HOW MACHINE LEARNING APPROACH IS BEING DEPLOYED BY THE STUDIES ON PROGNOSIS OF DEMENTIA: A SYSTEMATIC LITERATURE REVIEW

Dissertation Submitted to

The IIHMR University, Jaipur

for the partial fulfillment for the award of

the degree of Master of Business

Administration (MBA)

in

Hospital and Health Management

by

Bharti Verma

Under the Supervision and Guidance of

Dr. Alok Mathur

2021

HOW MACHINE LEARNING APPROACH IS BEING DEPLOYED BY THE STUDIES ON PROGNOSIS OF DEMENTIA: A SYSTEMATIC LITERATURE REVIEW

Dissertation Submitted to

The IIHMR University, Jaipur

for the partial fulfillment for the award of

the degree of Master of Business

Administration (MBA)

in

Hospital and Health Management

by

Bharti Verma

Under the Supervision and Guidance of

Dr. Alok Mathur

2021

DECLARATION BY STUDENT

I hereby declare that this dissertation titled **How Machine Learning Approach Is Being Deployed by The Studies on Prognosis of Dementia: A Systematic Literature Review** is the bonafide record of my original research work. I declare that it has not been submitted to any other university or institution for the award of any degree or diploma. Information derived from the published or unpublished work of others has been duly acknowledged in the text.

Bharti Verma

18-June-2021

CERTIFICATE

This is to certify that **Bharti Verma** in partial fulfillment of the requirements for the award of the degree of MBA (Hospital and Health Management from the IIHMR University, Jaipur has successfully completed her/his internship at (name of the organization) during March 22, 2021 to June 19, 2021.

Place:
Date:

Preceptor/Head of the Organization
Name of the organization

CERTIFICATE

This is to certify that dissertation titled **How Machine Learning Approach Is Being Deployed by The Studies on Prognosis of Dementia: A Systematic Literature Review** is a record of the research work undertaken by **Bharti Verma** in partial fulfillment of the requirements for the award of the degree of MBA (Hospital and Health Management) from the IIHMR University, Jaipur under my guidance and supervision and her approach to the research study has been sincere, scientific, and analytical.

Faculty Guide
IIHMR University
Date:

School Dean
IIHMR University
Date:

ACKNOWLEDGEMENT

The work on this thesis would not have been feasible without the great assistance of various people who contributed in some way to its completion. I'd like to express my gratitude to each of them individually.

First and foremost, I want to thank my mentor, Dr. Alok Mathur, for his support, guidance, and advice; without him, this dissertation would not have been possible, he had been a wonderful mentor as well as guide in my journey towards my research study. I would specially thank my industry guide Mr. Gaurav Mundra for his continuous support and belief on me throughout the study completion.

I'd also like to thank my 314e Corporation colleagues and fellow MBA Hospital and Health students for the pleasant work atmosphere, shared experiences, lively conversations, and coffee chats. Supriya Sen, Rashika Sharma, Purnima Rathore, Kanchan Gehani, and Narma Bhattacharya deserve special mention.

ABSTRACT

From its fundamental operations to management, Healthcare is a significant and high-cost sector that entails various decision-making tasks based on data analysis. Machine learning is a technology that can be effective in a data-intensive context like healthcare. This thesis looks into the use of machine learning in healthcare settings as a form of applied health technology. AHT refers to the use of scientific methodologies in the development of therapies that address real-world health and healthcare issues. The focus of this thesis' research is on key activity in healthcare systems: **prognosis.** The prognosis research context is focused on dementia prognosis, with the goal of providing prognostic estimations for older people who have developed dementia, in this study, machine learning applications were found to be beneficial. In the context of prognosis research, a study used machine learning techniques to undertake a review of the relevant data in dementia prognosis, indicating a focus on neuroimaging studies dedicated to confirming biomarkers for medical research.

- **Background:**

Dementia is a complex condition marked by poor patient outcomes and significant healthcare expenses. Little is known about its mechanics despite decades of investigation. Dementia prognostic estimations can assist researchers, patients, and government agencies in coping with the condition. As a result, health data, machine learning approaches could be used to create dementia prognostic estimations.

- **Objective:**

The purpose of this study is to give data on the state of the art of studies employing machine learning approaches to investigate dementia and its prognosis.

- **Method:**

To reach our goal, we conducted a comprehensive literature review in which we searched five large databases—Pubmed, ScienceDirect, ResearchGate, PLOS one, and Google

Scholar—for research that used machine learning approaches for dementia prognosis. Low-quality studies were deleted after a quality checklist was used to assess the quality of the evidence offered by the selected studies. Finally, summary tables were created using data from the final set of investigations.

- **Result**

There was a total of 20 papers in the collection. The data summary results revealed that the current research is focused on applying machine learning approaches to investigate people with moderate cognitive impairment that will progress to dementia. The most often used variable was neuroimaging.

- **Conclusion**

The major topic in the research included is the prediction of conversion from MCI to dementia. On neuroimaging data, the majority of studies employed machine learning approaches. Most research have only used a few data sources, with the ADNI database being the most widely used.

No study had looked into using machine learning to predict epidemiological elements of dementia. Finally, considering the various contexts of the investigations, caution should be exercised when evaluating the stated accuracy of ML approaches.

ABBREVIATIONS AND ACRONYMS

ADNI: Alzheimer's Disease Neuroimaging Initiative

AHT: Applied Health Technology

CDR: Clinical Data Reports

CIND: Cognitive impairment no Dementia

MCI: Mild Cognitive Impairment

MLP: Multi-layer perception

MRI: Magnetic Resonance Imaging

PET: Positron Emission Tomography

SLR: Systematic Literature Review

SVM: Support Vector Machines

WHO: World Health Organization

Table of Contents

List of Figures

List of Tables

1. Introduction

Research in Healthcare sector is valuable to society as it can lead to vital innovations like new treatments, tests, vaccines, prevention policies and other widespread advancements that affect healthcare and its dispensing to the common population. The information technology innovation into the health sciences was a substantial progress in this area as it permitted clinically abundant information to be accessible in a structured format letting the enhancement of information-centered research in this vicinity. [1] This type of research is faster and cheaper in its performance, while letting the analysis of big percentages of data to recognize unanticipated circumstances, paradigms in subcategories of subjects that would naturally not be included in controlled experiments, work with complex diseases which not much is known about. [1]

Modern healthcare experiences an increase of health information in terms of quantity, variety and accessibility, which indicates on the research's methodologies that require more compelling statistical techniques acceptable to use the best of this health data. [2,3] Unique example of such robust procedures is machine learning. [3]

1.1 Machine Learning

Artificial intelligence is a wide discipline that affects the insight and the construction of computer programs which demonstrate key aspects of intelligence. [4] The capability to understand is some of those essential aspects which is discovered in its sub-sphere called machine learning. The derivation of the word machine learning dates to 1950s along with its description given by Arthur Samuel as: "an area of study that offers computers the ability to learn without being explicitly programmed". [5] Decades later, in 1997, post numerous hardware and software advancements, the International Business Machines Corporation's (IBM) Deep Blue machine learning curriculum trounced the chess legend Garry Kasparov, an incident which was a historic milestone for machine learning. [6] This exemplifies the outstanding ability and progression of machine learning algorithms that instigated a paradigm shift in the Computer Science span, which mainly concentrated on 'manually programing computers', into evolving an entire novel field with the attention towards 'getting computers to program on their own' (grounded on earlier involvements and basic preliminary situations). [7]

While discussing around machine learning algorithms, a crucial consideration to be made regarding the issue of why machines should learn instead of just creating them to function as anticipated. The explanations for that have much to do with the restricted human capacity to deal with enormous number of records, several variables at the same time and ever-dynamic environments [8]; the whole of which would make manual coding unfeasible (if not impossible), such as in the following tasks:

