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Special Article

AI-augmented frameworks for enhancing Alzheimer's disease clinical trials: A memory clinic perspective

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ABSTRACT

Alzheimer's disease (AD) clinical trials continue to face major hurdles in patient identification, resulting in delayed timelines, underpowered studies, and escalating costs. This perspective explores these challenges through the lens of a memory clinic, where hundreds of cases often translate into only a handful of enrollments. We highlight the potential of artificial intelligence (AI) to address this gap by powering chatbots for awareness and pre-screening, decision support tools for case identification, and algorithms for matching patients to trial-specific criteria, automating and streamlining the recruitment process. We also examine critical considerations in developing such AI-driven tools, including data standardization, privacy protections, and ethical safeguards. With thoughtful implementation, these innovations could accelerate more inclusive and efficient AD trials, ultimately bringing therapies to patients faster.

1. Introduction

Consider a representative memory clinic tasked with managing a consistent influx of patients presenting with early cognitive impairments, including memory deficits or disorientation. Although assessing numerous potential participants annually, such clinics typically secure enrollment for only a limited number in Alzheimer's disease (AD) clinical trials. These recruitment difficulties arise from multifaceted practical barriers (Fig. 1): patients and their families often attribute mild symptoms to normative aging processes, thereby postponing medical consultation and contributing to diagnostic delays [1]; overburdened neurologists and other providers are constrained by time limitations, impeding thorough manual examination of electronic health records (EHRs) to determine eligibility amid broader system resource constraints; diagnostic obstacles, such as the requirement for costly biomarker evaluations, discourage patient referrals; and rigorous trial protocols, mandating precise cognitive thresholds or genetic indicators, contribute to elevated screen-failure rates [2]. These impediments reflect wider systemic challenges in AD therapeutic advancement, wherein a large majority of qualified candidates remain unreferred or uninvolved in trials [3], culminating in investigations that exhibit protracted enrollment periods, extended durations, and heightened expenditures relative to other medical domains.

Artificial intelligence (AI) provides a practical, actionable path forward by automating and enhancing key steps in the trial recruitment process [4–7]. In the memory clinic scenario, AI tools based on large language models (LLMs) and other analytical tools have the potential to integrate diverse data sources, EHRs, neuroimaging, genetics, and even digital biomarkers from apps, to identify and match patients efficiently. This perspective uses the memory clinic example to dissect these challenges and outline a vision for AI integration, guiding readers toward implementing more precise, inclusive, and accelerated AD trial recruitment to advance therapeutic breakthroughs. To facilitate user comprehension, we present a collection of technical terms with brief explanations in Table 1.

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2. Systemic barriers to effective clinical trial participant identification in AD

AD clinical trials face interconnected, system-wide barriers that accumulate across the patient journey, from community perceptions to data infrastructure, resulting in enrollment shortfalls (Fig. 1). In our representative memory clinic, these barriers manifest daily: despite seeing hundreds of patients with cognitive concerns annually, only a small fraction might be referred to trials, with even fewer enrolling due to delays, dropouts, and mismatches. Addressing these barriers is crucial for accelerating therapeutic development and ensuring trial populations reflect the diverse demographics affected by AD [8].

Community and healthcare system barriers. In the memory clinic setting, early AD symptoms such as subtle memory lapses or difficulty with daily tasks, are frequently misattributed to normal aging by patients and families [9], leading to delayed recognition and underreporting, particularly in preclinical or mild cognitive impairment (MCI) stages. First, many patients present at a much later stage in the disease continuum, often after significant cognitive decline has already occurred [1]. At that point, they may no longer meet eligibility criteria for early-intervention trials, which increasingly focus on prodromal or preclinical AD [3,8]. This likely postpones consultations, with many patients only seeking help when symptoms become severe, narrowing the window for trial eligibility. Stigma and fear surrounding an AD diagnosis further exacerbate this [10–12], as individuals worry about impacts on independence, employment, or insurability, often minimizing or concealing symptoms to avoid social or professional repercussions. For instance, in underserved communities served by the clinic, cultural misconceptions or historical mistrust of medical research can reduce initial visits [13,14], limiting the potential participant pool from the outset.

Within the healthcare system, clinicians report insufficient time and resources to thoroughly discuss AD with patients [15], especially those without overt symptoms, amid packed schedules. Structural disincentives, such as limited reimbursement for cognitive screenings or referrals, further discourage proactive involvement [16]. Many neurologists lack deep familiarity with preclinical AD indicators, contributing to delayed diagnoses and missed referral opportunities. The perceived absence of effective disease-modifying therapies diminishes the incentive for early screening among both providers and patients. Second, there is a lack of sophisticated investigational tools in routine clinical settings to help stratify patients accurately along the amyloid versus tau pathology axis. While plasma biomarkers are emerging as valuable tools, they are not yet widely adopted or reimbursed, and positron emission tomography (PET) or cerebrospinal fluid (CSF) analyses remain cost-prohibitive or inaccessible. This makes precise phenotyping difficult, thereby limiting appropriate trial assignments and resulting in referral drop-offs, higher costs, and identification of only a fraction of eligible patients. Third, the variability in cognitive testing, both in administration and patient performance, makes it challenging to predict with confidence whether a patient will meet cognitive thresholds for trial inclusion. Factors such as education, cultural background,

