

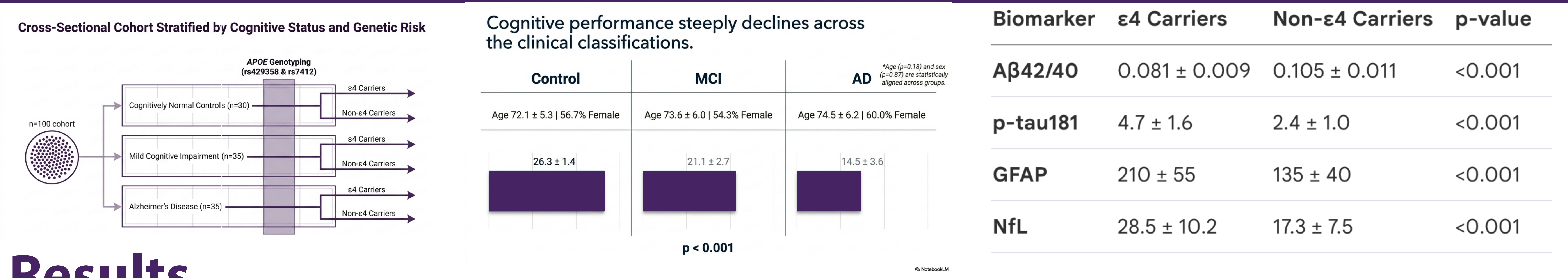
# Genetic Risk and Blood-Based Biomarkers in Alzheimer's Disease: Role of APOE in Amyloid Pathology



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## Introduction to the Biological Framework of Alzheimer's Disease

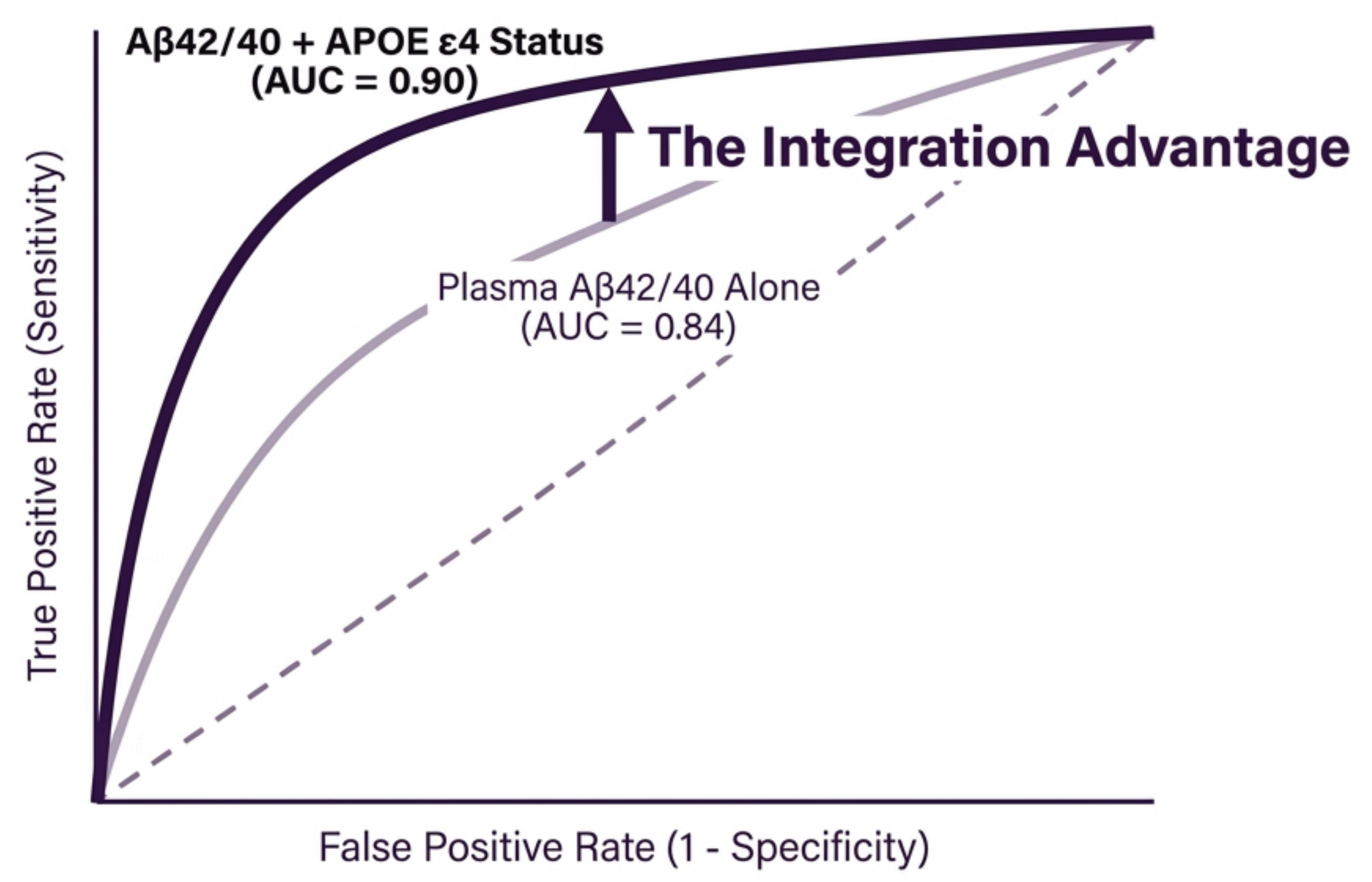
Alzheimer's disease is traditionally recognized by progressive cognitive decline linked to amyloid- $\beta$  (A $\beta$ ) deposition and tau pathology. However, modern clinical approaches are shifting toward a biological definition that prioritizes biomarkers over clinical symptoms alone.



