

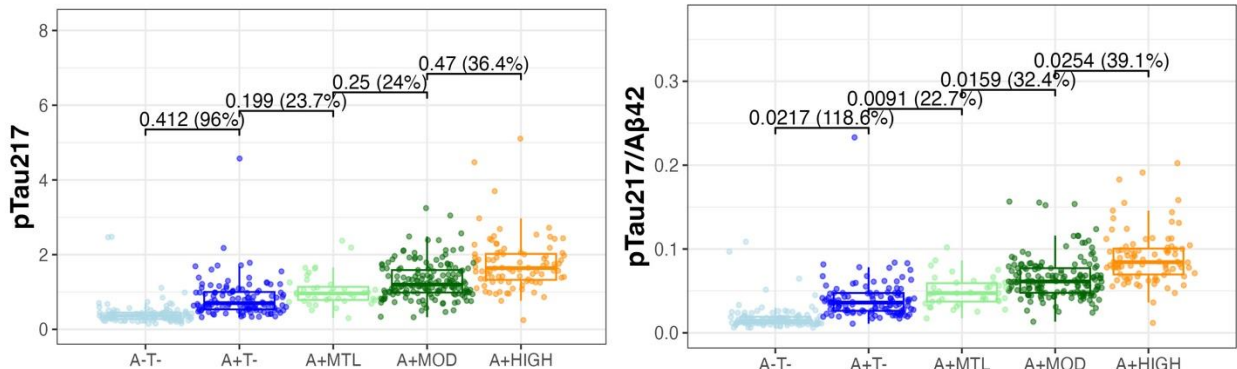
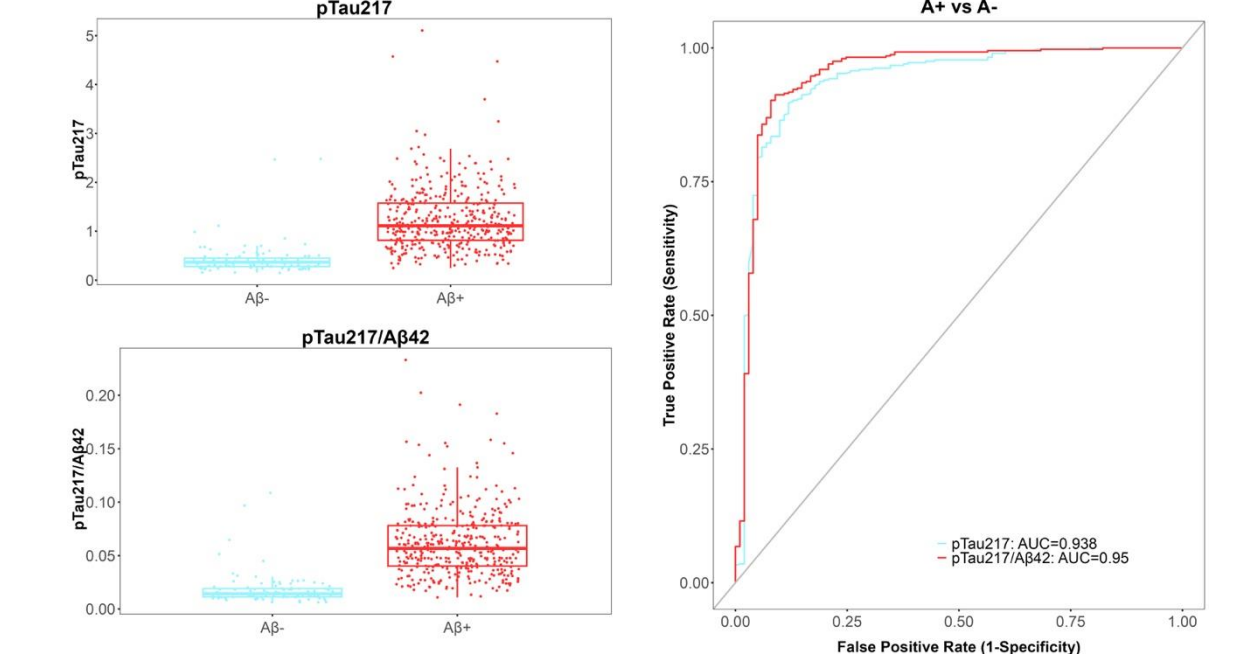
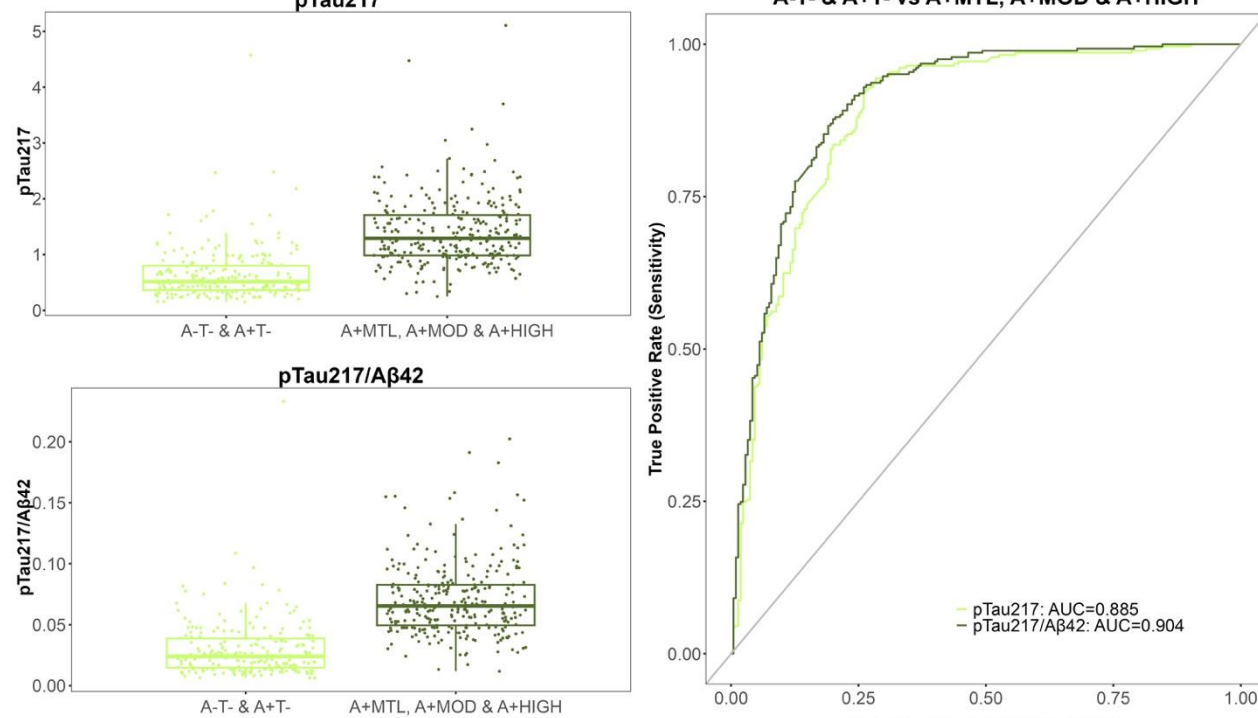
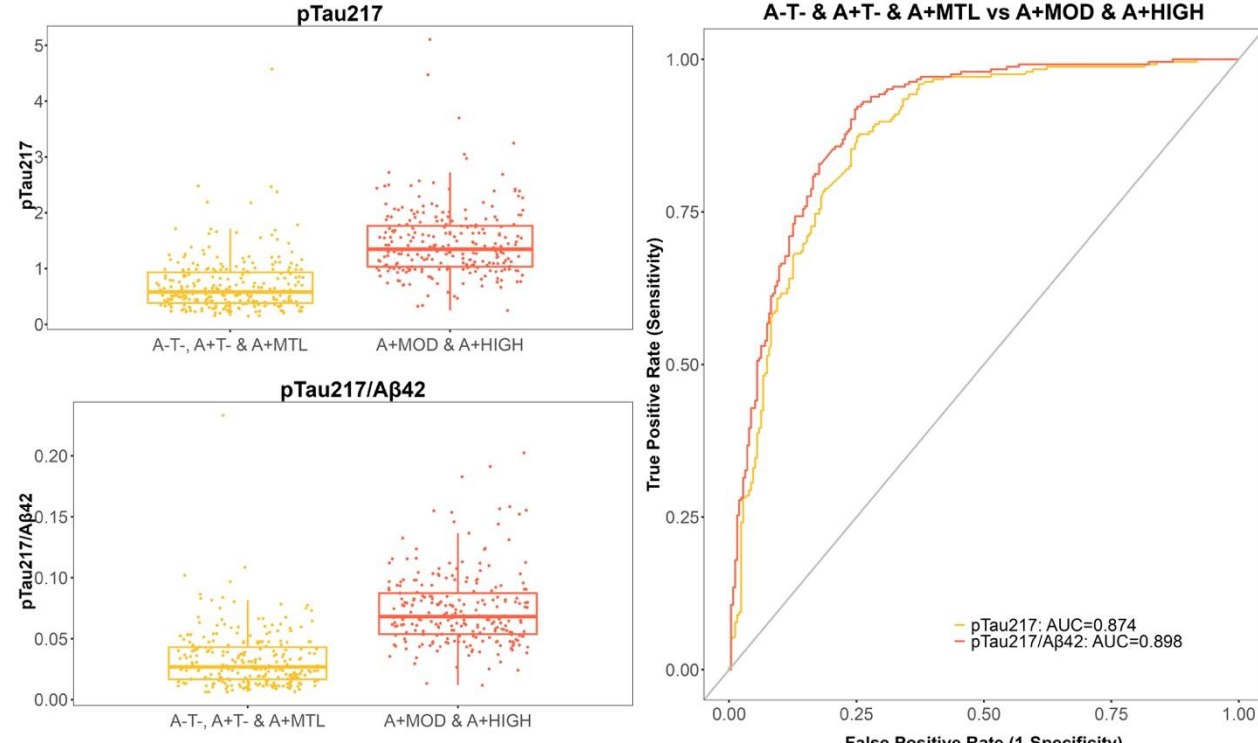
Plasma p-Tau217/Aβ42 Ratio Outperforms p-Tau217 Alone for Stage-specific Detection of Abnormal Tau Levels Across the AD Continuum