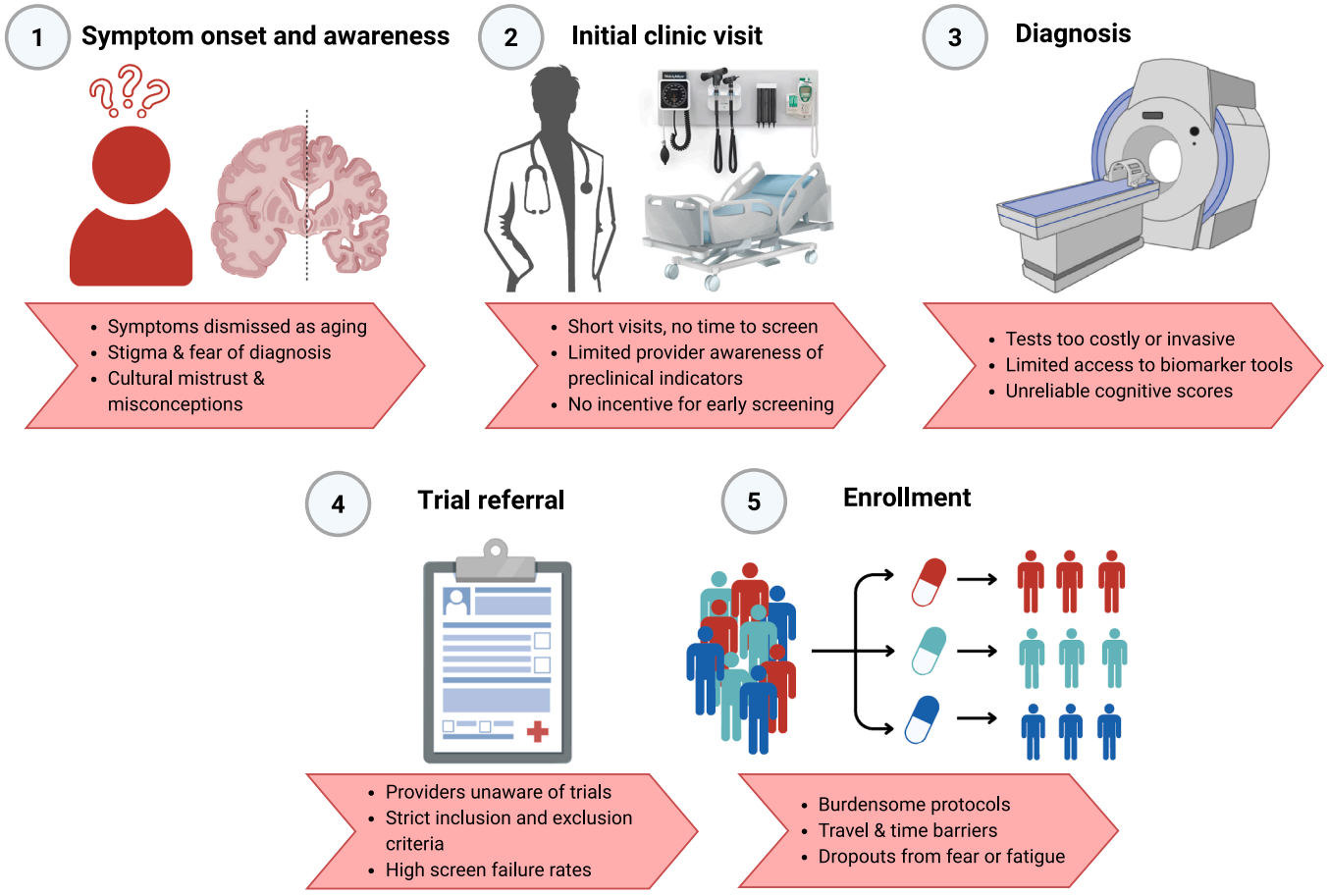

Fig. 1. Challenges in the Alzheimer's disease patient journey to clinical trial enrollment. This infographic outlines the progression of Alzheimer's disease (AD) patients from symptom onset to trial enrollment, highlighting barriers at each step. Symptom onset and awareness involve dismissing symptoms as aging, stigma/fear of diagnosis, and cultural mistrust. Initial clinic visit faces short durations without screening time, low provider awareness of preclinical indicators, and no early screening incentives. Diagnosis encounters costly/invasive tests, limited biomarker access, and unreliable cognitive scores. Trial referral includes provider unawareness of trials, strict eligibility criteria, and high screen failures. Enrollment is impeded by burdensome protocols, travel/time barriers, and dropouts from fear or fatigue.

Table 1
Glossary of technical terms.

Application programming interface (API)	A set of rules and communication standards that allow different software systems to communicate and share data.
Clinical decision support (CDS) system	A technology system that provides healthcare professionals with evidence-based knowledge and patient-specific recommendations to enhance clinical decisions and improve patient care.
Data fragmentation	The scattering of data across multiple disconnected systems, applications, and locations, which makes it difficult to manage, analyze, and integrate data effectively.
Data infrastructure	Systems and resources that enable the collection, storage, management, integration, processing, and accessibility of data. This includes hardware, software, standards, and governance policies.
Differential privacy	A method of adding carefully calibrated noise to the output of an algorithm to protect the privacy of individual data points, ensuring that the presence or absence of any single person's data does not significantly affect the algorithm.
Fairness-constrained modeling	Integration of mathematical fairness criteria directly into the training process of an AI model.
Federated learning	Computational approach where models are trained in a decentralized way without sharing source data.
Fast Healthcare Interoperability Resources (FHIR)	A standard for exchanging electronic health information that makes it easier for different healthcare systems to share data securely and efficiently.
Generalizability	A result is generalizable if it applies to both the sample under study and the population it is from, or similar populations.
Generative AI	Collection of AI techniques capable of creating new content, such as text or images, by learning patterns from existing data.
Ontology	A structured framework that organizes knowledge into categories and defines relationships between them. In AI, it helps machines interpret and use complex information consistently.
Regex	Regex, short for "regular expression," is a sequence of characters that defines a search pattern.
Retrieval grounding	Connecting a large language model to a verifiable, external knowledge base to generate more accurate, relevant, and trustworthy responses.
Scalability	The ability of a system to handle increased workload efficiently, without prohibitive cost or waiting times.
Structure-code crosschecks	Structure-code crosschecks verify that a program's code matches its intended architectural design to ensure consistency and reduce errors.

testing environment, and examiner differences can significantly impact results, often contributing to high screen-failure rates.

Clinical trial ecosystem barriers. Most physicians remain unaware of ongoing AD trials or lack the detailed knowledge to refer patients effectively [17,18], treating trials as an afterthought rather than a viable care option. In the memory clinic, this translates to ad hoc referrals, with neurologists relying on sporadic emails from sponsors rather than integrated systems, resulting in missed matches for a large fraction of suitable patients. Stringent inclusion and exclusion criteria often demanding biomarker positivity (e.g., amyloid or tau confirmation) and specific cognitive thresholds, exacerbate issues, leading to high screen-failure rates. Exclusion criteria frequently outnumber inclusions, such as barring patients with comorbidities common in older adults, compounding recruitment challenges. Even post-enrollment, participants may withdraw due to burdensome protocols (e.g., frequent visits or invasive monitoring), perceived risks, or logistical hurdles like transportation, further underpowering studies and straining clinic resources.

Data and operational barriers. Data fragmentation and operational inefficiencies pose additional hurdles in the clinic environment. Patient information is often siloed in disparate, unstructured formats across EHR systems, making it labor-intensive to identify candidates efficiently. While standards like Health Level Seven (HL7) and Fast Healthcare Interoperability Resources (FHIR) exist to facilitate integration, inconsistent adoption and varying versions hinder seamless data harmonization, as evidenced in efforts to align sources like the National Alzheimer's Coordinating Center (NACC) or the Alzheimer's Disease Neuroimaging Initiative (ADNI). Current practices rely on manual EHR reviews, which are time-consuming and error-prone; a single neurologist might spend hours weekly scanning records yet overlook key details. Furthermore, AD trials disproportionately enroll participants who are more educated, engaged, and research-positive, leading to underrepresentation of racial and ethnic minorities and underserved populations [19–22]. In the memory clinic, this bias means trials may not capture the full spectrum of AD, with minorities comprising only a small fraction of participants despite higher disease prevalence, limiting generalizability and perpetuating health disparities. Given these inefficiencies, there is a need for automated, scalable solutions to match patients against complex criteria in real-time.

3. Role of AI in enhancing trial readiness

Building upon the barriers outlined in the memory clinic context, AI emerges as a useful tool to enhance trial readiness by directly addressing these challenges through automation, precision, and scalability (Fig. 2). Numerous AI-based solutions for clinical trial recruitment are available and have shown promise in enhancing efficiency, yet the primary hurdles remain their adoption and integration into clinical workflows, influenced by factors such as implementation barriers, lack of uniform standards, and the need for clinician literacy [4,23,24]. In our representative memory clinic, serving approximately 500-1000 patients with cognitive concerns annually, such tools can transform recruitment from a manual, inefficient process yielding only 10-20 enrollments per year to a streamlined system identifying a much larger set of viable candidates, reducing timelines and costs. Below is a phased vision tailored to the clinic, leveraging tools like LLMs and predictive analytics:

Community-level AI for awareness building and pre-screening.

To expand the patient funnel and combat stigma, the clinic could deploy accessible AI tools on its website or app, such as LLM-based chatbots (e.g., built on open-source frameworks like Hugging Face models or commercial platforms) [25–29].

1. Patients or families input symptoms via text or voice; the AI analyzes responses to provide personalized education (e.g., "`The frequent forgetfulness you described may indicate early cognitive concerns rather than just typical aging. Here's a comparison based on common patterns. Disclaimer: This is not a diagnosis. Consult a doctor.`").
2. Integrated LLMs scan local social media or forums (with anonymized data) to detect misconceptions, enabling targeted outreach campaigns (e.g., emails or ads to high-risk demographics like those over 65 in underserved areas). To mitigate risks of LLMs generating content misaligned with clinical intentions, we recommend incorporating human oversight, such as clinician review of LLM outputs, to ensure alignment and accuracy.
3. Anonymized pre-screening via digital biomarkers such as speech analysis apps where users read prompts, and AI detects hesitations or patterns indicative of decline using models trained on neuropsychological data, stratifies risk levels (low/medium/high) while employing federated learning and differential privacy to safeguard identities. High-risk users receive gentle nudges (e.g., "`Schedule a visit for further evaluation.`") with links to clinic appointments or trial info.

