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Advances in Blood-Based Diagnostics for Alzheimer's Disease: Clinical Implications and Biomarker Integration

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Abstract

Alzheimer's disease (AD), the leading cause of dementia, presents important diagnostic difficulties with its subtle onset and limitation of traditional diagnostic methods such as cerebrospinal fluid (CSF) examination and PET scanning. These accurate methods are still invasive, costly, and mostly unavailable in the primary care environment. It is only recently that blood-based biomarkers have been the focus, targeting important pathological aspects of AD amyloid load, tau pathology, neuroinflammation, and neurodegeneration. By 2025, plasma biomarkers including phosphorylated tau (p-tau217), amyloid-β 42/40 ratio, neurofilament light chain (NfL), and glial fibrillary acidic protein (GFAP) have shown diagnostic accuracies greater than 90%, with FDA-cleared systems such as Lumipulse found in clinical practice. Such advances are transforming the diagnostics landscape allowing early detection, risk stratification, and monitoring therapeutic response in a minimally invasive and cost-efficient manner. Platforms like SIMOA, mass spectrometry, and future point-of-care biosensors enable research and clinical deployment. With their potential, however, comes difficulty in standardizing assays, validating them in population-specific contexts, ensuring ethical application, and making them available. In the future, AI-driven multimarker panels, home-testing solutions, and international policy endorsement might make Alzheimer's diagnostics more democratized. Blood-based biomarkers therefore constitute an AD care paradigm shift that holds promise for earlier intervention and better outcomes across a variety of healthcare settings.

Keywords: Alzheimer's Disease, Phosphorylated Tau (P-Tau217, P-Tau181), Neurofilament Light Chain (Nfl), Simoa Technology, Lumipulse Assay

1. Introduction

Alzheimer's disease (AD), a neurodegenerative condition affecting memory, cognition, and behavior, is the leading cause of dementia worldwide, accounting for 60–70% of cases [1]. Despite decades of research, accurate diagnosis remains a challenge, often confirmed only after significant cognitive and functional decline [2]. Conventional diagnostic tools, such as cerebrospinal fluid (CSF) analysis and positron emission tomography (PET) imaging, provide high sensitivity and specificity, but they are invasive, expensive, and largely inaccessible in primary care or low-resource settings [3,4].

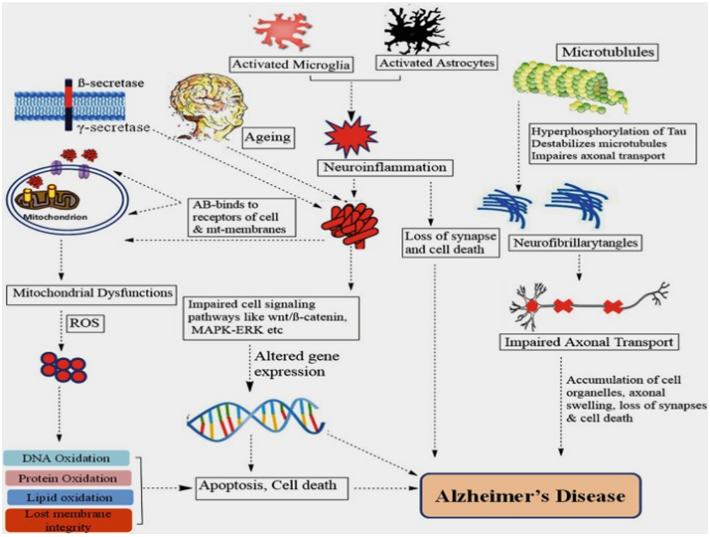
Recent advances have shifted focus toward blood-based biomarkers that reflect the core pathological changes of AD amyloid plaque deposition, tau pathology, neuroinflammation, and neurodegeneration [5,6]. These biomarkers are emerging as minimally invasive, cost-effective, and scalable alternatives for early detection, staging, and monitoring of Alzheimer's pathology [7].

By 2025, several blood tests including automated immunoassays like Lumipulse and ultrasensitive platforms such as SIMOA (Single Molecule Array) and mass spectrometry (MS) have demonstrated diagnostic accuracies exceeding 90% in differentiating AD from

other dementias [8,9]. For example, plasma p-tau217 and Aβ42/40 ratio tests now show equivalent performance to CSF and PET benchmarks, and are increasingly being adopted in clinical and research settings [10].

