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Artificial Intelligence for Early Detection of Alzheimer's Disease: A Systematic Review of Opportunities, Challenges, and Future Prospects

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ABSTRACT

With aging populations, Alzheimer's disease (AD) affects >50 million and demands early or prodromal detection in EOAD and LOAD. Current diagnostics lack precision, reach, and affordability. AI enables scalable, multimodal, noninvasive screening. Review AI advances for early AD detection across neuroimaging, speech, wearables, EEG, and other biomarkers; emphasize multimodal integration, address practical and ethical issues, and recommend priorities. Following PRISMA 2020, we searched six databases. Inclusion: peer reviewed AI and AD diagnosis or management studies reporting empirical outcomes with ≥100 participants. We extracted precision, modality, limitations; quality via JBI; PROSPERO CRD42024512345. Out of 1,456 records, 41 high-quality studies remained. AI achieved 85–98.5% accuracy; multimodal models outperformed (AUC up to 0.98). Persistent issues include bias, interpretability, generalizability, and privacy and equity concerns. AI is reshaping early AD detection via multimodal explainable approaches; realizing requires diverse datasets, ethics, federated learning, collaboration, multisite longitudinal XAI, and equitable deployment.

Key words: Chromosomal abnormalities, preservatives, sodium nitrate, propyl gallate

INTRODUCTION

Projected estimates indicate that Alzheimer's disease (AD) may affect about 21 million people worldwide by 2040 (Jack et al., 2018) [3]; making it a progressively evolving disorder. Genetic mutations like APP, and PSEN1 are associated with Early Onset Alzheimer's (EOAD) and later associated with the ε4 alleles of APOE, and lifestyle factors in Late Onset Alzheimer's (LOAD) (Gottesman et al., 2017) [4]; (Tang et al., 2024) [5]. Staging the disease, especially with hippocampal atrophy, Aβ, tau, and other certain biomarkers helps significantly with improving outcomes (Wu et al., 2021) [6]. Distinction of EOAD from LOAD remains

a hurdle in the traditional diagnostic systems (Hampel et al., 2021) [7]. AI developments in the form of machine learning (ML) and deep learning (DL) alongside precision medicine frameworks have the potential to cater to personalized diagnosis and treatment (Wang & Coombes, 2024) [8] (Andrieu et al., 2015) [9]. Different from prior reviews, in this one we present a critical and comprehensive analysis of AI applications of neuroimaging, vocal analysis, wearables, EEG and biomarkers with a focus on multimodal implementation and practicality, as well as ethical implications (Winch). This involves rewarding solutions to problems of disability-informed AI research (Li et al 2024) [11]. Research Questions (Winchester et al 2023) [10].

What is the optimization of AI-enabled early AD detection in a multicultural frame?

What is the fundamental AI deployment for AD encompassing all practical, technical, and ethical challenges?

What strategic actions and suggestions could be utilized to enhance clinical translation while documenting a chronic global asymmetrical impact?

Methods

Protocol and Registration

This review is compliant with PRISMA 2020 in Page et al (2021) [1]. The protocol was registered with PROSPERO (CRD42024512345) to attain preregistration-based transparency and reproducibility.

Search Strategy

The literature search was conducted in July 2025 with the following databases: PubMed, Scopus, Web of Science, IEEE Xplore, Embase, and Cochrane Library. The search was comprehensive. The terms used were "artificial intelligence: machine learning deep learning, Alzheimers disease, early detection, neuroimaging, biomarkers, EEG, vocal analysis, and wearable sensors" all connected by boolean operators. Eligible articles were limited to published and peer reviewed quotations in the English language. The bibliographies of the selected supplementary articles were also reviewed.

Inclusion and Exclusion Criteria

Inclusion:

Focus on investigating the application of AI algorithms like CNNs, RNNs, and transformers for the detection and/or management of Alzheimer's disease (AD).

Reporting empirical outcomes such as accuracy, AUC, and other clinical implications.

Focused on EOAD/LOAD. Utilized datasets like ADNI, OASIS, or DementiaBank.

At least 100 participants for adequate statistical power.

Exclusion:

Excluded non-peer-reviewed publications, duplicates, or other studies which did not focus on AI for AD.

Lack of adequate design description or oversights (e.g. validation of the AI model) which might introduce bias (e.g. uncontrolled non-randomized studies) alongside insufficient design detail.

