

Evaluating Biomarker Utility in a Real World Clinical Setting

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INTRODUCTION

- The advent of disease modifying treatments for Alzheimer's disease (AD) has created a **rapid increase in demand for clinical and biological confirmation**.
- Plasma blood-based biomarkers (BBMs) may support biological confirmation though uncertainty remains regarding their integration and performance against long-standing reference standards.
- We evaluated the "real-world" context of use and diagnostic performance of BBMs for AD in a multidisciplinary memory disorders clinic

METHODS

- We conducted a retrospective analysis of **patients evaluated at a single memory disorders clinic who underwent biomarker testing for suspected Alzheimer's disease**.
- Modalities included **plasma mass spectrometry (MS), CSF biomarkers obtained by lumbar puncture, plasma immunoassay, and amyloid PET imaging**.
- Demographics were extracted from the electronic medical record to **evaluate biomarker utilization, testing patterns, and influence on diagnosis and care planning**.

Modality	Clinical role	Practical considerations
Blood-based biomarkers	- Minimally invasive AD biomarker option - Supports diagnostic clarification - Flags patients needing confirmation	- Insurance coverage may be inconsistent - Performance varies by assay/platform - Discordant results may require CSF or PET
CSF biomarkers	- Biochemical evidence of AD pathology - Assesses multiple AD-related analytes - Clarifies blood-based results	- More invasive than blood-based testing - Requires lumbar puncture - May be less acceptable to some patients
Amyloid PET imaging	- Visual confirmation of amyloid burden - Useful when certainty affects care - Clarifies uncertain biomarker findings	- Higher cost and lower accessibility - Limited amyloid-specific radiotracer availability - Does not capture all etiologies

AD, Alzheimer's disease; CSF, cerebrospinal fluid; PET, positron emission tomography. Blood-based category includes plasma biomarker testing platforms.

Figure 1. Note. Adapted from "Selection and Interpretation of Biomarker Tests for Alzheimer Disease," by J. A. Tanner and S. E. Schindler, 2025, Practical Neurology, July 2025 issue.

RESULTS

- A total of **1,208 patients** were included. The median age was 76.8 years old, with the majority female 662; 62.6%) and White (928; 78.6%). Educational attainment included advanced education in 205 patients (20.6%), bachelor's degree in 248 (24.5%), high school in 323 (32.4%), and some college in 191 (19.2%). Among participants with available APOE genotyping, **360 (50.3%) were APOE ε4 carriers, including 50 homozygous (7.0%) and 310 heterozygous carriers (24.1%)**.
- Plasma mass spectrometry was the most commonly utilized biomarker modality (826 patients; 70.0%)**. Followed by CSF Lumbar puncture biomarkers was performed in 129 patients (10.9%), plasma immunoassay testing in 29 patients (2.5%), and amyloid PET imaging in 72 patients (6.1%).
- Most patients (982; 83.2%) completed a single biomarker modality, most commonly MS-based plasma biomarker testing alone. **Forty five patients (3.8%) completed multiple biomarker modalities**, typically to clarify diagnostic uncertainty following plasma results or indeterminate or intermediate findings from CSF or amyloid PET testing.
- Biomarker results influenced clinical decision making in over 75.9% of patients**, most commonly through revisiting established diagnoses 57.5%, and prescreening for anti-amyloid therapies or clinical trial eligibility 10.8%.
- Biomarker results prompted additional testing in 7.7%. **Among patients undergoing both MS-based plasma biomarker testing and amyloid PET imaging, overall percent agreement was 91.7% (11/12)**, with substantial agreement beyond chance (Cohen's κ = 0.625, p = 0.0195)

