

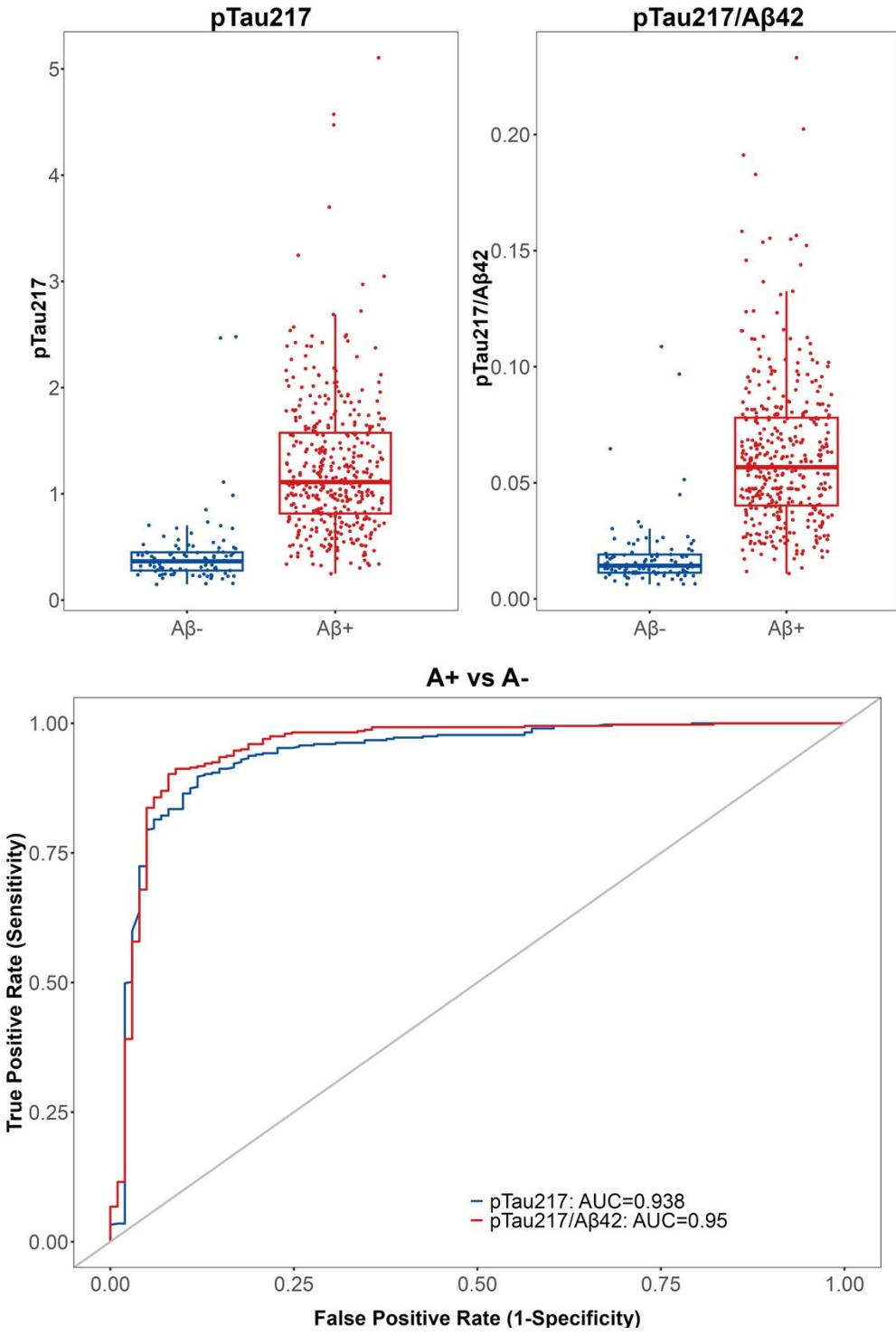
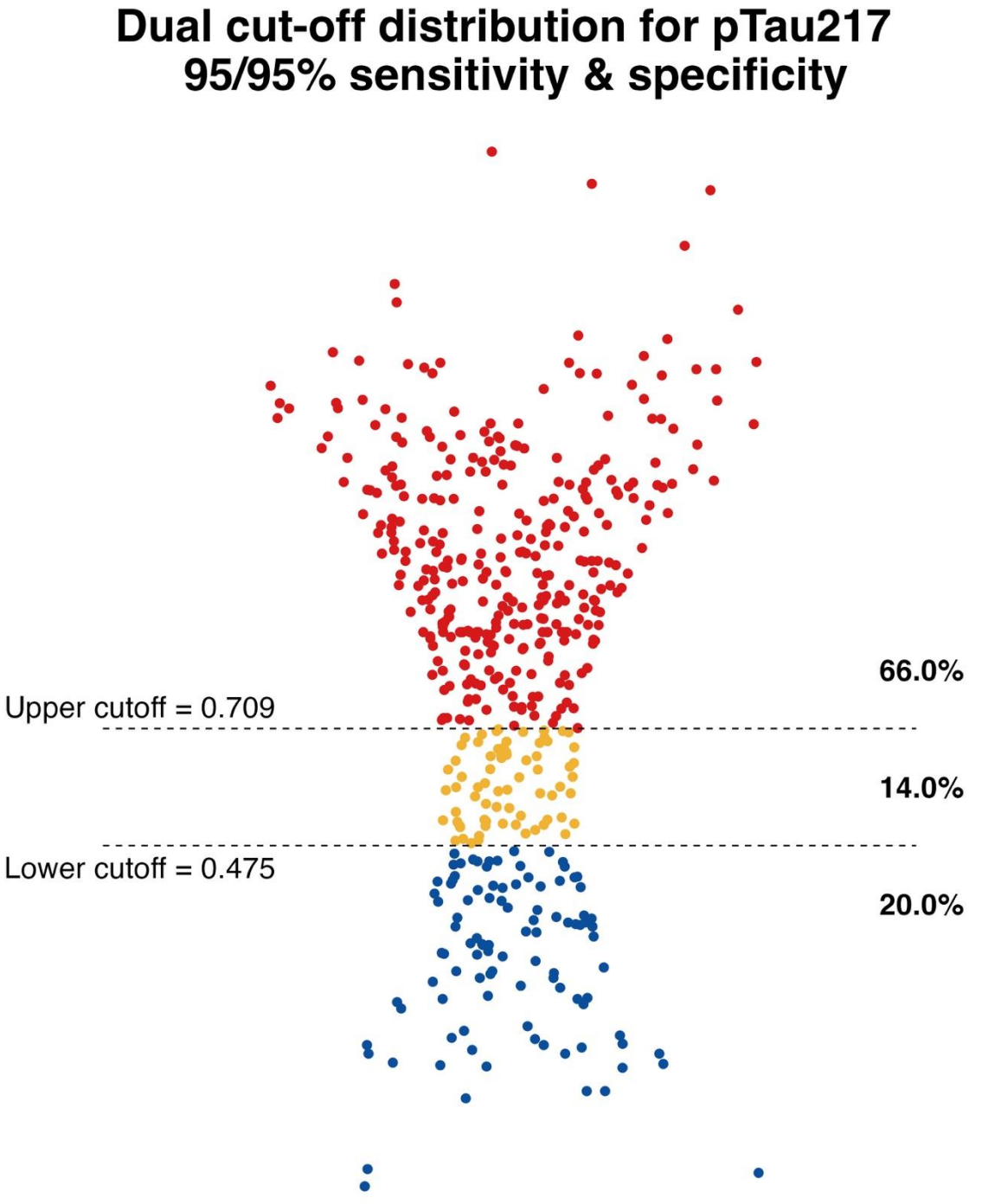
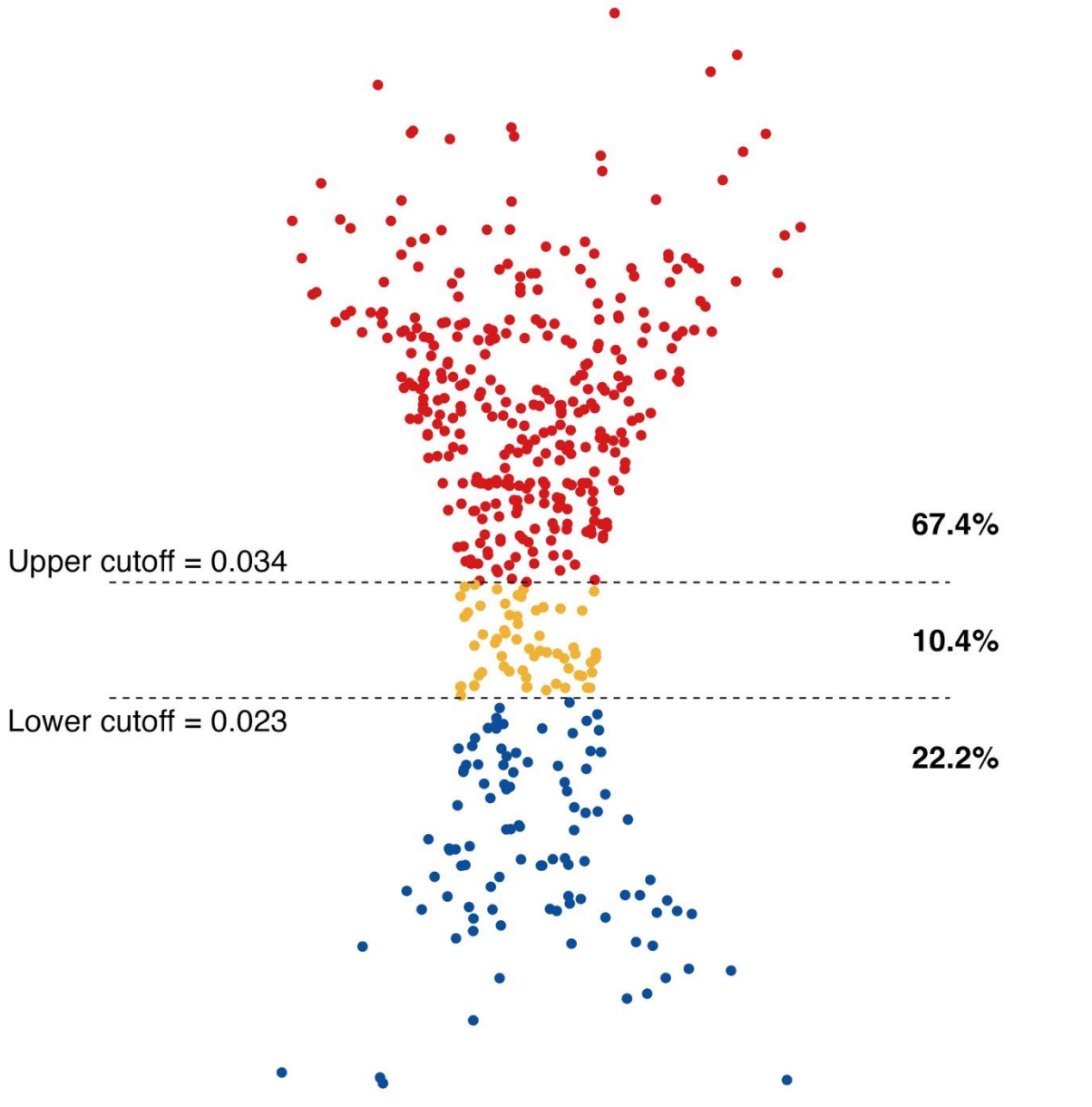
Beckman Coulter Plasma p-tau217 and p-tau217/Aβ42: Confirmatory Biomarkers for Clinical Trial Screening and Disease Modifying Treatment

P-0442

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Both pTau217 and the pTau217/Aβ42 ratio effectively distinguished Aβ-PET-positive from Aβ-PET-negative participants. Importantly, the conservative dual cut-off approach classified fewer than 20% of participants as intermediate, supporting the potential clinical utility of these biomarkers.

INTRODUCTION	RESULTS	RESULTS	RESULTS	CONCLUSIONS
p-Tau217 is a leading plasma biomarker for abnormal amyloid-β (Aβ) positivity in Alzheimer’s disease (AD) yet cut-off values and performance vary across platforms and laboratories. This study evaluates RUO p-Tau217 and Aβ 1-42 assays designed to predict Aβ positivity using a widely scalable platform already available worldwide.	