Regarding feasibility and timing, while LLMs are mature and widely available with proven applications in healthcare, their immediate

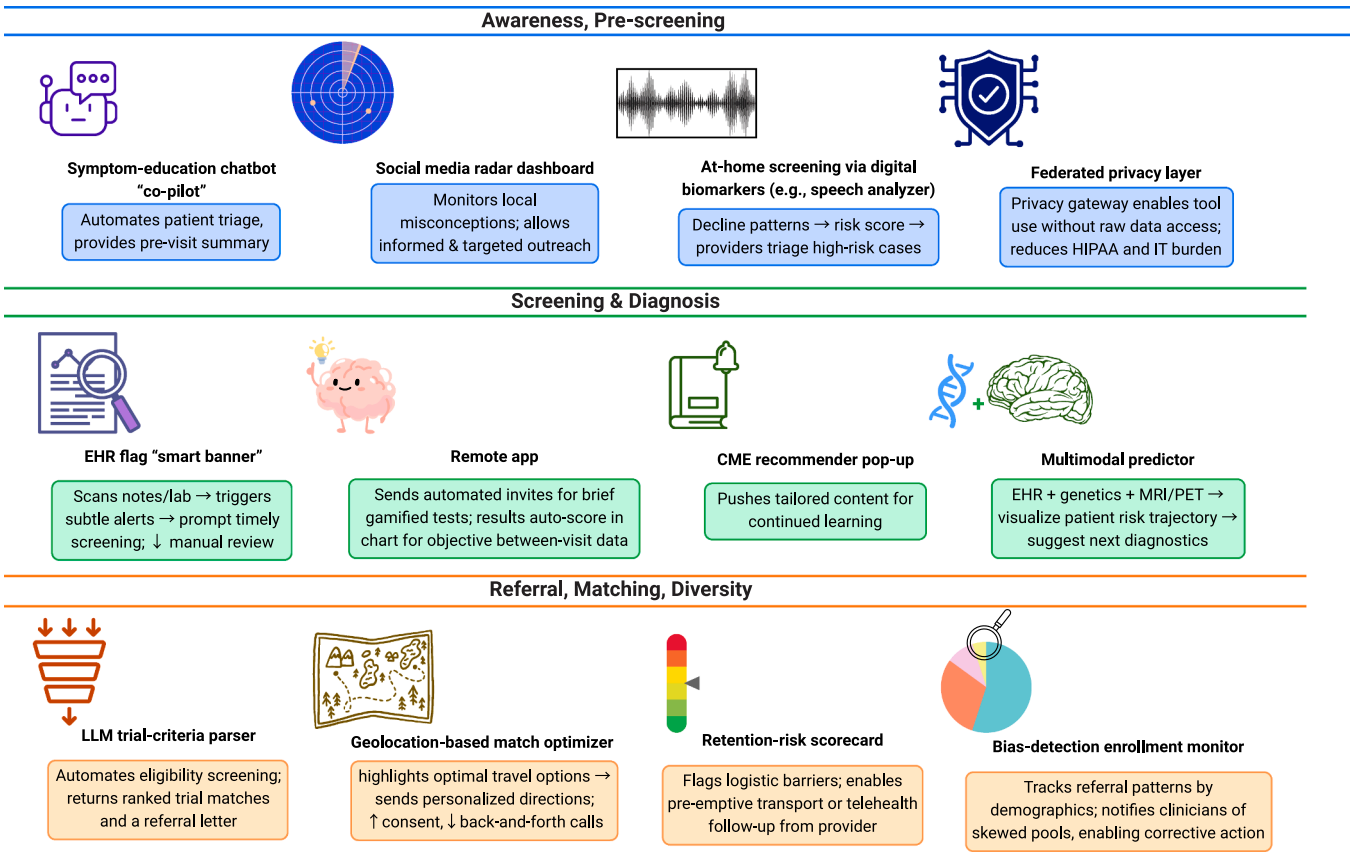

Fig. 2. AI-driven solutions to overcome barriers in the Alzheimer's disease patient journey for clinical trials. This diagram showcases AI-powered tools across three stages to streamline the Alzheimer's disease (AD) patient journey toward clinical trials. In "Awareness, Pre-screening," it features a symptom-education chatbot for triage and summaries, a social media dashboard for targeted outreach, an at-home biomarker screening tool for risk detection, and a privacy layer for secure data handling. The "Screening & Diagnosis" section includes an EHR alert banner for subtle detections, a remote gamified testing app for objective data, a CME recommender for provider education, and a multimodal predictor for risk visualization using EHR, genetics, and imaging. Finally, "Referral, Matching, Diversity" highlights an AI parser for trial eligibility and referrals, a geolocation optimizer for travel and consent, a retention-risk scorer for proactive support, and a bias monitor to ensure diverse enrollment.

implementation for chatbots and text-based pre-screening requires caution, particularly for vulnerable populations such as older adults with cognitive impairment, due to concerns including biases, privacy risks, and technical limitations in handling interactions with this group [30]. Speech-derived acoustic and linguistic markers, while promising and supported by ongoing research [31–38], are at a moderate maturity level, requiring additional clinical validation, and could be feasibly integrated as datasets expand and standardization improves [39]. Social media mining faces greater variability in maturity due to privacy constraints, data quality issues, and ethical challenges in health research, with effective deployment potentially taking a few years as tools, regulations, and frameworks advance [40–42].

Healthcare system-level AI for screening and workflow optimization.

Within the clinic, AI integrates into EHR systems (e.g., via APIs from vendors like Epic or Cerner, enhanced with tools from IQVIA) to alleviate resource strains and diagnostic gaps. Rather than deploying separate bots for each of the ICD-coded diseases, a common foundational chatbot with modular, disease-specific extensions (e.g., for AD-focused pre-screening) can provide efficient, scalable support across conditions.

1. During intake or visits, clinical decision support (CDS) tools use LLMs to scan unstructured notes, labs, and medication histories, flagging at-risk patients in real-time (e.g., "`Word repetition in notes suggests MCI; recommend MoCA screening`") [43].
2. Virtual assistants or chatbots pre-collect data (e.g., administering remote cognitive tests like digital memory assessments) and educate patients [44,45], freeing clinicians a few hours weekly for direct care.
3. To address diagnostic shortages, AI analyzes low-cost digital biomarkers (e.g., typing patterns from app-based tasks or eye movements via webcam) for non-invasive risk scores [46–48], prioritizing patients for advanced tests and reducing unnecessary procedures.
4. Predictive models integrate diverse data types (EHRs, genetics, neuroimaging) to forecast progression, tailoring physician education via medically focused LLMs [25], or personalized continuing medical education modules (e.g., "`Based on your query history, review this update on preclinical AD detection`"). This not only motivates screening by linking to emerging treatments but also counters perceived futility.

Clinical trial referral and matching.

For seamless referrals, AI platforms embed into the clinic's EHR for end-to-end matching.

- Post-screening, the system extracts patient data (age, biomarkers, medication use, neuroimaging reports, cognition scores) and uses LLMs to parse trial criteria from databases like ClinicalTrials.gov.
- It generates matches with probabilistic scores (e.g., "`92% eligibility for AMARANTH trial [NCT identifier], biomarker-positive MCI cohort, 15 miles away`").
- Real-time notifications alert physicians during visits, with LLM assistants answering queries (e.g., "`What are exclusion details?`") 24/7.

