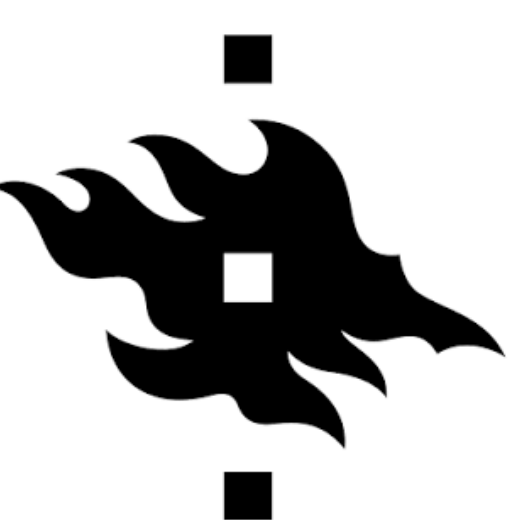


Short remote cognitive screening for early identification of Alzheimer’s disease in the population without dementia

Karin Lohi¹, Aino Aaltonen¹, Sanna-Kaisa Herukka^{2,3}, Tarja Kokkola², Sari Kärkkäinen², Aarno Palotie^{1,4,5}, Heiko Runz^{1,6}, Jaakko Kaprio¹, Valtteri Julkunen^{2,3}, Toni Saari¹, Eero Vuoksimaa¹

¹ Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Finland, ² Department of Neurology, Institute of Clinical Medicine, University of Eastern Finland, Kuopio, Finland, ³ Department of Neurology, NeuroCenter, Kuopio University Hospital, Kuopio, Finland, ⁴ Analytic and Translational Genetics Unit, Departments of Medicine, Neurology, and Psychiatry, Massachusetts General Hospital, Boston, MA, USA, ⁵ The Stanley Center for Psychiatric Research and Program in Medical and Population Genetics, The Broad Institute of MIT and Harvard, Cambridge, MA, USA, ⁶ European Molecular Biological Laboratories (EMBL), Heidelberg, Germany



UNIVERSITY OF HELSINKI



Institute for Molecular Medicine Finland
Nordic EMBL Partnership for Molecular Medicine

CONTACT



LinkedIn
Karin Lohi



Short remotely measured cognitive tests were associated with Alzheimer's plasma pathology and effectively identified in-person assessed cognitive impairment in a population-based setting.

