Review of Artificial Intelligence for Clinical Use in Alzheimer's Disease and Related Dementias

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ABSTRACT

As the U.S. population ages, Alzheimer's disease and related dementias (ADRD) cases are increasing, resulting in long wait times for specialist care. We review state-of-the-art artificial intelligence (AI) applications in ADRD care, from streamlining clinical diagnosis to pioneering novel digital biomarkers. Near-term AI applications include neuroimaging interpretation, conversational agents for patient interviews, and digital cognitive assessments. Large language models show promise as collaborative partners, helping clinicians interpret complex data while supporting patients and caregivers. Emerging digital biomarkers—speech analysis, passive monitoring through wearable devices, electronic health record analysis, and multiomics—offer potential for continuous monitoring to detect cognitive decline years before traditional assessments. Despite the acceleration of AI innovation, most of these systems are inaccessible in clinical practice. Implementation bottlenecks include limited external validation, technical challenges, model biases, infrastructure, and regulatory requirements. This review aims to help neurologists navigate this rapidly evolving AI landscape and prepare for implementation in ADRD care.

Keywords AI, ML, neurodegenerative disease, ADRD, digital biomarkers

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Introduction

As the U.S. population ages, the number of people with Alzheimer's disease and related dementias (ADRD) is rapidly increasing,[1,2] with lifetime dementia risk reaching 48% for women and 35% for men after age 55, and U.S. cases projected to double by 2060 to 1 million annually.[3] Early detection and precise diagnosis are crucial for proper access to quality care, eligibility for new and emerging disease-modifying therapies, and enabling research to advance the field. Unfortunately, more than 50% of dementia diagnoses are delayed until moderate or advanced stages in primary care,[4,5] with greater delays among racial and ethnic minorities.[6]

There are many challenges with diagnosing neurodegenerative diseases. Often, primary care providers (PCPs) are the first clinicians to hear concerns from patients and their informants, but most PCPs cite a lack of time and confidence for the diagnostic process,[7,8] preferring to refer patients to specialists. Consequently, the demand for dementia specialists greatly exceeds the available supply, with the gap continuing to widen.[9–11] The average wait times for dementia specialists are projected to exceed 40 months by 2027, with rural areas facing three times longer delays compared to urban regions.[12] Beyond access issues, diagnosis is challenging, requiring time-consuming data collection and nuanced interpretation.

After diagnosis, challenges with management are growing as new therapeutics with intensive requirements for monitoring are emerging, adding both urgency and complexity.[13,14] Many PCPs and general neurologists struggle to keep pace with the rapid advances in the field, which includes maintaining awareness of research studies that could potentially benefit their patients and the ADRD field. Furthermore, new care models such as those proposed by the Centers for Medicare and Medicaid Services[15] demand additional resources that our current workforce is ill-equipped to support.

Against this backdrop, artificial intelligence (AI) has garnered significant attention as a potential solution. AI encompasses a spectrum of complementary approaches, from traditional machine learning (ML) methods that excel with structured clinical data, to deep learning systems that identify complex patterns in neuroimaging, to generative AI based on large language models (LLMs). LLMs in particular have been advancing rapidly, which is AI trained on vast amounts of text, excelling at language understanding and generation. AI systems using LLMs can process multiple data modalities simultaneously—integrating clinical text, medical images, audio, and other data types. Advances across the spectrum of AI promise to enhance diagnostic accuracy, accelerate clinical workflows, and democratize access to specialized expertise.

In the field of ADRD, traditional ML paradigms have considerable utility in analyzing unified data modalities, including biomarkers,[16] genetic information (including emerging polygenic risk scores),[17] neuroimaging,[18] and connected speech.[19] Empirical evidence supporting the utility of LLMs in neurodegenerative disease characterization continues to emerge. For example, GPT-4 exceeded mean human performance on a neurology board-style examination[20] and provided neuropathologic differential diagnoses with high correlation to experts using human-curated clinical summaries.[21] There are also several techniques that can further improve an LLM's performance. A diagnostic pipeline that mimics the clinical process/reasoning of a physician, including chain of thought reasoning with LLM prompts, has shown performance boosts.[22] Retrieval augmented generation can be used to ground the LLM in the most up-to-date clinical diagnostic criteria for all neurodegenerative diseases.[23]

Many AI-based tools can now be used in the clinic; however, the level of evidence supporting their clinical use varies widely, and many implementation challenges prevent widespread use. While AI has yet to be integrated into routine ADRD clinical care, recent developments suggest this may soon change. AI capabilities have advanced at unprecedented rates over the past 2 to 3 years, coinciding with a sharp increase in FDA-cleared or approved AI-based medical devices.[24,25] With many promising applications on the horizon for ADRD, clinicians need to understand the current state of AI research in this field to prepare for responsible, evidence-based implementation and help shape how these technologies enter clinical practice.

