ISSN: 3107-6513
International Journal of Advanced Multidisciplinary Research and Educational Development
Volume 2, Issue 5 | September - October 2026 | www.ijamred.com

Machine Learning Driving Approaches to Early Alzheimer's Detection

Dr. Aliu Omowumi Hafsat
Department of Computer Science
School of Information and Communication Technology,

Hamza salim ismail
MIS - Unit, Auchi polytechnic, Auchi
Auchi Polytechnic, Auchi, Edo State, Nigeria.
Correspondence: aliu.omowumi.aoh@gmail.com

Abstract—
Alzheimer's disease (AD) represents a critical global health challenge, with early detection remaining pivotal for effective intervention and improved patient outcomes. Traditional diagnostic methods often identify the disease only after substantial neurodegeneration has occurred, limiting therapeutic efficacy. Machine learning (ML) approaches have emerged as transformative tools in revolutionizing early Alzheimer's detection through their capacity to analyze complex, multi-dimensional biomedical data. This paper provides a comprehensive examination of contemporary machine learning methodologies applied to early Alzheimer's detection, encompassing neuroimaging analysis, biomarker identification, cognitive assessment automation, and multi-modal data integration. Through systematic analysis of recent developments, this research demonstrates that ensemble learning models, particularly those integrating convolutional neural networks (CNNs) with support vector machines (SVMs), achieve diagnostic accuracies exceeding 92% in distinguishing mild cognitive impairment (MCI) from healthy controls. Deep learning architectures demonstrate superior performance in analyzing structural and functional magnetic resonance imaging (MRI) data, with classification accuracies reaching 94.7% for AD detection. However, significant challenges persist, including data heterogeneity, model interpretability, and clinical implementation barriers. This paper synthesizes current evidence, evaluates methodological approaches, and proposes future directions for advancing machine learning applications in early Alzheimer's detection within diverse clinical contexts.

Keywords Machine learning, Alzheimer's disease, early detection, neuroimaging, biomarkers

I. Introduction

Alzheimer's disease constitutes the most prevalent form of dementia, accounting for approximately 60 to 80% of all dementia cases globally (Alzheimer's Association, 2024). The World Health Organization estimates that over 55 million people worldwide currently live with dementia, with this number projected to reach 139 million by 2050 (World Health Organization, 2023). The progressive neurodegenerative nature of Alzheimer's disease manifests through irreversible cognitive decline, memory impairment, and behavioral changes that fundamentally compromise quality of life for both patients and caregivers. The socioeconomic burden associated with AD is substantial, with global costs exceeding $1.3 trillion annually and anticipated to double by 2030 (Alzheimer's Disease International, 2022).

Early detection of Alzheimer's disease represents a critical frontier in neurodegenerative disease management. The pathophysiological cascade of AD initiates decades before clinical symptoms emerge, with amyloid-beta plaque accumulation and tau protein hyperphosphorylation occurring during the preclinical phase (Jack et al., 2018). Traditional diagnostic approaches, including neuropsychological testing and clinical assessment, typically identify the disease only after substantial neural damage has manifested, significantly limiting therapeutic intervention opportunities. The mild cognitive impairment (MCI) stage, characterized by cognitive changes greater than expected for age but insufficient to interfere with daily activities, represents a crucial window for intervention, as approximately 10 to 15% of MCI patients progress to AD annually (Petersen et al., 2018).

The advent of machine learning technologies has catalyzed a paradigm shift in medical diagnostics, offering unprecedented capabilities for pattern recognition, predictive modeling, and data-driven decision support. Machine learning algorithms excel at identifying subtle, complex patterns within high-dimensional biomedical data that may elude conventional analytical methods or human perception. In the context of Alzheimer's detection, ML approaches leverage diverse data modalities including neuroimaging, genetic information, cerebrospinal fluid (CSF) biomarkers, cognitive assessment scores, and demographic variables to construct sophisticated predictive models (Rathore et al., 2017).

Recent advances in computational power, neuroimaging technologies, and algorithmic sophistication have positioned machine learning as a transformative force in early AD detection. Deep learning architectures, particularly convolutional neural networks (CNNs), have demonstrated remarkable proficiency in analyzing neuroimaging data, automatically extracting relevant features from brain scans without requiring manual feature engineering (Wen et al., 2020). Support vector machines (SVMs), random forests, and gradient boosting methods have shown consistent efficacy in integrating multi-modal data for enhanced diagnostic accuracy (Altaf et al., 2019). Furthermore, the development of

explainable artificial intelligence (XAI) techniques addresses the critical need for model interpretability in clinical applications, enabling clinicians to understand and trust algorithmic predictions (Tjoa & Guan, 2021).

Despite these promising developments, several challenges impede the widespread clinical adoption of ML-based diagnostic tools. Data heterogeneity across different imaging protocols, scanner manufacturers, and institutional settings introduces variability that can compromise model generalizability (Davatzikos et al., 2019). The scarcity of longitudinal datasets with comprehensive clinical annotations limits the development of robust temporal prediction models. Ethical considerations regarding algorithmic bias, patient privacy, and the potential for over-reliance on automated systems necessitate careful implementation frameworks (Char et al., 2018). Additionally, the integration of ML tools into existing clinical workflows requires significant infrastructure development, professional training, and validation studies.

This paper provides a comprehensive analysis of machine learning approaches to early Alzheimer's detection, examining current methodologies, performance metrics, implementation challenges, and future directions. The research synthesizes evidence from recent literature, evaluates the efficacy of various ML techniques, and proposes recommendations for advancing the field toward clinically viable, equitable, and effective diagnostic solutions.

II. Machine Learning Fundamentals in Medical Diagnostics

Machine learning encompasses a diverse array of computational methodologies that enable systems to learn patterns from data and make predictions without explicit programming. In medical diagnostics, ML algorithms serve multiple functions including classification, regression, clustering, and anomaly detection (Ghassemi et al., 2020). The fundamental taxonomy of machine learning divides approaches into supervised learning, unsupervised learning, and reinforcement learning, with supervised learning dominating applications in Alzheimer's detection.

Supervised learning algorithms learn from labeled training data, where input features are paired with known outcomes, to predict labels for new, unseen data. Classification algorithms such as support vector machines, decision trees, random forests, and neural networks have demonstrated particular utility in distinguishing between diagnostic categories (AD, MCI, healthy controls). SVMs construct optimal hyperplanes that maximize the margin between different classes in high-dimensional feature spaces, making them particularly effective for neuroimaging applications where feature dimensionality often exceeds sample size (Vapnik, 2013). Random forests employ ensemble learning by aggregating predictions from multiple decision trees, reducing overfitting and improving generalization performance (Breiman, 2001).

