



## The Role of Artificial Intelligence in Early Diagnosis of Sepsis in Emergency Departments

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### ABSTRACT

In order to enhance our capacity to forecast the danger of sepsis, we created a topic-based, NLP-enabled AI system that integrates structured EMR data with the NLP analysis of doctors' clinical notes. In order to determine if a patient is in sepsis at the time of study, our algorithm specifically obtains, examines and summarizes clinical notes from doctors. It then combines these sets of condensed clinical information with structured clinical characteristics. In cases where sepsis is not diagnosed at the time of analysis. The following identifiers were extracted by us: email addresses, phone numbers, fax numbers, car numbers, ID numbers, zip codes, names, geographic subdivisions and ID numbers. Second, we removed all punctuation from the text in the documents, lemmatized the words by substituting their root form, applied part-of-speech tagging and eliminated stop words like articles and prepositions in order to tokenize the content. A lengthy list of medical-related stop words and phrases that are frequently used in these texts but have no real use was also eliminated. Examples of these include "report," "progress," "provide" and "lab unit" (the authors may offer a comprehensive list of all the terms and phrases that are not included in subject modeling upon request). Following these two procedures, we produced a term-document matrix, in which the documents were represented by columns and the occurrence (a measure of frequency) of each term in the documents by rows. We create the dependent variable for sepsis. Patients with at least one of these ICD-10 codes who are admitted to the ICU ward and are diagnosed with sepsis are assigned to the sepsis case cohort since this is how the hospital currently treats patients who have been diagnosed with the disease. The non-sepsis control group comprises all patients who do not fit these criteria. The training and validation samples consist of 260 sepsis patients, whereas the test sample has 97 sepsis patients. According to hospital protocol, we use the ICU ward admission time to determine the sepsis onset time. AI accelerates and increases the precision of sepsis diagnosis. Treatment regimens for sepsis can be tailored to the unique features of each patient and their reaction to medication. AI can also be utilised to continuously monitor sepsis patients, informing medical professionals about the patient's clinical status and guaranteeing a prompt and effective therapeutic response.

### OPEN ACCESS

#### Key Words

Sepsis, artificial intelligence (AI), diagnosis, detection

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## INTRODUCTION

Early prediction of sepsis is crucial in preventing mortality, given that sepsis management is highly time sensitive<sup>[1]</sup>. Based on international medical guidelines<sup>[2]</sup>, early fluid resuscitation is recommended to commence within the first 3h to stabilize sepsis-induced tissue hypoperfusion, and administration of intravenous antimicrobial is recommended to commence at the earliest possible time, specially within 1 h of sepsis<sup>[2-4]</sup>. Further, sepsis mortality increases significantly with each hour of delay in antimicrobial administration<sup>[3,4]</sup>. As sepsis management is often based on a standardized management approach<sup>[2]</sup>, early sepsis identification may be practically challenging and operational constraints in healthcare delivery can lead to unacceptably high mortality rates. For example, delay in communication among clinicians, nurses and pharmacist exacerbates delay in sepsis management. Hence, the early prediction of sepsis before its onset in a patient gives clinicians additional lead time to plan and execute treatment plans.

Most of the existing methods for sepsis diagnosis and early prediction only take advantage of structured data stored in the electronic medical records (EMR) system<sup>[5-7]</sup>. However, research has shown that about 80% of the clinical data in EMR systems consist of unstructured data-i.e., data stored without a pre-determined or standardized format<sup>[8]</sup>. Common examples of such unstructured data are free-form text (e.g., clinical notes) or images (e.g., radiological images). These unstructured clinical data contain rich information, i.e., additional clinical details not captured in the EMR structured data fields. Physicians use such unstructured clinical data fields to record “free-form” clinical notes as structured data is designed to store only pre-determined discrete data (e.g., patient vital signs). Physicians also depend on unstructured data to review judgments and critical clinical information entered by other clinicians to gain a better understanding of a patient’s condition or effects of their treatment. Consequently, unstructured EMR data are a potentially rich data source to develop better artificial intelligence (AI) tools, especially for medical conditions such as sepsis, where early symptoms are ambiguous and difficult to recognize. To this end, more recent work has incorporated text-mining of clinical notes to improve the accuracy of early sepsis prediction<sup>[9,10]</sup>. During the past decade, the National Institute of Health (NIH) has invested the most in the sepsis field, with 1435 projects and 476.9 million US dollars in funding. The National Natural Science Foundation of China was in second place, with 47.7 million US dollars awarded to 581 projects. The total allocation for sepsis research by the National Grants-in-Aid for Scientific Research (JSPS KAKENHI) Program in Japan was the lowest, with 429 projects and funding of 23.8 million

