Longitudinal healthcare analytics for early detection and progression of neurological diseases: A clinical decision support system

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Abstract

Neurological diseases, including Alzheimer's disease (AD), are rising global health challenges. This study presents a two-stage decision support system (DSS) that uses machine learning and neuroimaging for early AD detection and monitoring. The first stage uses deep learning for predicting AD likelihood. The second leverages a 3D convolutional neural network to identify crucial brain regions in AD progression. Notably, the DSS offers a solution to machine learning's "black box" problem using an occlusion map explainability method, enhancing decision transparency. Its design is adaptable to other diseases using imaging data, underscoring its broad healthcare potential. By providing an innovative and interpretable tool for improved disease management, this research helps foster better patient care and outcomes.

Keywords: Neurological diseases, Alzheimer's disease, decision support system, disease management, machine learning, convolutional neural networks.

1. Introduction

Over the years, there have been numerous incurable diseases and disorders that persist due to diagnostic limitations and high costs. Globally, neurological diseases (NDs) affect about one billion individuals, including 50 million with epilepsy and 24 million with Alzheimer's disease (AD) and other neurologic disorders (Uygunoglu & Siva, 2021; World Health, 2006). NDs encompass conditions that impact the human brain and the central nervous system, such as epilepsy, AD, Parkinson's disease (PD), multiple sclerosis, and stroke. These diseases share similarities in causes, progression, and treatment strategies. Among them, AD and PD are the prevalent NDs predominantly affecting a substantial number of individuals aged 65 and above, underscoring their public health significance (Singh & Dash, 2023).

NDs are major contributors to global disability and rank as the second leading cause of death worldwide (Feigin et al., 2019). In 2020, over 6 million Americans were affected by progressive and irreversible neurodegeneration caused by AD and related dementias (ADRDs) (Gaugler et al., 2022). Among these dementias, AD is the most prevalent and is recognized as the sixth leading cause of death in the United States (Heron & Smith, 2013; Xu et al., 2010). However, the true impact of AD may be greater than reported due to factors like underdiagnosis and underreporting (James et al., 2014).

The need for early detection and intervention in NDs urgent, as timely diagnosis is crucial for identifying and preventing the development of these diseases (Olaniyan et al., 2023). While there hasn't been any discovered cure for certain NDs such as AD (Garg et al., 2023), and PD (Piri, 2020), detecting these diseases in their earlier or prodromal stages is vital to effectively manage their progression (Zhou et al., 2023). This is essential for providing effective care and implementing timely intervention strategies, leading to a higher quality of life for affected individuals and reducing the burden on caregivers.

NDs are chronic conditions that require careful management and early detection. Continuous monitoring and the adaptation of care strategies based on disease progression are essential to enhance the quality of life for individuals affected by these conditions. This forms the foundation for establishing standardized protocols for disease management in clinical settings (Epstein & Sherwood, 1996). Previous research on health information systems (HISs) have proposed various strategies to support effective health management, including the use of decision support systems (DSSs) (Meskens & Guinet, 2013; Wimmer et al., 2016).

Among HISs, DSSs are computerized systems designed to assist health professionals by utilizing various patient data sources to provide personalized advice during patient encounters or specific cases (Khan et al., 2023). DSSs have been widely studied and applied in different domains such as online social networks (Sadovykh et al., 2015), finance (Serrano-

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Silva et al., 2018), healthcare (Adeyemi et al., 2013; Bardhan et al., 2015; Zolbanin & Delen, 2018), and medical emergency management (Haghighi et al., 2013). Sutton et al. (2020) suggest that the rapid advancement and adoption of DSSs in healthcare signify a potential paradigm shift aimed at improving operational efficiency and care outcomes.

DSSs play a crucial role in disease management for several reasons, particularly in providing insights into projected progression of a condition. Firstly, integrating predicted disease progression into clinical decision-making allows for personalized treatment plans that consider individual variations in symptom presentation among patients (Croft et al., 2015). Secondly, DSSs enable health professionals to anticipate the potential evolution of the disease, empowering them to select appropriate treatment strategies in advance (Hamburg & Collins, 2010). By proactively addressing potential changes in the condition, healthcare providers can optimize treatment and care plans, ultimately leading to better patient outcomes. Lastly, patients benefit from understanding the expected course of their condition as it enables them to make informed decisions about their daily routines and actively participate in self-management of their health (Mueller-Peltzer et al., 2020). By incorporating patient education and engagement, DSSs promote a holistic approach to care and empower patients in modern medicine.