Deep learning represents a specialized subset of machine learning characterized by neural network architectures with multiple hidden layers capable of learning hierarchical feature representations. Convolutional neural networks have revolutionized medical image analysis through their capacity to automatically extract spatial patterns from images through convolution operations, pooling layers, and non-linear activation functions (LeCun et al., 2015). Recurrent neural networks (RNNs) and long short-term memory (LSTM) networks excel at processing sequential data, making them suitable for analyzing longitudinal patient records and temporal disease progression patterns (Hochreiter & Schmidhuber, 1997).

The typical machine learning workflow for Alzheimer's detection comprises several critical stages: data acquisition and preprocessing, feature extraction and selection, model training and validation, performance evaluation, and clinical deployment. Data preprocessing addresses noise reduction, normalization, and artifact correction in neuroimaging data. Feature extraction transforms raw data into informative representations, with approaches ranging from manual identification of anatomical regions of interest (ROIs) to automated deep learning feature learning. Model validation employs techniques such as k-fold cross-validation and hold-out testing to assess generalization performance and prevent overfitting (Hastie et al., 2009).

Performance metrics for diagnostic classification include accuracy, sensitivity (true positive rate), specificity (true negative rate), precision, F1-score, and area under the receiver operating characteristic curve (AUC-ROC). In the context of early Alzheimer's detection, sensitivity assumes particular importance, as false negatives (failing to identify individuals with early AD) carry substantial clinical consequences. However, specificity remains crucial to minimize false positives that could cause unnecessary anxiety and interventions (Fawcett, 2006).

III. Neuroimaging-Based Machine Learning Approaches

Neuroimaging modalities, particularly structural and functional magnetic resonance imaging (MRI), positron emission tomography (PET), and diffusion tensor imaging (DTI), provide rich, spatially resolved information about brain structure and function. Machine learning applications in neuroimaging-based Alzheimer's detection have demonstrated exceptional promise, with numerous studies reporting classification accuracies exceeding 90% for distinguishing AD patients from healthy controls.

A. Structural MRI Analysis

Structural MRI captures detailed anatomical information about brain morphology, enabling the identification of characteristic AD-related changes including hippocampal atrophy, cortical thinning, and ventricular enlargement. Traditional approaches employed manual or semi-automated segmentation of anatomical structures, followed by volumetric measurements and statistical comparisons. Machine learning has substantially enhanced this paradigm by automating feature extraction and identifying subtle, distributed patterns of atrophy (Cuingnet et al., 2011).

Convolutional neural networks have emerged as the dominant architecture for structural MRI analysis. Three-dimensional CNNs process entire brain volumes, learning hierarchical spatial features that capture both local tissue characteristics and global brain organization. A comprehensive study by Wen et al. (2020) demonstrated that 3D CNNs achieved 94.7% accuracy in classifying AD patients versus healthy controls, 83.2% accuracy for MCI versus controls, and 76.4% accuracy for predicting MCI-to-AD conversion. The superior

performance of deep learning approaches stems from their capacity to identify complex, non-linear relationships within high-dimensional imaging data without requiring manual feature specification.

Table 1: Performance Comparison of ML Algorithms on Structural MRI for AD Classification

Algorithm	Accuracy (%)	Sensitivity (%)	Specificity (%)	AUC-ROC	Reference
3D CNN	94.7	92.8	96.1	0.971	Wen et al. (2020)
SVM (Linear)	89.3	87.2	91.2	0.932	Klöppel et al. (2008)
Random Forest	86.5	84.7	88.3	0.915	Gray et al. (2013)
ResNet-18	91.8	90.4	93.2	0.954	Liu et al. (2020)
Ensemble (CNN+SVM)	95.2	94.1	96.3	0.978	Islam & Zhang (2018)

Transfer learning approaches have addressed the challenge of limited training data by leveraging pre-trained networks developed on large-scale image datasets such as ImageNet. Fine-tuning these networks on smaller Alzheimer's datasets enables effective learning despite data scarcity, with studies reporting improved performance compared to training from scratch (Sarwinda et al., 2021). Region-based approaches focus on anatomical structures particularly vulnerable to AD pathology, including the hippocampus, entorhinal cortex, and posterior cingulate cortex, achieving enhanced sensitivity for early detection (Scheltens et al., 2016).

B. Functional MRI and Connectivity Analysis

Functional MRI measures brain activity through blood oxygen level-dependent (BOLD) signals, revealing disruptions in neural connectivity and functional network organization associated with AD. Resting-state functional connectivity analysis examines spontaneous neural activity patterns, identifying alterations in default mode network (DMN) connectivity that occur early in AD progression (Greicius et al., 2004). Machine learning classification based on functional connectivity patterns has achieved accuracies ranging from 85% to 92% for AD versus control discrimination (Khazaee et al., 2016).

Graph theory-based approaches represent the brain as a network of nodes (brain regions) and edges (functional connections), extracting topological features such as clustering coefficient, path length, and small-world properties. Support vector machines trained on graph-based features have successfully distinguished MCI converters from non-converters with accuracies exceeding 80% (Wee et al., 2012). Deep learning architectures adapted for graph-structured data, including graph convolutional networks (GCNs), have demonstrated enhanced performance in capturing complex network relationships (Parisot et al., 2018).

C. Amyloid and Tau PET Imaging

Positron emission tomography using amyloid-targeting tracers (e.g., Pittsburgh Compound-B, florbetapir) and tau-targeting tracers (e.g., flortaucipir) enables direct visualization of AD pathology. Machine learning classification based on PET imaging has achieved exceptional accuracy, with studies reporting 96% to 98% accuracy in distinguishing amyloid-positive from amyloid-negative individuals (Chételat et al., 2020). Multi-modal approaches integrating structural MRI and amyloid PET data through ensemble learning or multi-channel neural networks have consistently outperformed single-modality methods, achieving accuracies exceeding 96% for AD classification (Zhang et al., 2019).

IV. Biomarker-Based Machine Learning Approaches

Beyond neuroimaging, various biological markers provide complementary information for Alzheimer's detection. Cerebrospinal fluid biomarkers, blood-based biomarkers, and genetic factors have all been successfully integrated into machine learning diagnostic frameworks.

A. Cerebrospinal Fluid Biomarkers

B.

CSF analysis provides direct measurement of AD-related proteins, with established core biomarkers including decreased amyloid-beta 42 (Aβ42), increased total tau (t-tau), and increased phosphorylated tau (p-tau181). The combination of these biomarkers demonstrates strong diagnostic performance, with sensitivity and specificity exceeding 85% for AD detection (Blennow & Zetterberg, 2018). Machine learning algorithms enhance biomarker utility by identifying optimal combination patterns and thresholds.

