

A Prospective Two-stage Cognitive and Blood-based Screening For Alzheimer's Risk In A Community Population

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INTRODUCTION

- Early detection of Alzheimer's disease (AD) remains challenging due to limited specialist capacity and reliance on costly or invasive diagnostic pathways.
- Community-based screening models integrated within primary care may improve access to AD risk assessment while supporting more efficient referral and care pathways.
- Prior retrospective analyses from Bio-Hermes showed that brief cognitive assessment combined with targeted blood-based biomarker testing can improve identification of individuals at elevated AD risk.
- This study prospectively evaluated the feasibility, operational performance, and clinical utility of a two-stage cognitive-plus-biomarker screening model in a real-world community setting.

METHODS

- Participants:** 520 adults age 55+ were recruited within The Villages®, FL through local PCP clinics between 1/12/26–3/27/26.
- Screening protocol:** Participants completed a self-report health/lifestyle survey, Cognivue Clarity® cognitive assessment with integrated Cognivue Amyloid Risk Measure (CARM), and LucentAD® Complete blood-based biomarker testing (CARM-L)
- Biomarker assessment:** LucentAD® Complete is a multi-analyte blood test that combines pTau217, Aβ42/40 ratio, NfL, and GFAP into a single AD risk score.
- A prospective decision-tree model** utilized cognitive performance as the initial triage, with BBM testing applied as a secondary adjudication step to refine amyloid risk into actionable categories.
- Derived categories** included Non-AD Dementia, AD Dementia, Probable Mixed Dementia, Preclinical AD, and True Control.
- Participant perceptions:** Utility, perceived value, and overall screening experience were also assessed.

Participant Characteristics and Clinical Stratification Outcomes

Table 1. Key participant characteristics

Characteristic	Total N=520
Age, mean ± SD	73.4 ± 7.0
Female, n (%)	282 (54.2%)
Cognivue Clarity® overall score, mean ± SD	72.1 ± 10.6
LucentAD® Complete score, mean ± SD	39.7 ± 24.5
pTau217, mean ± SD	0.05 ± 0.04
NfL, mean ± SD	22.1 ± 18.3
Overall experience, mean ± SD	9.8 ± 0.6

Table 2. Tree-derived categories

Category	n (%)
True Control	280 (53.8%)
Preclinical AD	105 (20.2%)
Non-AD Dementia	16 (3.1%)
AD Dementia	45 (8.7%)
Probable Mixed Dementia	74 (14.2%)

Tables 1 & 2. Participant Characteristics and Clinical Stratification Outcomes
Abbreviations: NfL = neurofilament light chain; AD = Alzheimer's disease.