These advances represent a paradigm shift: from diagnosing AD in its advanced stages to detecting it preclinically or at the mild cognitive impairment (MCI) stage, thereby enabling timely intervention, risk stratification, and monitoring of therapeutic efficacy offering new hope for patients, caregivers, and clinicians alike [11,12].

2. Pathophysiology of Alzheimer's Disease and Blood Biomarker



To understand the relevance of blood-based biomarkers, it's essential to know the pathological hallmarks of Alzheimer's disease:

2.1. Amyloid Plaques

Amyloid-β (Aβ) peptides, particularly Aβ42, are produced via sequential cleavage of amyloid precursor protein (APP) by β-secretase and γ-secretase [13]. Aβ42 has a higher tendency to aggregate than Aβ40 and forms extracellular plaques in the brain one of the earliest events in AD pathogenesis [14]. A decreased plasma Aβ42/Aβ40 ratio is strongly associated with brain amyloid positivity and is detectable using ultra-sensitive technologies such as mass spectrometry and SIMOA [10,15]. These peptides, though present in low concentrations in blood, are measurable with high precision and provide insight into preclinical AD pathology [11].

2.2. Neurofibrillary Tangles

The second hallmark of AD is the formation of neurofibrillary tangles (NFTs) composed of hyperphosphorylated tau proteins. This abnormal phosphorylation causes tau to dissociate from microtubules, leading to destabilization of the neuronal cytoskeleton and impaired axonal transport.[16] Plasma p-tau species such as p-tau181, p-tau217, and p-tau231 correlate with tau PET imaging and disease progression, making them highly specific and dynamic biomarkers for tau pathology in AD [8,9,16].

2.3. Neurodegeneration

As neuronal damage progresses, cytoskeletal proteins like neurofilament light chain (NfL) are released into CSF and peripheral blood [17]. Although not specific to AD, elevated NfL levels reflect axonal injury and overall neurodegeneration, and they correlate with both cognitive decline and brain atrophy across multiple studies [6,18]. Plasma NfL has been proposed as a longitudinal marker for tracking disease progression and monitoring therapeutic efficacy [19].

2.4. Neuroinflammation

Activated astrocytes and microglia mount an inflammatory response to Aβ and tau accumulation. This neuroinflammation contributes to further neuronal injury and synaptic dysfunction [12]. A key marker of astrocytic activation is glial fibrillary acidic protein (GFAP), which is elevated in the blood of individuals with amyloid-positive PET scans even before symptom onset [13,20]. GFAP is increasingly recognized as a preclinical marker of AD-related astroglial activation [21].

2.5. Emerging Targets

Beyond the core hallmarks, several emerging biomarkers are gaining traction:

- YKL-40, a glycoprotein secreted by activated glial cells, reflects neuroinflammatory processes and is elevated in early and late stages of AD [22].
- TREM2 (triggering receptor expressed on myeloid cells 2) is involved in microglial response to amyloid pathology and is associated with increased AD risk in mutation carriers [23].
- MTBR-tau243, a tau fragment derived from the microtubule-binding region of tau, shows strong correlation with tau PET findings and is under evaluation as a blood-based proxy for

neurofibrillary tangle burden [18,24].

3. Key Blood Biomarkers in Alzheimer's Disease Diagnosis

Blood-based biomarkers are transforming the way Alzheimer's disease (AD) is diagnosed, monitored, and potentially screened for in asymptomatic individuals. Several biomarkers now partially integrated into clinical care include phosphorylated tau (p-tau) species, amyloid-β (Aβ) peptides, neurofilament light chain (NfL), and glial fibrillary acidic protein (GFAP). Each of these reflects a specific pathological domain of AD and contributes to early detection, disease staging, and response monitoring [7,8,16].

3.1. Phosphorylated Tau (p-tau) – p-tau217, p-tau181, p-tau231

Among the plasma biomarkers, p-tau217 has consistently demonstrated the highest diagnostic performance. It mirrors tau pathology, correlates with tau-PET imaging, and distinguishes AD from other dementias [16].