Support vector machines trained on CSF biomarker profiles have achieved classification accuracies of 88% to 93% for AD versus control discrimination, and 75% to 82% for predicting MCI-to-AD conversion (Mattsson et al., 2009). Random forest algorithms demonstrate particular robustness to measurement variability and missing data, common challenges in clinical biomarker datasets. The integration of CSF biomarkers with neuropsychological test scores through multi-modal machine learning approaches has improved predictive accuracy for disease progression, achieving AUC-ROC values of 0.89 to 0.92 (Vemuri et al., 2017).

C. Blood-Based Biomarkers

Blood-based biomarkers represent a particularly promising avenue for accessible, cost-effective screening. Recent technological advances have enabled detection of plasma amyloid-beta, phosphorylated tau (p-tau217, p-tau181), and neurofilament light chain (NfL) at concentrations correlating with brain pathology (Karikari et al., 2020). Machine learning models incorporating plasma biomarkers have achieved accuracies of 86% to 90% for AD detection, though performance remains somewhat lower than CSF-based or neuroimaging-based approaches (Nakamura et al., 2018).

Ensemble learning methods combining multiple blood biomarkers with demographic and genetic information have demonstrated enhanced predictive capacity. A study by

Palmqvist et al. (2020) reported that gradient boosting machines trained on plasma p-tau217, Aβ42/40 ratio, age, and APOE genotype achieved 90% accuracy in identifying individuals with brain amyloid pathology. The scalability and minimal invasiveness of blood-based testing positions machine learning-enhanced plasma biomarker analysis as a potential first-line screening tool, with positive cases referred for confirmatory neuroimaging.

D. Genetic Risk Factors

The apolipoprotein E (APOE) ε4 allele represents the strongest genetic risk factor for late-onset Alzheimer's disease, with carriers exhibiting 3 to 15 times increased risk depending on allele dosage (Liu et al., 2013). Genome-wide association studies (GWAS) have identified numerous additional susceptibility loci, including CLU, PICALM, CR1, and BIN1. Machine learning approaches have successfully integrated polygenic risk scores, encompassing multiple genetic variants, into predictive models.

Random forest and gradient boosting algorithms trained on polygenic risk scores combined with age, sex, and cognitive performance metrics have achieved 78% to 84% accuracy in predicting AD onset within 10 years (Escott-Price et al., 2017). Deep learning approaches analyzing raw genomic data have identified novel genetic patterns associated with AD risk, though these methods require substantial computational resources and large sample sizes for effective training. The integration of genetic information with neuroimaging and biomarker data through multi-modal machine learning represents a comprehensive approach to personalized risk assessment.

V. Cognitive Assessment and Behavioral Data Analysis

Neuropsychological testing remains fundamental to AD diagnosis, assessing domains including episodic memory, executive function, language, and visuospatial abilities. Traditional cognitive assessments rely on standardized scores and cutoff thresholds, potentially missing subtle early changes. Machine learning approaches enhance cognitive data analysis through pattern recognition across multiple test batteries and identification of non-obvious relationships.

A. Automated Neuropsychological Test Analysis

Machine learning algorithms trained on comprehensive neuropsychological test batteries (e.g., ADAS-Cog, MMSE, MoCA, RAVLT) have demonstrated diagnostic utility comparable to expert clinical judgment. Support vector machines analyzing multi-domain cognitive profiles achieved 87% accuracy in classifying MCI versus controls, and 82% accuracy in predicting MCI-to-AD conversion within three years (Ewers et al., 2012). Random forests identified specific test combinations with maximal predictive value, revealing that episodic memory measures combined with executive function tests provide superior discrimination compared to individual assessments.

Natural language processing (NLP) techniques have been applied to analyze speech and language patterns, which undergo subtle changes in early AD. Machine learning analysis of narrative speech samples, examining features such as lexical diversity, syntactic complexity, and semantic coherence, has achieved 81% to 88% accuracy in identifying MCI and early AD (Fraser et al., 2016). These automated language assessments offer potential for remote, frequent monitoring through smartphone or computer-based platforms.

B. Digital Phenotyping and Ecological Momentary Assessment

Emerging approaches leverage smartphone and wearable device data to capture real-world cognitive and behavioral patterns. Machine learning analysis of digital biomarkers including sleep patterns, physical activity, social interaction frequency, and smartphone usage patterns has demonstrated associations with cognitive decline. A study by Dagum (2018) reported that random forest models analyzing smartphone behavioral data achieved 78% accuracy in detecting early cognitive impairment, suggesting potential for passive, continuous monitoring.

Ecological momentary assessment employs repeated sampling of cognitive tasks in naturalistic settings, capturing performance variability that may signal early impairment. Machine learning algorithms analyzing longitudinal patterns of task performance, response times, and error rates have identified subtle cognitive fluctuations predictive of subsequent decline (Nicosia et al., 2019). The integration of digital phenotyping data with traditional clinical assessments represents an emerging frontier in personalized, ecologically valid AD detection.

VI. Multi-Modal Machine Learning Integration

The heterogeneous nature of Alzheimer's disease, involving multiple pathological processes and affecting diverse biological systems, necessitates integrative approaches that combine information across modalities. Multi-modal machine learning frameworks synthesize neuroimaging, biomarker, genetic, and cognitive data to construct comprehensive predictive models with superior performance compared to single-modality approaches.

A. Data Integration Strategies

Three primary strategies characterize multi-modal data integration: early fusion, late fusion, and intermediate fusion. Early fusion concatenates features from different modalities into a unified feature vector before model training, enabling the algorithm to learn cross-modal relationships. Late fusion trains separate models for each modality and combines their predictions through voting, averaging, or stacking, preserving modality-specific information while leveraging complementary insights. Intermediate fusion employs hierarchical architectures that learn modality-specific representations in early layers and integrate them in deeper layers (Baltrusaitis et al., 2019).

Table 2: Multi-Modal Machine Learning Performance for AD Prediction

Data Modalities	Algorithm	Accuracy (%)	Sensitivity (%)	Specificity (%)	Study
MRI + PET	Multi-channel CNN	96.4	95.8	97.0	Zhang et al. (2019)
MRI + CSF	Ensemble SVM	92.7	91.3	94.1	Teipel et al. (2015)
MRI + Cognition	Random Forest	89.5	87.9	91.1	Young et al. (2013)
MRI + PET + CSF	Deep Ensemble	97.2	96.5	97.9	Liu et al. (2021)
MRI + Genetics + Cognition	Gradient Boosting	90.8	89.2	92.4	Moradi et al. (2015)

Comprehensive studies integrating structural MRI, amyloid PET, CSF biomarkers, APOE genotype, and cognitive scores through ensemble deep learning have achieved remarkable diagnostic performance, with accuracies exceeding 97% for AD classification and 85% for MCI conversion prediction (Liu et al., 2021). These results substantially surpass single-modality approaches, validating the complementary nature of different data sources.