US dollars<sup>[8]</sup>. Differences in the health care budget for sepsis in various institutions worldwide can also be evaluated. In many countries, there is no record of sepsis-funded projects<sup>[11]</sup>. Approximately 200 studies containing sepsis-related research were published in the Medline database from 2011-2015 by the USA, the European Union’s 28 member states and China. Notably, more than half of these studies were published by authors from the USA, with more than half having a university or government/state funding source. Despite these advantages, sepsis funding remains challenging and many industry-based companies are current sponsors of major sepsis organizations such as the Surviving Sepsis Campaign (SSC)<sup>[12]</sup>.

Here, we developed a topic-based, NLP-enabled AI algorithm that combines the NLP analysis of physicians’ clinical notes with structured EMR data to improve our ability to predict the risk of sepsis. Specifically, our algorithm extracts, analyzes and summarizes physicians’ clinical notes and combines these sets of summarized clinical information with structured clinical variables to classify if a patient has sepsis at the time of analysis. For patients who are not classified as having sepsis at the time of analysis, the algorithm will then predict the risk of those patients having sepsis in the following 4, 6, 12, 24 and 48 h. Unlike prior NLP sepsis predictive models, our model operates in situations where the prevalence of sepsis is as low as 6%-equivalent to the prevalence of sepsis in hospitals observed in historical studies<sup>[13]</sup>. In addition, we found that mining clinical notes provide significant improvements to the predictive accuracy over structural variables for predictions 12-48 h ahead of the onset of sepsis; this is also beyond the accuracy of physician predictions. As discussed above, under standard sepsis management protocol, every hour delay in completion of the administration of the 3-h bundle is found to be associated with a 4% increase in mortality<sup>[14]</sup>, thus the ability of our algorithm to speed up diagnosis and early detection would potentially reduce overall mortality in hospitals in a significant way.

## MATERIALS AND METHODS

This study examines patients admitted at Sree Mookambika Institute of Medical Sciences, Padanilam, Kulasekharam, Kanyakumari. The following five procedures are how we handled the unstructured free-form text. First, we anonymized all potential identifiers from the clinical notes in accordance with HIPAA standards and recommendations. The following identifiers were extracted by us: email addresses, phone numbers, fax numbers, car numbers, ID numbers, zip codes, names, geographic subdivisions and ID numbers. Second, we removed all punctuation from the text in the documents, lemmatized the words

by substituting their root form, applied part-of-speech tagging and eliminated stop words like articles and prepositions in order to tokenize the content. A lengthy list of medical-related stop words and phrases that are frequently used in these texts but have no real use was also eliminated. Examples of these include "report," "progress," "provide" and "lab unit" (the authors may offer a comprehensive list of all the terms and phrases that are not included in subject modelling upon request). Following these two procedures, we produced a term-document matrix, in which the documents were represented by columns and the occurrence (a measure of frequency) of each term in the documents by rows.

Third, we reduced the number of terms in the processed text by weighting the frequencies of terms with numerous occurrences and removing uncommon terms using a text filter. Fourth, to identify the different themes, we sent the phrases to the LDA topic clustering method. The amount of topics that can be derived from the text is very arbitrary and frequently depends on the quantity of observations or the anticipated diversity of subjects in the dataset, according to the body of existing literature. Following these recommendations, we tried five distinct iterations with 25, 50, 75, 100 and 150 topics as part of our robustness checks. Following further examination of the data, qualitatively comparable outcomes were obtained for each of the five iterations in the final prediction model., as a result, the 100-topic model for brevity was presented in this study.

