

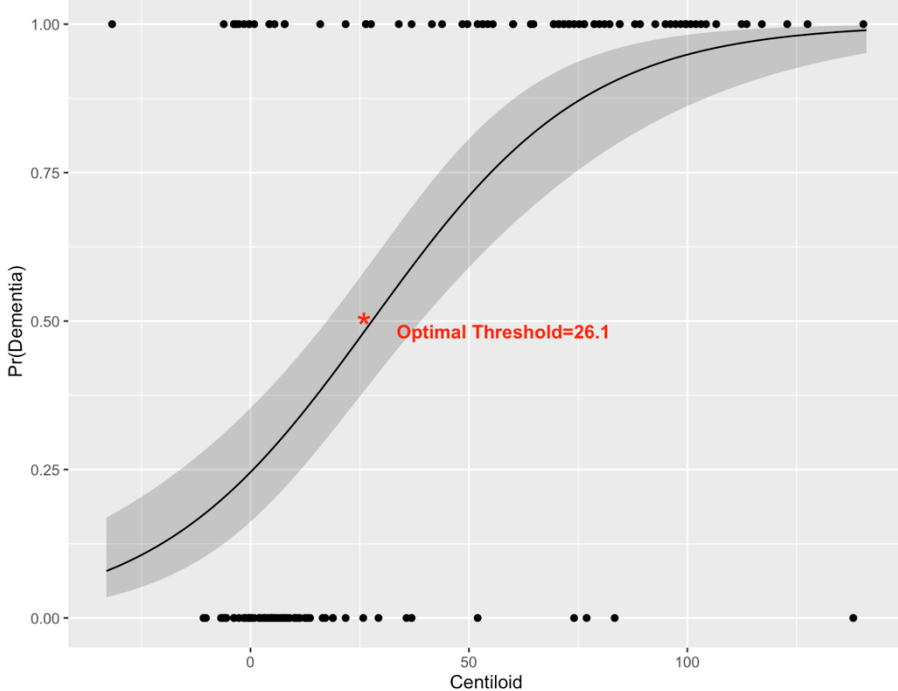
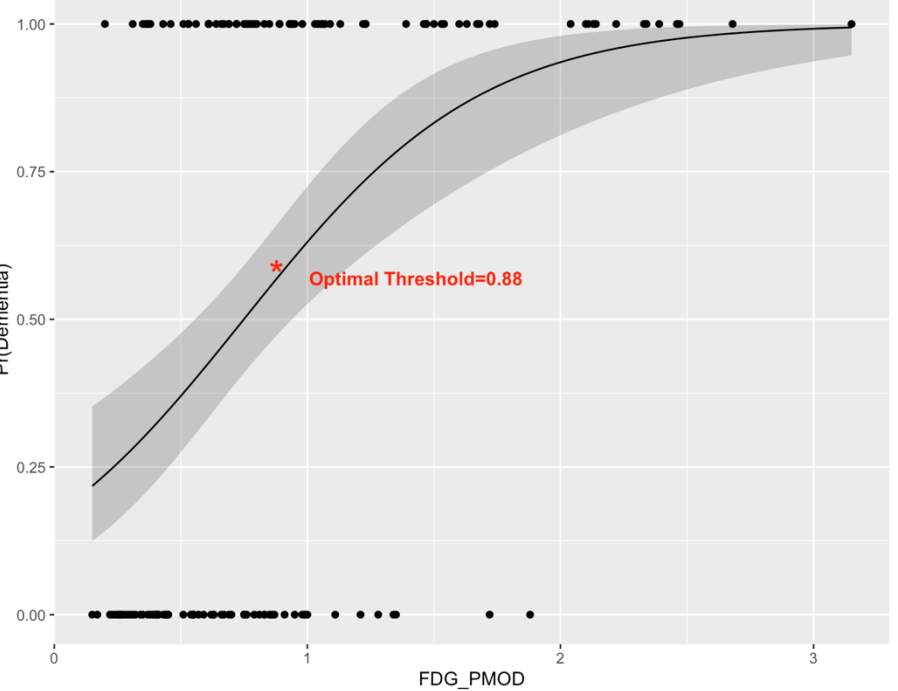
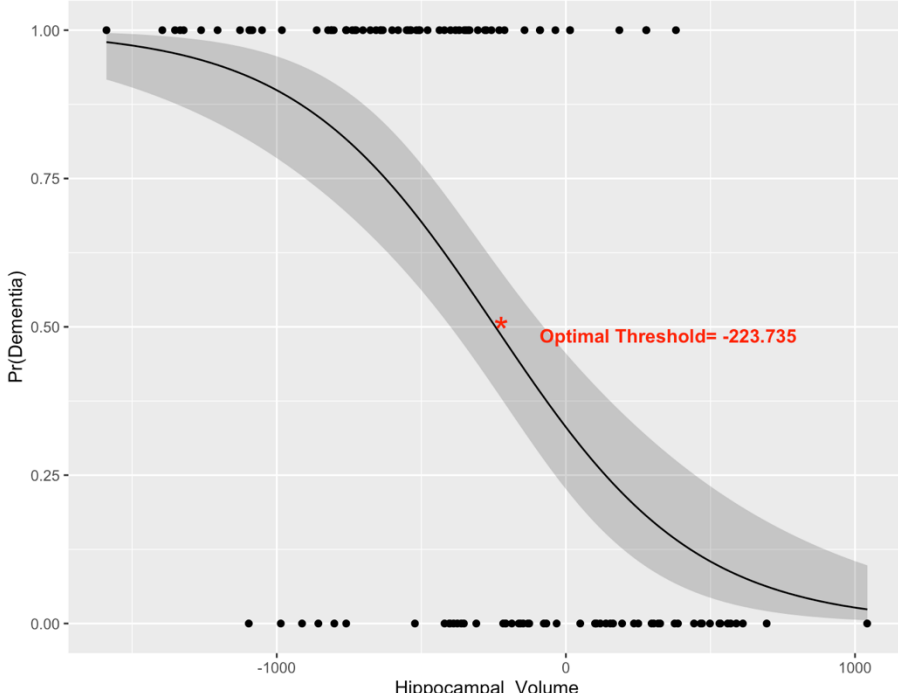
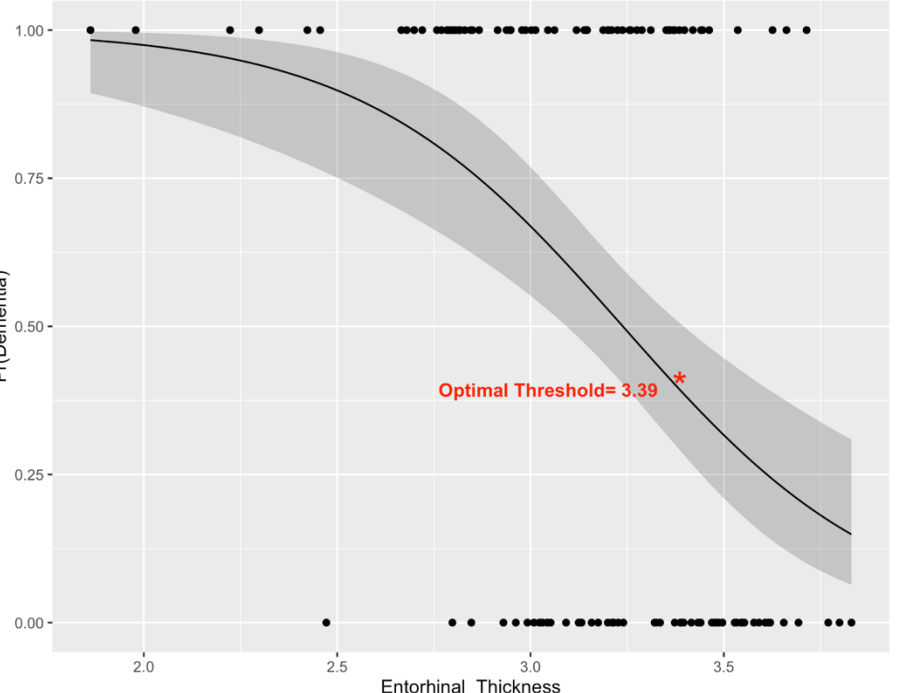
Utility Of Biomarker Predicted Probability Estimates
Compared To Cutoff Scores