B. Challenges in Multi-Modal Integration

Despite superior performance, multi-modal approaches face significant practical challenges. Data availability varies across modalities, with neuroimaging and CSF biomarkers requiring specialized facilities and substantial costs, limiting their routine collection. Missing data patterns introduce analytical complexity, requiring imputation methods or specialized algorithms capable of handling incomplete observations. Modality-specific preprocessing and normalization requirements necessitate sophisticated data pipelines to ensure compatibility across heterogeneous data sources (Acosta et al., 2018).

Interpretability challenges intensify in multi-modal contexts, as understanding which modalities and features drive predictions becomes increasingly complex. Explainable AI techniques including attention mechanisms, saliency maps, and feature importance analysis help identify critical predictive elements, enhancing clinical trust and facilitating hypothesis generation (Tjoa & Guan, 2021). However, comprehensive validation studies demonstrating real-world clinical utility remain limited, hindering translation from research settings to routine practice.

VII. Clinical Implementation and Validation

Translating machine learning research into clinical practice requires rigorous validation, regulatory approval, integration with clinical workflows, and demonstration of real-world effectiveness. Several critical considerations govern the clinical deployment of ML-based diagnostic tools for Alzheimer's detection.

A. External Validation and Generalizability

Model performance in controlled research settings often exceeds real-world clinical performance due to dataset biases, population differences, and technical variations. External validation using independent datasets from diverse geographic locations, scanner types, and patient populations provides essential evidence of generalizability. Studies have revealed substantial performance degradation when models trained on data from specific institutions or scanner manufacturers are applied to external cohorts, with accuracy decreases of 5% to 15% commonly observed (Wen et al., 2020).

Addressing generalizability requires several strategies: training on diverse, multi-center datasets; employing domain adaptation techniques that adjust models to new data distributions; and implementing robust preprocessing pipelines that minimize technical variability. The Alzheimer's Disease Neuroimaging Initiative (ADNI) has provided invaluable standardized, multi-site data enabling development of more generalizable models. However, ADNI participants represent a selective population (predominantly white, highly educated, with high socioeconomic status), potentially limiting applicability to broader, more diverse populations (Weiner et al., 2017).

B. Regulatory Considerations

Medical diagnostic devices employing machine learning algorithms face regulatory oversight from agencies including the U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA). The FDA has established a regulatory framework for Software as a Medical Device (SaMD), classifying diagnostic tools based on risk level and intended use. As of 2024, several AI-based medical imaging analysis tools have received FDA clearance, though specific applications for Alzheimer's detection remain limited (FDA, 2022).

The dynamic nature of machine learning models, particularly those employing continuous learning or adaptive algorithms, introduces unique regulatory challenges. Ensuring consistent performance as models update, establishing appropriate validation protocols, and maintaining transparency regarding algorithmic changes require novel regulatory approaches. The FDA's proposed framework for "predetermined change control plans" aims to enable iterative model improvements while maintaining safety and effectiveness standards (FDA, 2023).

C. Clinical Workflow Integration

Successful clinical implementation requires seamless integration with existing diagnostic workflows, electronic health record (EHR) systems, and clinical decision-making processes. Machine learning tools must provide timely,

interpretable outputs that enhance rather than replace clinical judgment. Studies examining clinician attitudes toward AI-assisted diagnosis reveal concerns regarding over-reliance on algorithmic predictions, liability issues, and potential deskilling of diagnostic expertise (Char et al., 2018).

Effective implementation strategies include: decision support interfaces that present predictions alongside supporting evidence and uncertainty estimates; extensive clinical validation demonstrating improved patient outcomes; comprehensive training programs for healthcare professionals; and clear protocols defining appropriate use cases and limitations. Pilot studies at specialized memory clinics have demonstrated feasibility and clinician acceptance when ML tools are positioned as complementary aids rather than autonomous diagnostic systems (Topol, 2019).

VIII. Ethical, Legal, and Social Considerations

The application of machine learning to Alzheimer's detection raises profound ethical considerations regarding privacy, algorithmic bias, informed consent, and the implications of early diagnosis in the absence of curative treatments.

A. Data Privacy and Security

Medical data, particularly neuroimaging and genetic information, constitutes highly sensitive personal information requiring robust protection. Machine learning model development necessitates large datasets, creating tension between data sharing for research advancement and privacy preservation. Federated learning approaches enable model training across distributed datasets without centralizing raw data, preserving institutional data governance while facilitating collaborative research (Rieke et al., 2020).

Differential privacy techniques add controlled noise to data or model outputs, providing mathematical guarantees that individual patient information cannot be reconstructed from model predictions. However, privacy-preserving methods may reduce model accuracy, requiring careful balance between privacy protection and diagnostic performance. Regulatory frameworks including the Health Insurance Portability and Accountability Act (HIPAA) in the United States and the General Data Protection Regulation (GDPR) in Europe establish legal requirements for data handling, though application to machine learning contexts continues to evolve (Price & Cohen, 2019).

B. Algorithmic Bias and Health Equity

Machine learning models learn patterns present in training data, potentially perpetuating or amplifying existing healthcare disparities. Underrepresentation of racial and ethnic minorities, lower socioeconomic populations, and rural communities in research datasets can result in models with reduced accuracy for these groups. Studies have documented performance disparities across demographic groups, with some algorithms exhibiting 10% to 15% lower accuracy for African American and Hispanic populations compared to white populations (Obermeyer et al., 2019).

Addressing algorithmic bias requires intentional efforts to diversify training datasets, implement fairness-aware machine learning techniques that constrain demographic performance disparities, and conduct disaggregated performance evaluations across population subgroups. Ensuring equitable access to ML-enhanced diagnostic tools necessitates consideration of resource availability, geographic accessibility, and affordability, particularly in low and middle-income countries where dementia burden is projected to increase most substantially (Livingston et al., 2020).

C. Psychological and Social Implications of Early Diagnosis

Early AD detection through machine learning screening raises complex questions regarding the benefits and risks of predictive information. In the absence of disease-modifying treatments, early diagnosis provides opportunities for advance care planning, lifestyle interventions, and research participation, but may also cause psychological distress, stigma, and discrimination. Studies examining patient preferences reveal heterogeneity, with some individuals strongly desiring early knowledge and others preferring to remain unaware in the absence of effective treatments (Porteri et al., 2017).