- Geolocation and predictive analytics prioritize local trials, forecast retention risks (e.g., based on travel distance or comorbidities), and suggest outreach to sponsors for clinics with high eligible pools. To enhance diversity, bias-detection algorithms flag underrepresented groups (e.g., by zip code or ethnicity) and recommend targeted pre-screening campaigns. Case studies, including AI-stratified trials [49], demonstrated reductions in recruitment time, lower screen failures, and cost savings, while improving inclusivity.

When evaluating LLMs versus other AI approaches in healthcare, they perform best for language-focused tasks [50–52]. These include developing patient- and clinician-facing chatbots, where retrieval grounding and rule-based guardrails enhance safety. LLMs also excel at converting unstructured text, such as EHR notes, into structured fields through parsing and entity extraction, with validation using rule-based dictionaries, regex, and structured-code crosschecks. Additionally, LLMs aid in interpreting narrative eligibility criteria for normalization, often paired with rules and ontologies for formalization. However, LLMs have limitations in areas like calibrated risk prediction [53,54], fairness-constrained modeling, and regulated decision support, where probabilistic and auditable models are preferred. Instead, traditional ML is superior for tabular risk scoring, reproducible cohort definitions, and deterministic pre-screening, with optional LLM assistance for filling missing text values [55–57]. Traditional ML also manages compliance-critical workflows effectively and excels in bias detection and monitoring, limiting LLMs to textual explanations. For clinical decision support prompts, combining LLM summarization with rules and validated models enforces thresholds. Multi-source, diverse data pipelines can integrate LLM-based text extraction with non-LLM models to improve prediction and question-answering, incorporating rule checks as guardrails for reliability and compliance [58].

4. Technical and clinical considerations for implementation

Implementing an AI solution requires careful consideration of technical feasibility, clinical integration, and human oversight to ensure they augment rather than supplant professional judgment. While AI tools like LLMs and predictive models offer probabilistic outputs (e.g., eligibility scores or risk predictions) to boost efficiency, their deployment must prioritize seamless workflow fit, data security, and validation to avoid errors or biases that could undermine trust or outcomes. For instance, in a clinic handling 500-1000 cognitive cases yearly, starting with pilot integrations, such as embedding AI tools in EHRs, can yield faster identifications, but only if addressed through structured steps. A recent study showed that an AI-powered system coined as Automated Clinical Trial Eligibility Screener (ACTES) reduced patient screening time by 34 % compared to manual processes, while improving the numbers of subjects screened, approached, and enrolled by 14.7 %, 11.1 %, and 11.1 %, respectively [59]. These efficiencies not only expedite identifications but also alleviate clinician burden in resource-constrained memory clinics, where manual processes often yield low enrollment rates.

From a technical standpoint, successful AI implementation in memory clinics requires a foundational assessment of infrastructure readiness. Many clinics operate with legacy EHR systems that are incompatible with modern AI tools, necessitating a shift toward interoperable standards such as FHIR to enable standardized data exchange. This includes converting unstructured clinical notes into structured formats (i.e., JSON), using cloud-based platforms, though such adoption can involve costs (e.g., storage fees of $0.25-0.50 per GB per month), and accessibility challenges for smaller clinics, including integration complexities and the need for specialized IT expertise. For a broad audience including smaller clinics with limited AD expertise, resource pooling across multiple sites (e.g., via medical center consortia) can distribute costs and expertise. Beyond EHR standardization, AD-specific tuning may require an additional 3-6 months, involving fine-tuning models on AD-relevant datasets (e.g., for biomarker integration), customizing APIs for databases like ClinicalTrials.gov, and conducting iterative pilot tests to align with evolving regulations. Establishing such interoperability allows AI models to process diverse data types including EHRs, imaging, and biomarkers, without fragmentation. A typical implementation roadmap begins with auditing existing systems for API compatibility and, where necessary, using middleware or open-source NLP tools (e.g., spaCy) to bridge integration gaps. Models are then trained or fine-tuned on de-identified clinic data, often employing federated learning approaches to preserve patient privacy while ensuring robustness across demographic variations. Real-time inference can be supported through edge computing e.g., using on-site servers to analyze speech biomarkers during clinic visits, while more computationally intensive tasks, such as trial matching, can leverage cloud resources. Technical challenges, such as incomplete or noisy data, can be addressed by ensemble approaches that combine LLMs for text parsing with computer vision for imaging analysis, achieving high accuracy in eligibility assessments in pilot settings. Continuous model refinement ensures adaptability to evolving trial criteria, and scalability testing (e.g., simulating high query volumes) is essential to ensure operational reliability in busy clinical environments.

For AI to be effective in memory clinics, it must integrate seamlessly into clinical workflows, enhancing patient-centered care. This requires tailoring tools to provider needs. The first step involves conducting user training sessions (e.g., workshops) focused on interpreting AI outputs such as "`75% MCI risk, recommend trial NCT456,`" with an emphasis on the probabilistic and supportive nature of these outputs to avoid over-reliance. The next step entails piloting the system on a subset of patients, validating AI recommendations against manual review, and tracking key metrics such as false positives, which can be reduced through iterative tuning, along with clinician satisfaction. The subsequent step integrates feedback loops in which clinicians can override or annotate AI suggestions, feeding into model refinement for continuous improvement. A major concern is bias amplification. For example, models trained on non-diverse datasets may under-identify eligible patients from minority groups. This can be addressed through dataset audits and the application of debiasing techniques. Ethical considerations include obtaining informed consent (e.g., "`This tool analyzes your data to suggest relevant trials`") and monitoring impacts on clinical workflow, where initial increases in validation time are often offset by long-term gains, such as a reduction in administrative burden.

5. Data standardization and interoperability

Effective AI deployment for AD trial recruitment hinges on overcoming data fragmentation, as models based on LLMs require structured, consistent inputs to accurately parse eligibility from sources such as EHRs, lab results, and demographics. However, the healthcare data landscape remains plagued by inconsistencies, posing barriers to AI systems that must integrate heterogeneous information for patient matching. For a mid-sized clinic managing a few hundred cognitive cases annually, this means siloed, unstructured records lead to inefficient manual harmonization, delaying identifications and inflating errors in trial referrals. Below, we outline practical data challenges in this setting and a vision for standardization, leveraging tools like FHIR and privacy-preserving techniques to enable AI-driven efficiency.

Data issues in the clinic amplify recruitment hurdles, mirroring broader AD research obstacles. For instance, patient data scatters across incompatible systems, e.g., legacy EHRs with free-text notes varying in syntax, alongside disparate lab or imaging files, making it difficult to aggregate for AI analysis, often requiring hours of manual review per case and overlooking a good fraction of eligibility criteria. In the context of AD, this is exacerbated by diverse data inputs like longitudinal narratives on cognitive decline, leading to misinterpretations in assessments. Moreover, inconsistent adoption of standards (e.g., multiple HL7 versions) hinders data exchange with external trial databases or collaborators, such as NACC datasets not natively FHIR-formatted, causing

delays in matching patients to biomarker-positive trials and contributing to referral inefficiencies. Strict regulations limit data sharing for AI training, with siloed records restricting access to high-quality datasets; techniques like annotation add complexity, while noisy or biased data (e.g., underrepresenting minorities) reduces model accuracy in diverse clinic populations. EHRs blend structured data with clinical language, challenging LLMs to process lengthy documents or eligibility criteria in natural language, resulting in oversight of subtle AD indicators and prolonging recruitment by weeks. These challenges culminate in underpowered trials, with clinics like ours contributing fewer participants due to data silos, underscoring the need for standardized pipelines.