This review examines AI applications in ADRD through the lens of clinical practicality, organizing discussion around progress from familiar clinical data enhanced by AI to emerging digital biomarkers and novel data sources that may transform future practice. We address current limitations and provide clinically relevant AI knowledge to aid neurologists navigating this rapidly evolving landscape while maintaining appropriate skepticism about unvalidated or poorly validated technologies.

AI-Enhanced Collection and Interpretation of Standard Clinical Data

Understanding the Patient's History

The constraints of brief office visits present significant challenges for diagnosing neurodegenerative diseases. Physicians, faced with limited time, may struggle to effectively review a lengthy patient chart or gather comprehensive patient histories from distressed patients or their caregivers. AI could likely help with these limitations.

Even before the patient is seen, AI can extract value from large volumes of text, parsing scanned documents and synthesizing electronic health record (EHR) data to extract relevant history or generate targeted questions for assessment. AI-powered conversational agents are demonstrating the capabilities needed to gather an effective patient history, particularly using LLMs. LLMs can enable conversational agents to interview patients efficiently and empathetically,[26] adjust explanations to a patient's education level, and speak in most patients' preferred languages.[27] More recent advancements with voice-based conversational agents[28] could interact with patients over the phone to overcome barriers with the writing and typing typically required of traditional questionnaires, and also increase access for patients who are of lower socioeconomic status, limited English proficiency, or elderly.[29–32] Assuming unconstrained time, these agents may eventually be able to collect a history in a manner comparable to specialists. Still, significant work is needed. Most have been tested only with text-based, low-stakes interactions,[33–38] can perform worse with non-English speaking people,[39] and likely will require a monitoring system that detects emergency situations during these interviews, raising implementation challenges.

Once valuable information is collected from the EHR and interview, LLMs can summarize it into a history of present illness or outline, allowing a clinician to quickly identify concerning patterns.[40] Reliable summarization is critical in cognitive impairment contexts, as detection of subtle symptom changes over time is essential for early diagnosis and management. It will be challenging to ensure that generated summaries are consistently comprehensive and accurate, particularly as hallucinations (fabricated information) are still a concern with LLMs. Emerging promising solutions include the adoption of AI confidence scores and secondary AI models that critically evaluate the summaries.[41–43]

AI transcription and summarization are already being used during the visit as healthcare institutions are widely adopting ambient AI scribes.[44] A growing number of companies are offering this technology, which records the clinic visit between the patient and the clinician, then automatically transcribes and summarizes patient encounters just as an in-person medical scribe would. These AI scribes still make mistakes, but clinical implementation has moved forward as clinicians can feasibly check over the summaries and correct them before signing their notes.

LLMs as Collaborative Partners

A particularly promising development is the emergence of LLMs as intuitive interfaces between clinicians and complex data—both traditional clinical data as well as the outputs from AI-enabled digital biomarkers and emerging data sources. LLMs can serve as collaborative partners that help clinicians interpret familiar clinical information (e.g., neuroimaging, laboratory results, and clinical notes) by incorporating the latest evidence-based information and highlighting subtle patterns that might be overlooked in busy clinical settings.[45–47] Several companies are beginning to create such an interface, with some being used widely by clinicians using a text-only chat interface with responses grounded in clinical evidence.

Importantly, as new AI tools become validated and enter clinical practice, their analytical outputs will become part of the complex data landscape that clinicians must interpret. LLM capabilities have the potential to translate and integrate these AI-derived insights, explaining in natural language what various AI tools have detected and how these findings fit together with traditional clinical data to inform diagnosis and management decisions (**Fig. 1**).

Beyond supporting clinicians, LLMs also hold significant promise for directly assisting patients and caregivers throughout the dementia journey. The conversational abilities of these models