The recent advancement in artificial intelligence (AI) and machine learning (ML) technologies have opened up new possibilities for improving healthcare outcomes through IS research (Dwivedi et al., 2023). Previous studies have explored the integration of AI and ML into health DSSs to assist physicians in various tasks such as identifying cardiovascular disease risk factors (Hsu, 2018), predicting diabetic retinopathy (Piri et al., 2017), predicting colorectal cancer (Kalgotra et al., 2023), and assessing hospital readmissions (Todd et al., 2022). However, most of these studies have primarily focused on utilizing clinical data and have overlooked the inclusion of imaging data, which could limit their ability to accurately assess disease progression. Furthermore, many of the ML models used in these studies operate as "black-boxes", meaning that their decision-making process is not easily interpretable. However, in a clinical setting, interpretability is a crucial aspect of decision support, as healthcare professionals need to understand and trust the results provided by a system (Xu et al., 2023).

Motivated by the gaps identified in existing research, we present a novel two-stage DSS designed to support physicians and health practitioners in the identification of at-risk individuals, early detection/ prediction/monitoring of NDs, and personalized treatment recommendations. AD serves as an empirical example to showcase the integration of DSSs in a clinical setting for early detection and progression monitoring of NDs. Our proposed DSS represents a significant leap forward in leveraging advanced technologies to address the challenges posed by complex NDs.

In the first stage of DSS development, we employ an ML model that predicts AD based on longitudinal clinical data, including demographic information, medical history, cognitive assessments, and genetic data. The primary objective is to identify and classify patients into two categories: normal controls (NC) and mild cognitive impairment (MCI). MCI represents the early stage of AD, where individuals may either experience stable cognitive decline or progress to AD over time (Huang et al., 2019). In the second stage, we utilize a transfer learning approach to fine-tune a 3D convolutional neural network (3D-CNN) model using longitudinal AD brain imaging data, especially magnetic resonance imaging (MRI) and positron emission tomography (PET) scans. This allows us to track the progression of the disease and classify patients into healthy and unhealthy controls. Then, to enhance interpretability, we employ an occlusion map method (Zeiler & Fergus, 2014) to visualize and understand which regions of the brain the 3D-CNN model finds indicative of the progression of AD. This will further the trust and understanding of the outcomes of the DSS among medical practitioners.

AI and ML hold great potential in revolutionizing the management of NDs. Specifically, our objective is to harness the transformative power of AI, particularly deep learning techniques, to facilitate early detection and improve treatment strategies for these debilitating conditions. While the potential of our DSS in pioneering early detection of NDs is indeed noteworthy, it is equally imperative to address the techno-ethical considerations that arise in this context. The implementation of a well-executed technology impact assessment is essential to ensure that stakeholders can fully comprehend the implications of our DSS. This, in turn, empowers medical practitioners to make informed decisions that uphold ethical principles such as fairness, privacy, and autonomy.

The research structure is as follows: in section 2, we provide descriptions of relevant and related works, and in section 3, first, we provide a description of the data used in this research, then, we present the proposed methodology with an explanation of our research framework. We present discussion in section 4, expected contribution in section 5, and finally, the research is summarized in Section 6.

2. Literature Review

2.1. Healthcare Analytics

The central aim of healthcare analytics is to forecast health-related outcomes by employing both clinical and non-clinical data (Lin et al., 2017). Data can be sourced from two main types: clinical trial data, which is explicitly collected for analysis but often limited in size, and secondary healthcare data, like electronic health records (EHR), which is typically larger but comes with its own set of challenges for data analytics researchers. At the population level, previous studies have studied hospital readmission (Ben-Assuli & Padman, 2020; Zolbanin & Delen, 2018) and mortality rates (Dag et al., 2017; Zolbanin et al., 2015).

At the individual level, researchers attempt to predict and detect the occurrence of diseases. Delen et al. (2012) developed an advanced predictive model to interpret the post-surgical results of a coronary surgery patients. Leveraging seven well-known machine learning algorithms, Hsu (2018) created datasets ranked by attributes (risk-factors) to assist physicians in determining the significance of cardiovascular diseases (CVDs) risk factors. To aid physicians to ascertain whether the severity of symptoms may either remain consistent or continue to intensify, Mueller-Peltzer et al. (2020) developed a decision support system (DSS) that employed a cross-sectional time-series model to predict the expected course for low back pain among patients. Wang et al. (2020) suggested a model to forecast the risk associated with multiple diseases. Ahsen et al. (2019) investigated the diagnosis of breast cancer, considering the influence of human bias. Zhang and Ram (2020) presented a data-oriented structure that combines various ML methods to detect triggers and risk factors associated with asthma. Dag et al. (2016) presented a predictive model to assess of heart transplant. Likewise, Topuz et al. (2018) presented a predictive model to examine the survival outcome post kidney transplant.