- Responsibilities that are too complicated to be properly delineated, except for examples in a sequence of inputs and outputs
- Responsibilities that consist of extricating meaning (interactions and correlations) in huge amounts of information
- Responsibilities that include on-the-job betterment, as all the attributes of the environment are not known
- Responsibilities which have enormous volume of existing intelligence that makes explicit coding unviable; and
- Responsibilities which entail changing environments that would involve incessant reform

From a broad perspective, a machine learning technique works by learning how to accomplish a task from a set of instances or interpretations, and by enhancing its execution while executing the specified task. [9] To say that learning occurred implies that the structure in question altered its composition, programming or data, in order to enhance the execution upon the classified task, built on the illustrations or observations. The proficiency acquired on how to do the task in doubt is summarized in the manner of a prototype, so when given a completely new set of statistics, this model can bring out the task within an agreeable execution level, presuming that the teaching data is representative of the latest data. [10]

Here, are more than a few learning approaches inside machine learning, that are utilized in various sorts of troubles. Most frequent ones are regulated, unsupervised and reinforcement learning. Nevertheless, the articles which constitute this dissertation are

only **regulated** approaches. The left ones are contemplated out of the scope of this introductory description. In regulated learning, the illustrations or statements that are utilized to instruct the models have known labels which resemble to accurate outputs, and the algorithm will present in directive way to map the inputs to the outputs. [8] Significantly common sorts of problems amid this knowledge approach are categorization, in which the output is exemplified by a limited number of categories; and regression in which the productivity is a real-value number. [11]

Several machine learning concerns have a tendency to be well-constricted, exhibiting no considerable disputes in demonstrating the inputs into pertinent variables to be used in constructing models [12]. However, complicated real-world concerns tend to include information associated to spontaneous signals, spontaneous sounds, dialect, spontaneous images or visual events, these are tough to be transformed into explanatory measures.[12,13] To manage this challenge, a new modality of machine learning algorithms was pioneered: profound learning. Profound learning can be engaged with numerous learning approaches and has an important distinction from the various conventional machine learning modalities. Whereas the later one requires the realm of specialists to hand-craft elements, profound learning presents automated characteristic engineering, implying that it instinctively finds the essential enlightening elements in the data first, and then operates the specified task (e.g., categorization, regression). [14]

Both profound learning and additional conventional forms of machine learning work in order to develop models by the purpose of creating precise prognostications. [15] Different interest which may occur when developing a model is actually deciphering it to comprehend why the model functions and how are the elements combined together in order to assess the marked result. [15] Realizing the modeling significance is vital since around there is an important tradeoff to be deemed, ever since in almost all the cases, the more intricate the algorithms get, the less understandable they are. [16]

In nutshell, machine learning is no novel, and it is an area which has been progressing since the past decades, reacting on much more complicated and tough duties. This

proposes the capacity to resolve hitches that might be either infeasible or impractical to be unraveled by physical coding and it remarks the presence in contemporary life, from weather reports, to claims that contains the capacity to momentously affect individuals' lives, this is the case of healthcare.

1.2 Machine Learning in Healthcare

The health segment persists the expansion more rapidly than the economy itself. [17] Amidst 2000 and 2017, world's health expenditure in real percentage expanded by 3.9% in a year whilst the world economy expanded by 3.0% a year. The globe's healthcare expenditure in 2017 was anticipated to have touched US$ 7.8 trillion mark, that relates to nearly 10% of the global GDP in that year. [17] The rise in health expenditure in US till 2017, was mainly depended on o healthcare service's shooting prices along with associated intensity. This rise can be termed as a multitude factorial rise linked with aging and increasing population, incidence and prevalence rate of diseases and escalation in pharmaceutical costs. [18] The ascendent inclination of the costs of care fetched problematic concerns associated to efficacy and efficiency towards the healthcare systems and it was the leading driving factors for bringing alteration in this segment as earlier it used to be largely focused on hospital care, in order to provide advanced importance to preventative activities and outpatient services. [19]

There are several tasks which together link in the formation of healthcare systems. At first, a patient goes through screening and diagnosis, that comprises of the categorization of patient's records via knowledge transmitted by assessments, probes and past medical records. [20] After this, there are various treatments along with follow ups which includes adequate effective planning and management of detailed events, because of available presented information for future referrals for patients. But a perpetual issue in health information is interoperability – the non-existence of a universal data scheme for health care organizations needs to be rendered it tough for combining data throughout a health structure. [20] Existing approaches in healthcare does not support the current integration of data requirements and it ought to be reevaluated for supporting the extraneous information needs of machine learning.

Incorporation of machine learning to healthcare functions and services isn't novel, further it is also facing a continuity of enhancement in both civic and non – civic segments. [21] The increase in the advancement was made practically feasible through enormous volumes of health records and informational data available in both structured and non – structured forms. [19]

1.3 Prognosis

How pivotal prognosis activities can be focused on through machine learning will be dealt with in this section of the introduction.

Prognosis in the medical loop serves the purpose of laying evidence – based interpretation for a person's chances of forming various results and further leads to information regarding the formation of interventions and strategies for betterment of diagnosing health concerns and managing patients. [22] The prognosis process is an important element in medical science, which marks the assessment of the uncertainties, for population of developing typical results relied on clinical and nonclinical characteristics. Chiefly it is reflected as the expected result of an illness, also prognosis is essential in predicting the possible outcomes of healthy people. [22]

For constructing a reliable estimation of prognosis, a longitudinal perspective of the individuals ought to be taken into consideration, with various other factors, that sets strong foundation for the application of machine learning. [23] Through these trajectories to unravel the pattern of patient's medical concerns, we can estimate the usefulness of machine learning in prognosis level of the treatment cycle at both individual and population level. [23]

1.4 Dementia

Dementia is a convoluted illness that influences the brain's neurological system. It is highly prevalent amongst the aged population, liable for a radical cognitive deterioration severely chronic enough to affect the patient's regular operations and liberation. [24] Despite of years of research committed towards examining it, not much is renowned regarding its processes and at hand there is still not a single accurate illness modifying

medication or therapy which can halt or drastically slow down its progression. [25] The extremely familiar kind of dementia pathology is the growth of amyloid plaques in the brain along with tau proteins in the inner side of neurons. [26]

Further, many studies which were assessed on dementia states that the population suffering from dementia is prone to higher mortality risks than similar population in that specific age spectrum. [27] Even beyond the concerns of general mobility and daily functioning, dementia patients additionally suffer from other several chronic illnesses which can escalate their further deterioration in daily life functioning. [24,28]

One thing to keep in mind is that most studies that use ML approaches for prognosis use persons as their unit of analysis. Prognosis, on the other hand, can be applied to population as well as individuals. When dealing with the dementia family of diseases, for example, focusing on populations may be a good idea because their long-term presence and high direct and indirect costs necessitate large investment, economic arrangements, and the creation of care facilities and infrastructure.

As a result, in order to address dementia prognosis in populations, additional prediction methods that have traditionally been used for population prediction should be included.

As, mentioned that dementia is severe illness which generates so many uncertain chores for patients, the caretakers, families and even public bodies. Therefore, it is of utmost significance to examine the prognosis of dementia. This prognostic assessment will assist researchers in exploring different dimensions of disease progression, management of healthcare programs and will also help patients and their families to understand the condition better. So, machine learning innovative computing advancement which may aid the prognosis of dementia, its analysis and diagnostic decision making. [25]

2. Rationale of the Study

This systematic literature review research on prognosis of dementia through machine learning was conducted since dementia requires multidisciplinary approach as it is a

multifactorial illness. Also, very little is known regarding the whole fundamental procedures involved in the treatment of dementia. Therefore, this study presents the concept of machine learning in order to augment the human abilities for handling complicated issues, either through expanding the knowledge base or through revelation of new concepts for filling the gaps of previously conducted studies for uncovering associated benefits.

Through this research we can also analyze various baseline attributes involved in the development of dementia and how machine learning can be deployed throughout the prognosis.