Participant Profiles Across Tree-Derived Screening Categories

Table 3. Compact Outcomes + Key Characteristics

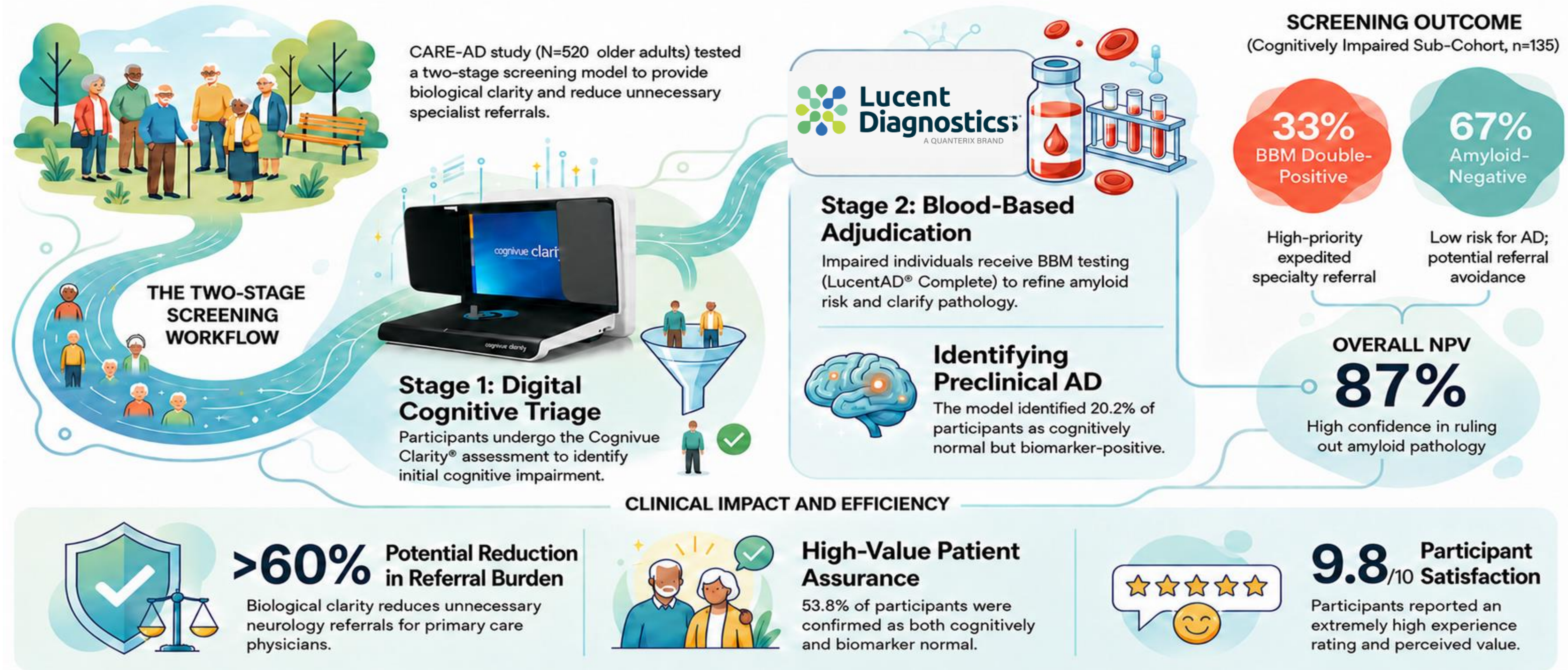
Group	n (%)	Mean age	Cognivue Clarity® score	LucentAD® Complete	Interpretation
True Control	353 (67.9%)	72.2 ± 6.5	77.1 ± 6.5	25.8 ± 7.8	Normal cognition + lower BBM risk profile
Preclinical AD	32 (6.2%)	76.6 ± 6.0	75.8 ± 6.3	72.3 ± 17.3	Normal cognition + elevated BBM risk profile
Non-AD Dementia	17 (3.3%)	66.2 ± 6.0	67.1 ± 5.2	25.1 ± 7.2	Impairment + lower AD-BBM risk profile
AD Dementia	22 (4.2%)	79.3 ± 5.9	57.3 ± 7.6	76.7 ± 17.8	Impairment + elevated AD-BBM risk profile
Probable Mixed Dementia	96 (18.5%)	76.6 ± 7.0	58.3 ± 10.0	26.6 ± 7.9	Impairment + mixed-risk profile

Table 3. Participant Profiles Across Tree-Derived Screening Categories
Abbreviations: BBM = blood-based biomarker; AD = Alzheimer's disease.

IMPLICATIONS

- This study demonstrates the feasibility of a two-stage community-based screening model to support AD risk assessment in a primary care-linked setting.
- By providing biological clarification of cognitive impairment at the local level, the model may help prioritize high-probability patients for specialty referral while offering reassurance to lower-risk participants.
- This scalable approach may help address specialist backlogs and support earlier intervention when therapeutic impact may be greatest.
- Future work should evaluate how two-stage cognitive and blood-based classifications influence participant health behaviors, clinical referrals, care planning, early intervention, and costs over time.