- A 2025 multi-center study using the Lumipulse G platform reported 92–94% accuracy in detecting AD pathology using a dual-threshold strategy [16].
- The same study showed that plasma p-tau217 effectively distinguishes AD from frontotemporal dementia (FTD), Lewy body dementia (LBD), and vascular dementia (VaD) with high specificity [16].
- **p-tau181** also performs well, though with slightly lower specificity, especially in early disease [9].
- **p-tau231** is gaining interest for its ability to detect preclinical AD, possibly rising earlier than p-tau217 in the biomarker cascade [25].

3.2. Amyloid-β 42/40 Ratio

The **Aβ42/40 ratio** serves as an early and reliable indicator of amyloid plaque accumulation in the brain.

- A decrease in this ratio reflects increased Aβ42 deposition, a key pathological hallmark of AD [10,15].
- While moderately predictive on its own, combining Aβ42/40 with p-tau217 significantly boosts diagnostic accuracy [16].
- In 2025, p-tau217/Aβ42 ratio tests achieved AUC values of 0.96–0.97, comparable to CSF-based amyloid and tau assessments [16].

3.3. Neurofilament Light Chain (NfL)

NfL is a non-specific but sensitive marker of axonal degeneration that reflects the rate of neuronal damage.

- Elevated in AD and other disorders (e.g., multiple sclerosis, TBI), NfL levels track neurodegeneration across the brain [18].
- Longitudinal studies, such as the Swedish BioFINDER cohort, have shown that NfL levels rise with disease severity and correlate with cognitive decline [19].
- In cognitively normal individuals, high NfL levels predict conversion to MCI or dementia within 3–5 years [26].

3.4. Glial Fibrillary Acidic Protein (GFAP)

GFAP is an astrocytic protein that reflects neuroinflammation and glial activation, often in response to amyloid pathology.

- Plasma GFAP is elevated early in the disease process, even prior to overt clinical symptoms [20,21].
- GFAP correlates with amyloid PET positivity and is emerging as a marker of early risk and progression [20].
- Recent work highlights GFAP's utility in screening asymptomatic individuals and enhancing risk stratification algorithms [21].

3.5. Other Emerging Biomarkers

Several novel blood-based biomarkers are in development or early validation:

- **MTBR-tau243 (crystalized tau):** A truncated tau species derived from the microtubule-binding region. In 2025, it was shown to distinguish AD from controls with ~92% accuracy and high correlation to tau PET burden [24].
- **YKL-40:** A glycoprotein produced by astrocytes and microglia; reflects **chronic inflammation**, though it lacks AD specificity [22].
- **TREM2/sTREM2:** These microglial receptors modulate immune response to amyloid plaques. Variants in TREM2 are associated with AD risk and show potential as markers of disease progression and therapeutic response [23].
- Plasma synaptic markers (e.g., neurogranin, SNAP25) are being evaluated for their role in synaptic dysfunction, an early feature of cognitive decline in AD [27].

4. Analytical Platforms for Blood-Based Biomarker Detection

The reliable detection of Alzheimer's disease (AD) biomarkers in blood requires highly sensitive platforms, as the target proteins (e.g., ptau, Aβ) exist in very low concentrations and are susceptible to interference from other serum components [6,7,16]. Over the past decade and particularly by 2025 technologies have evolved to provide accurate, scalable, and clinically translatable detection platforms for research and diagnostic purposes.

4.1. Fully Automated Immunoassays (e.g., Lumipulse)

The Lumipulse G platform (Fujirebio) is a fully automated chemiluminescent enzyme immunoassay (CLEIA) system, recently FDA-cleared in 2024–2025 for measuring plasma ptau217 and Aβ42/Aβ40 ratio [16,28].

- Allows high-throughput, standardized, and batch-consistent testing in clinical labs.
- Utilizes a dual-cutoff strategy to reduce the impact of borderline or indeterminate values.
- In real-world studies, it showed 92–94% diagnostic accuracy in differentiating AD from other dementias in both primary and specialty care settings [16].
- Regulatory status: Cleared by the U.S. FDA in 2025 for use in symptomatic adults aged ≥55 [28].