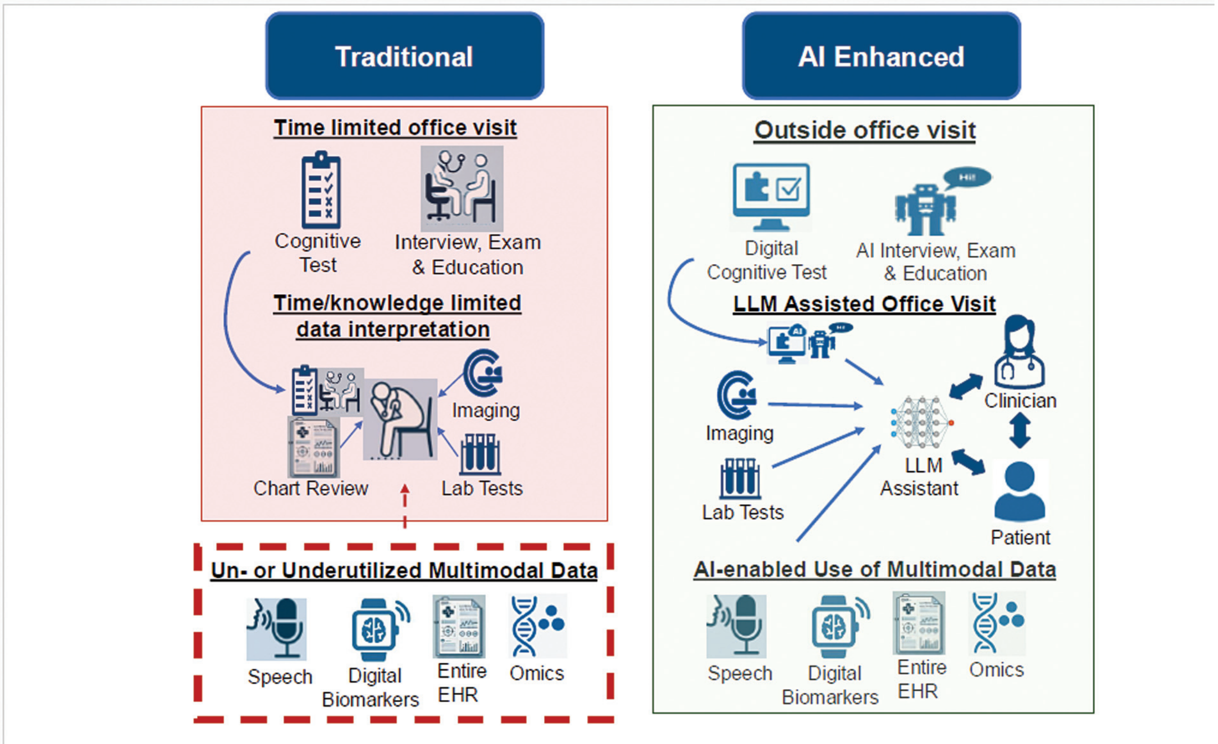

Fig. 1 Comparison of traditional versus AI-enhanced methods. Left panel (traditional care): brief cognitive testing (e.g., MMSE, MoCA), clinical interviews, physical examinations, and patient education are constrained by time-limited office visits. Clinicians must manually interpret heterogeneous data sources—cognitive test results, history, neurological examination findings, neuroimaging, electronic health record (EHR) information, and laboratory or biomarker results such as cerebrospinal fluid and plasma assays. Experienced clinicians may notice subtle speech changes or consider patient-provided digital data (e.g., sleep tracking), yet these remain underutilized without artificial intelligence (AI) support. Parsing large EHRs or integrating omics-level information is rarely feasible in traditional workflows. Right panel (AI-enhanced care): artificial intelligence (AI) systems assist with collecting and integrating multimodal information from structured and unstructured data—including clinical text, speech, wearable devices, EHRs, imaging, and omics—to augment diagnostic reasoning and personalize care. Most of this data can be collected outside the time-limited office visit. A Large language model (LLM) system designed for medical assistance, grounded in the latest evidence, highlights and explains salient findings as well as assists with differential diagnosis. This integration reduces clinician burden, enhances diagnostic accuracy, and facilitates earlier detection and triage to appropriate care settings.

create opportunities for providing companionship, helping patients understand their diagnosis and treatment options, and guiding caregivers through complex care decisions.[48] As cognitive abilities decline, patients may find AI companions more accessible than traditional educational resources,[49] while caregivers can receive personalized guidance on managing behavioral symptoms or navigating healthcare systems. However, as AI becomes more integrated into dementia care, it's important to consider how these technologies will reshape care relationships and decision-making dynamics within families and care teams, ensuring that AI enhances rather than replaces the human connections central to quality dementia care.[50]

This dual capability—supporting both clinicians as well as patients and their families—positions LLMs as comprehensive tools that could address multiple challenges across the continuum of dementia care.[48]

Neuropsychological Testing

When concerning symptoms are identified, a cognitive assessment looking for objective evidence of cognitive impairment is required. Current challenges include cost, time required for clinicians to administer tests, specific training even for the most common assessments (e.g., MMSE, MoCA), and language and cultural biases that complicate interpretation in medically underserved populations.[6,32,51] Digital cognitive assessments can enable AI integration as they can capture potentially meaningful nuances in performance (e.g., trial-level data, response times) that are not possible to record or quickly interpret with traditional paper-based cognitive tests.