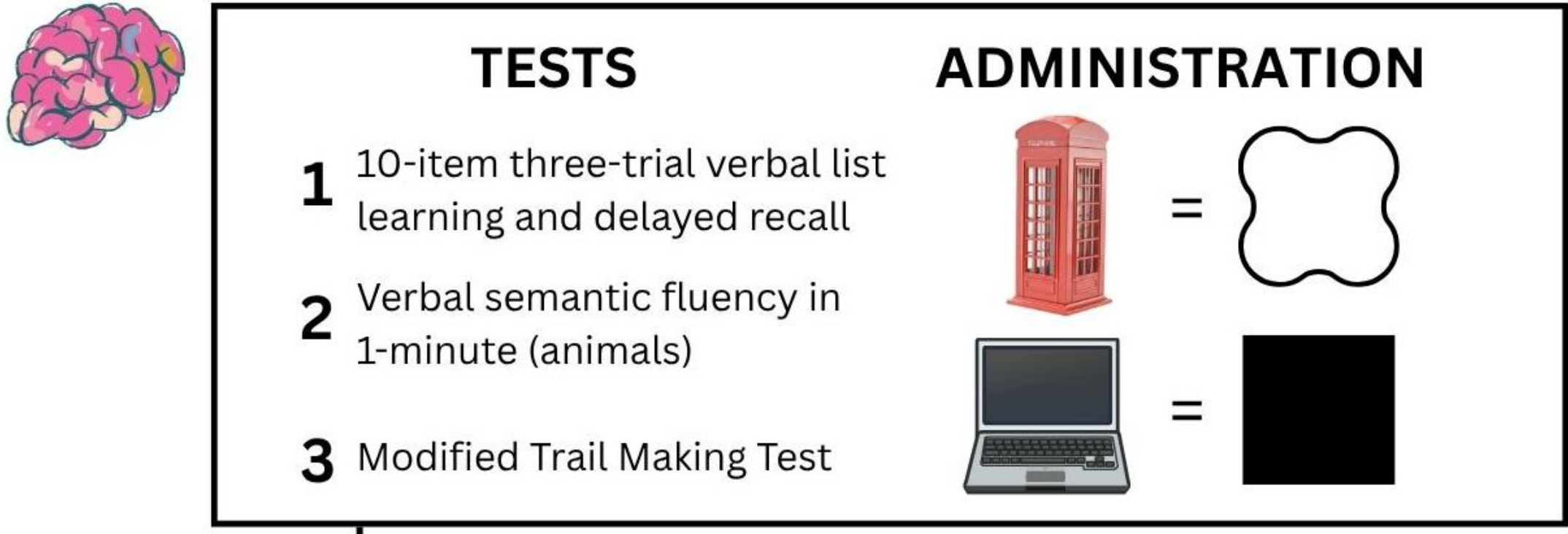
1 INTRODUCTION

- Remote cognitive testing and plasma biomarkers could enable an accessible and scalable screening approach for Alzheimer’s disease (AD) risk in aging populations. [1,2]
- Composite scores are a practical way to combine tests detecting typical AD cognitive impairment [3], especially for the amnesic AD variant. [4]
- To investigate opportunities for short cognitive assessment for primary care use, we investigated remote cognitive composite scores of multiple short tests [5,6] in a population-based sample of older twins without cognition-affecting disorders [7] by

1) exploring the association with a specific plasma biomarker [8], and

2) evaluating the accuracy for detecting impairment in in-person cognitive assessment used in the clinical setting.

2 METHDOS



TESTS

- 10-item three-trial verbal list learning and delayed recall
- Verbal semantic fluency in 1-minute (animals)
- Modified Trail Making Test

ADMINISTRATION

Telephone = Verbal list learning and delayed recall

Computer = Verbal semantic fluency and Modified Trail Making Test

standard scoring

Remote Cognitive Composite Scores	t-PACC	c-PACC	mem-PACC
	1 2	1 3	1 1

 **ALZpath Simoa pTau-217 v2 Assay**
Simoa HD-X analyser

4 CONCLUSIONS

- The following remote cognitive composite scores were significantly associated with plasma p-tau217 levels:
 - t-PACC:** telephone word list learning and delayed recall + verbal fluency tasks
 - mem-PACC:** telephone and computer word list learning and delayed recall tasks
- Remote cognitive composite scores comprising short AD-sensitive cognitive measures achieved acceptable accuracies for in-person cognitive impairment, with minimal differences between the composite scores, with the following having the highest performance based on area under the curve (AUC) value:
 - c-PACC:** computer word list learning and delayed recall + modified trail making test
- These results from a population-based sample of twins aged 65–85-years suggest that remote assessment of cognition—including a telephone interview—could be useful for screening individuals at increased risk of Alzheimer’s disease, especially in the context of population aging.

5 REFERENCES

[1] Aarland, D., Sunde, A. L., Tovar-Rios, D. A., Leuzy, A., Fladby, T., Zetterberg, H., Blennow, K., Tan, K., De Santis, G., Yakoub, Y., Arslan, B., Huber, H., Pola, I., Grötschel, L., Di Molfetta, G., Skjellegriind, H. K., Selbaek, G., & Ashton, N. J. (2026). Prevalence of Alzheimer’s disease pathology in the community. *Nature*, 650(8100), 182–186. <https://doi.org/10.1038/s41586-025-09841-y>