4.2. SIMOA (Single Molecule Array)

SIMOA (Single Molecule Array) developed by Quanterix is a digital immunoassay platform capable of detecting proteins at femtomolar concentrations [29].

- It enables ultra-sensitive quantification of ptau181, ptau217, NfL, and GFAP in plasma.

- Extensively used in research programs such as BioFINDER, DIAN (Dominantly Inherited Alzheimer Network), and ADNI (Alzheimer's Disease Neuroimaging Initiative) [6,18].
- Despite its precision, clinical use remains limited due to high cost, complexity, and the need for centralized labs [29].
- Research gold standard: Especially valued for longitudinal tracking and multi-site biomarker standardization.

4.3. Mass Spectrometry (MS)

LC-MS/MS (liquid chromatography–tandem mass spectrometry) is a powerful analytical technique used primarily for quantifying Aβ42/Aβ40 and validating immunoassay results [15,30].

- Provides high specificity, avoiding cross-reactivity common in antibody-based assays.
- Often used in reference laboratories to establish assay standards and cutoff thresholds.
- Requires advanced equipment and expertise, limiting its routine diagnostic use [30].

Role: Essential for biomarker discovery, validation, and regulatory qualification.

4.4. Nanopillar & Photonic-Crystal Biosensors (Emerging POC Technology)

In 2025, a novel class of nanopillar photonic-crystal biosensors demonstrated label-free detection of Aβ42/Aβ40 in undiluted human serum with picogram/mL sensitivity [31].

- These sensors rely on light diffraction changes upon binding of amyloid peptides to the nanopillar surface.
- Offer rapid, portable, and low-cost diagnostic possibilities—suitable for point-of-care (POC) or home testing.
- Although still experimental, they hold great promise for mass screening and global accessibility [31].

Status: Preclinical stage with proof-of-concept completed.

4.5. Dried Blood Spot (DBS) Sampling

DBS technology is gaining attention as a minimally invasive, home-collectible alternative for Alzheimer's biomarker testing [32].

- Involves collecting capillary blood on filter paper and shipping it to central labs.
- Facilitates remote monitoring, population studies, and low-resource diagnostics.
- Ongoing efforts are validating DBS for ptau181, Aβ42/Aβ40, and NfL, although performance still lags behind plasma-based assays [32].

Platform	Sensitivity	Throughput	Clinical Use	Comments
Lumipulse	High	High	FDA-cleared	Best for clinical labs
SIMOA (Quanterix)	Ultra-high	Moderate	Research use	Leading research platform
Mass Spectrometry (MS)	Very High	Low	Validation only	Precise, but technically complex
Nanopillar Biosensors	High (emerging)	High (future)	In development	Portable & cost-effective
Dried Blood Spot (DBS)	Moderate (TBD)	Very High	Experimental	Ideal for population-level use

Table 1: Potential: May enable scalable community-based screening and longitudinal monitoring

5. Clinical Utility of Blood-Based Biomarkers in Alzheimer's Disease

Blood-based biomarkers have transitioned from research tools to clinically actionable diagnostics, informing care across diagnosis, early detection, risk stratification, treatment monitoring, and clinical trials. By 2025, several studies have confirmed the value of biomarkers like ptau217, Aβ42/40, NfL, and GFAP in real-world settings [16,19,20].

5.1. Diagnosis in Primary and Specialty Care

Clinicians now use blood biomarkers to:

- Confirm Alzheimer's disease (AD) in symptomatic individuals.
- Differentiate AD from frontotemporal dementia (FTD), Lewy body dementia (LBD), and vascular dementia (VaD).
- Reduce dependency on PET imaging and CSF lumbar punctures, which are invasive, costly, and less accessible [3,4,16].
- Evidence: A 2025 Swedish multi-center cohort study demonstrated that plasma ptau217, when used with a dual-threshold ("rule-in/rule-out") approach, identified AD pathology with 92–94% accuracy—across both general neurology and memory clinic populations [16].