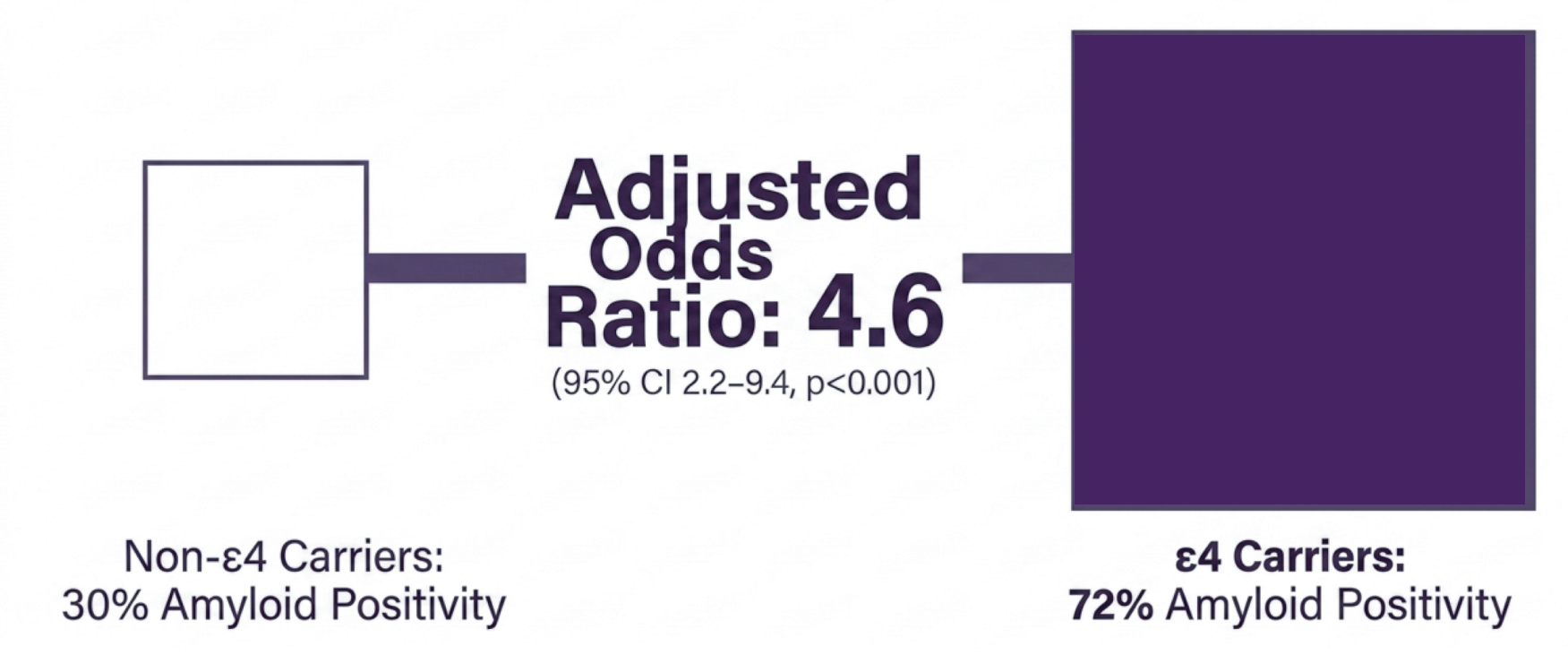
## Results

### The $\epsilon$ 4 Allele Drives a Coordinated Pathological Signature in the Blood

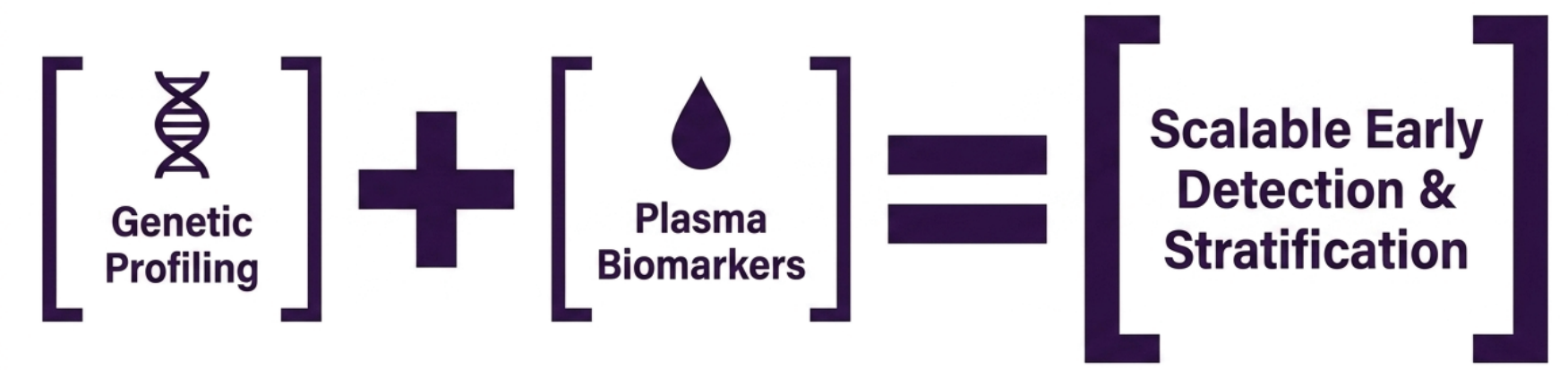
|                 | Non- $\epsilon$ 4 (Baseline) | $\epsilon$ 4 Carriers (Elevated Risk) |       |
|-----------------|------------------------------|---------------------------------------|-------|
| A $\beta$ 42/40 | 0.105                        | 0.081                                 | ratio |
| p-tau181        | 2.4                          | 4.7                                   | pg/mL |
| GFAP            | 135                          | 210                                   | pg/mL |
| NfL             | 17.3                         | 28.5                                  | pg/mL |