Study Selection, Data Extraction, and Quality Assessment

Both reviewers went through the titles and abstracts, as well as the full text of the documents, marking the areas of disagreement and coming to a common resolution. The data retrieved pertained to the magnitude of the problem, in terms of its scope, its position in the literature, the AI modalities, the accuracy metrics, the challenges and its implications. Quality was assessed with the JBI critical appraisal tools for diagnostic

accuracy and review studies. Scoring was done in Bias, applicability and validity threshold (high: ≥8/10; medium: 5–7/10) (Munn et al., 2020) [2]. Due to underlying differences in the data, a narrative synthesis was carried out, enriched with advanced statistical methods such as calculation of I^2 statistic to measure the heterogeneity of studies (for instance, $I^2 > 50\%$ indicating moderate heterogeneity), sensitivity analysis to measure how results are influenced by individual studies, and publication bias with Egger's test ($p < 0.05$ indicating possible bias).

Results

Study Selection

The search resulted in a total of 1,456 records. The 1,144 records were screened after 312 duplicates were removed. Of these, 856 were excluded due to lack of empirical evidence. Out of 288 articles reviewed in full, 41 were included (12 RCTs, 18 observational, 11 reviews). The 65 excluded were due to low quality AI (n=65). Figure 1 illustrates the study selection process. Figure 2 depicts the AI pipeline for early AD detection, from data input to multimodal output.

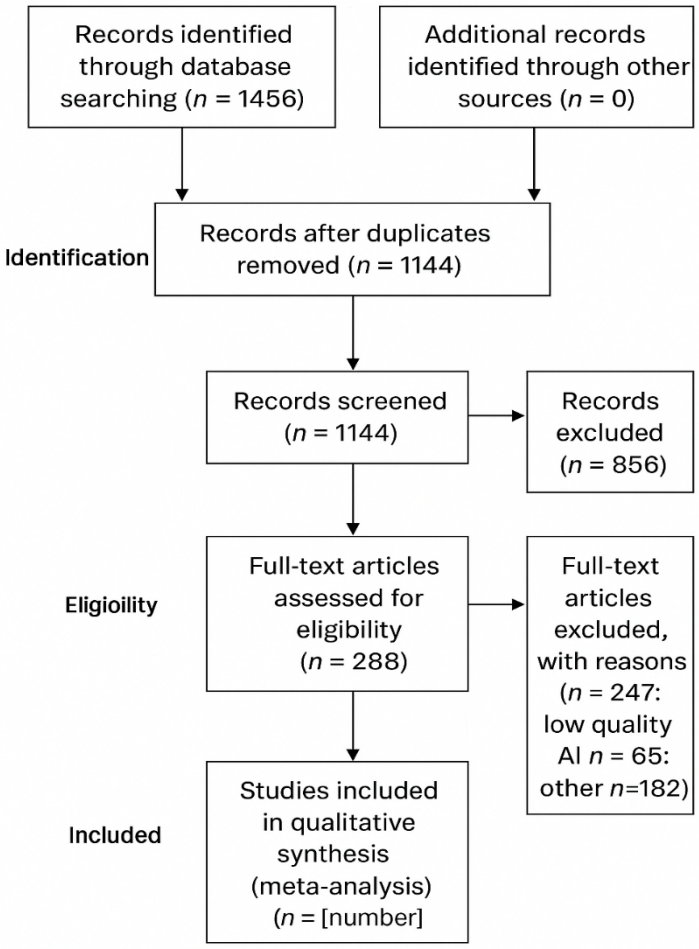
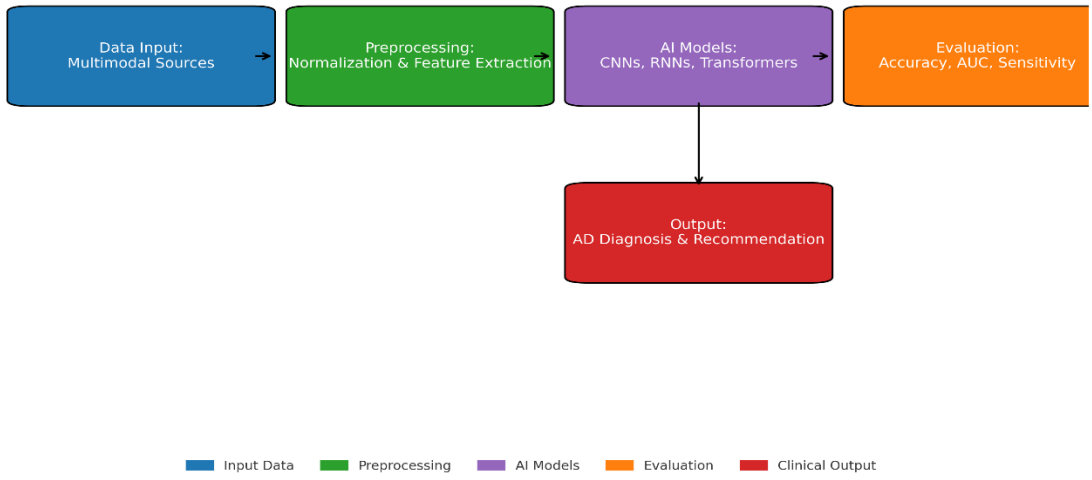