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James D. Doecke¹, Rodrigo Canovas², Christopher J. Fowler³, Vincent Dore², Larry Ward³, Kinal Bhatt, MD, MPH⁴, Christopher Rowe⁵, Colin L. Masters⁶.

¹Health and Biosecurity, CSIRO, Australian E-Health Research Centre, Herston, Australia, ²Health and Biosecurity, CSIRO, Australian E-Health Research Centre, Parkville, Australia, ³The Florey Institute of Neuroscience and Mental Health, Parkville, Australia, ⁴Medical & Scientific Affairs, Beckman Coulter, Miami, FL, USA, ⁵Department of Molecular Imaging & Therapy, Austin Health, Heidelberg, Australia, ⁶Alzheimer’s Research Australia, University of Western Australia, Nedlands, WA, Australia.

Both Beckman Coulter pTau217 and the pTau217/Aβ42 ratio accurately predicted amyloid-β status and progression across biological disease stages. Notably, the pTau217/Aβ42 ratio enhanced predictive performance in individuals with established amyloid-β positivity.

INTRODUCTION	RESULTS	RESULTS	RESULTS	CONCLUSIONS
Plasma tau, phosphorylated at position 217 (p-Tau217), is a sensitive marker of Amyloid-Beta (Aβ) positivity, yet its changes across the stages of tau aggregation remain poorly defined. This study evaluates the performance of p-Tau217 and the p-Tau217/Aβ42 ratio for potential clinical trial pre-screening.	Participant groups (classified by Aβ (A) and tau (T) PET status) included 101 A-T- (20%), 114 A+T- (23%), 40 A+T_{MTL} (8%), 157 A+T_{MOD} (31%), and 88 A+T_{HIGH} (18%). Large increases in both pTau217 and the pTau217/Aβ42 ratio across biological stage (Figure 1).  Figure 1: Box and whisker plot of biomarker values across biological disease stage. In early-stage comparisons (A-T- vs. all other groups) the p-Tau217/Aβ42 ratio demonstrated a higher AUC than p-Tau217 alone (AUC p-Tau217: 0.938, p-Tau217/Aβ42: 0.95, p=0.075, Figure 2).  Figure 2: Box and whisker plot of biomarker values between A- & A+ (left). ROC curves of biomarkers to predict A+ from A- (right).	When A-T- and A+T- participants were combined and compared with all other tau-PET+ groups, the p-Tau217/Aβ42 ratio again outperformed p-Tau217 (AUC p-Tau217: 0.885, p-Tau217/Aβ42: 0.904, p=0.002, Figure 3).  Figure 3: Box and whisker plot of biomarker values for A-T- & A+T- vs A+T_{MTL} & A+T_{MOD} & A+T_{HIGH} (left). ROC curves of biomarkers to predict A+T_{MTL} & A+T_{MOD} & A+T_{HIGH} from A-T- & A+T- (right).	Including participants with early tau deposition (A+T_{MTL}) in the tau-PET negative group, and comparing them with those with moderate/high tau burden (A+T_{MOD}, A+T_{HIGH}), produced slightly lower AUC values for both biomarkers, however the ratio remained significantly higher (AUC p-Tau217: 0.874, p-Tau-217/Aβ42: 0.898, p<0.0001, Figure 4). Lastly, identifying participants with high tau burden (A+T_{HIGH}) against all others, analogous to clinical trial pre-screening, the AUC values decreased further, yet the ratio continued to outperform p-Tau217 alone (AUC p-Tau217: 0.849, p-Tau217/Aβ42: 0.882, p=0.0007, Figure 5).  Figure 4: Box and whisker plot of biomarker values for A-T- & A+T- & A+T_{MTL} vs A+T_{MOD} & A+T_{HIGH} (left). ROC curves of biomarkers to predict A+T_{MOD} & A+T_{HIGH} from A-T- & A+T- & A+T_{MTL} (right).	The p-Tau217/Aβ42 ratio outperformed p-Tau217 alone at every stage comparison, demonstrating superior ability to differentiate biological disease stages across the AD continuum. This positions the ratio as a strong candidate biomarker for both early detection of tau positivity and exclusion of individuals with advanced tau burden in clinical trial pre-screening.
CONTACT  James.Doecke@csiro.au (+61) 3253 3697 Team Leader, Biostatistics Australian E-Health Research Centre, CSIRO 				