### APOE $\epsilon$ 4 is an Independent, High-Magnitude Predictor of Amyloid Pathology

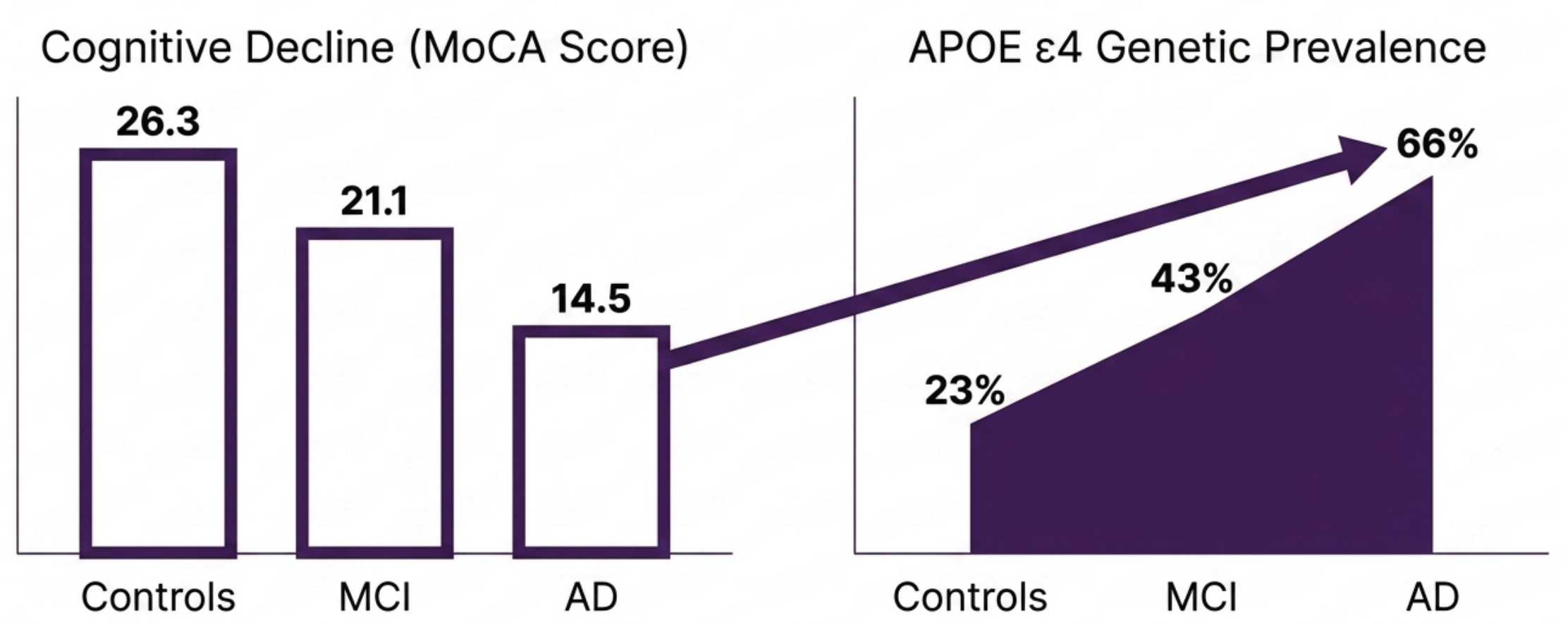


### A Scalable Framework for the Future of Early Detection



APOE  $\epsilon$ 4 orchestrates a multi-dimensional biological signature. Combining these modalities provides the necessary paradigm shift for highly accurate, accessible Alzheimer's diagnostics.

### APOE $\epsilon$ 4 Prevalence Spikes as Cognitive Performance Declines



Plasma AB42/40 alone discriminated amyloid positivity (AUC=0.84). Incorporating APOE e4 status significantly improved performance (AUC = 0.90), highlighting the added value of integrating genetic and plasma biomarkers.

## Conclusion

APOE  $\epsilon$ 4 strongly influences amyloid pathology, neurodegeneration, and cognitive decline. Integration of genetic risk with blood-based biomarkers provides a powerful and scalable approach for early detection and stratification of Alzheimer's disease.

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