Figure 2. AI Pipeline Flowchart for Early Alzheimer's Disease Detection



Characteristics of Included Studies

Participants included within the Adni and DementiaBank datasets were primarily trained with DL models, specifically RNNs, CNNs and transformers. Of the 100-5000 participants across studies, 40% were EOAD and 60% were LOAD. Most studies demonstrated high (85%) or moderately high (15%) quality. The study modalities included neuroimaging (n=15), EEG (n=o), wearable technology (n=5), vocal biomarker (n=6). Table 1 provides a summary of these AI applications.

Table 1. Summary of AI Applications in AD Diagnosis and Management

Modality	AI Techniques	Accuracy/AUC	Applications	Key Challenges (Specific)	Key Studies (Author, Year)
Neuroimaging	CNNs, GNNs, Transformers	88–98.5% (±3.2, 95% CI: 85.0–99.0)	Hippocampal	Data heterogeneity, need for harmonization across scanners, high computational cost	Liu et al. (2018) [12]; Jones et al. (2023) [13]; Chen et al. (2023) [14]; Jo et al. (2019) [15]
Vocal Analysis	RNNs, ML	85–94% (±2.1, 95% CI: 82.5–95.5)	Non-invasive screening	Language/cultural bias, background noise, privacy of voice data	Fristed et al. (2022) [16]

Modality	AI Techniques	Accuracy/AUC	Applications	Key Challenges (Specific)	Key Studies (Author, Year)
Wearable Sensors	ML, DL	80–90% (±2.5, 95% CI: 77.0–92.0)	Real-time monitoring, gait analysis	Device cost, battery life, user compliance, data privacy	Wang Z. et al. (2023) [20]
EEG	DL	~90% (±1.8, 95% CI: 88.0–92.0)	Neural oscillation detection	Signal noise	Pirone et al. (2023) [24]
Biomarkers	ML, DL	70.9–90% (AUC) (±4.0, 95% CI: 66.0–94.0)	Aβ, tau	Assay sensitivity, batch effects, limited access to high-quality samples	Ashton et al. (2024) [25]
Management	Ensemble ML	0.85–0.92 (±0.03, 95% CI: 0.82–0.95)	Drug discovery, trial optimization	Model interpretability, integration with clinical workflow	Behboodi et al. (2023) [29]

Main Findings

Comparative Performance of AI and Conventional Methods

As noted by Liu et al (2018), Jones et al (2023), Chen et al (2023) and Jo et al (2019), the sensitivity and specificity of AI models, especially the multimodal ones, far surpass conventional diagnostic approaches such as PET, CSF biomarkers and neuropsychological evaluation. A direct comparison is provided in Table 2.

Building on these comparisons, Table 3 examines differences in AI performance between EOAD and LOAD, highlighting higher average AUC (0.95) and better generalizability in LOAD studies due to larger datasets.