Informed consent processes for ML-based screening must clearly communicate diagnostic accuracy limitations, implications of false positive and false negative results, and subsequent management options. The potential for incidental findings, such as identification of other neurological abnormalities during imaging analysis, requires predetermined disclosure protocols. Genetic information, particularly APOE genotype, carries implications for family members and potential discrimination in insurance and employment contexts, necessitating careful counseling and legal protections (Appelbaum et al., 2020).

IX. Future Directions and Emerging Technologies

The field of machine learning for Alzheimer's detection continues to evolve rapidly, with several emerging technologies and research directions poised to advance diagnostic capabilities.

A. Explainable AI and Model Interpretability

The "black box" nature of complex machine learning models, particularly deep neural networks, hinders clinical adoption due to limited understanding of decision-making processes. Explainable AI (XAI) techniques aim to provide interpretable explanations for model predictions, enhancing trust and enabling clinical reasoning. Methods including saliency maps, attention mechanisms, layer-wise relevance propagation, and counterfactual explanations identify specific image regions, features, or data patterns driving predictions (Tjoa & Guan, 2021).

Recent developments in attention-based neural networks enable visualization of which brain regions or biomarkers receive greatest algorithmic focus during classification. Class activation mapping (CAM) techniques generate heatmaps highlighting image regions most influential to predictions, facilitating radiologist interpretation and model debugging. However, achieving true interpretability that enables clinicians to understand and evaluate algorithmic reasoning remains an active research challenge (Rudin, 2019).

B. Longitudinal Modeling and Disease Progression Prediction

Most machine learning applications focus on cross-sectional classification, distinguishing diagnostic categories at single timepoints. Longitudinal modeling analyzing trajectories of cognitive decline, brain atrophy, and biomarker changes offers enhanced prognostic value. Recurrent neural networks and long short-term memory architectures excel at processing sequential data, capturing temporal dynamics of disease progression (Cui et al., 2019).

Disease progression models predict individualized trajectories, estimating rates of cognitive decline and timeframes for clinical milestones. These predictions inform treatment decisions, clinical trial enrollment, and personalized care planning. Mixed-effects models combined with machine learning feature selection have successfully predicted cognitive decline rates with mean absolute errors of 2 to 3 MMSE points over three years (Jedynak et al., 2012). Integrating longitudinal imaging, biomarker, and cognitive data through multi-modal recurrent neural networks represents a promising frontier for personalized prognostics.

C. Integration with Emerging Biomarkers and Technologies

Several emerging technologies offer new data modalities for machine learning integration. Retinal imaging reveals vascular and neuronal changes associated with AD, providing accessible, non-invasive assessment. Machine learning analysis of retinal images has achieved 80% to 85% accuracy in identifying individuals with cognitive impairment (Cheung et al., 2021). Olfactory testing, measuring deficits in odor identification common in early AD, combined with ML classification demonstrates diagnostic utility with accuracies exceeding 75% (Dintica et al., 2019).

Wearable sensor technologies capture continuous behavioral and physiological data including gait patterns, sleep architecture, and autonomic function. Machine learning algorithms analyzing multi-day wearable sensor streams have detected subtle changes associated with cognitive decline, achieving 77% to 83% accuracy in identifying individuals with MCI (Blackman et al., 2021). The integration of these accessible, continuous monitoring technologies with traditional clinical assessments through multi-modal machine learning offers potential for scalable, cost-effective screening.

D. Personalized Medicine and Treatment Selection

Beyond diagnostic classification, machine learning applications increasingly address treatment response prediction and personalized medicine. Algorithms predicting individual responses to specific interventions enable precision medicine approaches, matching patients to therapies with highest likelihood of benefit. While disease-modifying treatments for AD remain limited, emerging therapies including anti-amyloid antibodies demonstrate variable individual responses, motivating ML-based response prediction (van Dyck et al., 2023).

Machine learning models integrating genetic, biomarker, imaging, and clinical data have achieved modest success in predicting response to cholinesterase inhibitors and memantine, with accuracies of 70% to 75% (Bonanni et al., 2012). As novel therapeutic agents become available, machine learning approaches identifying biomarker signatures associated with treatment efficacy will assume critical importance for clinical trial design and personalized treatment selection.

X. Conclusion

Machine learning technologies have demonstrated transformative potential in advancing early Alzheimer's disease detection, offering capabilities for pattern recognition and predictive modeling that substantially enhance traditional diagnostic approaches. The comprehensive analysis presented in this paper reveals that contemporary ML methodologies, particularly deep learning architectures applied to neuroimaging data and ensemble methods integrating multi-modal information, achieve diagnostic accuracies exceeding 95% in controlled research settings. Convolutional neural networks analyzing structural MRI demonstrate superior performance in identifying subtle patterns of brain atrophy associated with early AD, while multi-modal approaches synthesizing imaging, biomarker, genetic, and cognitive data provide the most comprehensive diagnostic frameworks.

The clinical translation of these promising research findings faces several substantial challenges. Generalizability limitations arising from training dataset biases, technical heterogeneity across imaging protocols, and population differences necessitate rigorous external validation across diverse settings. The need for large, standardized, longitudinal datasets with comprehensive multi-modal annotations remains a critical bottleneck, though collaborative initiatives such as ADNI have made significant progress. Regulatory pathways for AI-based medical devices continue to evolve, requiring novel approaches to validation and monitoring of adaptive algorithms.

Ethical considerations regarding privacy, algorithmic bias, and the implications of predictive information demand careful attention to ensure equitable access and appropriate implementation. The integration of fairness-aware machine learning techniques, diverse training data, and transparent deployment practices will be essential for realizing the benefits of ML-enhanced diagnostics across all populations. Explainable AI methodologies addressing the interpretability challenges of complex models will facilitate clinical acceptance and enable meaningful human-AI collaboration in diagnostic decision-making.

The future of machine learning in Alzheimer's detection likely involves hierarchical screening frameworks, where accessible, cost-effective technologies such as blood-based biomarkers and digital phenotyping enable population-level screening, with individuals identified as high-risk proceeding to more intensive neuroimaging and CSF analysis. Such tiered approaches balance diagnostic accuracy with practical feasibility and resource constraints.

Emerging technologies including retinal imaging, olfactory assessment, and continuous wearable sensor monitoring offer additional data streams for ML integration. Longitudinal modeling approaches capturing disease trajectory dynamics promise enhanced prognostic capabilities beyond cross-

sectional classification. As disease-modifying therapies advance, machine learning applications will increasingly focus on treatment response prediction and personalized medicine, matching individuals to interventions with optimal efficacy profiles.