3. Study Outline

This thesis is a framework based on 20 research articles that has been synthesized. The following is how the rest of this work is organized: Chapter 1 (introduction) introduces key concepts and background information for this work's motivation, as well as the thesis's research contexts. The overall and specific goals of this thesis are detailed in chapter 5 (Research Aims). Chapter 4 (Research context in prognosis: prediction of the onset of dementia in older people) provides similar information, but in the context of prognosis research. Chapter 10 (Discussion) discusses the major findings in relation to the research contexts and the work as a whole, while another chapter discusses threats to validity. The concluding reflections of the thesis work are included in chapter 12 (Conclusion); finally, chapter 14 (Future Work) offers proposals for prospective future investigations.

4. Study Context

Dr. Henderson noted at the time that dementia was a very prevalent condition with an unknown origin, limited palliative therapy, and a considerable social impact. The WHO has designated dementia as a public health priority, citing worrying rates of 7.5 million new cases per year. Dementia is a term used to describe a group of neurological illnesses

that cause gradual cognitive decline and memory loss. As dementia progresses, the affected individuals experience an accumulation of disabilities and cognitive impairment to the point where it interferes with their social and professional functioning, and it can proceed to the point where they even lose their independence completely. Furthermore, little is known about its processes, and no approved symptomatic medication has been shown to be effective in addressing cognitive decline.

In light of this scenario, preventive and risk-reduction efforts are critical, as are prognostic estimations in combating the dementia epidemic. Individuals and their development or lack of development of dementia can be used to discover predictors and their relative importance. Doing this prediction considering a time frame that is large enough for the application of interventions may lead to positive results as to prevent or delay the dementia onset. But, the challenge with this technique is that dementia is thought to be a complex condition, and some elements thought to impact its progression cannot be studied in typical SLR.

5. Study Aim

The main purpose of the prognosis research was to give prognostic estimates for older people in terms of whether or not they will develop dementia.

The aim of the study was to give a systematic literature evaluation of the state of the art, trends, and gaps in dementia prognostic research using machine learning approaches.

6. Research Question

"How Machine Learning approach is being deployed by the studies on Prognosis of Dementia: A Systematic Literature Review"

General Objective: The aim of the literature review is to observe the articles from authors who have conducted primary studies on the employment of machine learning on prognosis of dementia, in order to discern some key aspects of application of machine

learning in healthcare and to understand the major gaps of the previously conducted primary studies.

Specific Objectives:

i) To identify most frequently used ML technique in the prognosis of dementia
ii) To study what data determinants are considered while applying ML technique
iii) To determine the aim of these studies which deploy ML technique for prognosis of dementia
iv) To ascertain the way in which censor data was handled
v) To understand whether these studies primarily focused on individual or population level

7. Literature Review

Table 1: Literature Review of the Study

S. No	Source	Author	Tittle	Study Design	Findings
1.	PubMed	Susan Jongstra *et al. (2018)*	Improving prediction of Dementia in Primary care	Longitudinal Study	The study was based on MMSE (mini-mental state examination), which revealed that administration of VAT among patients who have small percentage decline in their MMSE since last 2-years possess a significant incremental value in order to identify elevated risk among patients for developing dementia.
2.	PubMed	Jussi Tohka *et al. (2016)*	Comparison of feature selection techniques in Machine Learning for anatomical brain MRI in dementia	Cross-sectional study	The study was based on two classification problems; Dementia and MCI (mild cognitive impairment). It was found that in Dementia illness, the variation in the accuracy of test due to

					subject sample did not vary. Also, for MCI, embedded feature selection technique outperformed SVM-based ones.
3.	ScienceDirect	Carlos Cabral *et al. (2015)*	Predicting conversion from MCI to AD with FDG-PET brain images at different prodromal stages	Cross-sectional study	This study synthesizes findings which executes that MCI to AD conversion have the chances to be predicted in a time span of 24 months before conversion. Further, the differentiating power of ML techniques decreases as the temporal distance of the conversion time (TC) increases.
4.	ResearchGate	Bo Cheng *et al. (2016)*	Domain transfer learning for MCI conversion prediction	Experimental Research	The paper proposed general domain transfer learning-based framework for the conversion of MCI prediction. The study was conducted using 202 ADNI subjects, the experimental study shows that the proposed method (SVM and DT) showcases better performance significantly than old methods of MCI converters.
5.	PubMed	R. Guerrero *et al. (2014)*	Manifold population modeling as a neuro-imaging biomarker: application to ADNI and ADNI-Go	Experimental Research	Till then it was for the first time that classification of pMCI (progressive mild cognitive impairment) and sMCI (stable mild cognitive impairment) was shown. In addition to this, classification accuracies between cognitive normal and eMCI (early mild cognitive impairment) were presented.
6.	PLOS one	Laura. L	Predicting	Longitudinal	The superlative execution

		Symonds *et al. (2016)*	Progression from Mild Cognitive Impairment to Alzheimer's Dementia Using Clinical, MRI, and Plasma Biomarkers via Probabilistic Pattern Classification	Research	model merged an amalgamation of cognitive/functional indicators and morphometric MRI procedures projected estimated progression with 80% accuracy (83% sensitivity, 76% specificity, AUC = 0.87). Further, Calibration analysis discovered that the archetypal is proficient in creating probabilistic estimates that consistently imitate the definite risk of advancement.
7.	PubMed	Johan Berglund *et al. (2015)*	Machine leaning and microsimulation techniques on the prognosis of dementia: A systematic literature review	Literature Review	In entire 37 articles which were studied. The information summary outcomes reflected that the contemporary research was fixated on the examination of the people with mild cognitive impairment that might progress to Alzheimer's disease, by means of machine learning techniques. Microsimulation studies on the other hand were focused towards cost containment and they had a populational view. In the presented studies Neuroimaging was the most frequently rummage-sale variable.
8.	ResearchGate	Yash Liu *et al. (2014)*	Hierarchical Interactions Model for Predicting Mild Cognitive Impairment (MCI) to Dementia	Experimental Research	The research synthesized the results regarding the efficacy of tiered collaboration models for estimating the conversion from MCI to probable

			Conversion		Dementia and recognizing a small subdivision of most prognostic biosignatures and pertinent exchanges.
9.	PubMed	Hongming Li *et al. (2019)*	A deep learning model for early prediction of Alzheimer's disease Dementia based on MRI data	RCT Research	The foreseen development susceptibility clustered people subject into subcategories with substantial alterations in their progression time to dementia ($P < .0002$). Enhanced performance in order to predict progression of dementia (concordance index = 0.864) was found when the deep learning-grounded development susceptibility was collective with baseline medical events.
10.	PubMed	Asim M Mubeen *et al. (2017)*	Prediction of incipient Alzheimer's disease Dementia in patients with MCI	RCT Research	The procedures executed in this study can be efficiently utilized for separating stable MCI patients from the ones who are at primary stage of dementia with high accurateness. There were strong pointers of impending dementia in women with MCI in comparison to men.
11.	Google Scholar	Bencie Woll *et al. (2020)*	A Multi-modal Machine Learning Approach and Toolkit to Automate Recognition of Early Stages of Dementia	Experimental Research	The study demonstrated a new approach through multi-modal toolkit based on machine learning's automatic recognition. This was done through several motoric contribution from body to the sign envelope, e.g., hand-arm movement and facial expressions in combination.
12.	Google	Danial	Early Diagnosis of Dementia from	Observational	The study proposed two-

	Scholar	Hooshyar *et al. (2017)*	Clinical Data by Machine Learning Techniques	Research	layered predictive modal for diagnosing Dementia through machine learning technique. The demonstrated modal was found to be efficient in simplifying the prediction or interpretation of the results. This was done through categorizing the patients in different classes, thus enhancing the clinical practice.
13.	Google Scholar	Serge Gautheir *et al. (2017)*	Identifying incipient dementia individuals using machine learning and amyloid imaging	Experimental Research	The study proposed machine learning –grounded probabilistic approach intended to evaluate the prognosis of dementia progression in 24 months, relied on the provincial data from a sole amyloid positron tomography scan. significantly, the projected approach was considered to overawed the intrinsic hostile imbalance proportions among stable and progressive MCI patients in a quick observational time.
14.	ScienceDirect	Jane Stocks *et al. (2021)*	Transfer learning for predicting conversion from mild cognitive impairment to dementia of Alzheimer's type based on a three-dimensional convolutional neural network	Experimental Research	The study established a deep learning model to estimate translation from MCI to DAT (Dementia of Alzheimer's type). Operational MRI scans were utilized as per contribution to 3D convolutional neural network. The 3D convolutional neural grid was proficient for the use in transmission learning;

