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Use of Predictive Modelling in Alzheimer's Detection

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Abstract:

Alzheimer’s disease is an irreversible, progressive brain disorder that slowly destroys memory and thinking skills, and, eventually, the ability to conduct the simplest tasks [1] .The changes related to Alzheimer’s disease can occur in an individual much before the onset of the disease. Identifying individuals in pre-symptomatic stages is important to slow the progression of the disease and in some cases prevent the occurrence of the symptoms. Therefore, accessibility and availability of right information is vital for early interventions and achieving patient-centered care. The use of predictive modeling facilitates access to such information and more importantly shares information easily with the patient’s healthcare team thus benefiting patient’s outcomes. The aim of this paper is to understand how the use of predictive models can help with Alzheimer’s detection and discuss the challenges with the models.

Keywords: Predictive modeling, Patient-centered care, Machine Learning, Coordination of care, Alzheimer's Disease, Dementia

1. Introduction

Predictive modeling can be used to calculate the probability of an outcome or occurrence of an event based on the input data, capture relationships between various data sets and identify patterns with the use of statistical models and algorithms. In healthcare, predictive modeling can help aid with actionable insights using the data and is thus useful in identifying individuals at risk for diseases such as Alzheimer's. Despite the progress made in terms of the identification of AD and the medications, there is no straightforward way of way of determining a person's rate of cognitive decline once the patient is identified with Alzheimer's thus making it increasingly difficult for the doctors to add or modify the patient treatment plan. Some of the current treatments include helping people maintain mental function, managing behavioral symptoms and slowing down memory loss. If the predictive models can help identify the onset of the cognitive decline of the patients with Alzheimer's it aids the doctors in ensuring the participant’s cohorts

for clinical trials. Machine learning and predictive analytics offer promise to boost enrollment by predicting which patients have prodromal AD, and which will go on to develop AD [2] for example the model developed by the Massachusetts Institute of Technology (MIT) can help predict if patients at risk for Alzheimer's disease will experience clinically significant cognitive decline due to the disease, by predicting their cognition test scores up to two years in the future [3].

While this disease is a concern for the entire population, the risk is almost double for women. The figure below shows the lifetime risk for Alzheimer’s disease by gender [4].

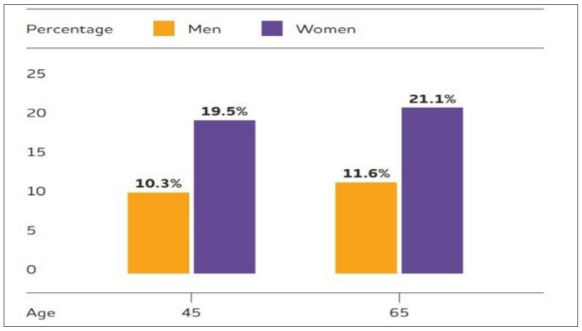

Figure 1: Illustration of the estimated lifetime risk for Alzheimer's by gender

2. Predictive Modeling for Alzheimer's Disease

Since there are no known preventive interventions for AD, diagnosing it at the earlier stages will reduce the risk associated with it [5]. The diagnosis for AD requires extensive evaluation, which includes patient and their family history, physical examination, a sizable number of laboratory and neuropsychological tests, and neuroimaging by MRI, CT, or PET scan. This is time consuming, and the possibility of accurate diagnosis is low. The Predictive models can help parse and process overly complex clinical data, such as free form text and biomedical information.

The early diagnosis of dementia improves the quality of patient care. More than half of those living with this disease did not receive a timely diagnosis, which supports using predictive modeling to advance diagnosis times, interventions, and access to services. The results from a study in 2012 support the use of machine learning to help identify those with dementia. From 2213 healthy patients, the expectation of a positive diagnosis of early dementia was thought to be approximately 161 people; however, the evidence indicated machine-learning was able to identify 295 [6].

As discussed by Hong and team, predicting progression from subjective memory impairment (SMI) to mild cognitive impairment (MCI) or AD can be enhanced by combining four predictors including advanced age, poor baseline memory scores, cognitive status, and apolipoprotein E4 (APOE4) carrier status [7] .In developing a modeling strategy, clinicians will be able to identify patients at higher risk of progression to determine if further evaluations are needed.

The failure to identify AD patients at initial stages is believed to be a primary reason for the frequent failure of AD clinical trials. To reduce clinical trial failure rates and advance research that provides medical benefits, large scale data sets are combined with advanced predictive modeling to generate maximum impact. These techniques can be used to determine patients at risk for AD and to obtain good subjects for AD clinical trials with the hope of finding the most effective treatments of AD.

The predictive modelling for Alzheimer's involves a systematic process from data collection to model evaluation. The process of data collection includes gathering data about the patients' genetics, environmental factors, past medical history, demographics such as age and gender, lifestyle and finally the cerebrospinal fluid proteins. These data elements form the basis for identifying the variables for the feature selection. Correlation analysis or the methods such as principal component analysis (PCA) will be used to identify the variables from the data set. Once the feature selection is complete, algorithms such as logistic regression, neural networks, and support vector machines (SVM) can be used to develop the models. These models are trained to identify the target variable of the AD presence using the data collected.