More broadly, several validated digital cognitive assessment tools with and without AI integration are now available for clinic or remotely at home, though with varying levels of validation.[52,53] Some of these tools have demonstrated great potential to scale. For example, the TabCAT-Brain Health Assessment developed at UCSF is an iPad-based in-clinic assessment that includes immediate scoring, outperforms traditional paper-based assessments, has had organic adoption across several UCSF-affiliated PCP clinics, and is free for primary care use.[54–57] Remote, self-administered cognitive tasks delivered on participants' own devices are also proving both practical and psychometrically sound in AD research. A recent scoping review[58] showed encouraging adherence rates among research participants and moderate correlations with gold-standard neuropsychological batteries ($r=$ approximately 0.53–0.70).

Further studies show promise of AI applications in optimizing cognitive test administration and scoring across diverse cultures and health literacy levels.[59,60] For example, PENSIEVE-AI uses an image-based deep learning model to detect mild cognitive impairment (MCI) and dementia based on touch-screen tablet drawing tasks,[60] the Novoic app collects speech recordings from story recall tasks and analyzes them with a fully automated AI-based transcription and analysis pipeline for detection of Alzheimer's disease,[61] and the Altoida app delivers augmented reality tasks and analyzes functional motor behaviors collected via accelerometer, gyroscope, and touch screen interactions to detect MCI with AI models.[62] Linus Health also developed a brief digital cognitive battery that used AI models to identify subtypes of MCI.[63] Beyond task performance, a growing number of studies are also using AI to evaluate eye tracking data during digital cognitive and oculomotor tasks.[64]

A particularly promising emerging tool is Virtual Reality, which can be an immersive and engaging experience with almost limitless possibilities for testing cognition.[65] There is growing evidence that VR-based cognitive assessments exhibit ecological validity by simulating real-world tasks and aligning with established neuropsychological and functional measures.[65,66] Incorporation of LLMs in virtual reality has enabled engaging virtual companions for persons living with dementia,[49] which makes virtual psychometrists particularly promising.

The landscape of digital cognitive assessments continues to evolve, with emerging tools increasingly incorporating AI to enhance the administration, scoring, and feedback of results.[67] Digital cognitive assessments can be used to evaluate for clinical manifestations of neurodegenerative disease or other cognitive disorders, but clinical follow-up is always needed to make a diagnosis. Also, more validation of remote and AI-powered cognitive assessments in clinical populations outside highly engaged research registries is needed to support widespread clinical deployment.

Physical Examination

Physical examination continues to be important in obtaining a diagnosis, including the motor findings associated with Lewy body disease, corticobasal syndrome, progressive supranuclear palsy, amyotrophic lateral sclerosis, and many other conditions. In addition, the absence of motor findings in AD is also important. While an in-person physical exam is ideal, physical exam findings for these syndromes can often be uncovered through video visits, which can increase accessibility for patients who cannot feasibly travel to see a specialist. Possibilities include video interpretation of speech patterns, motor planning and execution, gait, balance, and others. New multimodal AI models have made significant progress in describing video content, such as surgeries, making video data a promising method for AI decision support with further research.[68] Recent studies have shown that short videos captured on consumer-grade technology can detect Parkinsonism.[69,70] Additionally, passive data collection, discussed below, may soon augment or even replace some physical exam findings.

Neuroimaging

Neuroimaging with MRI and PET is a cornerstone of the diagnosis of etiologies of neurodegenerative disease, including the exclusion of readily treatable causes of dementia, assessing vascular etiologies of dementia, and observing spatial patterns of atrophy (MRI) or biomarker presence and location (PET). The complexity of neuroimaging interpretation in neurodegenerative diseases has made it an active area of AI research, with investigators exploring automated approaches to detect subtle changes that may be missed in routine clinical reading.

However, consistent imaging protocols are essential for AI model accuracy, as systematic variation can significantly impact performance. Initiatives like the Alzheimer's disease imaging initiative (ADNI) have established best practices for acquisition and preprocessing, while large-scale studies such as the UK Biobank have advanced standardization for diverse MRI techniques.[71–74] These standardization efforts have greatly aided in advancing reliable AI imaging research.

Traditional AI methods (i.e., ML models) have made significant progress with the classification of disease states. Notably, logistic regression models are finding widespread research application in binary classification scenarios, particularly in distinguishing between healthy controls and individuals with Alzheimer's disease using MRI.[18] For example, support vector machines have demonstrated particular efficacy in identifying imaging biomarkers associated with frontotemporal dementia.[75]

The emergence of deep learning architectures, particularly convolutional neural networks (CNNs), has revolutionized neuroimaging analysis, including MRI and PET scan interpretation.[76] These sophisticated models demonstrate remarkable precision in identifying disease-specific features, such as patterns of brain atrophy characteristic of Alzheimer's disease. CNNs trained on structural MRI data have shown particular prowess in detecting subtle patterns of cortical thinning associated with various neurodegenerative conditions.[18]

Substantial work has been done to develop AI models that can aid in neurological diagnoses based on multi-sequence brain MRI or PET, and more recent efforts involve the development of multimodal AI models that incorporate clinical, laboratory, and imaging data for differentiating etiologies of dementia.[77–79] A recent example is work from the Mayo Clinic highlighting an AI model that can detect nine different neurodegenerative phenotypes from FDG-PET images, with initial validation from ADNI with AUC of 0.93.[80] Incorporating AI interpretation of MRI atrophy patterns, in particular, as part of an AI diagnostic tool will be of great value to clinicians.