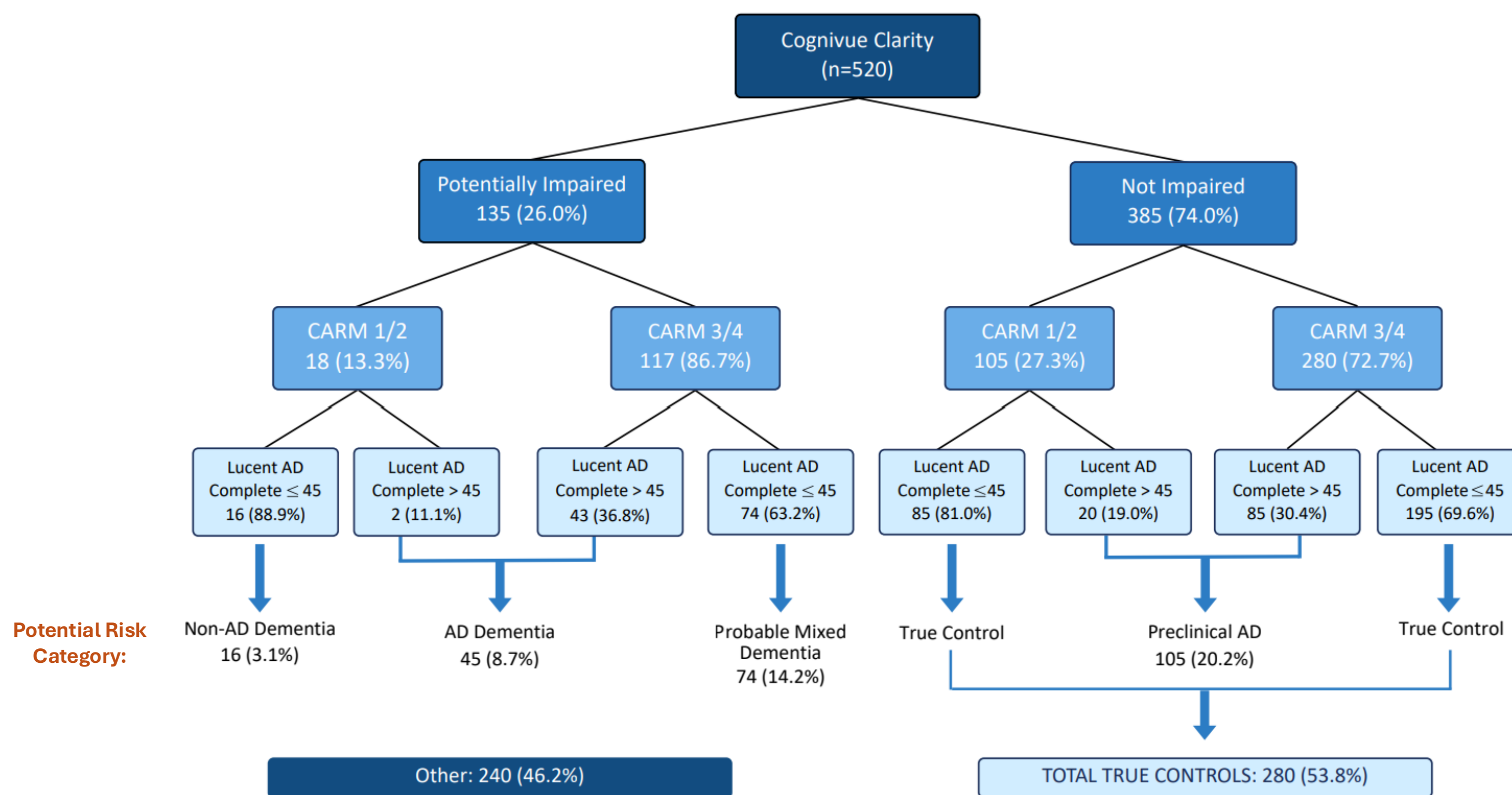
A New Frontier in Community-Based Alzheimer's Screening



RESULTS

- Risk differentiation:** Using the two-stage paradigm, the performance of 26.0% (n=135) were identified as potentially cognitively impaired by Cognivue Clarity®. For this sub-cohort:
 - BBM testing identified 45 cognitive test +/BBM+ individuals (33%), representing a high-priority group for potential expedited specialty referral.
 - Conversely, 90 impaired participants (67%) were BBM-; given the 87% NPV, AD pathology was unlikely, potentially reducing AD-focused specialty referrals by >60%.
 - Linear regression revealed Cognivue-impaired participants had higher NfL than True Controls, with a right-shifted distribution and approximately 11% higher age-adjusted log-NfL ($p = .016$). This supports the need for follow-up pathways beyond AD-focused referral alone, including evaluation of vascular, cardiovascular, structural, or other non-AD contributors (median difference = 4.41 pg/mL, Mann Whitney $p < .001$)
- BBM adjudication among impaired participants:** Within this sub-cohort, BBM testing identified 45 participants with an AD Dementia screening profile and 90 participants with BBM-negative impaired profiles, including Non-AD Dementia (n=16) and Probable Mixed Dementia (n=74).
- Early risk identification:** Although the intended workflow targets cognitively impaired participants, the study also identified 20.2% (n=105) as Preclinical AD (cognitively normal/BBM-positive), offering a critical window for future intervention or inclusion into clinical trials.
- Reassurance:** 53.8% of participants received high-value assurance as both cognitively and biomarker normal supporting impactful quality-of-life reassurance for the majority of participants screened.
- Participant perceptions:** 2-step CARM-L screening was favorably received with an overall experience rating of 9.8/10.