To transform fragmented data into AI-powered assets, the clinic can implement interoperability frameworks. Here's a practical vision:

- Begin by auditing EHRs for fragmentation, then adopt FHIR as a core standard to convert heterogeneous sources into unified formats (e.g., transforming free-text notes and labs into FHIR resources via APIs). Step 1: Use cloud platforms to ingest and normalize data from multiple systems, creating a centralized repository where AD-specific elements (e.g., cognitive scores, biomarkers) are structured for AI querying. Step 2: Employ LLMs for automated harmonization, parsing unstructured eligibility criteria into operationalizable rules, reducing manual effort and enabling real-time trial matching.
- Integrate legacy and modern systems through FHIR-compliant pipelines (e.g., JSON conversions for inputs like NACC data). Step 1: Implement hybrid integrations to bridge HL7 gaps, allowing seamless exchange with trial sponsors or registries. Step 2: Use AI to flag inconsistencies (e.g., semantic variations in clinical notes), automating corrections and improving accuracy for analyses like combining EHRs with neuroimaging. This fosters collaborative research and enhances clinic contributions to diverse trials.
- To address data silos and confidentiality, apply federated learning and differential privacy for model training without centralizing sensitive information. Step 1: Train AI on distributed datasets (e.g., across clinic sites) using federated approaches, adding noise via differential privacy to protect identities while maintaining utility for AD detection. Step 2: Validate with de-identified clinic data, ensuring compliance with HIPAA/GDPR and reducing bias through diverse annotations.
- Leverage advanced AI architectures for complex data. Step 1: Use LLMs to process complex texts and integrate with structured elements, e.g., extracting AD risk from narrative histories. Step 2: Invest in quality datasets via collaborations, fine-tuning models to handle clinic-specific variations and cutting eligibility oversights [49].

6. Ethical and regulatory considerations

Integrating AI into AD trial recruitment workflows such as using LLMs for patient matching or digital biomarkers for pre-screening, introduces ethical and regulatory challenges that must be navigated to protect patient well-being, ensure equity, and sustain trust in healthcare. A robust framework is essential for responsible deployment, balancing innovation with safeguards like informed consent and bias mitigation. For a mid-sized clinic handling 500-1000 cognitive cases annually, these issues can manifest in daily operations, potentially eroding patient participation if unaddressed, while compliance with regulations like HIPAA and GDPR adds operational layers. Below, we outline practical challenges in this clinic context and a step-by-step vision for ethical integration, drawing on privacy-preserving techniques and explainable AI (XAI) to foster trust and inclusivity.

Ethical and regulatory hurdles in the clinic significantly amplify recruitment barriers, contributing to hesitancy among both patients and providers. The collection of sensitive data such as genomics, EHRs, and behavioral metrics, for use in AI tools raises privacy concerns under HIPAA and GDPR. Beyond HIPAA and GDPR, evolving AI-specific regulatory frameworks, such as the FDA's guidance on AI/ML-based software as a medical device (SaMD) [60–63], and the European Union AI Act [64–67], must be integrated; these classify AI tools by risk (e.g., Class I minimal risk for low-stakes chatbots, which may not require rigorous RCTs, but still necessitate local validation to mitigate risks like hallucinations) and mandate requirements for transparency, clinical validation, robustness, and ongoing post-market monitoring to ensure safety and efficacy. As discussed by Shuren et al., for MCI/AD [68], SaMD like digital therapeutics are regulated via a risk-based approach, with no clearances yet for AD treatment, emphasizing breakthrough programs and benefit-risk assessments in diverse populations. Health systems should implement safeguards such as rule-based constraints, human oversight for outputs, and pilot testing to prevent misinformation, particularly given the potential for patient over-reliance with serious consequences.

Patients, particularly those from certain subgroups, are often less trusting of AI systems, which can deter participation, especially since retracting data once incorporated into AI models is difficult [69]. Furthermore, the "black box" nature of many AI algorithms obscures decision-making, making it challenging for clinicians to explain why a patient was flagged for a trial. This undermines informed consent and fosters "therapeutic misconception [70]," where patients overestimate the certainty of AI predictions especially in preclinical AD assessments, posing autonomy risks for individuals, particularly those with lower health literacy [71]. Over-reliance on AI may also erode trust in clinicians, with some patients perceiving them as less competent, potentially leading to "de-skilling" and a diminished emphasis on human skills like empathy [72–75]. In some cases, this can increase clinician workload for validating AI outputs, negating promised efficiencies and contributing higher participant withdrawal rates. Given that only a few health systems have the capacity for ongoing monitoring, responsibility should involve multidisciplinary teams or external partners, potentially utilizing a CMS Registry to track safety, performance, and risks post-installation, ensuring neurologists are not solely burdened. Finally, AI-generated pre-symptomatic predictions echo ethical dilemmas seen in Huntington's disease testing [76,77], where disclosing risk in the absence of treatments can provoke anxiety or stigma. This not only threatens patients' right not to know but also raises the specter of discrimination in insurability or employment, deterring engagement of at-risk individuals who fear unequal access or social repercussions. Additionally, generative AI's tendency to fabricate human-like experiences (e.g., claiming personal anecdotes) poses deception risks [78], especially for vulnerable AD patients; safeguards such as disclaimers, prompt restrictions, and family oversight are essential to prevent exploitation [79].

These challenges, if unaddressed, risk perpetuating disparities and regulatory violations, underscoring the need for proactive, ethics-driven frameworks. Misaligned financial incentives must be countered by independent vetting to prevent recruitment into potentially unsafe trials; chatbots should transparently discuss high failure rates and historical risks, programmed by multidisciplinary teams including patient advocates and lawyers for balance. Clinics can mitigate these issues by adopting a structured approach that emphasizes AI as a tool for augmentation anchored in human oversight. First, a secure data ecosystem should be established using techniques like federated learning and differential privacy to enable AI training without transmitting identifiable data. This includes auditing data flows for HIPAA/GDPR compliance, encrypting digital biomarkers, and collaborating on de-identified datasets, practices that can reduce breach risks and foster trust via transparent, opt-in data policies. Second, integrating explainable AI ensures that clinicians can communicate how and why decisions are made, for instance, using saliency maps to show why certain speech features suggest cognitive impairment. In parallel, patient consent must be redesigned with clarity and tailored literacy, supported by clinician training modules that reduce therapeutic misconceptions and align with consent standards for analogous conditions like HD. Consent should occur at multiple steps: for non-standard assessments (e.g., digital

biomarkers or speech analysis) that may inform models beyond immediate care; an explicit opt-in for trial eligibility screening, with disclosures on procedures specific to recruitment to avoid therapeutic misconception; and a separate consent for aggregating de-identified data with others for research purposes. Third, AI should be explicitly framed as an assistive tool that preserves human strengths like empathy and judgment. Hybrid workflows should allow clinicians to override AI in some cases, with regular staff feedback and soft-skills training to counter overreliance, strategies that may reduce patient withdrawals. Finally, clinics must adapt protocols for preclinical predictions by offering patients the option to decline results, ensuring access to psychosocial support, and partnering with ethicists to protect against stigma and discrimination.

7. Future directions

AI's role in AD trial recruitment promises significant advancements, but realizing this requires strategic investments in technology, policy, and partnerships to scale beyond current limitations. For our mid-sized clinic, future tools could evolve from basic matching to proactive, personalized systems that predict trial success and address diversity gaps, potentially doubling enrollments while halving timelines. Below, we outline emerging challenges and a step-by-step vision for future AI integration, emphasizing multimodal enhancements, regulatory evolution, and collaborative ecosystems to drive inclusive AD therapeutic progress.