AI-Enabled Digital Biomarkers and Emerging Data Sources

Speech

Speech is a rich source of cognitive and behavioral information, integrating both linguistic content and vocal motor features. As such, it is increasingly recognized as a promising digital biomarker for the early detection and monitoring of ADRD.[81,82] Automated speech analysis can capture deviations in speech and language specific to dementia syndromes. In AD, early language changes include word-finding difficulties, reduced lexical diversity, and vague or empty speech.[83–85] Acoustic features in AD may include slower articulation rate, increased pauses, and reduced prosody,[86] though these are typically more subtle than in disorders with prominent motor speech involvement, such as Parkinson's disease[87] or the nonfluent variant of primary progressive aphasia (PPA), which is additionally marked by agrammatism.[88] In the logopenic variant PPA, speech is characterized by frequent pauses, word-finding failures, and impaired repetition,[89] while in the semantic variant PPA, spontaneous speech is fluent but marked by semantic errors, reduced specificity, and loss of content due to degradation of conceptual knowledge.[90] Even in dementia syndromes where language symptoms are not dominant, such as the behavioral variant of frontotemporal dementia, automated speech analysis can detect subtle linguistic and acoustic patterns that reflect underlying cognitive, behavioral, or socio-emotional changes.[91,92]

Automated speech analysis enables the quantification of both how something is said through acoustic features (e.g., pitch variation, timing) and what is said through linguistic features (e.g., lexical diversity, semantic specificity, and syntactic complexity). Most pipelines follow a two-stage process: speech feature extraction—using natural language processing (NLP) and acoustic signal processing—followed by statistical analysis using ML modeling or inferential statistics, including general(ized) linear models.

Both traditional ML approaches (e.g., support vector machines, logistic regression, XGBoost) and deep learning methods (e.g., convolutional and recurrent neural networks, transformers) have shown success in distinguishing individuals with AD, MCI, FTD, including PPA, or PD from healthy controls.[93–96] While classification tasks are common in automated speech analysis in neurodegenerative research, several studies have employed regression models to predict continuous cognitive outcomes (e.g., MMSE)[97,98] or to explore relationships with imaging and biomarker measures.[99–101] Additionally, recent approaches have generated high-dimensional representations—known as embeddings—that capture nuanced relationships within audio (e.g., wav2vec2) or text (e.g., BERT) to extract complex patterns,[102–104] enabling a more holistic approach to speech analysis than using individual features, yet at the cost of transparency.

Growing access to speech data through mobile platforms, telehealth, and ambient voice technology is accelerating progress in this domain.[105,106] Although most studies to date are cross-sectional and research-focused—and important ethical challenges must be addressed prior to clinical implementation[107]—speech remains one of the most clinically viable digital biomarkers given its scalability, ecological validity, ease of longitudinal collection, and potential for passive capture in real-world settings.

Passive Digital Biomarkers

Passive monitoring via digital health technology is a complementary approach to overcome the limitations of traditional neuropsychological and neurologic evaluations.[108] Emerging methods have shown excellent feasibility to unobtrusively capture objective and naturalistic behavioral data in older adults through the use of sensors that are either worn or embedded within objects that people use regularly, such as smartwatches, smartphones, and other placeable sensors (e.g., a GPS sensor placed in one's car).[109] These technologies can capture multi-domain clinical data reflecting cognitive, behavioral, social, and physical function without any added patient burden, allowing for the development of digital biomarkers of ADRD.[110] A growing number of studies suggest these passive monitoring methods can detect subtle changes in neurodegenerative disease as they are happening in real time, even before symptoms become noticeable to individuals or their loved ones. For example, changes in physical activity and movement patterns, driving behavior, sleep patterns, everyday speech, eye tracking, facial expressions, technology use, writing, texting, and keyboard typing dynamics have all been shown to differentiate those with and without neurodegenerative disease.[111–119] Further, these passive digital biomarkers could also be applied across culturally and linguistically diverse populations, as they are less affected by the cultural and language biases that limit active cognitive testing approaches. Passive approaches to data collection are also low-burden and scalable, with great potential to be utilized as clinical diagnostic and monitoring tools with continued validation.