2.2. Decision Support Systems

DSS typically fall into two categories: knowledge-based and non-knowledge-based systems (Sutton et al., 2020). Knowledge-based systems are structured around IF-THEN rules, with the system extracting data to assess these rules and subsequently generating an action or result. On the other hand, Non-knowledge-based systems necessitate a data source, but the final decisions or outputs are derived using AI, ML, or statistical pattern recognition methods (Berner & La Lande, 2016).

Numerous DSSs have been introduced for diverse fields, encompassing finance, business processes, online social networks, healthcare and clinical applications, medical emergency management, among others. For example, in finance, Ben-Assuli (2012) evaluated the perceived influence of investment counselors' decision-making in the context of a banking DSS. Additionally, in business process, Ghattas et al. (2014) applied data mining techniques to improve the efficiency of business processes by extracting decision-making criteria from the insights gained through previous process executions. Finally, in online social networks, Sadovykh et al. (2015) employed netnography to investigate the capability of health online social networks as a tool to aid the decision-making process.

Healthcare analytics has the potential to tailor decision-making in disease management according to individuals' specific health profiles by drawing conclusions from patient data (Mueller-Peltzer et al., 2020). As a result, it offers decision support that is expected to be more efficient than the traditional approach of providing uniform care to everyone (Delen et al., 2012). A wide variety of recently introduced DSSs in healthcare are non-knowledge based and utilized AI and ML and other data driven methods due to the wide availability and accessibility of patient data (Agarwal & Dhar, 2014).

Heart et al. (2022) proposed a clinical decision support system (CDSS) to aid physicians in assessing CVD risk factors by integrating an AI-based back-end engine with a visual analytics and human-in-the-loop intelligent augmentation (IA) front-end component. Piri et al. (2017) created a CDSS to identify diabetic retinopathy and suggested an ensemble method to enhance the performance of the CDSS even more. Piri (2020) propose a framework for addressing missing data in EHR data and develop a CDSS for detecting Parkinson's disease (PD). Wang et al. (2012) formulated an advanced multitask learning model to estimate cognitive abilities using phenotypic markers in individuals suffering from AD. Zazon et al. (2023) used neurological methods to build a DSS to classify cognitive functions into levels. Ben-Assuli et al. (2023) proposed a CDSS for the selection and integration of features to boost the accuracy of congestive heart failure risk prediction. Wang et al. (2023) developed a DSS to assist physicians to enhance the efficiency of hospital triage at the initial assessment stage, thereby improving the transition from primary to secondary care. Kalgotra et al. (2023) developed a model for categorizing people into risk groups developing colorectal cancer, which serves as a DSS for gastroenterologists to accelerate diagnostic procedures and personalize patient care.

In summary, most of the previous studies in healthcare analytics and DSSs have utilized patients' clinical numerical data to build causal models to make predictions. However, the early detection and tracking of progression of NDs such as AD and PD goes beyond predicting clinical data. Neuroimaging techniques provide invaluable insights into the structural details of brain tissue such as size, volume, and shape (Garg et al., 2023). The capabilities of neuroimaging not only enhance the precision of AD clinical diagnosis but also to track disease progression and the impact of treatments (Mueller et al., 2005). MRI provides the structural details of brain tissues whilst PET provides functional imaging details of brain tissues (Mueller et al., 2005).

Hence, our study offers a unique contribution to the field of healthcare analytics by utilizing longitudinal clinical and neuroimaging data to develop a DSS that aids physicians in the early detection and monitoring of AD in patients. While many ML-based DSSs face criticism for their lack of interpretability, our study addresses this concern by incorporating an explainable AI (XAI) method. This XAI approach enhances the understandability and interpretability of the proposed DSS, providing healthcare professionals with supplementary visual aids to address emerging issues and questions related to NDs. The inclusion of time series models in DSSs has been suggested by previous researchers as a means to improve system effectiveness (Fisher et al., 2016; Mueller-Peltzer et al., 2020). By incorporating longitudinal data, the proposed DSS longitudinal data, our DSS considers the temporal aspect of disease progression, enabling more accurate predictions and monitoring. Through our study, we aim to complement the existing field of healthcare analytics and make a significant contribution to the literature. A summary of relevant studies is presented in the ***Appendix***.