As AI matures, new hurdles will arise in clinic settings, building on existing barriers. For example, current models may struggle with real-time multimodal data (e.g., integrating live speech analysis with EHRs), risking biases in underrepresented groups and reducing accuracy as patient volumes grow. In diverse clinics, this could perpetuate under-enrollment of minorities, limiting trial generalizability. Evolving guidelines (e.g., FDA's AI frameworks) may lag innovations like generative AI, complicating validation and increasing compliance burdens without clear sandboxes for testing. Without longitudinal data on AI's effects (e.g., on patient trust or outcomes), clinics risk unintended harms like increased anxiety from predictive tools, potentially raising withdrawals. Siloed advancements hinder global sharing, with clinics missing out on large-scale datasets, slowing progress in AD-specific AI.

To overcome these challenges, clinics can adopt phased, stakeholder-engaged innovations that support scalable and ethical AI integration. Advanced models that fuse LLMs, computer vision, and sensor data can enable precise, real-time participant matching by analyzing modalities such as speech, gait, and EHRs. Embedding bias-detection algorithms trained on diverse datasets helps correct underrepresentation and has been shown to improve minority enrollment [80]. Edge-AI devices, such as wearables for continuous biomarker monitoring, allow proactive risk flagging during clinical visits [81–84]. Participation in regulatory sandboxes (e.g., FDA or EMA) provides a safe environment to test AI protocols, while generative AI enables virtual trial simulations through synthetic patient profiles with ethical oversight to minimize risks like hallucination. Longitudinal studies tracking AI's clinical and psychosocial effects (e.g., annual patient trust surveys) inform iterative refinements. Ongoing input from ethicists supports responsible tool development, while adaptive clinician training ensures AI augments empathy-driven care, potentially increasing trial retention. Engagement in data-sharing consortia such as ADNI, NACC or the Critical Path Institute helps standardize tools and access high-quality datasets. Community-focused applications, including VR tools to destigmatize AD, can extend outreach to underserved populations, and clinic-led policy advocacy for inclusive trial incentives may accelerate global progress through unified benchmarks.

8. Conclusion

The memory clinic scenario illustrates the challenges in AD clinical trial recruitment, from community stigma and resource constraints to data silos and ethical dilemmas, that collectively hinder therapeutic advancement, often resulting in a small number of enrollments annually despite evaluating several potential participants. AI offers a practical solution by automating identification, enhancing matching precision, and promoting inclusivity through tools like LLMs integrated into everyday workflows. By addressing barriers step-by-step, from community pre-screening chatbots that boost early awareness to EHR-embedded CDS systems reducing screen failures and interoperable platforms ensuring data readiness, AI can accelerate enrollment, cut costs and ensure diverse representation, ultimately alleviating the global AD burden affecting millions. Ethical deployment, with privacy safeguards and human oversight, is paramount to building trust, while future directions in multimodal AI and collaborations promise even greater efficiencies. Through coordinated adoption in clinics worldwide, AI-augmented strategies can pave the way for faster breakthroughs in AD treatments, turning persistent obstacles into broader access to timely, inclusive AD therapies.

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Declaration of interests

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: V. B.K. is a co-founder and equity holder of deepPath Inc., and Cognimark, Inc. He also serves on the scientific advisory board of Altoida Inc. The remaining authors declare no competing interests.

References

[1] Bradford A, Kunik ME, Schulz P, Williams SP, Singh H. Missed and delayed diagnosis of dementia in primary care. Alzheimer Dis Assoc Disord. 2009;23:306–14.
[2] Langbaum JB, Zissimopoulos J, Au R, Bose N, Edgar CJ, Ehrenberg E, Fillit H, Hill CV, Hughes L, Irizarry M, Kremen S, Lakdawalla D, Lynn N, Malzbender K, Maruyama T, Massett HA, Patel D, Peneva D, Reiman EM, Romero K, Routledge C, Weiner MW, Weninger S, Aisen PS. Recommendations to address key recruitment challenges of Alzheimer's disease clinical trials. Alzheimer's Dement. 2022;19:696–707.
[3] Watson JL, Ryan L, Silverberg N, Cahan V, Bernard MA. Obstacles and opportunities In Alzheimer's clinical trial recruitment. Health Aff 2014;33:574–9.
[4] Lu X, Yang C, Liang L, Hu G, Zhong Z, Jiang Z. Artificial intelligence for optimizing recruitment and retention in clinical trials: a scoping review. J Am Med Inform Assoc. 2024;31:2749–59.
[5] Beattie J, Neufeld S, Yang D, Chukwuma C, Gul A, Desai N, Jiang S, Dohopolski M. Utilizing large language models for enhanced clinical trial matching: a study on automation in patient screening. Cureus 2024.
[6] Harrer S, Shah P, Antony B, Hu J. Artificial intelligence for clinical trial design. Trends Pharmacol Sci 2019;40:577–91.
[7] Lu X, Chen M, Lu Z, Shi X, Liang L. Artificial intelligence tools for optimising recruitment and retention in clinical trials: a scoping review protocol. BMJ Open 2024:14.
[8] Grill JD, Karlawish J. Addressing the challenges to successful recruitment and retention in Alzheimer's disease clinical trials. Alzheimers Res Ther 2010;2.
[9] Arenaza-Urquijo EM, Vemuri P. Resistance vs resilience to Alzheimer disease. Neurology 2018;90:695–703.
[10] Herrmann LK, Welter E, Leverenz J, Lerner AJ, Udelson N, Kanetsky C, Sajatovic M. A systematic review of dementia-related stigma research: can we move the stigma dial? Am J Geriatr Psychiatry 2018;26:316–31.
[11] Werner P, Heinik J. Stigma by association and Alzheimer's disease. Aging Ment Health 2008;12:92–9.
[12] Rosin ER, Blasco D, Pilozzi AR, Yang LH, Huang X. A narrative review of Alzheimer's Disease stigma. J Alzheimer's Dis. 2020;78:515–28.
[13] Scharff DP, Mathews KJ, Jackson P, Hoffsuemmer J, Martin E, Edwards D. More than Tuskegee: understanding mistrust about research participation. J Health Care Poor Underserved 2010;21:879–97.