One barrier to the clinical implementation of passive digital biomarkers, however, has been the lack of computing resources for storing and automatically processing and analyzing the large amount of data collected from passive digital tools that continuously monitor behavior over long periods of time.[120] AI represents a powerful part of the solution, with potential to identify data-driven patterns of behavioral change associated with AD and other neurodegenerative diseases through passive digital data.[121] Given the large amount of data that could be collected per person with digital devices, AI-powered analytic methods also have the potential to detect person-specific changes—that is, shifts in behavioral patterns unique to an individual—which could be used as a screener to connect a patient with a clinician for follow-up. This would be a powerful step toward a personalized medicine approach for dementia prevention, diagnosis, and treatment. While the integration of AI analytics in passive digital biomarker research is still only being used in research settings,[122] this methodology could eventually be used to improve detection and monitoring of neurodegenerative disease-related changes in clinical practice, as well as to monitor treatment outcomes in clinical trials in the near future.

Novel Use of EHR Data

Recent work applying ML to real-world EHRs shows that inexpensive, routinely collected data can flag patients at elevated risk for future Alzheimer's disease. Recent studies have used gradient boosting trees and random-forest models to predict ADRD up to 5 years in advance ($AUC > 0.85$) or to predict AD 7 years in advance (AUC: 0.72), the latter using only diagnosis codes, prescriptions, and common laboratory results.[123,124] Complementing these findings, another study incorporated functional scales (iADLs/ADLs) and common labs from the EHR to separate MCI (AUC: 0.75) and dementia (AUC: 0.96) from controls.[125] Unsupervised AI approaches have also been applied to EHRs to characterize dementia heterogeneity, identifying distinct disease subtypes and progression patterns for patients with Alzheimer's disease and Parkinson's disease.[126–129]

Unstructured EHR data is being increasingly utilized for dementia as well. Advanced NLP models, such as AD-BERT, are beginning to boost EHR-based prediction of Alzheimer's disease by mining the free-text of clinical notes.[130] AD-BERT had impressive accuracy for predicting whether an MCI patient would ever convert to AD (AUROC: 0.883 in an external cohort). This model highlighted phrases such as "memory," "MCI," and "difficulty recalling dates," indicating that it captures linguistic cues of emerging cognitive decline. Models such as AD-BERT could use free text from notes to complement structured-data risk scores and potentially flag high-risk MCI patients earlier, provided future work validates these models. Unstructured data can also be used for subphenotyping, as shown in the identification of three ADRD subtypes in a recent study.[131]

A key caveat is that most EHR studies rely on ICD-9/10 codes for progression labels rather than biomarker-confirmed diagnoses, and any diagnostic misclassification in routine practice would place an upper bound on reported AUROCs. High variations in data quality may also introduce confounding covariates (e.g., age, detection bias, indication bias) and technical biases (e.g., extent of missingness, imputation approaches, ontology mappings) that can also contribute to overly optimistic AUROCs reported. Furthermore, given that neurodegeneration is a chronic disease process, there is often heterogeneity in identifying an index date, particularly for different neurodegenerative syndromes. This can lead to AI models that excel in learning physician behaviors (e.g., ordering for a cognitive test) that predict subsequent diagnosis in downstream visits (e.g., ICD code for dementia given).[132] Nevertheless, EHR research holds promise in highlighting optimal care trajectories and pathways that can describe and improve dementia management. Furthermore, the integration of EHR datasets with biomarkers and neuropathology results will greatly improve model specificity and clinical utility in the future.[133]

Omics

AI-powered omics approaches hold significant promise for transforming dementia care, from biomarker discovery to risk stratification. Different types of -omics data, such as genomics, epigenomics, transcriptomics, proteomics, metabolomics, and lipidomics, can provide readouts of a patient's biological state that are not readily apparent from existing clinical laboratory measures. AI-based approaches are uniquely suited to leveraging such high-dimensional -omics data for potential clinical use, given their ability to reveal nonlinear relationships across different biological features that are difficult to observe by standard linear or logistic association analyses.[134] The use of AI for interpretation of omics data for clinical use is in early development, but AI models have already been applied to genomic data to derive polygenic risk scores for different diseases that outperform traditional risk scores generated from linear models,[135] and different types of blood-based -omics data have been combined with neuropathology and imaging data in a multi-modal AI model to identify subtypes of AD and co-pathology.[136,137] In certain early-onset or atypical dementia cases, the presence of genetic variants of unknown significance (VUSs) may represent undiagnosed pathogenic causes of disease, but their uncertain classification limits clinical actionability. Emerging AI models trained on evolutionary constraints, structural features, or functional data are increasingly used to resolve the significance of VUSs,[138,139] and could help reclassify VUSs in known ADRD risk genes (e.g., APP, PSEN1/2, MAPT).[140,141]