Figure 1: Two-Stage Screening Classification Pathway



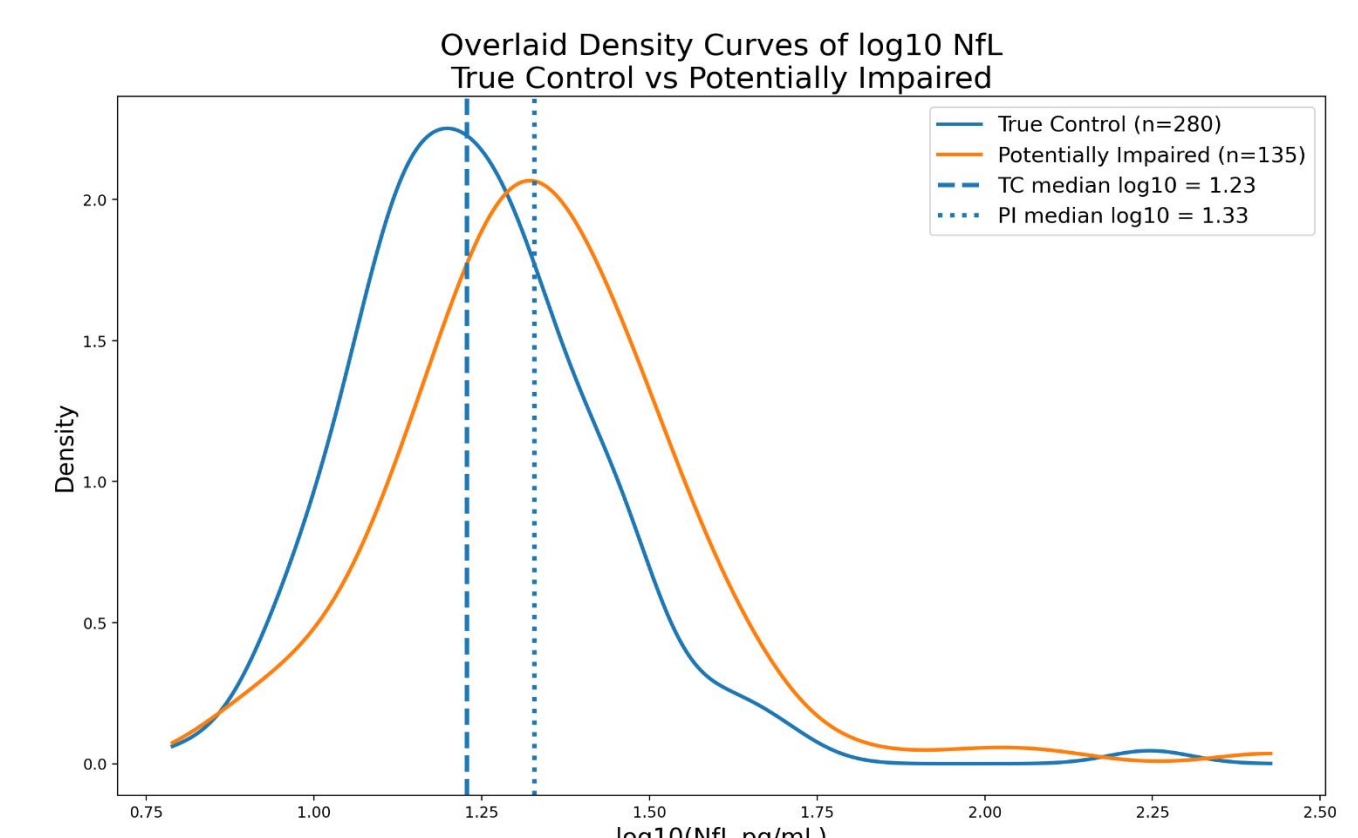
Exploratory Analysis of NfL in True Control vs Potentially Impaired Groups

Table 4. NfL Levels - True Control vs. Potentially Impaired Groups

Group	Mean NfL	Median NfL	Q1	Q3	Max
True Control	19.74	16.90	13.13	21.95	181.14
Potentially Impaired	25.87	21.31	16.34	28.38	266.70

Abbreviations: NfL = neurofilament light chain

Figure 2: NfL Burden in True Control vs Potentially Impaired Groups



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