Cut-off values using Youden's Index for p-Tau217 and p-Tau217/Aβ42 were 0.53 (AUC:0.94 (95%CI: 0.90-0.97) and 0.027 (AUC:0.95 (95%CI: 0.93-0.98), respectively; the AUC for the ratio was higher than for p-Tau217 alone (p=0.07). AUC values were not altered by adjusting for age, sex, and APOE ε4 status. 	Using single cut-offs, p-Tau217 achieved 90% sensitivity and 87% specificity, while p-Tau217/Aβ42 was slightly higher (91% sensitivity, 92% specificity). Using the conservative dual cut-off (95/95% sensitivity and specificity) for pTau217, only 14% of participants were in the intermediate zone. 	Using the conservative dual cut-off (95/95% sensitivity and specificity) for the pTau217/Aβ42 ratio, only 10% of participants were in the intermediate zone. Dual cut-off distribution for pTau217/Aβ42 95/95% sensitivity & specificity 	Utilizing the conservative 95% sensitivity and specificity cut-offs, the Beckman Coulter RUO p-tau217 assay, both alone and in an Aβ42 ratio, left <20% of participants in the intermediate zone. This demonstrated assay’s robust performance in identifying Aβ positivity within a research context, positions it as a practical tool for streamlining clinical trial pre-screening and investigating disease-modifying therapy.
METHODS	CONTACT			
The study included 500 participants from the Australian Imaging, Biomarkers and Lifestyle (AIBL) study (223 cognitively unimpaired, 171 mild cognitive impairment, 104 AD). EDTA plasma samples were collected within 12 months of Aβ-PET scans. Plasma p-Tau217, Aβ42, and APOE were measured with RUO assays on the Beckman Coulter Dxl 9000 Access Immunoassay Analyzer. As Aβ-PET+ prevalence was high (~80%), bootstrap resampling (to achieve ~62% Aβ-PET+ prevalence) was performed, reducing the number of Aβ-PET+ participants randomly in each iteration to ~100 Aβ-PET- and 160 Aβ-PET+. Performance of plasma p-Tau217 and the p-Tau217/Aβ42 ratio, adjusted for age, sex, and APOE allele ε4 status, was evaluated for predicting Aβ-PET positivity (Centiloid ≥25). Receiver operating characteristic analyses were used to calculate area under the curve (AUC), sensitivity, specificity, positive and negative predictive values, and overall accuracy. Additionally, dual cut-offs targeting sensitivity and specificity of 85%, 90%, or 95% were evaluated.	 James.Doecke@csiro.au (+61) 3253 3697 Team Leader, Biostatistics Australian E-Health Research Centre, CSIRO 			