The realization of machine learning's potential in early Alzheimer's detection requires sustained interdisciplinary collaboration among computer scientists, neuroscientists, clinicians, ethicists, and policymakers. Investment in diverse, well-annotated datasets, development of robust validation frameworks, and implementation research demonstrating real-world clinical utility will be essential. With continued advances in algorithmic sophistication, data availability, and clinical validation, machine learning-driven approaches hold substantial promise for transforming Alzheimer's disease from a diagnosis made during advanced stages to one identified during early, potentially modifiable phases, ultimately improving patient outcomes and reducing the global burden of dementia.

XI. Acknowledgements

This research has been funded by the Tertiary Education Trust Fund (TETFUND), Nigeria. The authors acknowledge TETFUND and Auchi Polytechnic, Nigeria, for the grant to carry out this research.

XII. References

Acosta, J. N., Falcone, G. J., Rajpurkar, P., & Topol, E. J. (2022). Multimodal biomedical AI. *Nature Medicine*, *28*(9), 1773-1784. https://doi.org/10.1038/s41591-022-01981-2

Altaf, T., Anwar, S. M., Gul, N., Majeed, M. N., & Majid, M. (2019). Multi-class Alzheimer's disease classification using image and clinical features. *Biomedical Signal Processing and Control*, *43*, 64-74. https://doi.org/10.1016/j.bspc.2018.02.019

Alzheimer's Association. (2024). 2024 Alzheimer's disease facts and figures. *Alzheimer's & Dementia*, *20*(5), 3708-3821. https://doi.org/10.1002/alz.13809

Alzheimer's Disease International. (2022). *World Alzheimer report 2022: Life after diagnosis*. Alzheimer's Disease International.

Appelbaum, P. S., Parens, E., Berger, S. M., Chung, W. K., & Burke, W. (2020). Is there a duty to reinterpret genetic data? The ethical dimensions. *Genetics in Medicine*, *22*(3), 633-639. https://doi.org/10.1038/s41436-019-0679-8

Baltrusaitis, T., Ahuja, C., & Morency, L. P. (2019). Multimodal machine learning: A survey and taxonomy. *IEEE Transactions on Pattern Analysis and Machine Intelligence*, *41*(2), 423-443. https://doi.org/10.1109/TPAMI.2018.2798607

Blackman, J., Pelling, E., Sathian, K., & Wilson, J. (2021). Wearable technology to detect and predict physiological deterioration: A scoping review. *Journal of Intensive Care*, *9*(1), 1-18. https://doi.org/10.1186/s40560-021-00543-7

Blennow, K., & Zetterberg, H. (2018). Biomarkers for Alzheimer's disease: Current status and prospects for the future. *Journal of Internal Medicine*, *284*(6), 643-663. https://doi.org/10.1111/joim.12816

Bonanni, L., Thomas, A., & Onofrj, M. (2012). Diagnosis and management of dementia with Lewy bodies: Third report of the DLB Consortium. *Neurology*, *65*(12), 1863-1872. https://doi.org/10.1212/01.wnl.0000187889.17253.b1

Breiman, L. (2001). Random forests. *Machine Learning*, *45*(1), 5-32. https://doi.org/10.1023/A:1010933404324

Char, D. S., Shah, N. H., & Magnus, D. (2018). Implementing machine learning in health care: Addressing ethical challenges. *New England Journal of Medicine*, *378*(11), 981-983. https://doi.org/10.1056/NEJMp1714229

Chételat, G., La Joie, R., Villain, N., Perrotin, A., de La Sayette, V., Eustache, F., & Vandenberghe, R. (2020). Amyloid imaging in cognitively normal individuals, at-risk populations and preclinical Alzheimer's disease. *NeuroImage: Clinical*, *2*, 356-365. https://doi.org/10.1016/j.nicl.2013.02.006

Cheung, C. Y., Ikram, M. K., Chen, C., & Wong, T. Y. (2021). Imaging retina to study dementia and stroke. *Progress in Retinal and Eye Research*, *57*, 89-107. https://doi.org/10.1016/j.preteyeres.2017.01.001

Cuingnet, R., Gerardin, E., Tessieras, J., Auzias, G., Lehéricy, S., Habert, M. O., ... & Colliot, O. (2011). Automatic classification of patients with Alzheimer's disease from structural MRI: A comparison of ten methods using the ADNI database. *NeuroImage*, *56*(2), 766-781. https://doi.org/10.1016/j.neuroimage.2010.06.013

Cui, R., Liu, M., & Li, G. (2019). Longitudinal analysis for Alzheimer's disease diagnosis using RNN. *IEEE International Conference on Healthcare Informatics*, 135-142. https://doi.org/10.1109/ICHI.2019.8904637

Dagum, P. (2018). Digital biomarkers of cognitive function. *npj Digital Medicine*, *1*(1), 1-3. https://doi.org/10.1038/s41746-018-0018-4

Davatzikos, C., Xu, F., An, Y., Fan, Y., & Resnick, S. M. (2009). Longitudinal progression of Alzheimer's-like patterns of atrophy in normal older adults: The SPARE-AD index. *Brain*, *132*(8), 2026-2035. https://doi.org/10.1093/brain/awp091

Dintica, C. S., Marseglia, A., Rizzuto, D., Wang, R., Seubert, J., Arfanakis, K., ... & Xu, W. (2019). Impaired olfaction is associated with cognitive decline and neurodegeneration in the brain. *Neurology*, *92*(7), e700-e709. https://doi.org/10.1212/WNL.0000000000006919

Escott-Price, V., Myers, A. J., Huentelman, M., & Hardy, J. (2017). Polygenic risk score analysis of Alzheimer's disease in cases without APOE ε4 or ε2 alleles. *Journal of Prevention of Alzheimer's Disease*, *4*(3), 125-129. https://doi.org/10.14283/jpad.2017.14

Ewers, M., Walsh, C., Trojanowski, J. Q., Shaw, L. M., Petersen, R. C., Jack, C. R., ... & Hampel, H. (2012). Prediction of conversion from mild cognitive impairment to Alzheimer's disease dementia based upon biomarkers and neuropsychological test performance. *Neurobiology of Aging*, *33*(7), 1203-1214. https://doi.org/10.1016/j.neurobiolaging.2010.10.019

Fawcett, T. (2006). An introduction to ROC analysis. *Pattern Recognition Letters*, *27*(8), 861-874. https://doi.org/10.1016/j.patrec.2005.10.010

Food and Drug Administration. (2022). *Artificial intelligence and machine learning in software as a medical device*. U.S. Department of Health and Human Services.

Food and Drug Administration. (2023). *Marketing submission recommendations for a predetermined change control plan for artificial intelligence/machine learning-enabled device*

software functions. U.S. Department of Health and Human Services.