5.2. Early Detection and Risk Stratification

Several biomarkers are now validated for identifying at-risk individuals before symptom onset:

- Elevated ptau217 and GFAP in cognitively normal adults correlate with amyloid PET positivity and future cognitive decline [20,21].
- NfL levels, especially when tracked longitudinally, predict conversion from mild cognitive impairment (MCI) to dementia [26].
- Combined panels (e.g., ptau217 + Aβ42/40 + NfL) improve the accuracy and specificity of risk stratification models [6,19].
- Notable Study: In the BioFINDER and ADNI cohorts, combining blood biomarkers with APOE genotype data yielded AUC values > 0.90 for predicting MCI-to-AD conversion [19].

5.3. Screening in Population Health and Primary Care

Blood-based AD diagnostics are now being considered for population-level screening, particularly among:

- Adults over 60 with subjective memory complaints.
- Individuals with APOE ε4 genotype or positive family history.
- Participants in early-intervention clinical trials, where preclinical enrollment is crucial [10,16,33].
- Example: Spanish memory clinics began offering plasma ptau217 screening as a first-line assessment before advanced imaging in 2025, aiding in triage and reducing diagnostic delays [33].

5.4. Clinical Trial Enrichment and Monitoring

Blood biomarkers now play a major role in trial optimization:

- Screening tool: Biomarkers like ptau217 and Aβ42/40 are used to pre-select amyloid-positive individuals, reducing PET screen failures and study costs [6,16].
- Therapy monitoring: In trials of lecanemab and donanemab, plasma biomarker reductions tracked with cognitive improvement, making them viable surrogate endpoints [34].
- Progression tracking: Serial measurements of NfL and GFAP correlate with neuronal injury and can reflect drug response better than cognitive scores alone [19,34].
- Recent Insight: In a 2025 Phase III trial, reductions in plasma ptau217 and GFAP were significantly associated with slower cognitive decline, validating their use in pharmacodynamic monitoring [34].

5.5. Limitations in Current Clinical Application

Despite their promise, several limitations persist:

- False positives in non-AD tauopathies like FTD, where ptau markers may be elevated without amyloid pathology [23].
- Demographic variability: Biomarker levels vary by age, sex, and ethnicity, requiring population-specific reference ranges [14,21].
- Limited reimbursement: Clinical plasma biomarker tests are not yet covered widely by insurers, especially outside the U.S. and Europe [28].
- Ethical concerns: Detecting preclinical AD in asymptomatic individuals raises questions around disclosure, counseling, and treatment access [12,35].
- Consensus Recommendation: Pre-test counseling and follow-up support are recommended for all individuals undergoing biomarker-based screening, especially if results indicate preclinical AD risk [35].

Clinical Application	Biomarker(s) Used	Status (2025)
Diagnostic confirmation	p-tau217, Aβ42/40 ratio	Validated, FDA-cleared
Differential diagnosis	p-tau217 vs. FTD, DLB	High specificity
Risk prediction in healthy adults	p-tau217, NfL, GFAP	Emerging
Trial recruitment	p-tau217, Aβ42/40	Actively used
Treatment monitoring	NfL, GFAP, p-tau181/217	Validated in trials
Routine screening	p-tau217 (POC and DBS)	In pilot implementation

Table 2: Clinical Uses of Key Biomarkers

6. Challenges and Limitations

Despite their transformative potential, the use of blood-based biomarkers in Alzheimer's disease (AD) diagnosis is accompanied by scientific, technical, clinical, and ethical challenges. Addressing these limitations is critical to ensure accurate, equitable, and responsible implementation at scale [6,12,35].

6.1. Analytical and Technical Variability

6.1.1. Assay Standardization

Different analytical platforms such as Lumipulse, SIMOA, and mass spectrometry (MS) may produce non-interchangeable values for the same biomarker due to variations in sensitivity, calibration, and detection principles [29,30].

- The absence of universal reference standards makes it difficult to harmonize thresholds and compare results across cohorts or geographic regions [6].
- This limits the development of global guidelines and impairs multi-center clinical trials [18].

6.1.2. Pre-analytical Factors

- Plasma biomarker levels are sensitive to collection, storage, and processing conditions [32].
- Factors such as hemolysis, anticoagulant type, delayed centrifugation, and freeze-thaw cycles can introduce variability and bias, especially in low-abundance proteins like ptau217 and Aβ42 [20,36].