[2] Lohi, K., Aaltonen, A., Herukka, S.-K., Kokkola, T., Kärkkäinen, S., Urjansson, M., FinnGen, Palotie, A., Daly, M., Riley-Gillis, B., Jacob, H., Viollet, C., Petrovski, S., Berton, A., Ramakrishnan, S., Tsai, E., Ding, Z., Holzinger, E., Plenge, R., ... Vuoksimaa, E. (2026). Scalable biological-cognitive profiling for Alzheimer’s disease in the population. *Brain Communications*, 8(3), fcag168. <https://doi.org/10.1093/braincomms/fcag168>

[3] Juganavar, A., Joshi, A., & Sheekar, T. (2023). Navigating Early Alzheimer’s Diagnosis: A Comprehensive Review of Diagnostic Innovations. *Cureus*. <https://doi.org/10.7759/cureus.44937>

[4] Drago V, Babiloni C, Bartrés-Faz D, et al. Disease Tracking Markers for Alzheimer’s Disease at the Prodromal (MCI) Stage. *J Alzheimers Dis*. 2011;26(s3):159-199. doi:10.3233/JAD-2011-0043

[5] 14. Requena-Komuro MC, Jiang J, Dobson L, et al. Remote versus face-to-face neuropsychological testing for dementia research: a comparative study in people with Alzheimer’s disease, frontotemporal dementia and healthy older individuals. *BMJ Open*. 2022;12(11):e064576. doi:10.1136/bmjopen-2022-064576

[6] Saari, T. T., Aaltonen, A., Lohi, K., Palviainen, T., Schwarz, C., Urjansson, M., Palotie, A., Runz, H., Julkunen, V., Kaprio, J., Vuoksimaa, E., & FinnGen. (2026). Validity of telephone-administered word list learning measures for assessment of episodic memory in aging and Alzheimer’s disease. *Neuropsychology*, 40(1), 17–35. <https://doi.org/10.1037/neu0001019>

[7] Vuoksimaa, E., Saari, T. T., Aaltonen, A., Aaltonen, S., Herukka, S.-K., Iso-Markku, P., Kokkola, T., Kyttälä, A., Kärkkäinen, S., Liedes, H., Ollikainen, M., Palviainen, T., Ruotsalainen, I., Toivola, A., Urjansson, M., Vasankari, T., Vähä-Yppä, H., Forsberg, M. M., Hiltunen, M., ... Julkunen, V. (2024). TWINGEN: Protocol for an observational clinical biobank recall and biomarker cohort study to identify Finnish individuals with high risk of Alzheimer’s disease. *BMJ Open*, 14(6), e081947. <https://doi.org/10.1136/bmjopen-2023-081947>

[8] Danilidou, M., Öhlund-Wistbacka, U., Hagman, G., Rosenberg, A., Ashton, N., Zetterberg, H., Blennow, K., Matton, A., & Kivipelto, M. (2025). Enhancing diagnostic precision in Alzheimer’s disease: Impact of comorbidities on blood biomarkers for clinical integration. *Alzheimer’s & Dementia*, 21(12), e70931. <https://doi.org/10.1002/alz.70931>

[9] Ashton NJ, Brum WS, Di Molfetta G, et al. Diagnostic Accuracy of a Plasma Phosphorylated Tau 217 Immunoassay for Alzheimer Disease Pathology. *JAMA Neurol*. 2024;81(3):255. doi:10.1001/jamaneurol.2023.5319

3 RESULTS

Demographics (TWINGEN)

N = 660 (all)					N = 191 (subsample)
Age	Education	APOE ε4	P-tau217	ADNPC by p-tau217	In-person Cognitive Impairment
Mean (SD)	Median (IQR)	Frequency (%)	Median (IQR)	Frequency (%)	Frequency (%)
76.2 (4.6)	10 (6)	206 (29.3)	0.34 (0.30)	269 (38.6)	18 (9.4%)