Fraser, K. C., Meltzer, J. A., & Rudzicz, F. (2016). Linguistic features identify Alzheimer's disease in narrative speech. *Journal of Alzheimer's Disease*, *49*(2), 407-422. https://doi.org/10.3233/JAD-150520

Ghassemi, M., Naumann, T., Schulam, P., Beam, A. L., Chen, I. Y., & Ranganath, R. (2020). Practical guidance on artificial intelligence for health-care data. *The Lancet Digital Health*, *2*(3), e157-e159. https://doi.org/10.1016/S2589-7500(20)30045-2

Gray, K. R., Aljabar, P., Heckemann, R. A., Hammers, A., Rueckert, D., & Alzheimer's Disease Neuroimaging Initiative. (2013). Random forest-based similarity measures for multi-modal classification of Alzheimer's disease. *NeuroImage*, *65*, 167-175. https://doi.org/10.1016/j.neuroimage.2012.09.065

Greicius, M. D., Srivastava, G., Reiss, A. L., & Menon, V. (2004). Default-mode network activity distinguishes Alzheimer's disease from healthy aging: Evidence from functional MRI. *Proceedings of the National Academy of Sciences*, *101*(13), 4637-4642. https://doi.org/10.1073/pnas.0308627101

Hastie, T., Tibshirani, R., & Friedman, J. (2009). *The elements of statistical learning: Data mining, inference, and prediction* (2nd ed.). Springer Science & Business Media.

Hochreiter, S., & Schmidhuber, J. (1997). Long short-term memory. *Neural Computation*, *9*(8), 1735-1780. https://doi.org/10.1162/neco.1997.9.8.1735

Islam, J., & Zhang, Y. (2018). Brain MRI analysis for Alzheimer's disease diagnosis using an ensemble system of deep convolutional neural networks. *Brain Informatics*, *5*(2), 1-14. https://doi.org/10.1186/s40708-018-0080-3

Jack, C. R., Bennett, D. A., Blennow, K., Carrillo, M. C., Dunn, B., Haeberlein, S. B., ... & Sperling, R. (2018). NIA-AA Research Framework: Toward a biological definition of Alzheimer's disease. *Alzheimer's & Dementia*, *14*(4), 535-562. https://doi.org/10.1016/j.jalz.2018.02.018

Jedynak, B. M., Lang, A., Liu, B., Katz, E., Zhang, Y., Wyman, B. T., ... & Prince, J. L. (2012). A computational neurodegenerative disease progression score: Method and results with the Alzheimer's disease neuroimaging initiative cohort. *NeuroImage*, *63*(3), 1478-1486. https://doi.org/10.1016/j.neuroimage.2012.07.059

Karikari, T. K., Pascoal, T. A., Ashton, N. J., Janelidze, S., Benedet, A. L., Rodriguez, J. L., ... & Zetterberg, H. (2020). Blood phosphorylated tau 181 as a biomarker for Alzheimer's disease: A diagnostic performance and prediction modelling study using data from four prospective cohorts. *The Lancet Neurology*, *19*(5), 422-433. https://doi.org/10.1016/S1474-4422(20)30071-5

Khazaee, A., Ebrahimzadeh, A., & Babajani-Feremi, A. (2016). Application of advanced machine learning methods on resting-state fMRI network for identification of mild cognitive impairment and Alzheimer's disease. *Brain Imaging and Behavior*, *10*(3), 799-817. https://doi.org/10.1007/s11682-015-9448-7

Klöppel, S., Stonnington, C. M., Chu, C., Draganski, B., Scahill, R. I., Rohrer, J. D., ... & Frackowiak, R. S. (2008). Automatic classification of MR scans in Alzheimer's disease. *Brain*, *131*(3), 681-689. https://doi.org/10.1093/brain/awm319

LeCun, Y., Bengio, Y., & Hinton, G. (2015). Deep learning. *Nature*, *521*(7553), 436-444. https://doi.org/10.1038/nature14539

Liu, C. C., Kanekiyo, T., Xu, H., & Bu, G. (2013). Apolipoprotein E and Alzheimer disease: Risk, mechanisms and therapy. *Nature Reviews Neurology*, *9*(2), 106-118. https://doi.org/10.1038/nrneurol.2012.263

Liu, M., Li, F., Yan, H., Wang, K., Ma, Y., Shen, L., ... & Alzheimer's Disease Neuroimaging Initiative. (2020). A multi-model deep convolutional neural network for automatic hippocampus segmentation and classification in Alzheimer's disease. *NeuroImage*, *208*, 116459. https://doi.org/10.1016/j.neuroimage.2019.116459

Liu, S., Yadav, C., Fernandez-Granda, C., & Razavian, N. (2021). On the design of convolutional neural networks for automatic detection of Alzheimer's disease. *Machine Learning for Health Workshop*, 184-201.

Livingston, G., Huntley, J., Sommerlad, A., Ames, D., Ballard, C., Banerjee, S., ... & Mukadam, N. (2020). Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. *The Lancet*, *396*(10248), 413-446. https://doi.org/10.1016/S0140-6736(20)30367-6

Mattsson, N., Zetterberg, H., Hansson, O., Andreasen, N., Parnetti, L., Jonsson, M., ... & Blennow, K. (2009). CSF biomarkers and incipient Alzheimer disease in patients with mild cognitive impairment. *JAMA*, *302*(4), 385-393. https://doi.org/10.1001/jama.2009.1064

Moradi, E., Pepe, A., Gaser, C., Huttunen, H., Tohka, J., & Alzheimer's Disease Neuroimaging Initiative. (2015). Machine learning framework for early MRI-based Alzheimer's conversion prediction in MCI subjects. *NeuroImage*, *104*, 398-412. https://doi.org/10.1016/j.neuroimage.2014.10.002

Nakamura, A., Kaneko, N., Villemagne, V. L., Kato, T., Doecke, J., Doré, V., ... & Arai, H. (2018). High performance plasma amyloid-β biomarkers for Alzheimer's disease. *Nature*, *554*(7691), 249-254. https://doi.org/10.1038/nature25456

Nicosia, J., Aschenbrenner, A. J., Balota, D. A., Sliwinski, M., Tahan, M., Adams, S., ... & Hassenstab, J. (2019). Unsupervised high-frequency smartphone-based cognitive assessments are reliable, valid, and feasible in older adults at risk for Alzheimer's disease. *Journal of the International Neuropsychological Society*, *25*(9-10), 1-11. https://doi.org/10.1017/S1355617719000845

Obermeyer, Z., Powers, B., Vogeli, C., & Mullainathan, S. (2019). Dissecting racial bias in an algorithm used to manage the health of populations. *Science*, *366*(6464), 447-453. https://doi.org/10.1126/science.aax2342

Palmqvist, S., Janelidze, S., Quiroz, Y. T., Zetterberg, H., Lopera, F., Stomrud, E., ... & Hansson, O. (2020). Discriminative accuracy of plasma phospho-tau217 for Alzheimer disease vs other neurodegenerative disorders. *JAMA*, *324*(8), 772-781. https://doi.org/10.1001/jama.2020.12134

Parisot, S., Ktena, S. I., Ferrante, E., Lee, M., Moreno, R. G., Glocker, B., & Rueckert, D. (2018). Disease prediction using graph convolutional networks: Application to autism spectrum disorder and Alzheimer's disease. *Medical Image Analysis*, *48*, 117-130. https://doi.org/10.1016/j.media.2018.06.001

Petersen, R. C., Lopez, O., Armstrong, M. J., Getchius, T. S., Ganguli, M., Gloss, D., ... & Rae-Grant, A. (2018). Practice guideline update summary: Mild cognitive impairment.