6.2. Biological and Demographic Variability

6.2.1. Population-Specific Differences

Plasma biomarker levels vary across age, sex, ethnicity, and comorbidities [14,21].

- Studies in 2025 flagged concerns about reduced diagnostic accuracy in Black and Hispanic populations, largely due to underrepresentation in biomarker discovery cohorts [3,37].
- This lack of diversity may contribute to systematic misclassification and health disparities in AD detection.

6.3. Clinical Interpretation Challenges

6.3.1. Intermediate or Borderline Results

- Biomarker thresholds often result in a "gray zone" of intermediate values, particularly near clinical cutoffs [16,28].
- While dual-threshold models (i.e., "rule-in" and "rule-out")

improve diagnostic clarity, they still require clinical context and follow-up testing [16].

6.3.2. Non-AD Conditions Elevating Biomarkers

- NfL is a non-specific marker elevated in conditions like stroke, multiple sclerosis (MS), traumatic brain injury (TBI), and other neurodegenerative diseases [18,19].
- GFAP may rise in response to brain inflammation or reactive astrocytosis not related to AD pathology [20].
- Co-existing comorbidities, particularly in older adults, can lead to false positives or diagnostic uncertainty.

6.4. Ethical and Psychological Considerations

6.4.1. Preclinical Diagnosis

- **Detecting AD biomarkers in asymptomatic individuals raises important ethical questions:**
  - Should individuals be informed if no definitive treatment is available?
  - How do we counsel people at risk of future dementia?
  - Does early diagnosis empower preventive planning or increase anxiety and stigma?

6.4.2. Insurance and Discrimination Risks

- In the absence of clear regulations, there is concern that biomarker data could be misused by insurers or employers, especially in countries lacking genetic privacy laws [12,35].

6.5. Cost and Reimbursement Barriers

- Though blood-based biomarker tests are cheaper than PET imaging, they still cost USD 300–500 per assay in many regions [28,38].
- Inconsistent insurance reimbursement makes these tests inaccessible to many patients, particularly in low- and middle-income countries (LMICs) [39].
- Most national health systems have yet to define coverage criteria or establish cost-effectiveness thresholds for plasma-based diagnostics [6,38].

Challenge	Impact	Emerging Solution
Assay variability	Inconsistent results	Global standardization efforts (WHO, ADNI)
Biological heterogeneity	Lower accuracy in diverse groups	Multi-ethnic reference ranges
Indeterminate results	Diagnostic uncertainty	Dual-cutoff strategies
Ethical and psychological concerns	Distress from early diagnosis	Pre- and post-test counseling
Cost and access	Limited use in underserved areas	Insurance reimbursement and POC testing

Table 2: Key Challenges and Proposed Solutions

7. Future Directions

The use of blood-based biomarkers in Alzheimer's disease (AD) is accelerating beyond research and early diagnosis. By 2025, several assays have reached clinical translation, but the future holds promise for scalable screening, personalized treatment, and global equity in AD care [6,16,38].

7.1. Expansion of Point-of-Care (POC) Testing

Efforts are underway to decentralize biomarker testing through POC technologies such as:

- Nanopillar photonic biosensors capable of detecting Aβ42/Aβ40 at picogram/mL sensitivity in undiluted serum using label-free detection [31].
- Paper-based microfluidics and lab-on-a-chip systems that allow finger-prick sampling for home or primary care use [39].
- Dried blood spot (DBS) methods enabling mail-in testing, with ongoing validation for plasma ptau181, Aβ42, and NfL [32].

Impact: These tools promise low-cost, wide-scale access, especially in low-resource settings.

7.2. Multimarker Panels and AI-Based Risk Models

Future diagnostic models are trending toward multi-analyte integration:

- Panels combining ptau217, Aβ42/Aβ40, GFAP, NfL, and emerging markets like YKL-40 and neurogranin increase diagnostic depth and disease staging accuracy [6,16].
- Machine learning algorithms can incorporate biomarker profiles with clinical features (e.g., APOE status, age, cognitive scores) to:
- Predict cognitive decline,
- Stratify patients for trials,
- Guide personalized care plans [19,40].

