

Plasma P-tau 181 Positivity In A Brazilian Primary Care Population

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TAKE HOME-MESSAGE: Plasma p-Tau181 reveals biological heterogeneity beyond clinical diagnosis in primary care, highlighting that dementia in real-world Global South populations often reflects diverse, non-Alzheimer etiologies.

Introduction

Blood-based biomarkers (BBMs) such as plasma p-Tau181 are increasingly proposed to support Alzheimer's disease (AD) detection beyond specialized memory clinics. As these biomarkers are considered for use across diverse community-based primary care populations, characterizing their behavior in real-world clinical contexts represents an important next step for informed interpretation and implementation

Table 1. Sociodemographic, and clinical characteristics of participants by cognitive status.

	CU No. 85	MCI No. 26	DEM No. 28
Age, mean years (SD)	68.7 (±6.4)	69.5 (±7.3)	77.8 (±7.0)
Women, n (%)	61 (71.8%)	19 (73.1%)	18 (64.3)
Race, n (%)			
Black	15 (17.6%)	7 (26.9%)	9 (32.1%)
Brown	11 (12.9%)	5 (19.2%)	2 (7.1%)
White	59 (69.4%)	14 (53.8%)	17 (60.7%)
Education, mean years (SD)	8.4 (±3.6)	7.3 (±4.0)	4.8 (±3.5)
Illiterates, n (%)	0 (0.0%)	0 (0.0%)	7 (25.0%)
Income, minimum wages mean (SD)	2.0 (±1.7)	1.3 (±0.7)	1.3 (±0.6)
Previous dx dementia, n (%)	0 (0.0%)	0 (0.0%)	5 (17.9%)

Methods

We conducted a cross-sectional study of 139 older adults receiving primary care-based home assistance in Brazil (Tab.1). Older adults were classified in cognitively unimpaired (CU), mild cognitive impairment (MCI), or dementia. Plasma pTau181 concentrations were analyzed using finite mixture modeling (FMM) to identify latent biomarker subpopulations and derive an empirical cutoff for biological AD positivity. The distribution of p-Tau181 classifications (negative, indeterminate, positive) was examined across diagnostic groups, and associations with demographic variables were explored.

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Results

Plasma p-Tau181 levels demonstrated a heterogeneous distribution with substantial overlap across cognitive categories. Two latent subpopulations were identified with mean p-Tau181 concentrations of 21.6 pg/mL (95% CI 19.3–23.9) and 55.9 pg/mL (95% CI 48.5–63.5), yielding an empirical cutoff of 35.3 pg/mL (95% CI 34.1–36.6) Fig.1. The proportion of individuals classified as p-Tau181-positive increased across diagnostic groups, from 17% in CU to 25% in MCI and 38% in DEM (Fig. 2). Increasing age (modeled as a continuous variable) was independently associated with p-Tau181 positivity in logistic regression analyses ($p < 0.0001$), while no significant differences were observed by gender. Notably, most participants with clinically diagnosed dementia did not meet biological criteria for AD based on plasma p-Tau181. Among clinically diagnosed dementia cases with negative plasma p-Tau181, vascular comorbidities were heterogeneous, supporting non-AD and potentially vascular-driven etiologies.

Figure 1. Estimated cutoff for pTau181 using finite mixture modeling.