					This proficient model was then reinstructed on the marked duty of classifying which MCI patients was converted to DAT. This model synthesized 80.4% cataloging accurateness at the marked task. Then, the study focused on visualization of brain parts which importantly contributes to the estimate of MCI.
15.	Google Scholar	Luca Presotto *et al. (2018)*	FDG-PET and CSF biomarker accuracy in prediction of conversion to different dementias in a large multicenter MCI cohort	Cohort Research	The use of topographical (FDG-PET) and CSF attributes, personalized on patient scenarios and measured with corroborated methods which can unusually progress initial discrepancy prognosis and estimation or exclusion of progression susceptibility to dementia in MCI focuses. The futuristic approach states that the improved automatic procedures for CSF quantification may condense inter-centers logical variability.
16.	Google Scholar	Yunus Miah *et al. (2020)*	Performance Comparison of Machine Learning Techniques in Identifying Dementia from Open Access Clinical Datasets	Observational Research	The study reports a proportional result of performance of various ML methods, including support vector machine (SVM), artificial neural network, Naive Bayes, decision tree and K-nearest neighbor, when they are working in recognizing dementia from clinical database. It has been initiated that SVM

					and random forest performed relatively better than other techniques
17.	PubMed	Dina Silva *et al. (2017)*	Predicting progression of MCI to Dementia using neuropsychological data: a supervised learning approach using time windows	Experimental Research	The study stated 4-time windows of; 2, 3, 4 and 5 years. Then, a prognostic model was developed for each time window with the use of clinical and neuropsychological data. The result of the study revealed that Prognostic models utilizing time windows have more prominent presentation when prognosticating progression of dementia from MCI, in contrast to the general prognostic method which is frequently used in the literature like; first last approach. Moreover, the proposed Time Windows approach is more pertinent from a medical perspective, for predicting progression in a sequential period.
18.	PubMed	Richard Smith *et al. (2020)*	Applying Deep learning to predicting dementia and MCI	Descriptive Research	The intention grounds of the research were to demeanor an examination on ADNI database and acknowledge the efficacy for constructing sorting models to unprecedented categories; Cognitively Normal (CN), Mild Cognitive Impairment (MCI), and Dementia (DEM), on the basis of three Deep Learning models: two Multi-Layer Perceptron (MLP1 and MLP2) models and a

					Convolutional Bidirectional Long Short-Term Memory (ConvBLSTM) model. The results demonstrated that the MLP models more precisely differentiate the DEM, MCI and CN classes, with precisions as accurate as 0.84 (SD 0.01). The ConvBLSTM model was slightly less precise than MLPs.
19.	MDPI	Jihye Lim *et al. (2014)*	A Deep Neural Network-Based Method for Prediction of Dementia Using Big Data	Cohort Research	A deep neural-based method for prediction of dementia was found to be more accurate than well-known prognostic machine learning algorithms. The projected approach shows 86.8% of the area under the curve (AUC), much better result than other algorithms can demonstrate.
20.	IOS Press	Sophie Hu *et al. (2020)*	Using machine learning to predict dementia from neuropsychiatric symptom and neuroimaging data	Descriptive Research	The study used baseline symptoms of neuropsychiatric in order to investigate baseline mild behavioral impairment (MBI) in association with brain morphological features, and it was found that reference neuropsychiatric symptoms, considered for MBI sphere and duration, have predictive utility along with brain morphological measures for prognosticating progression change using machine learning. MBI total score dysregulation were most extrapolative for

future prognosis.

With this literature review we can infer that there are many different proposed models of prognostic machine learning for predicting the progression of MCI into Dementia.

8. Methodology

A systematic literature review (SLR) recognizes, assesses and clarifies a considerable and symbolic sample of all the appropriate primary findings regarding the literature involving a dementia. SLRs perform a holistic examination followed by a predetermined approach which stipulates dedicated study questions, criteria for the assortment of articles and carry out the data extraction along with conclusion synthesis.

Conducting a SLR embraces the subsequent steps:

(i) Ascertain the requirement for executing the SLR
(ii) Articulate research questions
(iii) perform a thorough search of the selected primary studies
(iv) Interpretation of the results
(v) Presenting the report on SLR

An examination of various published quantitative and qualitative articles was done in this systematic literature review in order to critically analyze the perspective of various authors on prognosis of dementia through machine learning approach. The study emphasizes on answering some fundamental questions like; techniques of machine learning deployed in the prognosis of dementia, different variables that needs to be considered along with exploration of regions of curiosity through literature. A search string was mapped for clearly defining the inclusive studies

8.1 Search Strategy

PubMed, Google scholar, Medline, and to some extent lancet, all were used to carry out the search. The following search terms or search string was created keeping all the components of the research intact.

([“DEMENTIA” OR “DEMENTIA MORBIDITY” OR “ALZEIHEMER”] AND [“MACHINE LEARNING” OR “DECISION SUPPORT SYSTEM” OR “MACHINE LEARNING MODELS” AND [“PROGNOSIS” OR “PROGNOSTIC ESTIMATES”])

8.2 Article Selection Strategy

The research was conducted from 1st April 2021 to 15th June 2021and included articles since 2013. Following figure explains the process of article selection for this study.

100 study articles were found to be relevant for the SLR but, due to time constraints exclusion and inclusion criteria was decided for conflict resolution which brought down the search to 20 articles which were thoroughly read and assessed. The ones which effectively accepted through the created criteria were specified as pertinent and relevant for data extraction.

Table 2: Inclusion, Exclusion and Variable Definition

Inclusion Criteria	**Exclusion Criteria**
Should be a validated study in English; AND	Published before 2013; OR
Should have been published within the last 8 years; AND	Studies published in language other than English; OR
Address the prognosis associated to at least one machine learning technique; AND	Studies that don’t address at least one machine learning technique; OR
Prognosis related to dementia and its comorbidities	Articles focuses on cognitive impairment rather than Dementia
Variable	**Definition**
Attribute studied	Which dementia disease is being studied to determine a prognosis
Dataset used in the study	Name and origin of the data source utilized to calculate the dementia prognosis
Database categories	The data units were classified into classes
Handling Censored data	The manner in which censored data was handled is described.
Analysis technique	The prognostic models were built using machine learning techniques.

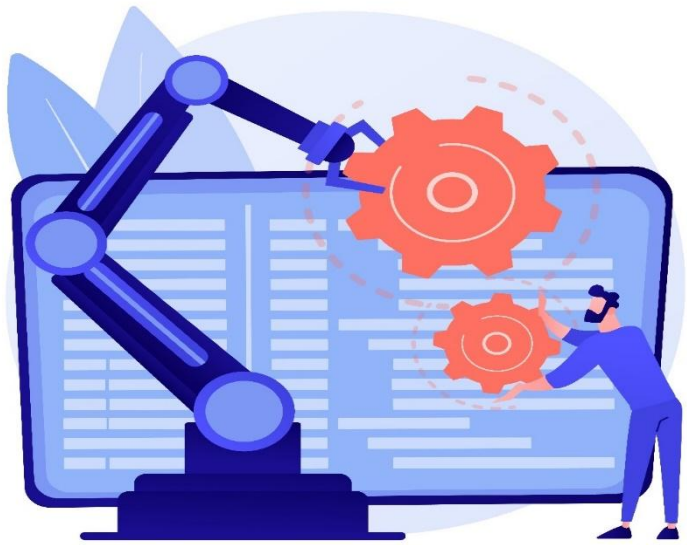
Variable Model	The variables that were used to create the prognostic models
Study Goals	The built-in prognostic models' purpose
Focus of the research	If the created prognostic models target individual or population-level predictions.

