

From Diagnostic Accuracy to Clinical Utility: A Comparative Review of Blood-Based Biomarkers in Alzheimer’s Disease Care in LMICs



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Background

Alzheimer’s disease (AD) is a leading cause of dementia worldwide, with 65% of the global economic burden expected to fall on low- and middle-income countries (LMICs) by 2050.¹ In these settings where positron emission tomography (PET) and cerebrospinal fluid (CSF) analytical infrastructure are largely unavailable, blood-based biomarkers (BBMs) are essential tools for early detection, yet their clinical adoption has lagged behind diagnostic validation. This narrative review examines the determinants shaping the clinical use of BBMs in LMICs and critically compares leading biomarker candidates within these constraints.

Methods

A comprehensive literature search was conducted using PubMed, Scopus, Web of Science, and the Cochrane Library. Search terms included combinations of “Alzheimer’s disease,” “blood-based biomarkers,” “phosphorylated tau,” “neurofilament light chain,” “clinical utility,” “cost-effectiveness,” and “low- and middle-income countries.” Peer-reviewed original studies, systematic reviews, meta-analysis, and international guidelines published between 2014 and 2026 were included. Evidence was synthesized using a multi-dimensional conceptual framework evaluating biomarkers across diagnostic performance, analytical feasibility, clinical interpretability, affordability, and scalability.

Table 1. Comparative Analysis of p-Tau and NfL

Determinant	Plasma p-tau	Plasma NfL	Implication for LMICs
 Diagnostic performance	High AD specificity; excellent discrimination (AUROC ≈0.80–0.90)	Moderate accuracy; sensitive to neurodegeneration but less AD-specific	p-tau preferred for AD diagnosis; NfL for staging and monitoring
 Analytical feasibility	Requires ultra-sensitive platforms (Simoa/IP-MS); technically demanding	Compatible with multiple assay platforms; more robust	NfL easier to implement in routine laboratories
 Clinical interpretation	Cut-offs vary; affected by comorbidities; often requires confirmatory testing	Consistently reflects neurodegeneration but not disease cause	p-tau needs specialist interpretation; NfL suitable for broader clinical use
 Affordability	Higher assay and infrastructure costs	Lower testing costs and simpler workflow	NfL more cost-effective for large-scale deployment
 Accessibility & scalability	Mainly available in research/tertiary centres	Greater potential for integration into primary and secondary care	NfL more scalable; p-tau best reserved for referral pathways

Abbreviations: p-tau = phosphorylated tau; NfL = neurofilament light chain; AD = Alzheimer’s disease; AUROC = area under the receiver operating characteristic curve; IP-MS = immunoprecipitation–mass spectrometry; LMICs = low- and middle-income countries.

Results

Plasma phosphorylated tau (p-tau) and neurofilament light chain (NfL) demonstrated complementary profiles across these determinants. p-tau showed high diagnostic accuracy for Alzheimer’s pathology, with area under the receiver operating characteristic curve (AUROC) values frequently exceeding 0.85 – 0.90. However, its use is constrained by assay complexity, higher per-test costs, and dependence on advanced laboratory platforms. In contrast, NfL exhibited high sensitivity to neurodegeneration, broader assay availability, and greater scalability, favouring deployment in resource-limited settings. Its limited specificity for AD pathology, however, reduces standalone diagnostic utility and necessitates its use in disease staging or prognostic monitoring. Comparative evaluation highlighted that no single biomarker optimally satisfies all determinants of clinical utility, particularly in LMIC contexts

Conclusion

Blood-based biomarkers have the potential to transform Alzheimer’s disease care, but real-world impact depends on alignment with system-level determinants beyond diagnostic accuracy alone. A tiered strategy leveraging the operational robustness of NfL for population-based screening and aetiological precision of p-tau for triaging in specialized care clinics within LMICs can advance equitable AD care globally.

References

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