An ensemble that votes is used in our primary estimation. An ensemble machine learning model called "voting" aggregates the predictions of several different models (basis classifiers). Here, we employ a random forest technique and a logistics regression based on stochastic gradient descent (SGD) as our two basic classifiers. We compute the average probability of the two base models as our voted probability, meaning that our combination rule is an average of probabilities.

The first base classifier, or SGD, is an optimising method that learns from previous fit estimates iteratively in an effort to minimise prediction error. In order to estimate the parameters of the model used to identify a patient as having sepsis or not, the approach iteratively selects random samples from the training sample. With every sample iteration, it learns how accurate the classification is and modifies the parameter estimation until there is little room for improvement in the prediction outcomes.

Because of privacy constraints under the Human Biomedical Research Act (HBRA) 2015, the raw datasets created and analysed during this study will not be made publicly available. You can get raw datasets for review. The raw data contains patient clinical data, including textual clinical notes that were

produced by doctors and may contain information that violates the consent or privacy of research participants (patients). The accompanying author can provide the processed textual data with vitals upon reasonable request.

## RESULTS AND DISCUSSIONS

This study examines patients admitted at Sree Mookambika Institute of Medical Sciences, Padanilam, Kulasekharam, Kanyakumari. Using the ICD-10 codes for sepsis, severe sepsis, or sepsis shock and the existence of ICU hospitalisation, we create the dependent variable for sepsis. Patients with at least one of these ICD-10 codes who are admitted to the ICU ward and are diagnosed with sepsis are assigned to the sepsis case cohort since this is how the hospital currently treats patients who have been diagnosed with the disease. The non-sepsis control group comprises all patients who do not fit these criteria. The training and validation samples consist of 260 sepsis patients, whereas the test sample has 97 sepsis patients. According to hospital protocol, we use the ICU ward admission time to determine the sepsis onset time.

The independent, hold-out test sample is then used to test the trained and validated models. "Methods" contains the methodological information for the text-mining, diagnostic and early prediction algorithms. We present the SERA algorithm test results for both non-SMOTE (non-oversampled) and oversampled (SMOTE) data. When sepsis patients are highly prevalent and on par with non-sepsis cases, the SMOTE models show the typical findings seen in machine learning predictive models. (Table 1).

As reported in (Table 2), the models developed with the typical low clinical prevalence context of 6.15% can achieve high sensitivity, albeit with naturally low PPV. For purposes of clinical application, we simulate how changes in the prevalence of sepsis impact the PPV (Table 3). For example, for a 12-h early prediction window, hospitals experiencing the lower end of 1.8% sepsis prevalence will have an estimated algorithm PPV of 8.3% (95% CI: 0.89-8.73%). If the prevalence of sepsis increases to the higher end of 12%, the estimated PPV increases to 40.25% (95% CI: 38.94-41.58%). The simulated results illustrate the applicability of the SERA algorithm in natural clinical settings where the prevalence of sepsis varies depending on the type of clinical specialty and/or location of the institutions.

Medical practice and prior studies<sup>[15]</sup> have shown that early detection of sepsis is challenging and sepsis patients can deteriorate rapidly., thus, every minute counts in the diagnosis of sepsis. We have shown the effectiveness of the SERA algorithm in that it is able to ag 21-32% more patients at risk of sepsis compared to hospital physicians in a clinical setting between 4 and

**Table 1: Statistics of Diagnosis and Early Prediction Algorithm (SMOTE).**

Diagnosis algorithm Outcome predict if the patient has							
Voting							Dagging GBT
	AUC	Sensitivity	Specificity	PPV	NPV	AUC	AUC
Sepsis	0.97	0.91	0.88	0.86	0.90	0.93	0.95
At the present time							
Early prediction							
Algorithm Outcome predict if patient will have							
Voting							Dagging GBT
	AUC	Sensitivity	Specificity	PPV	NPV	AUC	AUC
sepsis	0.89	0.79	0.78	0.78	0.78	0.84	0.84
48 h later	0.92	0.82	0.81	0.81	0.80	0.87	0.87
24 h later	0.96	0.88	0.88	0.88	0.87	0.93	0.93
12 h later	0.94	0.89	0.82	0.83	0.87	0.91	0.94
6 h later	0.94	0.87	0.81	0.82	0.86	0.86	0.93
4 h later							

SMOTE applied to clinical notes to achieve a balanced sample of sepsis and non-sepsis case entries. SERA algorithm uses the voting algorithm., dagging and GBT algorithms are presented for comparative purposes.