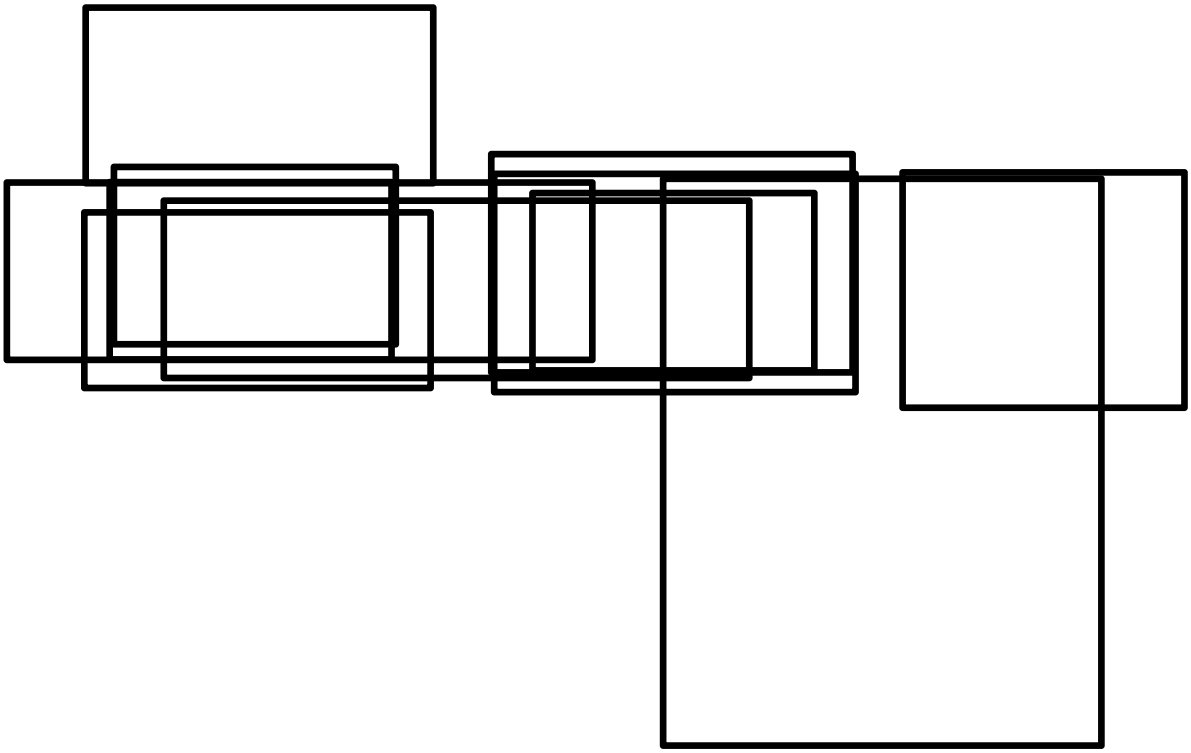
9. Result

The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow chart was used to define the assortment of the studies. At first 100 studies were selected and from these 42 full research articles were assessed for SLR eligibility, where 20 final articles were selected to be inculcated in the SLR, rest of the studies were excluded as they were found to be out of the threshold of the quality assessment, for not being in relevance with the research objective, some were not a prognostic estimation studies, some were excluded because they didn't use proper machine learning technique and one criteria for exclusion was for those studies who emphasizes on overall cognitive decline, but not dementia in particular.

Most frequently mentioned technique in the articles were SVM (Support Vector Machines) and Decision Trees.

Fig 1: Machine Learning Vector Illustration





Outcome of the final synthesis of 20 articles presented in this study revealed the perspective of the dementia prognosis through machine learning approach, along with recognizing the disparities among various perspectives presented in these papers. Findings from the studies outlines that the concentration of the whole research of the prognosis of Dementia was on the utilization of neuroimaging, in order to forecast the Dementia cases from MCI, by using data resource from ADNI data reserve. Through this research it was also inevitable that the attempts towards prevention of Dementia is practically unavailable, further this analysis of various articles laid out that the key concentrate of the studies were primarily those individuals who were possessing some sort of cognitive relapse and not the ones who were healthy and suddenly have the probability of developing dementia in future. Also, there were some associated uncertainties involving framework of prediction models because they did not present any accurate time for intervention and another major gap of the research was the lack of exploring of behavioral and social aspects in the presented models. The major attention of the studies included in this dissertation was vastly on individuals rather than the whole population projection regarding dementia prognosis.

9.1 Identified Machine Learning Technique

On the Subject of ML techniques, the generation of the extricated data indicates that the extremely frequent used ML methods were Support Vector Machines (SVM) (15 articles) and Decision Trees (DT) (5 articles).

The Support Vector Machine (SVM) was first introduced as a classification algorithm; it is a relatively young technique when compared to other machine learning techniques. SVMs, unlike some regression techniques, do not require a pre-determined model to fit data, while there are still algorithm requirements to consider (e.g., Radial function selection).

In terms of the SLR findings, SVMs were found in 20/37 papers, in some proposed models, and are by far the most often utilized machine learning technology in dementia prognostic research. The standard SVM is taken into account in these figures. SVMs were utilized in all 30 trials to discriminate between mild cognitively impaired (MCI) patients who will or will not acquire dementia.

Table 3: SVM Technique Identification

Technique Modifications	Featuring study in SLR
SVM	1-15
Radial basis function SVM	17, 13-15
Relevance Vector Machines	7
Domain Transfer SVM	7
Other approaches of SVM	7

A Decision Tree (DT) is a classification technique that represents learned knowledge as a tree structure that can be translated into if-then rules. The recursive learning process of DT begins with a test of each input variable to see how well it can classify the labelled instances on its own. The best one is chosen as the tree's root node, and its daughter nodes are defined as the input variable's possible values (or relevant ratios). Following that, the training set is divided into descendant nodes based on the values of the given input variable. This method is repeated until there are no more feasible splits in the tree.

Fig 3: DT Classification explication

DTs were the next most commonly utilized ML technique in this SLR, appearing in 5/20 of the trials. In the selected studies, the variants of this type of technique are presented

Table 4: DT Technique Identification

Technique Modifications	Featuring study in SLR
Random Forests	17
Decision Trees	16-20
Boosted Trees	18,19

9.2 Characteristics of The Data Used in The Models

In this section, machine learning (ML) attempt to understand the connection between various distinct variables, and the result variable, known as covariate. The articles used in

this thesis mainly focused primarily on binary prognosis variable (typically signifying development/no development to Dementia).

Following table encapsulates the relationship amid variables and articles. Note that variables which are not studied in the article and made no contribution to the outcome are not mentioned. Distinct characteristic variables termed as; neuroimaging, neuropsychological, genetic variable, lab testing and demographical variables are included in the articles which were studied.

Also, there were certain articles which contributed more than once for the subcategories but, the input to categories was only counted once. Thus, resulting in smaller number for categories than overall sum of numbers of the subcategories.

Table 5: Major characteristics studied in the SLR articles

Category of Variable	Subcategory of Variable	No. Of Studies	Studies, featuring variable category
Neuroimaging	MRI, PET, Neural-based models	9	2, 5, 6, 9, 14, 15, 17, 19, 20
Cognitive measures	Dementia assessment scale	1	12
Genetics	Family history, Hierarchical medical history	5	7,8,10,12,16
Lab Tests	Clinical tests	4	1,6,10,12
Demographics	Age	1	7

9.3 The Objectives of Dementia Prognostic Studies

The accumulated gathered information reveals that most of the studies, meant to scrutinize the progression of MCI to Dementia. The identified articles mention the need

for the Dementia prognosis and suggested patterns for the prediction, generally amid 8 to 36 months till growth. Exclusions are Adaszewski et al. [24], and Chen et al. [62], as these two created models for 42- and 60-months prognostication, respectively.