[14] Hamel LM, Penner LA, Albrecht TL, Heath E, Gwede CK, Eggly S. Barriers to clinical trial enrollment in racial and Ethnic Minority patients with cancer. Cancer Control 2016;23:327–37.
[15] Wollney EN, Armstrong MJ, Bedenfield N, Rosselli M, Curiel-Cid RE, Kitaigorodsky M, Levy X, Bylund CL. Barriers and best practices in disclosing a dementia diagnosis: a clinician interview study. Health v Insights 2022:15.
[16] Okpalauwaekwe U, Franks H, Kuo Y-F, Raji MA, Passy E, Tzeng H-M. What helps or hinders annual wellness visits for detection and management of cognitive impairment among older adults? A scoping review guided by the consolidated framework for implementation research. Nurs Rep 2025:15.
[17] Galvin JE, Meuser TM, Boise L, Connell CM. Predictors of physician referral for patient recruitment to Alzheimer disease clinical trials. Alzheimer Dis Assoc Disord. 2009;23:352–6.
[18] Park L, Kouhanim C, Lee S, Mendoza Z, Patrick K, Gertsik L, Aguilar C, Gullaba D, Semenova S, Jhee S. Implementing a memory Clinic model to facilitate recruitment into early phase clinical trials for mild cognitive impairment and Alzheimer's disease. J Prev Alzheimers Dis 2019;6:135–8.
[19] Shaw AR, Perales-Puchalt J, Moore T, Weatherspoon P, Robinson M, Hill CV, Vidoni ED. Recruitment of older African Americans in Alzheimer's Disease clinical trials using a community education approach. J Prev Alzheimers Dis 2022;9:672–8.
[20] Dabiri S, Raman R, Grooms J, Molina-Henry D. Examining the role of community engagement in enhancing the participation of racial and ethnic minoritized communities in Alzheimer's Disease clinical trials; a rapid review. J Prev Alzheimers Dis 2024;11:1647–72.
[21] Franzen S, Smith JE, van den Berg E, Rivera Mindt M, van Bruchem-Visser RL, Abner EL, Schneider LS, Prins ND, Babulal GM, Papma JM. Diversity in Alzheimer's disease drug trials: the importance of eligibility criteria. Alzheimer's Dement. 2021;18:810–23.
[22] Raman R, Aisen P, Carillo MC, Detke M, Grill JD, Okonkwo OC, Rivera-Mindt M, Sabbagh M, Vellas B, Weiner M, Sperling R. Tackling a major deficiency of diversity in Alzheimer's disease therapeutic trials: an CTAD Task Force report. J Prev Alzheimers Dis 2022;9:388–92.
[23] Wenderott K, Krups J, Weigl M, Wooldridge AR. Facilitators and barriers to implementing AI in routine medical imaging: systematic review and qualitative analysis. J Med Internet Res 2025:27.
[24] Hu Z, Hu R, Yau O, Teng M, Wang P, Hu G, Singla R. Tempering expectations on the medical artificial intelligence revolution: the medical trainee viewpoint. JMIR Med Inf. 2022:10.
[25] Jia S, Bit S, Searls E, Lauber MV, Fan P, Wang WM, Claus LA, Jasodanand VH, Veerapaneni D, Au R, Kolachalama VB. PodGPT: an audio-augmented large language model for research and education. NPJ Biomed Innov 2025;2:26.
[26] Nievas M, Basu A, Wang Y, Singh H. Distilling large language models for matching patients to clinical trials. J Am Med Inf Assoc 2024;31:1953–63.
[27] Jin Q, Wang Z, Floudas CS, Chen F, Gong C, Bracken-Clarke D, Xue E, Yang Y, Sun J, Lu Z. Matching patients to clinical trials with large language models. Nat Commun 2024;15:9074.
[28] Rybinski M, Kusa W, Karimi S, Hanbury A. Learning to match patients to clinical trials using large language models. J Biomed Inf. 2024:159.
[29] Chen H, Li X, He X, Chen A, McGill J, Webber EC, Xu H, Liu M, Bian J. Enhancing patient-trial matching with large language models: a scoping review of emerging applications and approaches. JCO Clin Cancer Inform. 2025.
[30] Abadir PM, Battle A, Walston JD, Chellappa R, Lipsitz LA. Enhancing care for older adults and dementia patients with large language models: proceedings of the National Institute on Aging—Artificial Intelligence & Technology Collaboratory for Aging Research Symposium. J Gerontol A: Biol Sci Med Sci. 2024:79.
[31] Karjadi C, Xue C, Cordella C, Kiran S, Paschalidis IC, Au R, Kolachalama VB. Fusion of low-level descriptors of digital voice recordings for dementia assessment. J Alzheimers Dis 2023;96:507–14.
[32] Xue C, Karjadi C, Paschalidis IC, Au R, Kolachalama VB. Detection of dementia on voice recordings using deep learning: a Framingham Heart Study. Alzheimers Res Ther 2021:13.
[33] Amini S, Hao B, Zhang L, Song M, Gupta A, Karjadi C, Kolachalama VB, Au R, Paschalidis IC. Automated detection of mild cognitive impairment and dementia from voice recordings: a natural language processing approach. Alzheimer's Dement. 2022;19:946–55.
[34] Tavabi N, Stück D, Signorini A, Karjadi C, Al Hanai T, Sandoval M, Lemke C, Glass J, Hardy S, Lavallee M, Wasserman B, Ang TFA, Nowak CM, Kainkaryam R, Foschini L, Au R. Cognitive digital biomarkers from automated transcription of spoken language. J Prev Alzheimers Dis 2022;9:791–800.
[35] Kiyoshige E, Ogata S, Kwon N, Nakaoku Y, Hayashi C, Blaylock N, Brueckner R, Subramanian V, Joseph Oconnell H, Yoshikawa Y, Teramoto K, Nakatsuka K, Saito S, Ihara M, Takegami M, Nishimura K. Developing and testing AI-based voice biomarker models to detect cognitive impairment among community dwelling adults: a cross-sectional study in Japan. Lancet Reg Health - West Pac. 2025:59.
[36] Eyigoz E, Mathur S, Santamaria M, Cecchi G, Naylor M. Linguistic markers predict onset of Alzheimer's disease. EClinicalMedicine. 2020. p. 28.
[37] Fraser KC, Meltzer JA, Rudzicz F, Garrard P. Linguistic features identify Alzheimer's disease in narrative speech. J Alzheimer's Dis. 2015;49:407–22.
[38] Guo Z, Ling Z, Li Y, Peña-Casanova J. Detecting Alzheimer's disease from continuous speech using language models. J Alzheimer's Dis. 2019;70:1163–74.
[39] Qi W, Zhu X, Wang B, Shi Y, Dong C, Shen S, Li J, Zhang K, He Y, Zhao M, Yao S, Dong Y, Shen H, Kang J, Lu X, Jiang G, Boots LMM, Fu H, Pan L, Chen H, Yan Z, Xing G, Cao S. Alzheimer's disease digital biomarkers multidimensional landscape and AI model scoping review. NPJ Digit Med. 2025;8.
[40] Ford E, Shepherd S, Jones K, Hassan L. Toward an ethical framework for the text mining of Social Media for health research: a systematic review. Front Digit Health 2021;2.
[41] Azizi M, Jamali AA, Spiteri RJ. Identifying X (Formerly Twitter) posts relevant to dementia and COVID-19: machine learning approach. JMIR Form Res. 2024;8.
[42] Alharthi NH, Alanazi EM, Liu X. Awareness level of Huntington disease: comprehensive analysis of tweets during Huntington Disease Awareness month. Comput Methods Progr Biomed Update 2023:4.
[43] Du X, Novoa-Laurentiev J, Plasek JM, Chuang Y-W, Wang L, Marshall GA, Mueller SK, Chang F, Datta S, Paek H, Lin B, Wei Q, Wang X, Wang J, Ding H, Manion FJ, Du J, Bates DW, Zhou L. Enhancing early detection of cognitive decline in the elderly: a comparative study utilizing large language models in clinical notes. eBioMedicine 2024:109.
[44] Serafimovska A, Swavley K, Zhang Qian Ao A, Challinor KL, Florio T. Cognitive status assessment of older adults - test administration by conversational artificial intelligence (AI) chatbot: proof-of-concept investigation. J Clin Exp Neuropsychol 2025;47:472–84.
[45] Hasan WU, Zaman KT, Wang X, Li J, Xie B, Tao C. Empowering Alzheimer's caregivers with conversational AI: a novel approach for enhanced communication and personalized support. NPJ Biomed Innov. 2024:1.
[46] Alfalahi H, Khandoker AH, Chowdhury N, Iakovakis D, Dias SB, Chaudhuri KR, Hadjileontiadis LJ. Diagnostic accuracy of keystroke dynamics as digital biomarkers for fine motor decline in neuropsychiatric disorders: a systematic review and meta-analysis. Sci Rep 2022:12.
[47] Tripathi S, Acien A, Holmes AA, Arroyo-Gallego T, Giancardo L. Generalizing Parkinson's disease detection using keystroke dynamics: a self-supervised approach. J Am Med Inform Assoc. 2024;31:1239–46.
[48] Li Q, Yan J, Ye J, Lv H, Zhang X, Tu Z, Li Y, Guo Q. Construction of a prediction model for Alzheimer's disease using an AI-driven eye-tracking task on mobile devices. Aging Clin Exp Res 2024:37.
[49] Vaghari D, Mohankumar G, Tan K, Lowe A, Shering C, Tino P, Kourtzi Z. AI-guided patient stratification improves outcomes and efficiency in the AMARANTH Alzheimer's Disease clinical trial. Nat Commun 2025:16.
[50] Dennstädt F, Hastings J, Putora PM, Schmerder M, Cihoric N. Implementing large language models in healthcare while balancing control, collaboration, costs and security. NPJ Digit Med. 2025;8.
[51] Singhal K, Tu T, Gottweis J, Sayres R, Wulczyn E, Amin M, Hou L, Clark K, Pfohl SR, Cole-Lewis H, Neal D, Rashid QM, Schaekermann M, Wang A, Dash D, Chen JH, Shah NH, Lachgar S, Mansfield PA, Prakash S, Green B, Dominowska E, Agüera y Arcas B, Tomašev N, Liu Y, Wong R, Semturs C, Mahdavi SS, Barral JK, Webster DR, Corrado GS, Matias Y, Azizi S, Karthikesalingam A, Natarajan V. Toward expert-level medical question answering with large language models. Nat, Med 2025;31:943–50.
[52] Wornow M, Xu Y, Thapa R, Patel B, Steinberg E, Fleming S, Pfeffer MA, Fries J, Shah NH. The shaky foundations of large language models and foundation models for electronic health records. NPJ Digit Med. 2023:6.
[53] Brown KE, Yan C, Li Z, Zhang X, Collins BX, Chen Y, Clayton EW, Kantarcioglu M, Vorobeychik Y, Malin BA. Large language models are less effective at clinical prediction tasks than locally trained machine learning models. J Am Med Inform Assoc. 2025;32:811–22.
[54] Liu M, Ning Y, Teixayavong S, Liu X, Mertens M, Shang Y, Li X, Miao D, Liao J, Xu J, Ting DSW, Cheng LT-E, Ong JCL, Teo ZL, Tan TF, RaviChandran N, Wang F, Celi LA, Ong MEH, Liu N. A scoping review and evidence gap analysis of clinical AI fairness. NPJ Digit Med. 2025;8.
[55] Yuan C, Ryan PB, Ta C, Guo Y, Li Z, Hardin J, Makadia R, Jin P, Shang N, Kang T, Weng C. Criteria2Query: a natural language interface to clinical databases for cohort definition. J Am Med Inform Assoc. 2019;26:294–305.
[56] Borisov V, Leemann T, Seßler K, Haug J, Pawelczyk M, Kasneci G. Deep neural networks and tabular data: a survey. IEEE Trans Neural Netw Learn Syst 2024;35:7499–519.
[57] Lopez I, Swaminathan A, Vedula K, Narayanan S, Nateghi Haredasht F, Ma SP, Liang AS, Tate S, Maddali M, Gallo RJ, Shah NH, Chen JH. Clinical entity augmented retrieval for clinical information extraction. NPJ Digit Med. 2025;8.
[58] Adam H, Lin J, Lin J, Keenan H, Wilson A, Ghassemi M. Clinical information extraction with large language models: a case study on organ procurement. AMIA Annu Symp Proc 2024;2024:115–23.
[59] Ni Y, Bermudez M, Kennebeck S, Liddy-Hicks S, Dexheimer J. A real-time automated patient screening system for clinical trials eligibility in an emergency department: design and evaluation. JMIR Med Inf. 2019:7.
[60] Gerke S, Babic B, Evgeniou T, Cohen IG. The need for a system view to regulate artificial intelligence/machine learning-based software as medical device. NPJ Digit Med. 2020:3.
[61] Yang S-R, Chien J-T, Lee C-Y. Advancements in clinical evaluation and regulatory frameworks for AI-driven software as a medical device (SaMD). IEEE Open J Eng Med Biol. 2025;6:147–51.
[62] Singh V, Cheng S, Kwan AC, Ebinger J. United States Food and Drug Administration regulation of clinical software in the era of artificial intelligence and machine learning. Mayo Clin Proc.: Digit Health 2025:3.
[63] Muehlematter UJ, Bluethgen C, Vokinger KN. FDA-cleared artificial intelligence and machine learning-based medical devices and their 510(k) predicate networks. Lancet Digit Health 2023;5:e618–26.
[64] Cancela-Outeda C. The EU's AI act: a framework for collaborative governance. Internet Things 2024:27.
[65] Kusche I. Possible harms of artificial intelligence and the EU AI act: fundamental rights and risk. J Risk Res 2024:1–14.