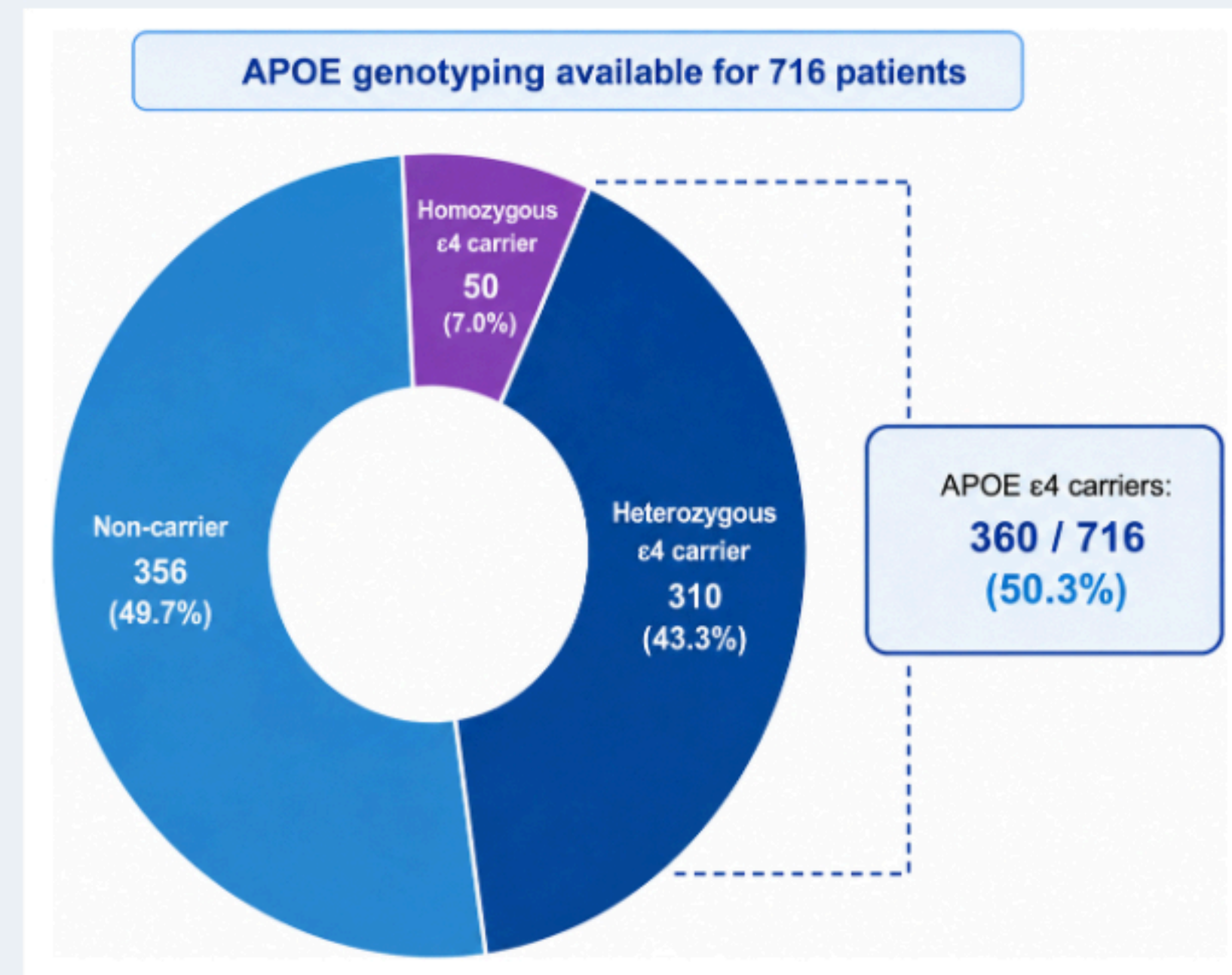


Figure 2. APOE ε4 Carrier Status in Genotype Patients. Among patients with available APOE genotyping, 50.3% were APOE ε4 carriers, while 49.7% were non-carriers.