Almost all the articles included in this study have extracted their data from ADNI (Alzheimer's disease neuroimaging initiative) for their predictive models, leading to restricted time-period for prediction due to limited follow up time. In certain study articles, there were also variation of the goal. In these studies, the aim was the prediction of Alzheimer and not Dementia from MCI.

Further, some studies use patient's prolonged informational records to design the predictive model based on course of action of Dementia with regards to its cerebral operations.

Table 6: Goals of the studies in SLR with respect to Prognosis of Dementia

Goal of the Studies	Study Count	Measures Studied	Type of Data Analysis	Featuring Studies
Mild Cognitive Impairment can be used to predict the onset of Dementia disease.	17	Dementia Disease, MCI	ML	1,2, 5-14, 16-20
Model illness stage using the score from the FDG-PET imaging	2	Dementia Disease	ML	3,15
Modeling illness progression based on events	1	MCI Conversion	ML	4

9.4 Addressing Data that has been Censored

When some individuals are unaware of their own personal time to the event of interest, data censoring occurs. This can happen when data on the time to event is unavailable due to a lack of follow-up or when the outcome event does not occur before the trial ends. Only two of the 22 studies included in this SLR explicitly addressed censored data. The Craig-Schapiro et al. study and the Plant et al. study. The former study employed Cox proportional hazard models to determine which baseline biomarkers should be included in ML multivariate models for predicting the transition from cognitive normality to very mild or moderate dementia. Participants who did not acquire very mild or mild dementia during the follow-up were statistically censored, while in the latter study the researchers and data censoring is addressed as a danger to validity, stating that for shorter follow-ups, there may be patients labelled as MCI with an MRI pathological pattern who have not yet acquired Dementia. The other papers considered in this review made no specific remarks about data censoring.

9.5 Focus of the Studies

The last objective of the SLR was to analyze the focus of the studies included in this research, and it was discovered that all the 20 studies sincerely focused on prognosis of dementia at an individual level and no study focused on population level.

10. Discussion

This section of the thesis represents the discussion concerning the findings accomplished through the study perspectives on prognosis of dementia, through the application of machine learning approach in healthcare, along with threats to validity for the studies included in this thesis.

The secondary research of this thesis was a systematic literature review which was done to present the cumulative evident results on prognosis of dementia through machine learning approach.

In order to tackle an issue like dementia which is sensitive, it is very significant that the interpretability and performance of prognosis must be thoroughly deemed. In the earlier conducted studies this arbitration was taken care of. Most importantly it is a matter of consideration that dementia is a mental cognitive disorder which eventually leads to severely grave outcomes for the individual who has it plus their families, as due to this illness a person tends to lose their basic mobility and daily functionality of performing routine activities, offering poorest of health markers with time. Secondly, there has been so far no absolute treatment or medication for dementia nor any illness-modifying treatments for treating the disease symptoms. Even analyzing or predicting the development of dementia among individuals who are susceptible without acknowledging their true circumstances is not affective nor applicable amidst various situations. Additionally, some sources also reveals that there are high chances of risks associated with mental stress, suicidal tendencies and even claims for demanding euthanasia among patients who are diagnosed with early dementia.

This concern is being considered like a significant problem because many have been detected by an extremely incapacitating ailment, deprived of the possibility of medication and cure or even a process for the mitigation of the early indicators, may perhaps be contended to be in contradiction of the medical ethical deportment. With regards to all these mentioned facts, it was conventional that the foremost center of examining prognostic evaluations of dementia will be the model based on interpretability besides the exposure of probable adaptable factors which are capacitated to be proceeded upon in exertions of deferring or preventing the dementia onset. This study concept operated to attain satisfactory results, contemplating the time for projection, which are extremely interpretable and deliver base for different hypotheses to be extensively investigated in trials with respect to adjustable risk aspects and important patient subdivisions. The significance of these conclusions relies on the actuality that they do not affect pharmacological ventures regarding individuals that even now represent some extent of cognitive impairment, which are the core of the study on the prognosis of dementia (evidenced by the SLR).

The key outcomes after this Systematic literature review are abridged below:

(i) Almost all the studies mentioned, utilizes neuroimaging for forecasting the occurrence of dementia from MCI, with the use of ADNI data reserve

(ii) Evaluations are generally rendered for about 36 months prior to the onset of dementia

(iii) Behavioral and social attributes were missing or neglected in the evaluated presented models

(iv) The locus of the whole thesis was based on individual level and not on population level

The overall study of prognosis of dementia which extensively uses ML techniques had their key focus on the use of neuroimaging in order to predict the onset of dementia through MCI, typically using the ADNI data surplus. The combined affect of this situation is the nearly absolute focus of the latest research in validating biomarkers which is to be utilized in the trials of medical care, as it is the overall concern of ADNI. This rigorous examination on biomarkers was vital to make the pharmaceutical study swifter while reducing the disclosure of ineffectual experimental medicines.

Additional considerable aspect concerning the whole predilection towards the neuroimaging variables, during the incorporated articles in the SLR, was that much of the prognostic study is involved with a specific attribute of dementia, and prognosis approximates should deliberate a multivariable method. The explanation for that is the inconsistency among people that might turn the sole predictor variable not exceptionally effective. Moreover, ADNI ensures not to contain important comorbidities in its data subjects with, contemplating dementia like cancer and cardiological conditions [75]. Furthermore, as ADNI is a non-epidemiologic study, therefore it possessed high risk regarding the effectiveness of methods applied in the findings which might be modified to the ADNI's certain requirements.

As, we discuss about the subject of the development of dementia among individuals through MCI, one more significant attribute to be considered is regarding the recognition

of timespan in advance for the suggested models during current research that can predict this transformation. Most of them are believed to complete this task in a timespan of up to 36 months. Keeping at bay the characteristic of being accurate with respect to the predictions (as they are vital), could this period restraint be enough to utilize prophylactic approaches (pharmaceutical or non-pharmaceutical) on screened individuals in order to delay the progression to dementia? An essential concern in the examination for medications is that they lengthen the period individuals splurge in the most responsive levels of dementia and reduce the timespan where they stay in the extremely unadorned stages, in which patients suffer from a low-slung value of living amid expensive care.

The lack of articles on behavior and social variables in assessment models spots out about the gap in the current research for more comprehensive approaches towards prognosis of dementia. Different prospect is that studies which are scrutinizing these may merely affect more data analysis techniques for receiving the predictions that are not ML. There was also no factual information towards handling of censored information, giving rise to several concerns because most of the study demographics were differentiated into categories of controls, dementia patients, converters of MCI and non-converters of MCI. Furthermore, the group of MCI non-converters could necessitate when an individual does not encounter the scenario evidently. Moreover, with respect to ML techniques there were severe lack of number of studies on predicting the onset of dementia for population marking another gap for the study.

10.1 Machine Learning for Prognosis of Dementia

Through this thesis, I wanted to present the capacity of machine learning in augmenting the human ability in simple manners. In the case of prognosis, elements involved in the procedure of developing dementia among aged people (and practical interactions between them) are unfamiliar and the concept of applied machine learning was determined in order to reveal patterns of the information, reflecting a great number of characteristics that might be too unreasonable for physical analysis. The contexts of this emphasize on the significance of the application part in several determining phases that might lead the preferences of the technology which will be applied in order to act upon the troubles

currently present. The study concept that was part of this dissertation laid out distinct priorities based on provisions of the necessity of a superior execution or a better interpretability, which were presented by the consequence and peculiarities the case. In the practical health technology arena, the problem is equally the starting and the ending of the service for a certain technology. Additional significant aspect of the applied machine learning in healthcare concerns is the use multidisciplinary aspect for a holistic approach, where clinical and intellectual knowledge researchers interact. The use of machine learning to construct and validate models is an uncomplicated progression, though it is the sphere where professionals can generate and establish elevated standard examples which may permit the engagement of machine learning. Further, the domain specialist requires to be in the loop for adequate interpreting, validating and identifying feasible positions of progress or malfunction. Several crucial methodological considerations were to be rendered concerning the usage of machine learning in the healthcare sector. One of them is the vigorous exploratory aspect that could be contemplated as an inductive kind of study, but it is different from the true induction'. In the 'true induction' a hypothesis is there termed; h and a frame of evidence e which defines the problem if e rationalizes h. Nevertheless, in the machine learning's scenario the e is renowned, but there is no h to rationalize it. Therefore, the purpose is to utilize various processes to attain an appropriate h from e [105]. Machine learning hence, functions by being a robotic (or automated) way to find out new hypotheses in a manner that “is not merely carried as the conjecture from observations to give common rules. It comprises the search for the rules in a substantial setting of opportunities”. These innovative discovered hypotheses need to be more scrutinized and authenticated through trials before any additional application is converted to a medical applied concept. Machine learning is a technology which can develop the manual constraints about duties that are impossible or quite unfeasible for a human to perform. It extends terrific possibility in the medical sector by unraveling many futuristic hypotheses in complicated situations similar to the ones that is related to health.