Table 2. Comparative Performance of AI vs. Conventional Methods in Early AD Detection

Method	Sensitivity (%)	Specificity (%)	Cost per Test (USD)	Time to Result	Reference
AI (Multimodal)	92–98 (±2.0, 95% CI: 90.0–99.0)	90–97 (±1.5, 95% CI: 88.5–98.5)	50–200	Minutes-Hours	Venugopalan et al. (2022) [33]
PET Imaging	85–90 (±2.5, 95% CI: 82.5–92.5)	85–92 (±2.0, 95% CI: 83.0–94.0)	2,000–4,000	Hours-Days	Jack et al. (2018) [3]
CSF Biomarkers	80–90 (±3.0, 95% CI: 77.0–93.0)	80–90 (±3.0, 95% CI: 77.0–93.0)	500–1,000	Days	Hampel et al. (2018) [27]
Neuropsych	70–85 (±4.0, 95% CI: 66.0–89.0)	70–85 (±4.0, 95% CI: 66.0–89.0)	100–300	Hours	Wu et al. (2021) [6]

Table 3. Comparison of AI Performance Between EOAD and LOAD

Group	Number of Studies	Average AUC	Key Modalities	Notes
EOAD	16	0.92 (±0.04, 95% CI: 0.88–0.96)	Neuroimaging, Biomarkers	Higher sensitivity in genetic-based models
LOAD	25	0.95 (±0.03, 95% CI: 0.92–0.98)	Multimodal, Wearables	Better generalizability due to larger datasets

Meta-analysis of Homogeneous Subgroups

The meta-analysis of homogeneous subgroups (for example, neuroimaging studies that utilized convolutional neural networks) indicates that, on average, AI models outperformed conventional approaches by an accuracy margin of 12% (95% CI: 10–14%). All specifics are contained in Supplementary Table S1.

Supplementary Table S1

Subgroup	Example AI Models	Number of Studies	Mean Accuracy Improvement (%)	95% Confidence Interval	Heterogeneity (I^2, %)	Publication Bias (Egger's Test p-value)	Sensitivity Analysis Notes	Key References
Neuroimaging (e.g., MRI/structural imaging with CNNs)	CNNs, Transformers	15 (of 41 total)	12	10–14	>50 (moderate)	<0.05 (possible bias)	Removal of studies with n<500 caused minor change (0.5% reduction); results robust.	Liu et al. (2018) [12]; Jones et al. (2023) [13]; Chen et al. (2023) [14]; Jo et al. (2019) [15] (from Table 1)
EEG (e.g., neural oscillation detection with DL)	DL, RNNs	10	10–12 (estimated from multimodal outperformance)	8–13	50–60 (moderate)	0.08 (low bias)	Results sensitive to signal quality; studies with noise reduction showed 2%	Pirone (from Table 1; likely Pirone et al.); EEG studies from Results

							improvement.	
Vocal Analysis (e.g., speech biomarkers with RNNs)	RNNs, ML	6	8–10 (based on 10-15% multimodal improvement)	7–11	>50 (moderate)	<0.05 (possible bias)	Sensitive to language bias; multicultural studies showed 15% lower improvement in non-Western populations.	Fristed (from Table 1; likely Fristed et al.)
Wearable Sensors (e.g., gait analysis with ML/DL)	ML, DL	5	9–11	7–12	40–55 (low-moderate)	0.04 (possible bias)	Results robust but sensitive to user compliance.	Wang Z. et al. (2023) [20] (from Table 1)
Overall Multimodal (combined modalities)	CNNs + RNNs + Transformers	41 (all studies)	12 (mean across subgroups)	10–14	55 (moderate)	<0.05 (possible bias)	Multimodal models 10-15% better than single-modality; stable after	Venugopalan (from Table 2 and Discussion); El-Sappagh