3. Research design

3.1. Data collection

In this study, we collected data from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database (adni.loni.usc.edu) and Open Access Series of Imaging Studies (OASIS) database (oasis-brains.org). ADNI is a collaborative organization comprising universities and medical centers from Canada and the United States (Petersen et al., 2010). The overarching objective of the ADNI has been to investigate the feasibility of using serial MRI, PET, as well as other biological markers, alongside clinical and neuropsychological assessments, to track the advancement of mild cognitive impairment (MCI), the early-stage Alzheimer disease (AD). ADNI offers a longitudinal study where initial imaging is supplemented with yearly follow-up scans. The purpose of OASIS is to encourage future advancements in AD research by offering neuroimaging datasets to the scientific community at no cost (Marcus et al., 2007). The project made data available in three distinct phases: OASIS 1-Cross-sectional, OASIS 2-Longitudinal, and OASIS-3-Longitudinal.

To reiterate, our study proposes a two-stage DSS to aid physicians and health practitioners in early detection, identifying at-risk individuals, recommending personalized treatment, prediction, and monitoring of the progression of AD. The first stage will leverage a robust set of longitudinal clinical diagnostic data, cognitive assessment data, and doctor's notes provided by ADNI and OASIS study conducted over the span of several years and compare how the models perform on these different datasets. The second stage of the DSS will analyze longitudinal T1-weighted images of MRI and PET from the same ADNI and OASIS studies and similar analysis and comparisons will be made. We suggest that the strategic integration of these multimodal imaging techniques and multiple data sources will deepen the empirical rigor and multidimensional understanding of AD progression and early detection. Previous studies have shown that using multimodal imaging data can increase the performance and accuracy of models based on AD/healthy controls (HC) classification (Dukart et al., 2013; Liu et al., 2015). The ADNI and OASIS databases offer anonymized data from patients who have willingly consented to the use of their information for research purposes. Importantly, patients retain the exclusive right to participate or withdraw their consent at any stage, even after initially granting it. This approach places a high priority on and upholds the privacy of patient data.

3.2. Proposed methodology

Once we have collected the data, the next step in our study is data preprocessing. We will apply various advanced techniques to enhance the quality and reliability of the numerical and imaging data, ensuring its suitability for further analyses. Additionally, text mining techniques will be used to analyze doctor notes and create a variable representing the premedical condition. In the first stage of DSS development, our primary objective is to build a classifier that can accurately predict the likelihood of a patient developing AD based on the clinical diagnostic data, especially classifying individuals as either NL or MCI. To achieve this, we will employ two popular deep learning algorithms: artificial neural networks (ANN) and extreme learning machine (ELM). These models will be trained using the collected data, and their performance will be evaluated on a separate test dataset. We will assess their predictive performance using measures such as sensitivity, accuracy, and specificity. The model with the best performance will be selected, as this will aid physicians in accurately classifying patients into NL and MCI categories.

In the second stage, our objective is to identify the most important brain regions that change over time to track the progression of AD using longitudinal imaging data. To accomplish this, we will a transfer learning approach and fine-tune a 3D-CNN model using MRI and PET data from ADNI. CNN is a form of supervised multi-layered neural network that employs adaptable convolutional kernels to identify hierarchical features within images (Li et al., 2021). In the case of our study, we will use a 3D-CNN, which is specifically designed for handing 3D data, such as MRI and PET imaging data. Transfer learning is a machine learning method that repurposes a model, originally trained for a specific task, to improve learning in a different but related target problem by transferring knowledge from the source problem (Pan & Yang, 2010). Transfer Learning is typically employed when there's a new dataset that is smaller in size compared to the original dataset used for training the pre-existing model (Ravichandran et al., 2023). The transfer learning process in this study will use a pre-trained 3D CNN model built on the ResNext101 network structure (Xie et al., 2017). This structure is composed of 101 layers and was initially trained using 300,000 video clips from the Kinetics dataset.