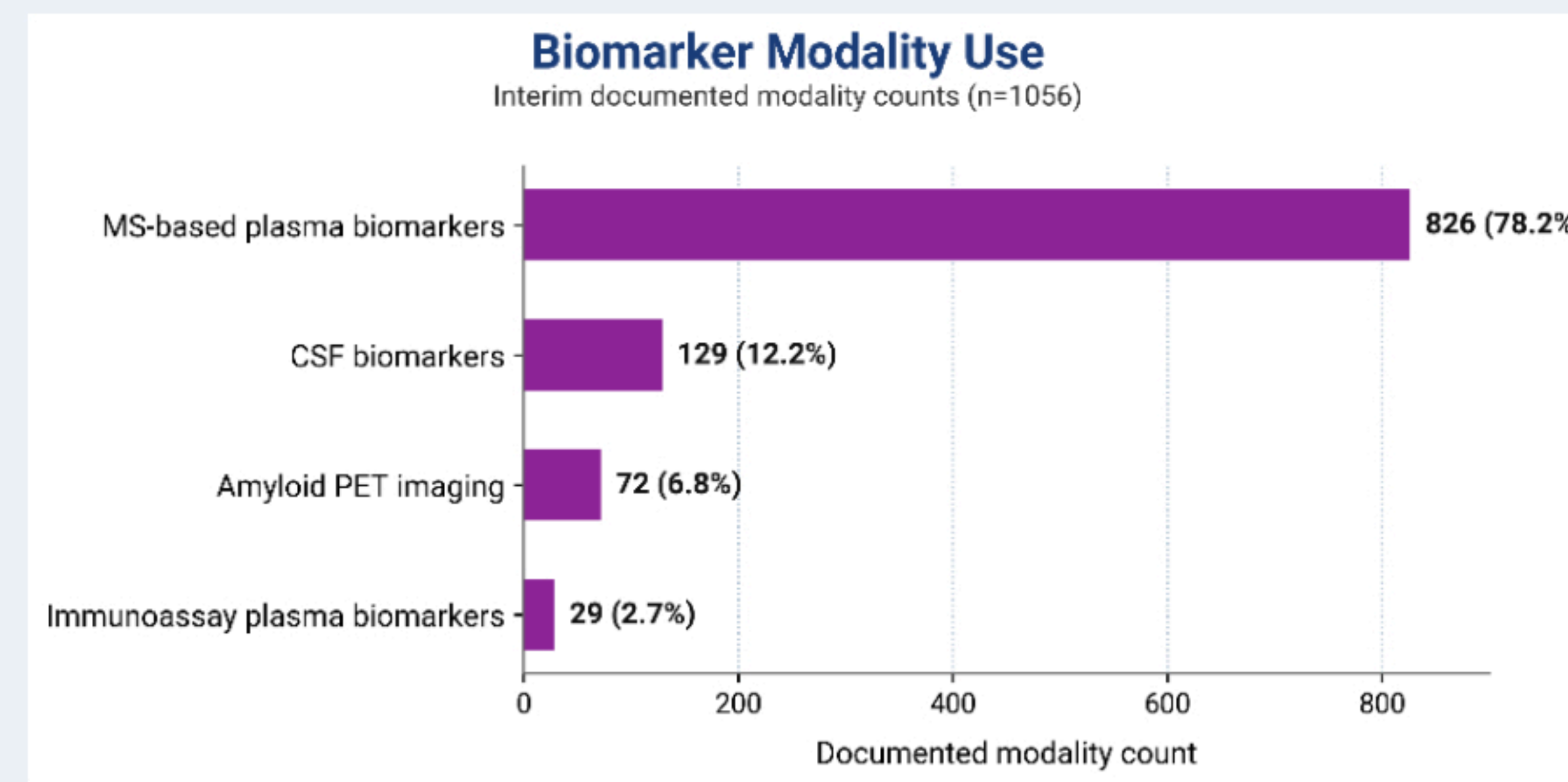


Figure 3. Biomarker modality use. Interim documented biomarker modality counts showed MS-based plasma biomarkers as the most frequently used modality, followed by CSF biomarkers, amyloid PET imaging, and immunoassay plasma biomarkers.