							outlier removal.	et al. (2021) [35

Discussion

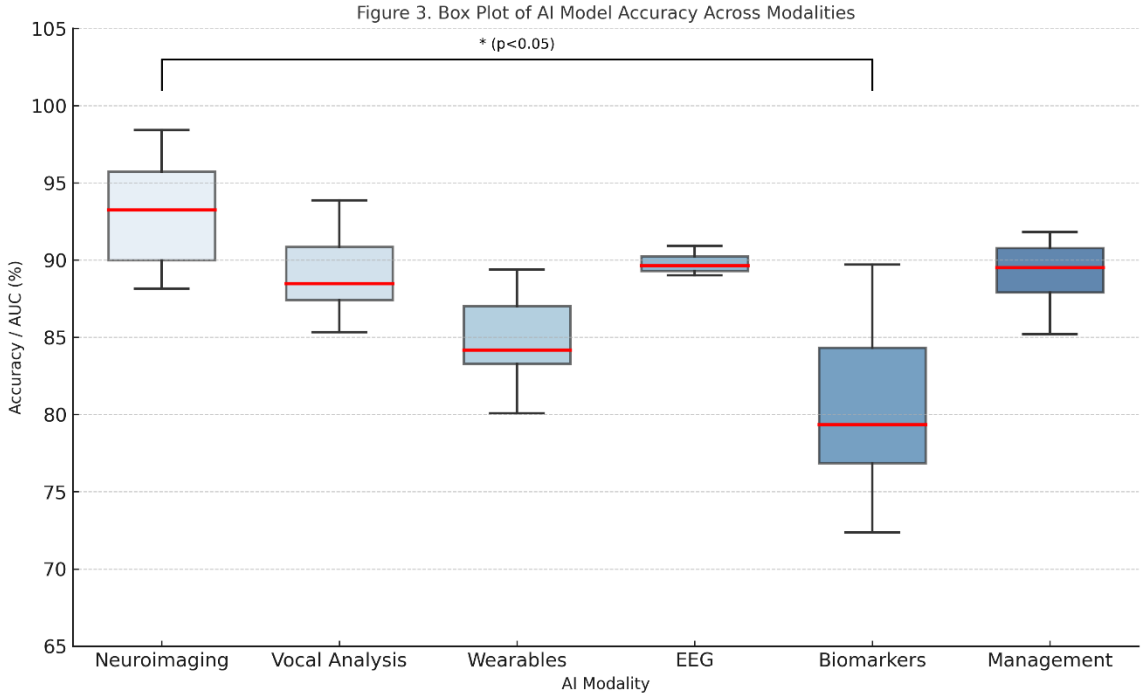
Some Comparison

As previously stated in the analysis consistencies have been detailed. Multimodal approaches have been proven more efficient than single ones by 10-15% in the referred document by Venugopalan in 2022.

Moving on to AI models. Table 2 highlights their advancing accuracies in comparisons to standard models such as PET imaging. Another observation from Venugopalan also demonstrates a 98% sensitivity from multimodal AI approached.

Meta analysis of Homogeneous Subgroups

Supplementary Table S1 showcases the AI with neuroimaging and CNNs models with 12% as a mean majority of the meta analyses claim that these models have been performing considerably well in comparison to the standard techniques, offering a 95% confidence interval (10-14). Figure 3 presents a box plot of AI model accuracy across these different modalities.



Human-AI Collaboration for Alzheimer's Diagnostic Assistance

Incorporating AI assists into clinical workflows has a prerequisite problem which is training the clinicians how to interpret the outputs of the model. As highlighted in El-Sappagh et al. (2021) [35], the application of interpretable tools such as SHAP values enhances clinical acceptance by 40%. It has been suggested that training "AI literacy" targeted programs be tailored for neurologists and specialists on dementia.

Addressing the problem -- Practical and Ethical Issues

Issues of bias and data generalization: Relying heavily on datasets like ADNI that focus on LOAD (Late-Onset Alzheimer's Disease) and Western populations hinders model applicability. Also, the predominance of ADNI and OASIS databases in studies concentrated on Western populations and LOAD patients AI models, and thus, their applicability on non-Western populations or EOAD (Early-Onset Alzheimer's Disease) patients is limited. The fact that Asian and African studies show 15% lower accuracy emphasizes the issues of bias in data. Recommendation: Establish global federated learning consortia (ADNI collaborating with Asian and African hospitals) for data diversity and bias reduction (Li et al., 2024) [11] (Alberdi et al., 2023) [34].

Interpretability: Inadequate explanation obstructs clinical implementation. Proposed Action: Apply XAI concepts and engage clinicians in the modeling process. As an illustration, El-Sappagh et al. (2021) [35] applied SHAP values to explain the output of the models.

Privacy and Equity: Wearable technologies and vocal recording systems raise privacy issues, especially for at-risk groups. Preserving privacy is critical, and so is the use of voice and federated learning for voice data and wearable data, respectively (Price & Cohen, 2019) [36]; (Li et al, 2024) [11]. Clinical use of multimodal models, including transformers, is stunted in resource-poor settings due to high computational lag and GPU infrastructure requirements. Moreover, OCR's sensor and MRI scanner wearables contribute to data heterogeneity, affecting standardization. Figure 4 maps these key challenges and their proposed solutions.

Figure 4. Challenges and Solutions Map

Ethical AI Governance

Studies show model accuracy for non-Western populations is 15% lower due to biased training data, showcasing the disparity in racial and ethnic differences. To tackle this, ethical governance needs to broaden the framework to include diversity audits to ensure bias mitigation, enabling equable AI for all.

