



In cognitively unimpaired A β - adults, baseline A β -PET informs who's heading toward positivity; cognition, on its own, does not.

- Predicting future A β positivity (A β +) can help enrichment of anti-amyloid trials
- We evaluated whether data-driven cognitive composites optimised for cognitively unimpaired (CU) older adults improve the prediction of time to A β positivity (≥ 20 centiloids) over eight years.

- Baseline data: 614 CU A β - older adults
- Data source: ADOPIIC consortium
- Cognitive composites derived through principal component analysis
- Analysis: Stratified Cox proportional hazards model
 - Outcome: Status (CU A β - or CU A β +) and Time to Status (years)
 - Strata: A β -PET centiloids (5-unit bins)
 - Cognitive predictors (Separate models): Learning & Memory (z), Executive Function (z), Attention & Processing Speed (z), and General Cognition (z)
 - Covariates: Age, sex, education, *APOE* ϵ 4 status (carrier or non-carrier), and baseline centiloids values
- Model performance – Harrell’s C-index

Overall probability of conversion to A β -Positivity

Time since baseline (years)

Time since baseline (years)	0	1	2	3	4	5	6	7	8
At Risk	614	611	567	526	402	330	256	175	16
Events	0	3	28	37	53	58	68	73	78

	General Cognition Hazard Ratio (exp) 95% CI	Learning & Memory Hazard Ratio (exp) 95% CI	Executive Function Hazard Ratio (exp) 95% CI	Attention & Processing Speed Hazard Ratio (exp) 95% CI
Age	1.05* (1.01 to 1.10)	1.06* (1.02 to 1.10)	1.07* (1.03 to 1.12)	1.05* (1.02 to 1.10)
Sex	0.65 (0.40 to 1.05)	0.60 (0.36 to 1.00)	0.75 (0.47 to 1.19)	0.77 (0.48 to 1.23)
Education	1.07* (1.00 to 1.15)	1.07 (0.99 to 1.14)	1.02 (0.95 to 1.10)	1.04 (0.98 to 1.11)
APOE ε4 (carriers)	2.22* (1.33 to 3.72)	2.22* (1.32 to 3.72)	2.20* (1.32 to 3.68)	2.18* (1.30 to 3.65)
General Cognition(z)	0.67 (0.43 to 1.05)	-	-	-
Learning & Memory (z)	-	0.76 (0.57 to 1.00)	-	-
Executive Function (z)	-	-	1.27 (0.92 to 1.74)	-
Attention & Processing Speed (z)	-	-	-	0.70* (0.52 to 0.95)
C-index (S.E)	0.66 (0.03)	0.67 (0.03)	0.67 (0.03)	0.67 (0.03)

- Of the 614 participants, 78 converted to A β positivity over eight years (Figure 1).
- Baseline centiloid, age, and *APOE* ϵ 4 were consistently associated with time to progression across all models ($p < 0.001$, Table 1).
- *APOE* ϵ 4 carriers had a two-fold higher hazard of progression (Table 1).
- Among cognitive predictors, only Attention & Processing Speed was associated with time to A β positivity (H.R = 0.70, $p < 0.001$).
- Model improvement by Attention & Processing Speed was minimal
- Once stratified, all models achieved a C-index of 0.67.

Baseline A β burden, age and APOE ϵ 4 status are the strongest predictors of time to A β +, whilst cognition added little in predicting time to A β +.

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