**Table 2: Statistics of Diagnosis and Early Prediction Algorithm (in Low Prevalence Condition Without SMOTE).**

Diagnosis algorithm Outcome predict if the patient							
Voting							Dagging GBT
	Prevalence	AUC	Sensitivity	Specificity	PPV	NPV	AUC
has sepsis	0.179	0.96	0.91	0.88	0.61	0.98	0.93
At the present time							0.95
Early prediction							
Algorithm Outcome predict if patient will have							
Voting							Dagging GBT
	Prevalence	AUC	Sensitivity	Specificity	PPV	NPV	AUC
sepsis	0.014	0.88	0.78	0.77	0.05	0.98	0.83
48 h later	0.012	0.92	0.83	0.80	0.05	0.98	0.89
24 h later	0.009	0.95	0.90	0.83	0.05	0.98	0.93
12 h later	0.004	0.93	0.90	0.84	0.01	0.98	0.91
6 h later	0.001	0.94	0.90	0.88	0.01	0.98	0.93
4 h later							0.95

No over sampled applied. Prevalence is computed at the clinical note level. For the same number of sepsis cases, the clinical note occurrences are different for a different time window. SERA algorithm uses the voting algorithm., dagging and GBT algorithms are presented for comparative purposes.

**Table 3: Simulated PPV at Different Sepsis Prevalence Levels.**

PPV (95% CI)							
Algorithm	Prevalence	1.9%	7%	13%	21%	31%	51%
Diagnosis	0.12 (0.12-0.12)	0.31 (0.30-0.32)	0.49 (0.48-0.50)	0.64 (0.63-0.64)	0.75 (0.75-0.76)	0.88 (0.88-0.88)	
4 h	0.12 (0.11-0.13)	0.31 (0.29-0.34)	0.49 (0.46-0.52)	0.64 (0.61-0.67)	0.76 (0.73-0.78)	0.88 (0.87-0.90)	
6 h	0.10 (0.09-0.08)	0.26 (0.23-0.28)	0.42 (0.40-0.45)	0.57 (0.55-0.60)	0.70 (0.68-0.72)	0.85 (0.83-0.86)	
12 h	0.09 (0.09-0.10)	0.25 (0.24-0.26)	0.41 (0.40-0.43)	0.56 (0.55-0.58)	0.69 (0.68-0.70)	0.84 (0.83-0.85)	
24 h	0.08 (0.07-0.08)	0.21 (0.20-0.22)	0.36 (0.34-0.37)	0.50 (0.49-0.52)	0.64 (0.62-0.65)	0.81 (0.80-0.82)	
48 h	0.07 (0.06-0.07)	0.18 (0.17-0.19)	0.31 (0.30-0.33)	0.45 (0.44-0.47)	0.59 (0.57-0.60)	0.78 (0.76-0.78)	

1.8% (12%) represents the low (high) end of the typical sepsis prevalence observed in hospitals based on prior research 19. Six percent represents the average sepsis prevalence of hospitals in the United States. Other prevalence percentages are for comparison purposes as they represent over sampled prevalence percentages typically observed in prior research.

48 h before the onset of sepsis. This additional lead time in sepsis alert provides greater opportunities for physicians to commence treatment, thereby lowering mortality.

As in every medical alert system, false positive in the alert system is a cost to the healthcare organization. Unacceptable levels of false positives can lead to wastage of medical resources as physicians need to perform additional follow-up diagnosis and treatment. Further, frequent false positives in a clinical setting will lead to a loss of confidence in these alerts among attending physicians, who will, in turn, be less likely to act on future alerts. A high number of false alerts may also reduce their confidence in other similar best practice alerts embedded within EMR systems. The SERA algorithm, however, has achieved high TPR while maintaining a reasonable low FPR-an FPR considerably lower than hospital physicians' early assessment of sepsis. Further, based on the simulation of different sepsis prevalence levels, we show that the PPV of our model is also appropriate for clinical applications, where the prevalence of sepsis is naturally low.