[66] Laux J, Wachter S, Mittelstadt B. Trustworthy artificial intelligence and the European Union AI act: on the conflation of trustworthiness and acceptability of risk. Regul Gov. 2023;18:3–32.
[67] Pham B-C, Davies SR. What problems is the AI act solving? Technological solutionism, fundamental rights, and trustworthiness in European AI policy. Crit Policy Stud. 2024;19:318–36.
[68] Shuren J, Doraiswamy PM. Digital Therapeutics for MCI and Alzheimer's disease: a regulatory perspective - highlights from the Clinical Trials on Alzheimer's Disease conference (CTAD). J Prev Alzheimers Dis 2022;9:236–40.
[69] Shah R, Robertson C, Woods A, Bergstrand K, Findley J, Balser C, Slepian MJ. Diverse patients' attitudes towards artificial intelligence (AI) in diagnosis. PLOS Digit Health 2023;2.
[70] Wilkins JM, Forester BP. Informed consent, therapeutic misconception, and clinical trials for Alzheimer's disease. Int J Geriatr Psychiat 2020;35:430–5.
[71] Gerke S, Minssen T, Cohen G. Ethical and legal challenges of artificial intelligence-driven healthcare. In Artif Intell Healthc. 2020:295–336.
[72] Reis M, Reis F, Kunde W. Public perception of physicians who use artificial intelligence. JAMA Netw Open 2025;8.
[73] Goddard K, Roudsari A, Wyatt JC. Automation bias: a systematic review of frequency, effect mediators, and mitigators. J Am Med Inform Assoc. 2012;19:121–7.
[74] Abdelwanis M, Alarafati HK, Tammam MMS, Simsekler MCE. Exploring the risks of automation bias in healthcare artificial intelligence applications: a Bowtie analysis. J Saf Sci Resil. 2024;5:460–9.
[75] Natali C, Marconi L, Dias Duran LD, Cabitza F. AI-induced deskilling in medicine: a mixed-method review and research agenda for healthcare and beyond. Artif Intell Rev 2025:58.
[76] Wusthoff C. The dilemma of confidentiality in Huntington disease. JAMA: J Am Med Assoc. 2003;290:1219–20.
[77] Kromberg JGR, Wessels T-M. Ethical issues and Huntington's disease. S Afr Med J. 2013:103.
[78] Williamson SM, Prybutok V. The era of artificial intelligence deception: unraveling the complexities of false realities and emerging threats of misinformation. Information 2024:15.
[79] Maddox T, Babski D, Embi P, Gerhart J, Goldsack J, Parikh R, Sarich T, Krishnan S, Elliott A. Gener Artif Intell Health Med. 2025.
[80] Chang CY, Yuan J, Ding S, Tan Q, Zhang K, Jiang X, Hu X, Zou N. Towards fair patient-trial matching via patient-criterion level fairness constraint. AMIA Annu Symp Proc 2023;2023:884–93.
[81] Mahajan A, Heydari K, Powell D. Wearable AI to enhance patient safety and clinical decision-making. NPJ Digit Med. 2025;8.
[82] Huang G, Chen X, Liao C. AI-driven wearable bioelectronics in Digital Healthcare. Biosensor 2025:15.
[83] Kovur P, Kovur KM, Rayat DY, Wishart DS. POC sensor systems and artificial intelligence—where we are now and where we are going? Biosensor 2025:15.
[84] Shajari S, Kuruvinashetti K, Komeili A, Sundararaj U. The emergence of AI-based wearable sensors for digital health technology: a review. Sensors 2023;23.