accompanied diseases
InSight	detection and prediction of sepsis, severe sepsis and septic shock,	Common clinical variables such as demographics, heart rate, pH, pulse pressure, respiration rate

V. FUTURE WORK

Investigating the related papers, it is apparent that the scientific community claims that a big problem concerning the use of machine learning and deep learning methods in medicine, especially in ICUs, is the lack of reproducibility. This is happening due to a variety of reasons. Alistair et al. highlight the need for improvement in models reported results with detailed technical description of data abstraction to facilitate the comparison among them. An effort towards solving this problem is also the development of an open-source pipeline for transforming the raw electronic health record (EHR) data from MIMIC-III database into data structures that are directly usable in common time-series prediction pipelines. At the same time, they are extensible for future research efforts [31].

Another reported issue is that most of the research is being conducted using data from one dataset (one hospital or ICU), possibly including patients of limited demographics and health history. In addition, in some cases, prescriptions, labs and vitals, various treatments and interventions or notes are excluded from the retrieved data [31] many times because of the limited timeframe that the research is conducted [32]. Moreover, nursing notes may present different characteristics because of variations in clinicians, experience, training and working environment, causing the results to be useful only to units where the research is taking place [33].

These three facts, by default, limit the potential of possible generalization of results to other hospitals or EHR systems [24]. As expected, to address these problems tests with data from different hospitals and medical centres [3] and further external validations to test the generalization need to be acquired [29]. Furthermore, future model development should consider more prospectively collected variables to evaluate the association of different clinical and laboratory characteristics, minimize any possible bias [7] and shorten prediction horizons about ICU mortality [32].

It is essential to mention that additional work is also required in methods that cope with free text notes, such as discharge summaries that predict the disease in each patient. Research on which words affect the probability of a prediction could improve the relationship between symptoms and diagnosis and consequently improve deep learning models [17]. This way, it would be possible to predict treatments and diagnosis codes for future visits. Also, it would greatly benefit the handling of non-standard writing to improve and document the structure of discharge summaries to be implemented in MIMIC III and IV [18].

Another issue the scientific community faces is that some diseases' diagnosis standards are unclear, with sepsis as the most prominent example [14]. Consequently, further research is necessary to determine the correct onset detection for cases like sepsis, as it varies depending on the number of accepted interpolations [5].

Finally, even though the machine and deep learning models seem very promising, further research on their performance is required. But even in that case, studies about clinicians' degree of acceptance of prediction methods must take place to evaluate whether they are prominent to new methodologies [8].

VI. CONCLUSION

The use of machine learning and deep learning methods for predicting outcomes in ICUs could offer great advantages in how they operate and deliver health care services. However, some limitations do not allow the methods that this review analyzed to be broadly adopted.

Probably the most important of those barriers is the lack of interoperability and reproducibility due to various reasons analyzed in the previous chapter. MIMIC III is a significant step towards reproducibility because its data are freely available and because there are data views, open-source libraries and freely available code that support information extraction from the database. However, as many researchers argue, current prediction models should be

tested in various conditions and data. Especially the missing data is the most common issue in machine learning during the analysis of healthcare data **[34]**. To confront this barrier, researchers tend to impute or remove the observation **[35]**. Therefore, the results of prediction models should be compared not only to the latest MIMIC IV but also to other databases such as National Inpatient Sample (NIS) or specific hospital records. In this way, it is possible to clarify whether a model can be widely adopted or is made for particular conditions that may still be useful in real-world conditions. In any case, the adoption of prediction models and their acceptance by the clinical staff as a prerequisite could improve health care in terms of quality, cost and final result.

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