Example: A 2025 AI-based study predicted MCI-to-AD conversion with >90% accuracy using integrated blood biomarkers and demographic features [40].

7.3. Integration into Preventive Healthcare

As data accumulate, blood biomarkers may enter routine health assessments, especially for older adults:

- Annual or biennial screening alongside cholesterol, glucose, and blood pressure.42
- Health systems in Sweden and Japan are piloting population-wide biomarker screening for adults ≥60 years with memory concerns or risk factors [33].

Goal: Enable early intervention before clinical onset.

7.4. Therapeutic Targeting and Biomarker-Guided Treatment

With recent FDA approval of anti-amyloid monoclonal antibodies (e.g., lecanemab, donanemab), biomarkers will guide treatment in 3 key ways:

1. Identifying eligible patients with confirmed amyloid pathology [34].
2. Monitoring therapeutic response via reductions in plasma ptau and GFAP.
3. Detecting treatment-related risks, such as amyloid-related imaging abnormalities (ARIA), using NfL and GFAP as safety markers [34].

Utility: Blood biomarkers may reduce dependence on repeated MRI and PET imaging.

7.5. Global Health Equity and Access

Equitable access to diagnostics is essential. Future directions include:

- Reducing cost barriers through local production and POC technologies [38].
- Ensuring ethnic validation of biomarker thresholds, especially in Africa, Asia, and Latin America [35,37].
- Expanding biobank diversity to improve algorithmic fairness in AI models and clinical studies [40].

Global efforts: The Global Alzheimer's Platform (GAP) and WHO Brain Health Initiative are investing in multi-ethnic cohort development and infrastructure.

7.6. Regulatory Approvals and Policy Integration

To become standard of care, biomarker assays must:

- Obtain approvals beyond the U.S. FDA, including EMA (Europe), PMDA (Japan), and regional regulators [28,41].
- Be included in clinical practice guidelines by organizations such as the Alzheimer's Association and European Academy of Neurology [41].
- Be reimbursed by public health systems and private insurers, with clearly defined cost-effectiveness thresholds [38].

Policy shift: Regulatory momentum is increasing in Canada, South Korea, and the EU, where coverage evaluations are underway.

Area	Advancements	Expected Impact by 2030
Point-of-care diagnostics	Nanotech biosensors, DBS kits	Universal screening access
AI integration	Predictive algorithms, digital platforms	Early, personalized risk scores
Clinical integration	Blood tests as part of annual check-ups	Early interventions
Treatment guidance	Biomarkers for drug selection/monitoring	Precision Alzheimer's medicine
Equity and access	Multinational validations, low-cost kits	Global AD risk mitigation
Policy and reimbursement	National coverage, updated guidelines	Clinical adoption worldwide

Table 4: Future Directions

8. Conclusion

The discovery of blood-based biomarkers represents a revolutionary change in the early diagnosis and treatment of Alzheimer's disease. Having verified plasma phosphorylated tau (p tau217), amyloid-β 42/40 ratios, neurofilament light chain (NfL), and glial fibrillary acidic protein (GFAP), we are seeing a transition from intricate, invasive, and costly diagnostics to minimally invasive, scalable, and affordable ones. Up to 2025, the fully automated assays like Lumipulse have attained regulatory approval, with diagnostic accuracies of over 90% and the onset of real-world clinical integration. In contrast, SIMOA and mass spectrometry continue to be critical instruments in research and validation. The clinical applications of blood biomarkers are already becoming a reality, not only for diagnosis and differential diagnosis, but also for early risk prediction, monitoring of treatment, and optimization of clinical trials. Still, challenges need to be overcome in the domains of standardization of assays, validation in specific populations, and ethical application. In the future, the intersection of AI-driven risk models, point-of-care technology, and multi-analyte panels will increasingly expand the limits of precision medicine. To make a global difference, however, efforts also need to extend to equity, access, and education, especially in underserved areas. Finally, blood-based diagnostics have the potential to democratize Alzheimer's treatment with the hope of earlier diagnosis, better results, and a brighter future for those at risk for or living with this debilitating condition.

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