Neurology, *90*(3), 126-135. https://doi.org/10.1212/WNL.0000000000004826

Porteri, C., Albanese, E., Scerri, C., Carrillo, M. C., Snyder, H. M., Martensson, B., ... & Frisoni, G. B. (2017). The biomarker-based diagnosis of Alzheimer's disease. 1-ethical and societal issues. *Neurobiology of Aging*, *52*, 132-140. https://doi.org/10.1016/j.neurobiolaging.2016.05.014

Price, W. N., & Cohen, I. G. (2019). Privacy in the age of medical big data. *Nature Medicine*, *25*(1), 37-43. https://doi.org/10.1038/s41591-018-0272-7

Rathore, S., Habes, M., Iftikhar, M. A., Shacklett, A., & Davatzikos, C. (2017). A review on neuroimaging-based classification studies and associated feature extraction methods for Alzheimer's disease and its prodromal stages. *NeuroImage*, *155*, 530-548. https://doi.org/10.1016/j.neuroimage.2017.03.057

Rieke, N., Hancox, J., Li, W., Milletari, F., Roth, H. R., Albarqouni, S., ... & Cardoso, M. J. (2020). The future of digital health with federated learning. *npj Digital Medicine*, *3*(1), 1-7. https://doi.org/10.1038/s41746-020-00323-1

Rudin, C. (2019). Stop explaining black box machine learning models for high stakes decisions and use interpretable models instead. *Nature Machine Intelligence*, *1*(5), 206-215. https://doi.org/10.1038/s42256-019-0048-x

Sarwinda, D., Paradisa, R. H., Bustamam, A., & Anggia, P. (2021). Deep learning in image classification using residual network (ResNet) variants for detection of colorectal cancer. *Procedia Computer Science*, *179*, 423-431. https://doi.org/10.1016/j.procs.2021.01.025

Scheltens, P., Blennow, K., Breteler, M. M., de Strooper, B., Frisoni, G. B., Salloway, S., & Van der Flier, W. M. (2016). Alzheimer's disease. *The Lancet*, *388*(10043), 505-517. https://doi.org/10.1016/S0140-6736(15)01124-1

Teipel, S., Grothe, M. J., Lista, S., Toschi, N., Garaci, F. G., & Hampel, H. (2015). Relevance of magnetic resonance imaging for early detection and diagnosis of Alzheimer disease. *Medical Clinics of North America*, *97*(3), 399-424. https://doi.org/10.1016/j.mcna.2012.12.013

Tjoa, E., & Guan, C. (2021). A survey on explainable artificial intelligence (XAI): Toward medical XAI. *IEEE Transactions on Neural Networks and Learning Systems*, *32*(11), 4793-4813. https://doi.org/10.1109/TNNLS.2020.3027314

Topol, E. J. (2019). High-performance medicine: The convergence of human and artificial intelligence. *Nature Medicine*, *25*(1), 44-56. https://doi.org/10.1038/s41591-018-0300-7

van Dyck, C. H., Swanson, C. J., Aisen, P., Bateman, R. J., Chen, C., Gee, M., ... & Shcherbinin, S. (2023). Lecanemab in early Alzheimer's disease. *New England Journal of Medicine*, *388*(1), 9-21. https://doi.org/10.1056/NEJMoa2212948

Vapnik, V. (2013). *The nature of statistical learning theory*. Springer Science & Business Media.

Vemuri, P., Wiste, H. J., Weigand, S. D., Knopman, D. S., Trojanowski, J. Q., Shaw, L. M., ... & Jack, C. R. (2017). Serial MRI and CSF biomarkers in normal aging, MCI, and AD. *Neurology*, *75*(2), 143-151. https://doi.org/10.1212/WNL.0b013e3181e7ca82

Wee, C. Y., Yap, P. T., Li, W., Denny, K., Browndyke, J. N., Potter, G. G., ... & Shen, D. (2012). Enriched white matter connectivity networks for accurate identification of MCI patients. *NeuroImage*, *54*(3), 1812-1822. https://doi.org/10.1016/j.neuroimage.2010.10.026

Weiner, M. W., Veitch, D. P., Aisen, P. S., Beckett, L. A., Cairns, N. J., Green, R. C., ... & Trojanowski, J. Q. (2017). Recent publications from the Alzheimer's Disease Neuroimaging Initiative: Reviewing progress toward improved AD clinical trials. *Alzheimer's & Dementia*, *13*(4), e1-e85. https://doi.org/10.1016/j.jalz.2016.11.007

Wen, J., Thibeau-Sutre, E., Diaz-Melo, M., Samper-González, J., Routier, A., Bottani, S., ... & Colliot, O. (2020). Convolutional neural networks for classification of Alzheimer's disease: Overview and reproducible evaluation. *Medical Image Analysis*, *63*, 101694. https://doi.org/10.1016/j.media.2020.101694

World Health Organization. (2023). *Dementia*. Retrieved from https://www.who.int/news-room/fact-sheets/detail/dementia

Young, J., Modat, M., Cardoso, M. J., Mendelson, A., Cash, D., Ourselin, S., & Alzheimer's Disease Neuroimaging Initiative. (2013). Accurate multimodal probabilistic prediction of conversion to Alzheimer's disease in patients with mild cognitive impairment. *NeuroImage: Clinical*, *2*, 735-745. https://doi.org/10.1016/j.nicl.2013.05.004

Zhang, D., Wang, Y., Zhou, L., Yuan, H., Shen, D., & Alzheimer's Disease Neuroimaging Initiative. (2019). Multimodal classification of Alzheimer's disease and mild cognitive impairment. *NeuroImage*, *55*(3), 856-867. https://doi.org/10.1016/j.neuroimage.2011.01.008