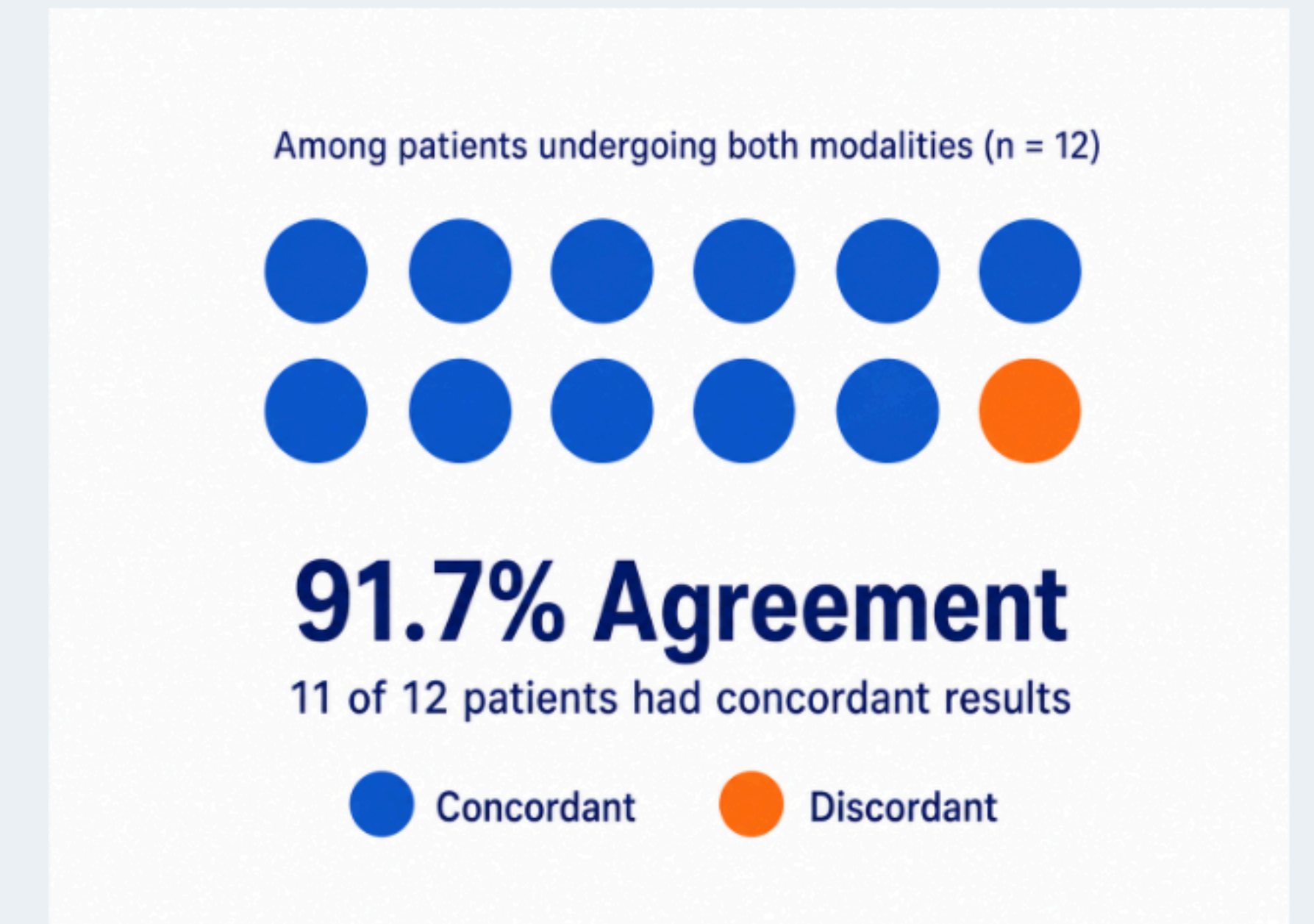


Figure 4. Concordance between MS-based plasma biomarkers and amyloid PET. Among patients who completed both modalities, 91.7% had concordant results, with 11 of 12 patients showing agreement between MS-based plasma biomarker testing and amyloid PET imaging.

CONCLUSION & DISCUSSION

- These findings explore the context of use of BBM integration in a real-world clinical practice
- MS plasma testing served as the primary entry point in support of a stepwise diagnostic approach, with multimodal testing reserved for cases requiring diagnostic clarification.**
- BBMs were frequently **considered in tandem with a full clinical work up to impact diagnostic certainty, clinical decision making, and eligibility for disease modifying therapy.**
- Navigation of concordant and discordant biomarker results will be essential as biomarker driven diagnosis and treatment becomes central to Alzheimer's disease care.
- Future studies may aim to include heterogenous populations and address confounding factors to **support development of a clinical practice guideline that balances robustness with the promising utility of BBMs**

LIMITATIONS

- This was a **retrospective study** completed at a single site
- Confounding factors** such as chronic kidney disease, obesity, and cardiovascular health history **were not explored within this study.**
- The study population was of **homogenous race.**

ACKNOWLEDGEMENTS

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Figure 1 was adapted from "Selection and Interpretation of Biomarker Tests for Alzheimer Disease," by J. A. Tanner and S. E. Schindler, 2025, Practical Neurology, July 2025 issue. C2N provided funding for conference attendance. The study design, data & analysis, and conclusions are entirely of the authors.