

Lopamudra Das¹, Trevor Burgon², Kinal Bhatt¹, Kelsy Gibson Ferrara², David Paculdo², Eric De Belen², Czarlota Valdenor²

¹Beckman Coulter Diagnostics, Brea, CA; ²QURE Healthcare, San Francisco, CA

KEY TAKEAWAY: Access to a high-performance blood-based p-Tau217/Aβ1-42 biomarker significantly improved diagnostic concordance of mild/early-stage Alzheimer’s disease (+26.2 pp, p=0.007) and reduced reliance on PET/CSF testing (–10.6 to –23.9 pp), with the most pronounced and statistically significant effects observed in clinical encounters where no other blood-based biomarkers were ordered (concordance +35.0 pp, p=0.049; PET/CSF –23.9 pp, p=0.046)

INTRODUCTION & METHODS

RESULTS

BACKGROUND

- Accurate diagnosis and staging of Alzheimer’s disease (AD) are increasingly critical with the emergence of disease-modifying therapies
- Current diagnostic approaches rely on PET imaging and CSF biomarkers, which are limited by cost, invasiveness, and accessibility
- Blood-based biomarkers (BBMs) offer a less invasive alternative and more scalable approach to aiding the diagnosis of AD
- Recent 2025 Alzheimer’s Association clinical guidelines support BBMs with high performance (≥90% sensitivity and specificity) for confirmatory use for use in diagnostic workflows¹
- There is limited prospective evidence on how BBM access influences clinician decision-making

STUDY OBJECTIVE

Evaluate how education and access to a novel BBM influence neurologists’ diagnostic accuracy and clinical decision-making

METHODS

- Study design:** Prospective, randomized controlled study using validated interactive virtual patient simulations (ClinicalTrials.gov: NCT07099001)
- Participants:** 142 U.S. board-certified neurologists (control n=70, intervention n=72) completed 6 virtual patient cases across 2 rounds (baseline + follow-up).
- Cases:** 6 unique presentations including mild/early-stage AD (n=2), intermediate/moderate-stage AD (n=2), and non-AD cognitive decline (n=2) — vascular dementia and hepatic encephalopathy.
- Intervention:** Participants received AD ratio p-Tau217/Aβ1-42 (≥90 sensitivity/specificity) test results at the start of Round 2 case workup. Control-arm participants did not receive the ratio test at the beginning, but were free to order BBMs
- Primary outcomes:** (1) diagnostic concordance with prespecified expert-defined case definitions, (2) CSF/PET ordering rates
- Analysis:** Encounter-level difference-in-differences (DiD) with arm × round interaction. Python 3.9 / statsmodels v0.14.6. All p-values two-sided, α=0.05.