In addition to risk stratification and disease subtyping, AI models have been proposed to align patient-specific omics signatures with therapeutic interventions.[142] This includes identifying drugs that could reverse disease-related gene expression or proteomic patterns through computational drug repurposing platforms,[143] as well as supporting patient stratification for ADRD clinical trials based on predicted drug response.[144] AI-informed treatment approaches, while still in early development, may become essential tools for optimizing dementia care but will need to be paired with rigorous validation and clinical testing to ensure safety and reliability.[145]

A number of challenges remain before more widespread use of AI and -omics in the clinic. Current limitations include the high cost of comprehensive biological testing, the lack of standardization across laboratories, and technical challenges that come with analyzing a huge amount of data where the number of measurements far exceeds the number of patients studied, leading to potential overfitting of the model and poor generalization across different groups of patients. While AI models can help with this dimensionality reduction, for example, by identifying the most important features to focus on, interpretability has been a challenge. However, costs are rapidly decreasing, and promising methods of dimensionality reduction are being developed. Despite these challenges, it is likely that AI models that incorporate multi-modal -omics data will eventually be developed for clinical use that prove superior to single or small panel biomarker measurements for risk stratification, diagnosis, staging, prognostication, and tailored treatment selection in neurodegenerative diseases.

See **Table 1** for a summary of AI approaches across modalities in ADRD, highlighting function, and clinical readiness.

Challenges and Considerations

Despite the successes with AI, there are still significant barriers to the safe adoption of AI in the clinic. There is a need for external validation, with one review finding that only 2 of 431 digital biomarker studies included validation at outside institutions.[122] Many models are trained on small, homogeneous datasets from single academic centers, likely limiting their generalizability to diverse clinical populations. The output of models can be difficult to interpret and, therefore, difficult to apply to clinical care.[146,147] Many AI techniques require sophisticated computational infrastructure that may not be readily available in typical clinical settings.[16] Furthermore, the optimistic performance reported in research studies may at times reflect methodological issues, including data leakage and selection bias, explaining why many models fail when tested prospectively in real-world settings.[148–150]

Ethical challenges around the use of AI in ADRD have been discussed in detail elsewhere,[48] but in brief, ethical considerations are particularly important in this time of rapid AI development before deploying in vulnerable populations with cognitive impairment. In response, numerous initiatives have developed frameworks and guidelines to ensure AI applications are fair, appropriate, valid, effective, and safe, which will at least in part require transparency with technical performance as well as organizational capacity to manage risks associated with deploying this

Table 1 AI applications in ADRD care—function and clinical readiness

Clinical domain/data type	AI application/technology	Function	Clinical readiness
Digital cognitive assessment	Cognitive tests are administered on an electronic device, in a clinic, or remotely	Cognitive screening, assessing for impairment by cognitive domain, and monitoring	Clinically available, validation ongoing
Patient history and documentation			
Electronic health record (EHR) review and synthesis	LLM-powered chart review and summarization	Previsit preparation, history extraction	Research stage, near-term
Patient/caregiver interviews	Conversational agents (LLM-based)	History gathering, symptom documentation	Research stage, near-term
Clinical documentation	Ambient AI scribes	Real-time clinician-patient interview transcription and note generation	Clinically available, validation ongoing
Data integration and interpretation	LLMs as collaborative partners	Synthesizing clinical data, integrating evidence, answering questions (future—explaining AI tool outputs)	Research stage, near-term (available in a narrower scope of medical, text-only chat interfaces)
Patient/caregiver education	Conversational AI companions	Education, emotional support, and care guidance	Research stage, near-term
Video-based physical examination	Multimodal AI video analysis	Remote detection of motor findings, Parkinsonism	Research stage, long-term
MRI analysis and PET scan interpretation	CNNs, traditional ML (logistic regression, SVM)	Atrophy pattern detection, biomarker detection, disease classification	Clinically available, validation ongoing
Automated speech analysis	Natural language processing, machine learning, and deep learning	Early detection, syndrome differentiation, and monitoring	Research stage, long-term
Passive digital biomarkers	Wearable/smartphone sensors, computer/smartphone usage tracking	Continuous behavioral/functional monitoring, early detection, risk stratification	Research stage, long-term
Electronic health records			
Structured EHR analysis	Gradient boosting, random forests	Risk prediction years before disease onset, and early detection of disease	Research stage, long-term
Unstructured clinical notes	NLP models (e.g., AD-BERT)	MCI-to-AD progression prediction, subphenotyping	Research stage, long-term
Genomics/proteomics/ metabolomics	Deep learning models, multi-modal AI	Risk stratification, disease subtyping, drug discovery, personalized treatment selection	Research stage, long-term