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Key point: Predicted probability estimates of biomarker status, created through logistic regression and associated with a specific clinical outcome, offer patients a more accurate assessment of dementia risk and more actionable insights than basic cutoff scores.

INTRODUCTION	METHODS	RESULTS	CONCLUSIONS
- Fluid and imaging biomarkers of Alzheimer’s disease (AD) are now essential for dementia diagnosis and risk assessment - Clinical decision-making typically evaluates whether a patient’s biomarker value exceeds a threshold value - Such binary decisions neglect the probabilistic relationship between biomarker values and the probability of a clinical outcome, such as dementia - In this <u>10-year prospective study</u>, we developed risk curves and equations estimating the 10-year probability of dementia using participants’ baseline values of four imaging biomarkers	- Participants were 153 adults (31 healthy controls, 35 with subjective cognitive decline, and 87 with mild cognitive impairment) aged 52 to 86 years (<i>M</i>=71 years, <i>SD</i>=7.5) - All participants underwent baseline fluorodeoxyglucose (FDG) and amyloid PET and structural MRI; detailed neuropsychological testing was performed at study entry and every 2 years for up to 10 years - We computed predicted probability curves using logistic regression for the 10-year risk of dementia, using amyloid PET Centiloid score, FDG-PET PMOD score, bilateral hippocampal volume, and entorhinal cortex thickness	- Over the 10-year observation period, 51% of participants developed dementia - All four biomarkers significantly predicted dementia onset (<i>p</i><0.0001). Their AUCs were: Centiloid (0.816), FDG-PMOD (0.760), Hippocampal Volume (0.821), and Entorhinal Cortex Thickness (0.741) - The curves below illustrate 10-year dementia risk estimates (± error) of dementia using baseline biomarker values; the ROC’s “optimal threshold”—marked by an asterisk—separates biomarker-positive from negative cases Amyloid PET Centiloid  FDG PMOD  Normalized and ICV-Corrected Hippocampal Volume  Entorhinal Cortex Thickness 	- Predicted probability curves offer more precise, actionable dementia risk information than threshold scores: 80% vs. 30% risk is clearer than “positive” or “negative” - The “optimal threshold” can lead to false hope or needless distress; values near the threshold may have similar decline probabilities but are treated differently if dichotomized - Multiple biomarkers can be combined, and separate curves can compare subgroup risk (e.g., sex, age tertiles)^{1,2,3,4} References ¹Jack et al. <i>Lancet Neurol</i> 2025; 24: 1016–25. doi: 10.1016/S1474-4422(25)00350-3 ²Borland et al. <i>Alzheimer's Dement</i>. 2024; 20:8625–8638. doi: 10.1002/alz.14305 ³Marion et al. <i>Statistics in Medicine</i> 2025; 44:1-10. doi: 10.1002/sim.70120 ⁴Efthimiou et al. <i>BMJ</i> 2023;386:e078276 doi: 10.1136/bmj-2023-078276
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