11. Threat to Validity

The validity threats determination will be deliberated in the following with regards to external validities in the encompassed articles of this dissertation, laterally with tasks involved in order to mitigate the threat.

11.1 External Validity

This validity explains the extent of achieved synthesized results as generalizable. The SLR of the studies included in this thesis are executed in a systematic manner along with defining the inclusive criteria, so to an extent we can mitigate the risk of external validity and consider the research to be generalizable.

12. Conclusion

The dissertation followed an approach of SLR which aimed at examining the machine learning's application in healthcare domain through its deployment in the field of prognosis of dementia. As the application of machine learning contemplates it as a modern healthcare technique, which can be utilized as the solution to peculiar applied issues.

In the research concept of prognosis of dementia, prognostic assessments were attempted to be examined and it was found that the required sufficient evident results reflected that the focus of most of the studies laid on the prediction models of MCI using ML techniques for patients who develop dementia, in usually 36 months, by the significant use of neuroimaging.

The 20 studies included in the SLR summarized the focus on the prognosis of dementia through the usage of ML technology, it executed various attributes including frequency in the type of ML technique, variables and aim of the various studies. There were only limited number of sets of data which were being utilized and most notably, it was ADNI database.

13. Limitations of the Study

The issue of whether a suitably large representative sample of all potentially relevant studies was included in the final set is the major limitation of this SLR.

To address the problem, a more inclusive selection approach was implemented. This means that in articles where the inclusive criteria were not clearly stated in the title or abstract, the study's substance was examined further for prospective inclusion or exclusion.

14. Recommendations and Scope for Future Work

Clinical studies should be the focus of future research in order to validate and examine the results acquired by estimating models developed in research contexts of the SLR in clinical trials, which should be the next step in the process of transferring discoveries to clinical practice.

The findings of this SLR revealed current trends and gaps in dementia prognostic research that should be addressed in the future. Further study should be conducted based on these findings to investigate other combinations of ML approaches, employing a multivariable approach that encompasses the indicated data qualities as well as lifestyle and social aspects.

BIBLOGRAPHY

1. Nass SJ, Levit LA, Gostin LO. Beyond the HIPAA Privacy Rule: Expanding Privacy, Taming Health Through Research. Washington (DC): Nationwide Academies Press (US); 2015.
2. Herland M, Khoshgoftaar TM, Wald R. A review of data mining using big data in health informatics. Journal Of Big Data. 2014. p. 2. doi:10.1186/2196-1115- 1-2
3. Crown WH. Probable application of machine learning in health outcomes research and some arithmetical cautions. Value Health. 2015;18: 137–140.
4. Panch T, Szolovits P, Atun R. Artificial intelligence, machine learning and health structures. J Glob Health. 2018;8: 020303.
5. Lee A, Taylor P, Kalpathy-Cramer J, Tufail A. When Machine Learning Has Arrived! 2017;124: 1726–1728.
6. IBM100 - Deep Blue. In: IBM Corporation [Internet]. 7 Mar 2013 [cited 15 Apr 2020].
7. Mitchell TM. The chastisement of machine learning. Conservatory of Computer Science. Carnegie Mellon University, Pittsburg, PA; 2017
8. Kotsiantis SB, Zaharakis I, Pintelas P. Administered machine learning: A review of cataloguing techniques. Emergent computer intelligence applications in computer commerce. 2018;160: 3–24.
9. Nilsson Nils J. Overview to Machine learning. Automation Research laboratory Section of Computer Science Stanford University. 2019;1.
10. Louridas P, Ebert C. Machine Learning. IEEE Software program. 2016. pp. 110–115. doi:10.1109/ms.2016.114
11. Kourou K, Exarchos TP, Exarchos KP, Karamouzis MV, Fotiadis DI. Machine learning submissions in MCI prognosis and prediction. Computer Structure. 2015;13: 8–17.
12. Deng L, Yu D. Profound Learning: Approaches and Applications. Signal Process Communication Network. 2014;7: 197–387

13. Miotto R, Wang F, Wang S, Jiang X, Dudley JT. Subterranean erudition for health care: review, prospects and challenges. Brief Bio information. 2018;19: 1236–1246.
14. Ravi D, Wong C, Deligianni F, Berthelot M, Andreu-Perez J, Lo B, et al. Deep Learning for Health Informatics. IEEE J Biomed Health Inform. 2017;21: 4–21.
15. Kuhn M, Johnson K. Practical Prognostic Modeling of Dementia. Springer, New York, NY; 2020.
16. Rowe M. An Introduction to Machine Learning for Medical professionals. Acad Med. 2019;94: 1433–1436.
17. World Health Organization. Global expenditure on health: a world in transition. 2019.
18. Dieleman JL, Squires E, Bui AL, Campbell M, Chapin A, Hamavid H, et al. Factors Linked to Rising Health-Care Spending in the United States, 2013. JAMA. 2017;318: 1668–1678.
19. Bhardwaj R, Nambiar AR, Dutta D. A Research on Machine Learning in Healthcare. 2017 IEEE 41st Yearly Processer Software and Applications Consultation. 2017. pp. 236–241
20. Panch T, Szolovits P, Atun R. Machine learning, artificial intelligence, and health-care systems. J Glob Health. 2018;8: 020303.
21. World Health Organization. An International Ethics Consultation on Big Data and Artificial Intelligence for Universal Health Coverage. 2018.
22. Moons KGM, Royston P, Vergouwe Y, Grobbee DE, Altman DG. What, why, and how do prognosis and prognostic research work? BMJ. 2020;338: b375.
23. Rajkomar A, Dean J, Kohane I. Pharmacology and Machine Learning. N Engl J Med. 2019;380: 1347–1358.
24. Melis RJF, Marengoni A, Rizzuto D, Teerenstra S, Kivipelto M, Angleman SB, et al. Multimorbidity's impact on dementia clinical development in a population-based cohort. PloS One. 2013; 8(12): e84014.
25. Ohno-Machado L. Modeling medical prognosis: approaches for survival analysis. J Biomed Inform. 2021 Dec; 34(6):428–39.