Finally, we address the limitation of the black-box nature of deep learning and ML models by adapting the occlusion map interpretability method to visualize the relevant brain region that significantly contributes to our model as AD progresses. This method involves systematically covering (occluding) different parts of the input image (MRI, PET) and observing the change in the model’s prediction. By doing this over the entire image, we create a heatmap that highlights the most important brain regions for the model's decision. The underlying idea is straightforward: if occluding a particular part of the image significantly alters the model's output, then that specific area of the image is likely important for the model's decision and thus represents a significant brain region that clinicians should pay attention to when assessing AD progression. The incorporation of this interpretability method into our DSS empowers medical professionals to autonomously interpret the model’s output more effectively.

Equally important, we are committed to addressing the techno-ethical challenges, ensuring transparency, patient autonomy, and the responsible use of advanced analytics in healthcare. The literature consistently underscores the importance of implementing AI in healthcare in an accountable and ethical manner (Lukkien et al., 2023; Obermeyer et al., 2019; Zou & Schiebinger, 2018). The framework of our research methodology is presented graphically in ***Figure 1***.

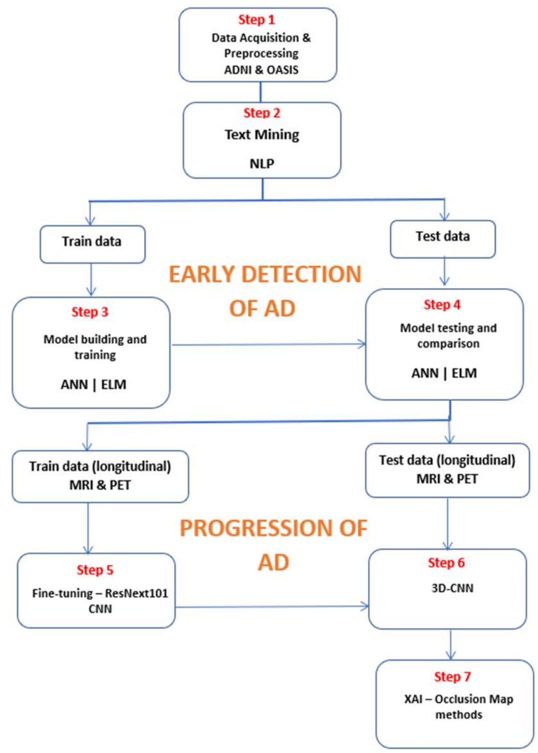

Figure 1. Research design.

4. Discussion

In the evolving domain of healthcare analytics for neurological diseases (NDs), our chosen methodology offers distinct advantages. Unlike many prevalent cross-sectional approaches, our methods are finely tuned to harness the temporal nature of longitudinal data, allowing for the early detection of disease and subsequently monitoring progression. This focus on time-sensitive data, combined with our emphasis on individual patient trajectories, facilitates a level of personalization that offers more accurate and timely interventions. Additionally, our approach seamlessly integrates diverse data modalities, from imaging to clinical notes, painting a comprehensive picture of disease progression.

Adapting our approach to the neurological context did pose unique challenges. Neurological data, especially in early disease stages, can be sparse. To counteract this, we incorporated data imputation and temporal smoothing, ensuring our analytics remain robust even with limited data. Furthermore, we introduced domain-specific feature extraction methods tailored to the unique markers of NDs. Optimized for real-time processing, our methods guarantee that clinicians receive actionable insights promptly, reinforcing the potential of our approach in a clinical setting.

5. Expected contribution

Our research presents a novel and important contribution to the advancement of AI in healthcare analytics. Previous studies on disease management have primarily focused on the utilization of clinical data, often neglecting the incorporation of imaging data. A distinctive aspect of our research is the integration of clinical diagnostic data with longitudinal imaging data. Additionally, the inherent black-box nature of ML models mentioned earlier presents a notable limitation, particularly in terms of interpretability. Interpretability plays a crucial role in a clinical setting as it ensures clear understanding of the results, which is essential for decision support. Our model introduces a significant advancement in this regard by incorporating occlusion map methods for interpretability. This addition enhances transparency, enabling healthcare professionals to trust and comprehend the underlying factors influencing the suggestions made by the DSS. Such an interpretability improves DSS applicability and acceptance in clinical settings.

Our DSS has a wide scope that goes beyond the application of AD. It is designed to be applicable to any diseases that utilizes imaging data, such as MRI and PET scans, for diagnosis and tracking disease progression. This versatility enables its use in various NDs and extends to other medical conditions, including cancer. The adaptability of our DSS highlights its value as a handy tool in disease management across different medical specialties.