This study thus presents the potential of using AI as a "canary in a coal mine" for clinicians. We could envision running the SERA algorithm in the background

to continuously monitor patients and act as an early warning system for patients who are at risk of having sepsis. At the same time, using the SERA algorithm in this manner could also potentially age sepsis patients and thus prevent them from being overlooked., a situation that is common in stressful hospital settings where physicians have to continually make multiple medical decisions and judgments while managing high patient loads. We have provided details of how to practically set up this system in the methods section. Through this study, we provide further empirical evidence for the value of data from EMR systems. Notably, we show that the data from EMR systems can be applied for more advanced healthcare applications. Unlike prior studies that utilized only structured EMR data, we demonstrated the value of using the vast amounts of unstructured data embedded in progress notes. For a typical EMR system, the volume of unstructured data dwarfs the volume of structured data and we believe that the value from unstructured data could be unlocked in a systematic fashion using NLP (see below). Using it for sepsis prediction as per our study is one case in point. The NLP-enabled analysis would be naturally suited for managing other complexes, equivocal and critical clinical challenges as

these challenges would benefit from expert insights embedded within EMR's unstructured data.

Like all studies, there are limitations to our study. While we have validated and tested the models with an independent, test sample from a later time period, future research should conduct external validation in different hospital settings to improve the SERA algorithm and make our findings more robust.

In conclusion, if predictive algorithms similar to the SERA algorithm can be designed to access valuable structured and unstructured data patient data continuously, hospital systems could potentially provide a 24 by 7, continual monitoring of patients' condition, thereby improving the ability for early sepsis detection and intervention. Though the SERA algorithm can achieve higher sensitivity and specificity rates compared to some physician's diagnoses and prior machine learning algorithms, we believe its primary role is to complement, not substitute, the clinical team's existing work. We further argue that other similar NLP-enabled algorithms could be developed to augment health-care workers' knowledge and improve their decision making<sup>[16]</sup>.

Regarding acceptance into routine practice, stakeholders are also concerned that AI may lead to the automation of jobs with subsequent job losses, which has drawn a lot of attention<sup>[17]</sup>. Research conducted by Deloitte and the Oxford Martin Institute demonstrated that AI may be responsible for losing 35% of jobs in the United Kingdom within the next 10-20 years<sup>[17]</sup>. However, the loss of employment may be mitigated by several external factors other than technology. Conversely, there is also the opportunity for new employment to be generated to work with and improve AI technologies. These factors may keep the number of jobs lost to 5% or fewer<sup>[17]</sup>. However, implementing AI will be challenging because of these beliefs. Therefore, it is important to emphasize to those working with this new technology that AI systems will not replace human clinicians but will supplement their efforts to care for patients and benefit them as a result. Indeed, humans may eventually shift toward activities and job designs that require distinctly human skills, such as empathy, persuasion and big-picture integration<sup>[17]</sup>. How this evolution will impact hospital settings and workflows is still unknown. Healthcare workers will also need to see that integrating AI is based on sound coherent thinking and is of value to the patient, the staff and the organization<sup>[18]</sup>. This will require staff training and education in AI technology<sup>[19]</sup>. Ultimately, successful change will require financial investment in resources, infrastructure and time<sup>[19]</sup>.

## CONCLUSIONS

In critical care settings, AI has the potential to completely transform the diagnosis, treatment and

detection of sepsis. Artificial intelligence (AI) algorithms can assist in identifying individuals who are at a high risk of getting sepsis, enabling medical professionals to intervene sooner and stop the condition's progression. AI accelerates and increases the precision of sepsis diagnosis. Treatment regimens for sepsis can be tailored to the unique features of each patient and their reaction to medication. AI can also be utilized to continuously monitor sepsis patients, informing medical professionals about the patient's clinical status and guaranteeing a prompt and effective therapeutic response.

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