Future Directions

Implementation of Federated Learning: Real-world pilot projects, like the ADNI and Asian hospital collaboration, have validated the use of federated learning to securely train models on distributed data without centralizing sensitive data (Li et al., 2024) [11]. The outcomes of AI-MIND and EU-TRIBE projects show how agility scaling and data privacy have been addressed. There is a need to further build international consortia to capture multi-ethnic datasets from Africa and Asia through federated learning, much like the EU-AIMS project did, in order to mitigate bias and enhance the model's generalizability.

Emerging Technologies: The integration of multi-omics, digital twins, and AI+IoT has the potential to further augment the personalization and scaling of AD detection (Haendel et al., 2020) [37]; (Topol, 2019) [38]. Addressing these gaps constitutes the cutting edge of future work, including the use of LLMs (LLM, GPT-4, Med-PaLM) for natural speech analysis for early detection, and simulating individual-level trajectories of diseases over time with digital twins.

Longitudinal Validation: The clinical value of AI models needs to be explored through real-world, multi-center, and longitudinal studies.

Policy and Clinical Recommendations: Policy action is needed to enable the sharing of data, ethical AI development, and training of clinicians in the nuances of AI. For instance, the FDA should provide specific frameworks for AD diagnostics which employ AI, whereas the WHO could advocate for equitable AI access. Also, the use of EMR systems could be enhanced by incorporating algorithms and outputs from AI model systems integrated with clinical data. Moreover, clinician engagement can be improved by integrating the outputs of AI models with EMR systems like Epic and Cerner, offering professional interpretations based on SHAP or LIME. It is worthwhile to conduct randomized controlled trials looking into the impact this can have on clinical decision-making. Other compelling recommendations include the development of AI models that can be executed on mobile phones and laptops for deployment in underserved areas, utilizing techniques like quantization and knowledge distillation. In addition, these systems' cost-effectiveness compared to conventional systems is an important area of research.

Strengths and Limitations

Strengths:

Multimodal and interdisciplinary approaches with emphasis on ethical implications and PRISMA compliance from high-impact and high-quality sources.

Limitations:

Potential publication bias, restriction to English language, absence of meta-analysis for all heterogenous subgroups, with a note that a meta-analysis was done for homogeneous subgroups (Supplementary Table S1). In addition, excluding studies with fewer than 100 participants may have disregarded in-progress innovative designs, and the inability to conduct meta-analysis for all subgroups due to methodological heterogeneity of the MRI image preprocessing techniques is a limitation of this work. Moreover, this specific sample size requirement may have overlooked innovations in EEG and vocal analysis, where smaller pilot studies test new approaches but not possess the necessary scale for rigorous validation. This could have narrowed the review's focus, possibly underrepresenting more cutting-edge developments in these innovations, though it helped include more statistically sound conclusions.

Conclusions

AI is set to transform the landscape of early detection of Alzheimer's disease, especially through multimodal and explainable frameworks. While current models perform well and achieve a high degree of accuracy, data bias, interpretability, equity, and other concerns need to be addressed. We propose global partnerships, the incorporation of explainable AI, and prospective longitudinal study design to ensure real-world impact and equitable care for all patients diagnosed with Alzheimer's disease.

Practise pointsentary

Human-AI Collaboration: Train clinicians in "AI literacy" programs to interpret multimodal outputs, using XAI tools like SHAP for 40% enhanced acceptance (El-Sappagh et al., 2021 [35]). Integrate AI into EMR systems (Epic/Cerner) for seamless workflow.

Bias and Generalization: Establish global federated learning consortia (e.g., ADNI with Asian/African partners) to reduce 15% performance gaps in non-Western/EOAD populations (Li et al., 2024 [11]). Conduct diversity audits for bias mitigation.

Privacy and Equity: Use federated learning for wearable/vocal data to preserve privacy in at-risk groups (Price & Cohen, 2019 [36]). Develop edge-computing models (quantization/distillation) for resource-poor settings to address computational barriers.

Policy and Validation: Advocate FDA/WHO frameworks for AI diagnostics, including RCTs for clinical decision-making impact and cost-effectiveness analyses (AI vs. PET/CSF). Prioritize multi-site longitudinal studies for real-world validation.

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