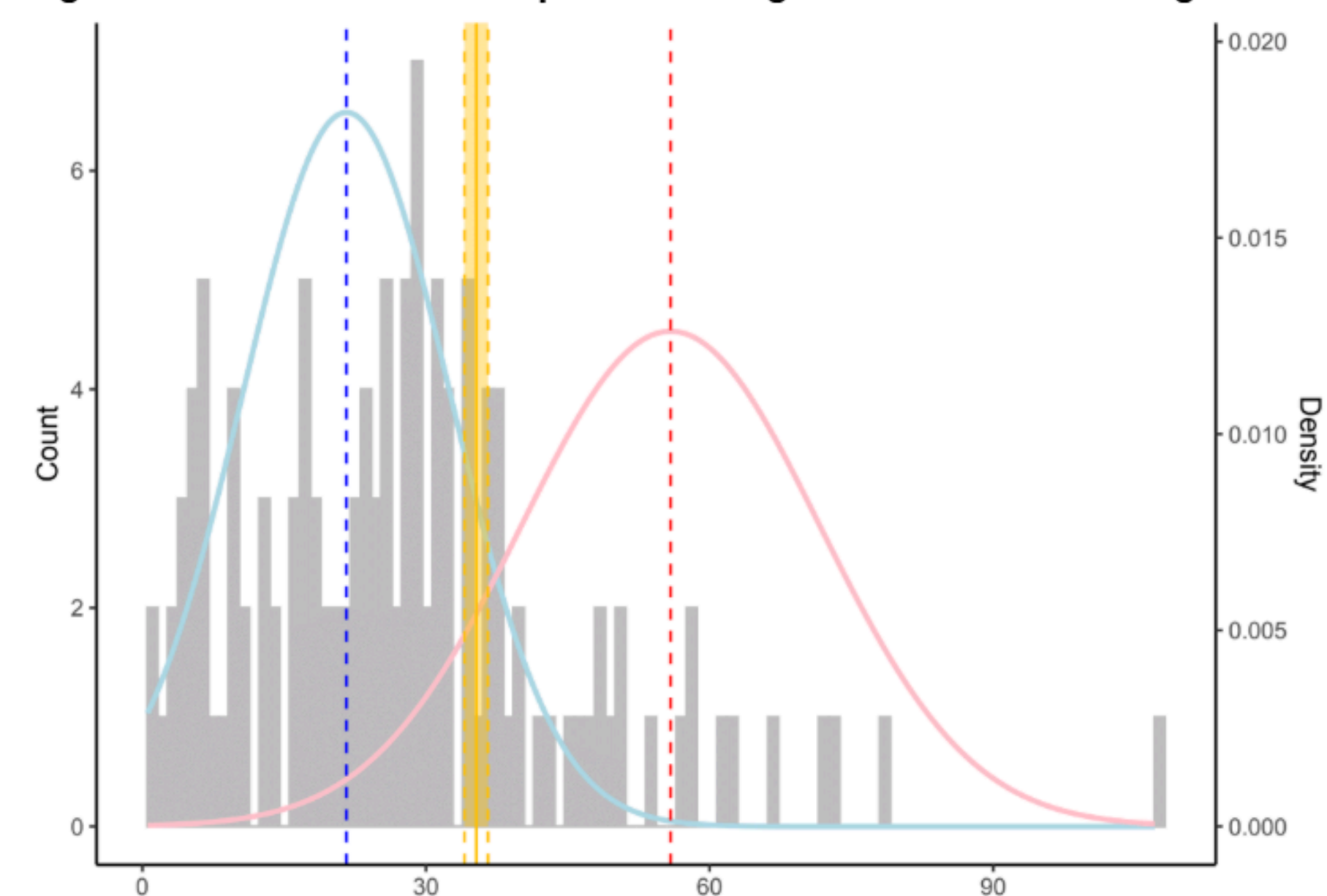
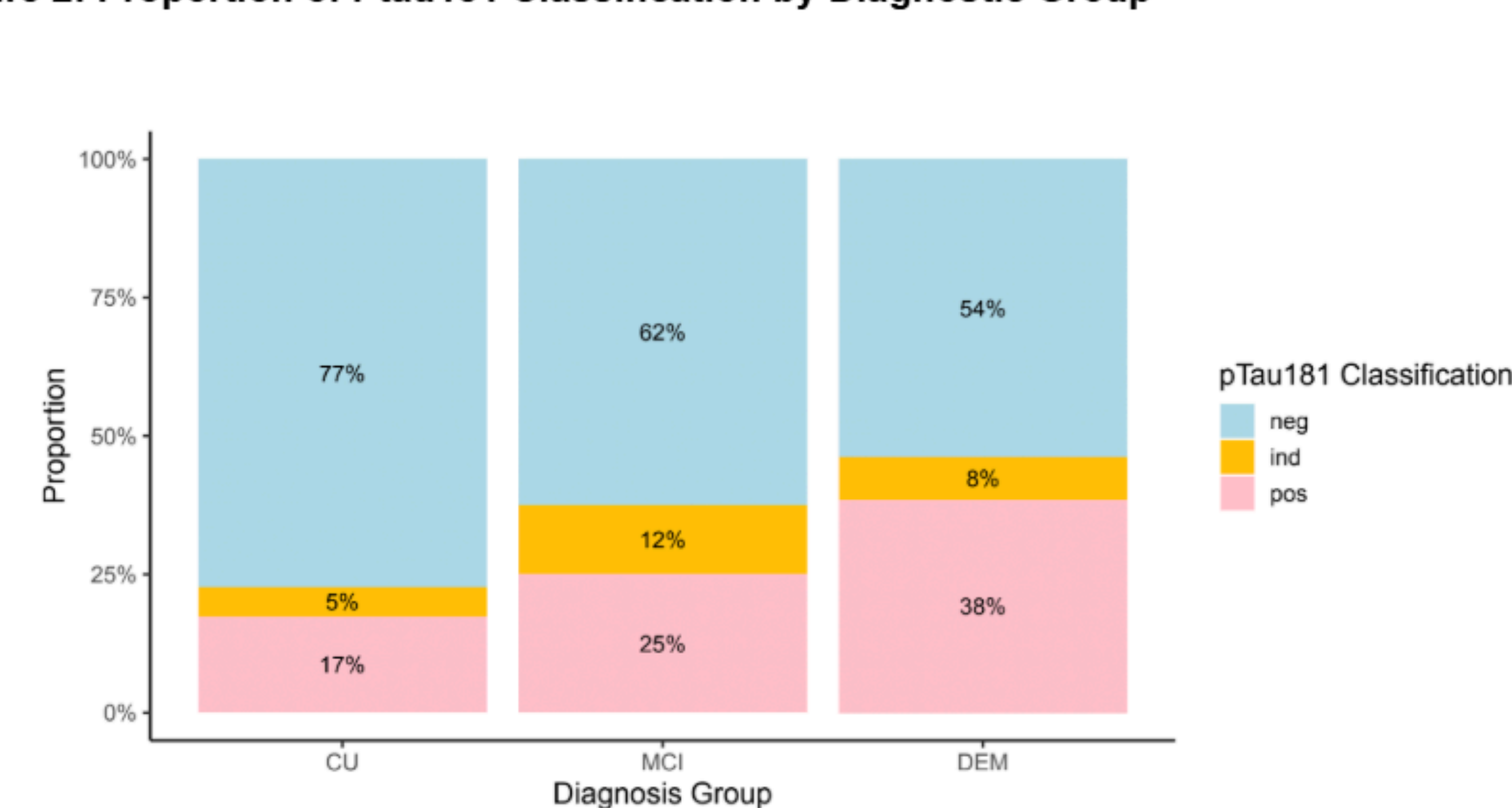


Figure 2: Proportion of Ptau181 Classification by Diagnostic Group



Conclusion

In a primary care population, plasma p-Tau181 reveals biological heterogeneity not fully captured by syndromic clinical diagnoses. The lower prevalence of biological AD among individuals with clinical dementia contrasts with specialized cohorts and may reflect a broader etiological spectrum, including non-AD and mixed pathologies, in community-based Global South settings. These findings highlight the need to interpret BBMs within the clinical and social realities of primary care populations, where diverse contributors to cognitive impairment may shape biomarker-phenotype relationships.

Acknowledgment