26. Winblad B, Amouyel P, Andrieu S, Ballard C, Brayne C, Brodaty H, et al. Dementia's disease and other MCI conditions must be eradicated as a priority for European research and society. Lancet Neurol. 2016 Apr; 15(5):455– 532.
27. Van de Vorst IE, Vaartjes I, Geerlings MI, Bots ML, Koek HL. Results of a prospective nationwide registry linkage research in the US on the prognosis of dementia patients. BMJ Open. 2015 Oct 1; 5(10): e008897.
28. Poblador-Plou B, Caldero´n-Larrañaga A, Marta-Moreno J, Hancco-Saavedra J, Sicras-Mainar A, Soljak M, et al. Dementia comorbidity in primary care patients: a cross-sectional study BMC Psychiatry. 2014; 14:84.
29. Jongstra S, van Gool WA, Moll van Charante EP, van Dalen JW, Eurelings LSM, Richard E, Ligthart SA. Improving Prediction of Dementia in Primary Care. Ann Fam Med. 2018 May;16(3):206-210. doi: 10.1370/afm.2224. PMID: 29760023; PMCID: PMC5951248.
30. Tohka J, Moradi E, Huttunen H; Alzheimer's Disease Neuroimaging Initiative. Comparison of Feature Selection Techniques in Machine Learning for Anatomical Brain MRI in Dementia. Neuroinformatics. 2016 Jul;14(3):279-96. doi: 10.1007/s12021-015-9292-3. PMID: 26803769.
31. Ottoy J, Niemantsverdriet E, Verhaeghe J, De Roeck E, Struyfs H, Somers C, Wyffels L, Ceyssens S, Van Mossevelde S, Van den Bossche T, Van Broeckhoven C, Ribbens A, Bjerke M, Stroobants S, Engelborghs S, Staelens S. Association of short-term cognitive decline and MCI-to-AD dementia conversion with CSF, MRI, amyloid- and ^{18}F-FDG-PET imaging. Neuroimage Clin. 2019; 22:101771. doi: 10.1016/j.nicl.2019.101771. Epub 2019 Mar 13. PMID: 30927601; PMCID: PMC6444289.
32. Cheng B, Liu M, Zhang D, Munsell BC, Shen D. Domain Transfer Learning for MCI Conversion Prediction. IEEE Trans Biomed Eng. 2015 Jul;62(7):1805-1817. doi: 10.1109/TBME.2015.2404809. Epub 2015 Mar 2. PMID: 25751861; PMCID: PMC4474791.
33. Guerrero R, Wolz R, Rao AW, Rueckert D; Alzheimer's Disease Neuroimaging Initiative (ADNI). Manifold population modeling as a neuro-imaging biomarker:

application to ADNI and ADNI-GO. Neuroimage. 2014 Jul 1;94: 275-286. doi: 10.1016/j.neuroimage.2014.03.036. Epub 2014 Mar 21. PMID: 24657351.

34. Korolev IO, Symonds LL, Bozoki AC; Alzheimer's Disease Neuroimaging Initiative. Predicting Progression from Mild Cognitive Impairment to Alzheimer's Dementia Using Clinical, MRI, and Plasma Biomarkers via Probabilistic Pattern Classification. PLoS One. 2016 Feb 22;11(2): e0138866. doi: 10.1371/journal.pone.0138866. PMID: 26901338; PMCID: PMC4762666.
35. Dallora AL, Eivazzadeh S, Mendes E, Berglund J, Anderberg P. Machine learning and microsimulation techniques on the prognosis of dementia: A systematic literature review. PLoS One. 2017 Jun 29;12(6): e0179804. doi: 10.1371/journal.pone.0179804. PMID: 28662070; PMCID: PMC5491044.
36. Li H, Liu Y, Gong P, Zhang C, Ye J; Alzheimers Disease Neuroimaging Initiative. Hierarchical interactions model for predicting Mild Cognitive Impairment (MCI) to Dementia Disease conversion. PLoS One. 2014 Jan 8;9(1): e82450. doi: 10.1371/journal.pone.0082450. PMID: 24416143; PMCID: PMC3885394.
37. Li H, Habes M, Wolk DA, Fan Y; Alzheimer's Disease Neuroimaging Initiative and the Australian Imaging Biomarkers and Lifestyle Study of Aging. A deep learning model for early prediction of Alzheimer's disease dementia based on magnetic resonance imaging data. Alzheimers Dement. 2019 Aug;15(8):1059-1070. doi: 10.1016/j.jalz.2019.02.007. Epub 2019 Jun 11. PMID: 31201098; PMCID: PMC6719787.
38. Ardekani BA, Bermudez E, Mubeen AM, Bachman AH; Alzheimer’s Disease Neuroimaging Initiative. Prediction of Incipient Alzheimer's Disease Dementia in Patients with Mild Cognitive Impairment. J PMID: 27662309.
39. Xing Liang, Tyron Wolfe; A Multi-modal Machine Learning Approach and Toolkit to Automate Recognition of Early Stages of Dementia among British Sign Language Users, ResearchGate October 2020.

40. Ju R, Hu C, Zhou P, Li Q. Early Diagnosis of Dementia from clinical data by ML technique. IEEE/ACM Trans Comput Biol Bioinform. 2019 Jan-Feb;16(1):244-257. doi: 10.1109/TCBB.2017.2776910. Epub 2017 Nov 23. PMID: 29989989.
41. Mathotaarachchi S, Pascoal TA, Shin M, Benedet AL, Kang MS, Beaudry T, Fonov VS, Gauthier S, Rosa-Neto P; Alzheimer's Disease Neuroimaging Initiative. Identifying incipient dementia individuals using machine learning and amyloid imaging. Neurobiol Aging. 2017 Nov; 59:80-90. doi: 10.1016/j.neurobiolaging.2017.06.027. Epub 2017 Jul 11. PMID: 28756942.
42. Bae J, Stocks J, Heywood A, Jung Y, Jenkins L, Hill V, Katsaggelos A, Popuri K, Rosen H, Beg MF, Wang L; Alzheimer's Disease Neuroimaging Initiative. Transfer learning for predicting conversion from mild cognitive impairment to dementia of Alzheimer's type based on a three-dimensional convolutional neural network. Neurobiol Aging. 2021 Mar; 99:53-64. doi: 10.1016/j.neurobiolaging.2020.12.005. Epub 2020 Dec 13. PMID: 33422894; PMCID: PMC7902477.
43. Caminiti SP, Ballarini T, Sala A, Cerami C, Presotto L, Santangelo R, Fallanca F, Vanoli EG, Gianolli L, Iannaccone S, Magnani G, Perani D; BIOMARKAPD Project. FDG-PET and CSF biomarker accuracy in prediction of conversion to different dementias in a large multicentre MCI cohort. Neuroimage Clin. 2018 Jan 28; 18:167-177. doi: 10.1016/j.nicl.2018.01.019. PMID: 29387532; PMCID: PMC5790816.
44. Miah Y., Prima C.N.E., Seema S.J., Mahmud M., Shamim Kaiser M. (2021) Performance Comparison of Machine Learning Techniques in Identifying Dementia from Open Access Clinical Datasets. In: Saeed F., Al-Hadhrami T., Mohammed F., Mohammed E. (eds) Advances on Smart and Soft Computing. Advances in Intelligent Systems and Computing, vol 1188. Springer, Singapore. October 2020.
45. Pereira T, Lemos L, Cardoso S, Silva D, Rodrigues A, Santana I, de Mendonça A, Guerreiro M, Madeira SC. Predicting progression of mild cognitive impairment to dementia using neuropsychological data: a supervised learning approach using

time windows. BMC Med Inform Decis Mak. 2017 Jul 19;17(1):110. doi: 10.1186/s12911-017-0497-2. PMID: 28724366; PMCID: PMC5517828.

46. Stamate D. et al. (2020) Applying Deep Learning to Predicting Dementia and Mild Cognitive Impairment. In: Maglogiannis I., Iliadis L., Pimenidis E. (eds) Artificial Intelligence Applications and Innovations. AIAI 2020. IFIP Advances in Information and Communication Technology, vol 584. May 2020.
47. Kim J, Lim J. A Deep Neural Network-Based Method for Prediction of Dementia Using Big Data. Int J Environ Res Public Health. 2021 May 18;18(10):5386. doi: 10.3390/ijerph18105386. PMID: 34070100; PMCID: PMC8158341.
48. Gill S, Mouches P, Hu S, Rajashekar D, MacMaster FP, Smith EE, Forkert ND, Ismail Z; Alzheimer's Disease Neuroimaging Initiative. Using Machine Learning to Predict Dementia from Neuropsychiatric Symptom and Neuroimaging Data. J Alzheimers Dis. 2020;75(1):277-288. doi: 10.3233/JAD-191169. PMID: 32250302; PMCID: PMC7306896.