The implementation of our DSS holds the potential to bring about significant improvements in health outcomes. By fostering early detection and accurately tracking disease progression, it provides healthcare professionals with valuable insights to optimize treatment strategies, leading to enhanced patient care. These improvements in patient care have the potential to result in better health outcomes, highlighting the practical and beneficial impact of our study in the field of healthcare analytics.

Finally, our DSS offers physicians a vital tool for predicting the progression of AD. This function plays a crucial role in guiding physicians in providing personalized care planning, sensitivity support, and medication adjustments. By tailoring care based on each patient's disease progression, the proposed approach promotes more effective and patient-centered care to improve patient experience and quality of life.

6. Conclusion

This paper presents a novel DSS designed to assist physicians in making clinical decisions related to the early detection and progression monitoring of AD. The primary purpose of this DSS is not to supplant the expertise of physicians but rather to augment their capabilities by assisting in the identification of at-risk individuals, offering personalized treatment recommendations, and predicting/monitoring the progression of AD and other NDs. This underscores the critical role of AI in complementing human skills, emphasizing the essential nature of AI-human collaboration (Fügener et al., 2022). The first stage of the DSS utilizes historical clinical data, including behavioral, cognitive, and neurological assessments, to develop an ML model for classifying patients into normal and those with mild cognitive impairment. Subsequently, the second stage employs medical imaging data to construct an interpretable deep learning model for classifying AD patients and monitoring the progression of AD. This combination introduces a novel approach to tracking the progression of NDs. By merging these diverse data types, our study achieves a more comprehensive and enriched understanding, enhancing the precision of diagnoses and, consequently, the effectiveness of disease management and treatment planning.

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Appendix. List of related studies on decision support systems for disease management

Research Paper	Disease	Method/classifier	Data source	Observations
(Heart et al., 2022)	CVDs	PCA, LDA	Sheba Medical Center EHR data	Clinical numerical data
(Delen et al., 2012)	Coronary surgery	ANN, SVM, CART, C5	NIS	Clinical numerical data
(Hsu, 2018)	CVDs	SVM, BN, RBF, Bagging	Mackay Mem. Hospital	Clinical numerical data
(Mueller-Peltzer et al., 2020)	Low back pain	Cross-sectional time-series	Hospital	Longitudinal pain data, and questionnaire
(Wang et al., 2020)	Multiple diseases	Network analysis	EHR data	Clinical numerical data
(Ahsen et al., 2019)	Breast cancer	SVM, ELM	Undisclosed	Clinical numerical data and mammograms
(Zhang & Ram, 2020)	Asthma	SVM, CNN	Social-media, environmental sensors, socioeconomic census, outpatient illness surveillance	Observational clinical data, and image data
(Dag et al., 2016)	Heart transplant	DT, ANN, SVM, LR	United Network for Organ Sharing	Clinical numerical data
(Topuz et al., 2018)	Kidney transplant	SVM, ANN, BT, BNN	United Network for Organ Sharing	Clinical numerical data
(Piri et al., 2017)	Diabetic retinopathy	LR, ANN, DT, RF	Cerner Health Facts - EHR data	Clinical numerical data
(Piri, 2020)	PD	LR, SVM-L, SVM-RBF, NN, RF, GB	Cerner Health Facts - EHR data	Clinical numerical data
(Lu et al., 2021)	Multiple diseases	Network analysis	Cerner Health Facts - EHR data	Clinical numerical data
(Ben-Assuli et al., 2023)	Congestive heart failure	XGBoost	Sheba Medical Center	Clinical numerical data
(Wang et al., 2023)	Hospital triage	LGBM, GNB, DT, LDA, SVM, EL	Undisclosed	Clinical numerical and blood data
(Kalgotra et al., 2023)	Colorectal cancer	MPNN, XGBoost	Center for Health Systems Innovation – EHR data	Clinical numerical data
(Zazon et al., 2023)	NDs	DNN, MDTW, KNN	Primary data collection – research lab	Electroencephalogram data, computer-based assessment data.
Proposed	AD and NDs	3D-CNN, LR, SVM, ANN, ELM, RF	ADNI	Clinical data, cognitive assessment data, Multimodal imaging data (MRI and PET)

Nationwide Inpatient Sample (NIS); Decision Tree (DT); Radial Basis Function (RBF); Extreme Learning Machine (ELM); Linear Regression (LR); Bayesian Neural Network (BNN); Light Gradient Boosting Machine (LGBM); Linear Discriminant Analysis (LDA).