Deep learning is becoming an increasingly popular form of machine learning for early detection and automation classification of AD due to its ability to process very large-scale neuroimaging data. Approaches like; Convolutional Neural Network (CNN) and Recurrent Neural Network (RNN) have achieved up to 96% AD classification accuracy, and an 84% MCI conversion prediction rate. With Deep Learning still evolving it will only continue to improve in performance and accuracy, creating a great deal of potential in the diagnostic classification of AD [5]. The pattern analysis methods, such as linear discriminant analysis (LDA), linear program boosting method (LPBM), logistic regression (LR), support vector machine (SVM), and support vector machinerecursive feature elimination (SVM-RFE) have been used and hold promise for early detection of AD and the prediction of AD progression [8].

Cross validation methods such as K-fold are used to measure the performance of the model and eliminate the unknowns in the data. The models will be constantly evaluated for accuracy, specificity and precision as these metrics will help determine the model's ability to segregate members with and without

AD. Fig. 2 below illustrates the various steps involved in AD diagnosis.

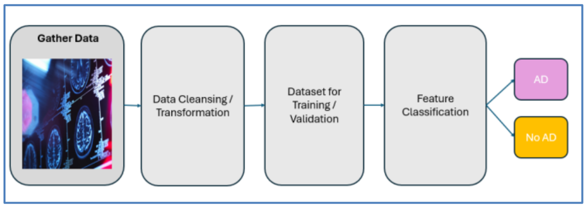

Figure 2: Illustration of the process of AD diagnosis

As the members with AD will be on the complex medication regime thus affecting patient safety predictive analytics can play a significant role in the medication management. By ensuring coordination among the multi-disciplinary teams the medication reconciliation will be more effective and improve patient safety

3. Challenges associated with Predictive Modeling

The key aspect of AD prevention is the need to treat disease years before the onset of cognitive, behavioral, or functional decline. Prediction of Alzheimer's risk and evaluation of long-term treatment outcomes requires models, but this is met with ethical concerns and social implication. The use of healthcare data over an extended period may present a privacy risk to the patients and becomes challenging to gain specific informed consent for the future possibilities for research. Even though analytics have been developed in the field of bioinformatics and pharmacology, specific case studies for brain disease are limited and these publications are typically written for a very narrow specialty audience [9]. Very few clinical trials are undertaken for AD therapy.

The use of predictive modeling for real-time clinical decision making is needed to improve health outcomes, enhance patients' experiences, and reduce health care costs. The development and validation of predictive models for clinical practice is the initial step in the implementation of point of care predictions. Integrating electronic health care predictive analytics (e-HPA) into the clinical workflow, testing e-HPA in a patient population, and subsequently disseminating e-HPA across US health care systems on a broad scale require thoughtful planning. Input is needed from policy makers, health care executives, researchers, and practitioners as the field evolves. With the implementation of such a large-scale initiative, there are challenges including the need to ensure privacy, oversite of implementation, incorporating predictive analytics into medical education, and transparency to make sure that electronic systems do not replace decision making by physicians and patients. Other considerations are interoperability to scale e-HPA across health care systems.

Global healthcare focus has shifted to gathering data to influence health outcomes. Although some progress has been made in the field of research related to Alzheimer's

Disease (AD), clinical trial failure rates are still problematic and slow. In the United States alone, 150 clinical trials are seeking 70,000 participants [10]. Having more data is always beneficial for data-based prediction modelling, but the amount of data available today is pushing the limits as it relates to scalability. The major problem associated with scaling algorithms is that communications and synchronization overheads go up and so a lot of efficiency can be lost, especially where the computation does not fit nicely into a map/reduce model.

4. Conclusion

As discussed throughout this paper, there is no treatment to prevent or reverse Alzheimer's. However, early interventions can help reduce symptoms such as confusion and loss of memory and give patients an opportunity to participate in a wider variety of clinical trials. If Alzheimer's disease were diagnosed when patients had MCI, it would collectively save $7 trillion to $7.9 trillion in health and long-term care costs [4].Proper data mining algorithms and predictive modeling can refine searches for targeted customers. Predictive modeling can help cut costs by

identifying patients at higher risk for the disease and allowing providers time to implement early intervention before problems develop.

While Predictive models help provide actionable insights for healthcare professionals by diagnosing the disease early on, providing risk stratification and providing a long-term care plan to monitor the disease progression, it is also essential that these models are validated on independent datasets to ensure accuracy and generalizability. Finally ensuring patient privacy, meaningful use principles of data sharing and adhering to HIPAA's ethical standards are particularly important in creating these models.

To summarize, predictive modeling offers great scope for early intervention from detection to management of Alzheimer's disease and improved patient care. However, it is important to mitigate the challenges related to research, data collection and the collaboration among the different teams involved in this process to benefit from these models.

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