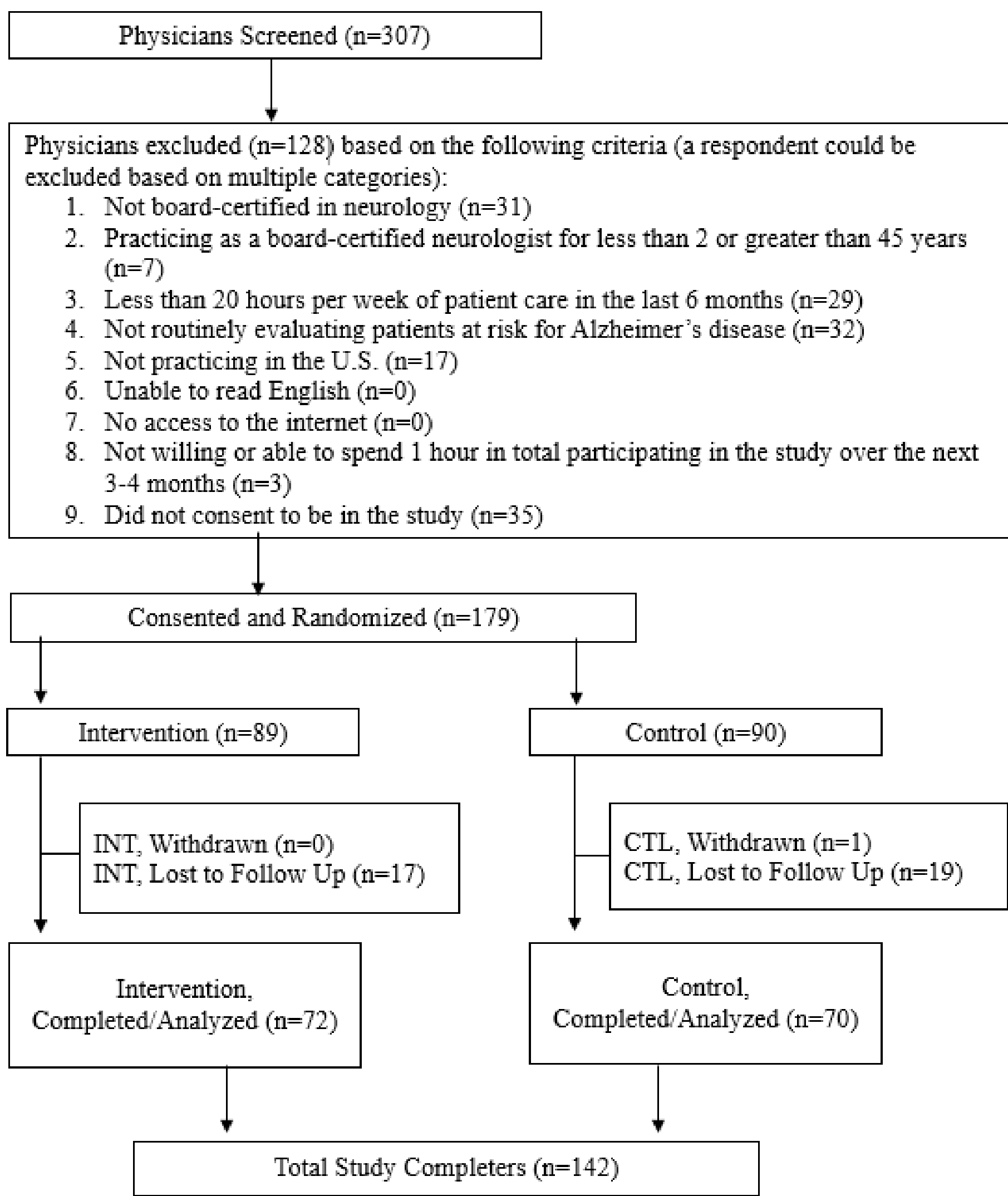


Figure 1: Participant Recruitment Flowchart

PARTICIPANT CHARACTERISTICS

- In total, 307 invitees were screened, and 142 neurologists completed 852 virtual patient encounters (**Figure 1**)
- There were no significant differences in baseline demographics or practice characteristics between groups

BASELINE PRACTICE ASSESSMENT

- Cognitive assessments were nearly universally ordered (97.9%) along with family history elicitation (96.7%)
- Baseline diagnostic engagement style was high:
 - BBM use was high (67.1%)
 - PET/CSF use: 69.0%
- Staging assessments concordant with case definitions 61.0% of the time, with variation by disease category and severity:
 - 81.7% for vascular dementia,
 - 80.8% for mild/early-stage AD
 - 18.3% for hepatic encephalopathy, and
 - 51.4% for intermediate/moderate-stage AD
- Disease-modifying therapies (DMT) were recommended 56.7% of time in all AD cases with more frequent orders for mild/early-stage patients than in more advanced disease stages (69.9% vs. 42.8%, p<0.001)

IMPACT ON DIAGNOSTIC CONCORDANCE and PET/CSF ORDERING

- A +26.2 percentage-point improvement in mild/early AD diagnostic concordance (p=0.007) — the clinical setting where accurate, timely diagnosis is most consequential for DMT eligibility decisions (**Table 1**)
- The AD ratio test was associated with a directional reduction in CSF/PET ordering across the full sample, with the strongest within-arm reduction in non-AD encounters (47.2% → 29.2%, p=0.026) (**Table 1**)
- In encounters where no additional commercially available BBMs were ordered (N=302, **Table 2**), access to the intervention AD ratio test was associated with:
 - +20.0 pp directional improvement in overall diagnostic concordance (p=0.116), with the largest significant gain observed in mild/early-stage AD (+35.0 pp, p=0.049, *not shown here*)
 - CSF/PET ordering significantly declined (DiD –23.9 pp, p=0.046)

Case Type	Control Baseline → F/U	Intervention Baseline → F/U	DiD (pp)	p-value
DIAGNOSTIC CONCORDANCE				
All encounters	63.8% → 57.6%	55.1% → 61.1%	+10.7	0.149
Mild/early AD	87.8% → 72.7%	73.6% → 84.7%	+26.2	0.007*
Intermediate/moderate AD	51.5% → 47.3%	41.7% → 48.6%	+4.2	0.702
Non-AD	50.0% → 54.3%	50.0% → 50.0%	–0.3	0.986
PET/CSF ORDERING				
All encounters	72.4% → 70.5%	65.7% → 53.2%	–10.6	0.078
Mild/early AD	87.8% → 83.3%	81.9% → 66.7%	–10.8	0.293
Intermediate/moderate AD	75.8% → 77.0%	68.1% → 63.9%	–5.4	0.576
Non-AD	52.9% → 51.4%	47.2% → 29.2%	–16.6	0.104

Table 1: Impact on Diagnostic Concordance and PET/CSF Ordering (N=852 encounters)

Sample	n	CSF/PET DiD	Concordance DiD
All encounters	852	–10.6 pp (p=0.051)*	+10.7 pp (p=0.149)
BBM-informed	652	–14.0 pp (p=0.078)	+2.8 pp (p=0.554)
No additional BBMs	302	–23.9 pp (p=0.046)*	+20.0 pp (p=0.116)

Table 2: Impact on Diagnostic Concordance and PET/CSF Ordering by BBM use status

CONCLUSIONS	REFERENCES/ CONTACT
- High-performance BBMs improve diagnostic concordance, with the greatest gains in early/mild AD - BBMs reduce reliance on PET/CSF testing enabling more efficient diagnostic pathways - Impact is most pronounced in: - Mild/early-stage disease - When no supplemental AD BBMs were ordered - Findings support BBMs as tools to: - Improve diagnostic precision - Enable earlier treatment decisions - Optimize healthcare resource utilization - High baseline adoption suggests readiness for real-world adoption - These findings demonstrate that BBMs can improve diagnostic concordance while simultaneously reducing reliance on invasive and high-cost confirmatory testing	1. Palmqvist S, et al. Alzheimer’s Association Clinical Practice Guideline on the use of blood-based biomarkers in the diagnostic workup of suspected Alzheimer’s disease within specialized care settings. Alzheimer’s & Dementia. 2025;21(7):e70535. Lopamudra Das, PhD, MPH Beckman Coulter Diagnostics ldas@beckman.com COI Disclosure: LD is an employee of Beckman Coulter Diagnostics