Abbreviations: AD, Alzheimer's disease; AD-BERT, Alzheimer's disease bidirectional encoder representations from transformers; AI, artificial intelligence; CNN, convolutional neural network; LLM, large language model; MCI, mild cognitive impairment; ML, machine learning; MRI, magnetic resonance imaging; NLP, natural language processing; PET, positron emission tomography; SVM, support vector machine.
Note: Clinical readiness definitions (clinically available): available in healthcare settings, though the level of evidence supporting clinical validation varies widely, and implementation challenges have hindered use in routine clinical care. Research stage: promising evidence but requires further validation and development, not clinically available. Clinical readiness categories represent a continuum, and individual tools within each category vary in their development stage.

technology.[151] Key concerns for the ADRD community include ensuring informed consent from patients with diminished decision-making capacity, protecting patient privacy beyond traditional de-identification methods, and maintaining transparency about AI decision-making processes.[152–154] In contrast to approving drugs with unclear but static mechanisms of action, AI performance can change over time, raising the importance of explainability and interpretability to ensure humans can identify signs of model deterioration or drift at the point of care.[155–157] Patient safety risks include potential misdiagnosis, inappropriate treatment recommendations, and adverse psychological effects from AI interactions. Legal liability remains unclear regarding responsibility when AI systems contribute to patient harm.

AI has the potential to exacerbate existing brain health inequities if leveraged incorrectly. Bias can be introduced through nonrepresentative health data, the absence of diverse perspectives in algorithm development, and inadequate oversight of AI-based decisions.[158] Implicit biases present in healthcare and research settings, from subjective decision-making to stigmatizing language and stereotypes, can be encoded into algorithms. These biases may also manifest as a lack of attention to culturally-relevant meanings of aging and care for the patient as well as the caregiver. For example, AI may flag a patient as "noncompliant" for integrating faith beliefs, family values, or culture into their understanding of disease and coping with dementia.[159] Additionally, racial and ethnic minority patients and those from socioeconomically disadvantaged backgrounds receive more fragmented medical care,[160] and may have limited access to online patient portals. This can lead to a systematic lack of data from medical records used to train AI, degrading performance for these populations.[161] Prior work has demonstrated lack of adequate representation of certain ethnoracial groups can lead to unfairness (fairness being the absence of favor or prejudice toward a group based on group characteristics) among ML models predicting progression along the AD continuum for ADNI participants.[162]

Utilization of AI technologies in dementia detection and diagnosis among marginalized populations may also be hampered by mistrust and concerns about privacy as well as other factors, even when these tools are designed with an emphasis on equity and fairness.[160] Great care must be taken to not further the digital divide and gaps in access to personalized cognitive monitoring and intervention based on who does or does not have access and or familiarity with technology and the internet. Careful consideration of language preferences, cultural beliefs, health literacy, and other factors that affect a patient or research participant's ability to interface with AI-based tools will be essential if AI-based tools are to be widely adopted among all groups. Context matters. It is important not to reinforce or exacerbate inequities by using prediction models that rely on historical data and patterns shaped by structural inequity.

Conclusion and Clinical Implications

The convergence of advancing AI capabilities with the urgent clinical need in ADRD presents an opportunity to transform dementia care across the entire continuum—from enhancing traditional diagnostic approaches to pioneering novel digital biomarkers for earlier, more precise detection. It is likely that the relatively near-term applications involve AI-enhanced processing of familiar data types that integrate with existing workflows: AI-assisted neuroimaging interpretation, conversational agents interviewing patients and caregivers, and digital cognitive assessments offering standardized, scalable alternatives to traditional testing. These, combined with the diagnostic as well as interactive capabilities of LLMs, could represent a shift toward AI as a collaborative partner that augments clinician capabilities rather than replacing clinical judgment.

Emerging digital biomarkers—including speech analysis, passive monitoring, and advanced EHR mining—hold transformative potential for continuous, unobtrusive monitoring that could detect cognitive decline years before traditional assessments. AI-powered omics approaches promise precision medicine capabilities. However, implementation may have a longer time horizon as these innovative approaches remain largely research-stage and require extensive validation before clinical deployment.

Despite significant promise, substantial barriers to implementation persist. The field suffers from limited external validation, with most studies conducted in single institutions or highly selected research cohorts. Technical challenges include ensuring model interpretability for clinical decision-making, addressing biases that could exacerbate health disparities, and developing robust safeguards against AI hallucinations in high-stakes medical decisions. Infrastructure requirements, including standardized data collection protocols and computational resources, may pose additional barriers, particularly for resource-limited healthcare settings.

The ultimate measure of success will be meaningful improvements in patient outcomes, care accessibility, and quality of life rather than technical accuracy alone. This necessitates close collaboration between clinicians, AI developers, and healthcare systems to ensure technological advances address real-world clinical needs while preserving the human elements central to compassionate dementia care. The ADRD community has a critical opportunity to shape how these technologies are developed and deployed, maintaining focus on clinical utility, ethical implementation, and patient-centered outcomes.

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Statements and Additional Information

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