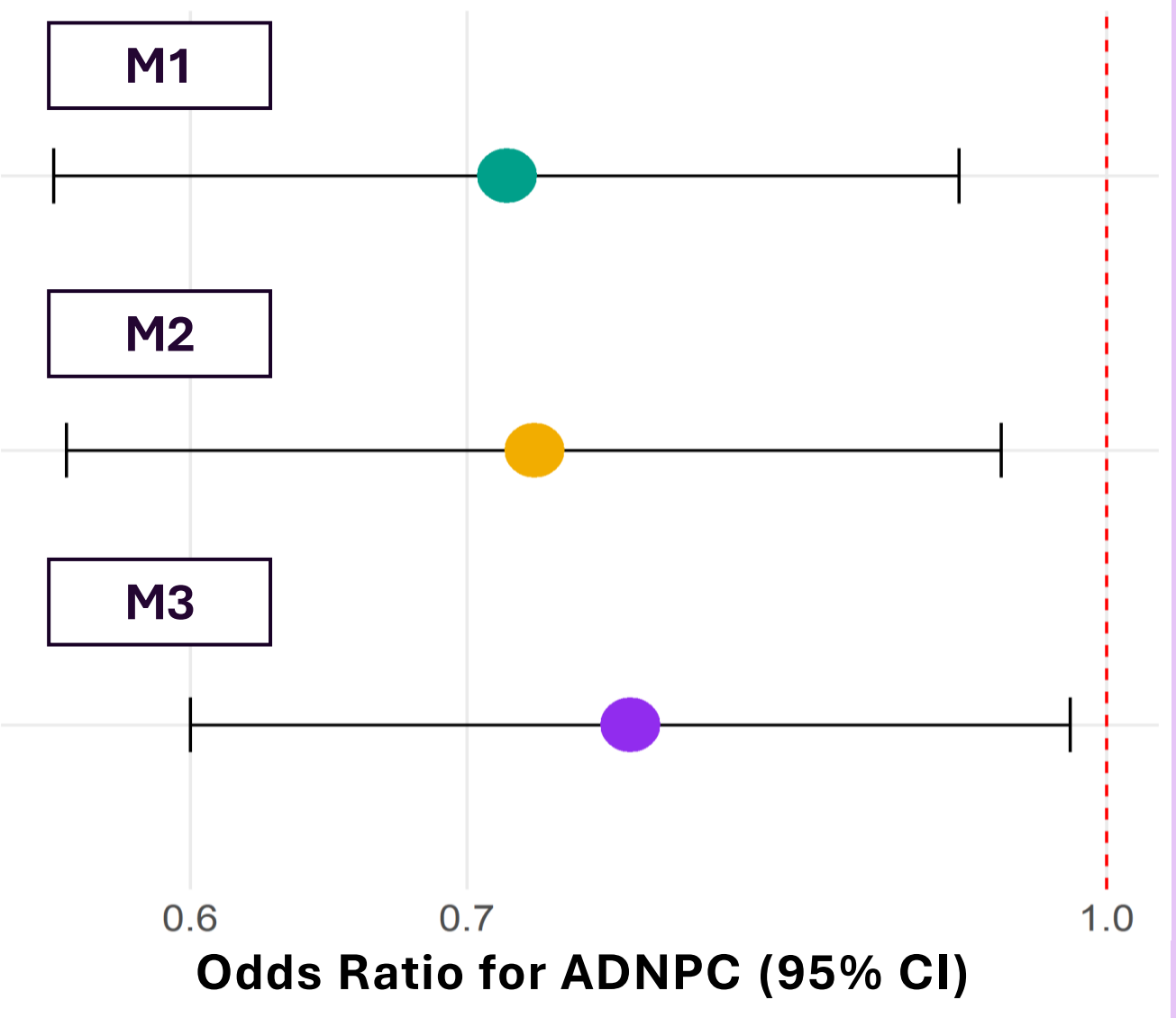
Generalized Estimating Equations analysis (N = 660)

	OR	95% CI
t-PACC (M1) *	0.716	0.556–0.921
mem-PACC (M2) *	0.727	0.560–0.943
c-PACC (M3)	0.767	0.600–0.980
Age *	1.770	1.438–2.180
Sex	0.929	0.645–1.337
Education	1.208	1.005–1.453
APOE ε4 allele (yes/no) *	3.976	2.714–5.826

M1

M2

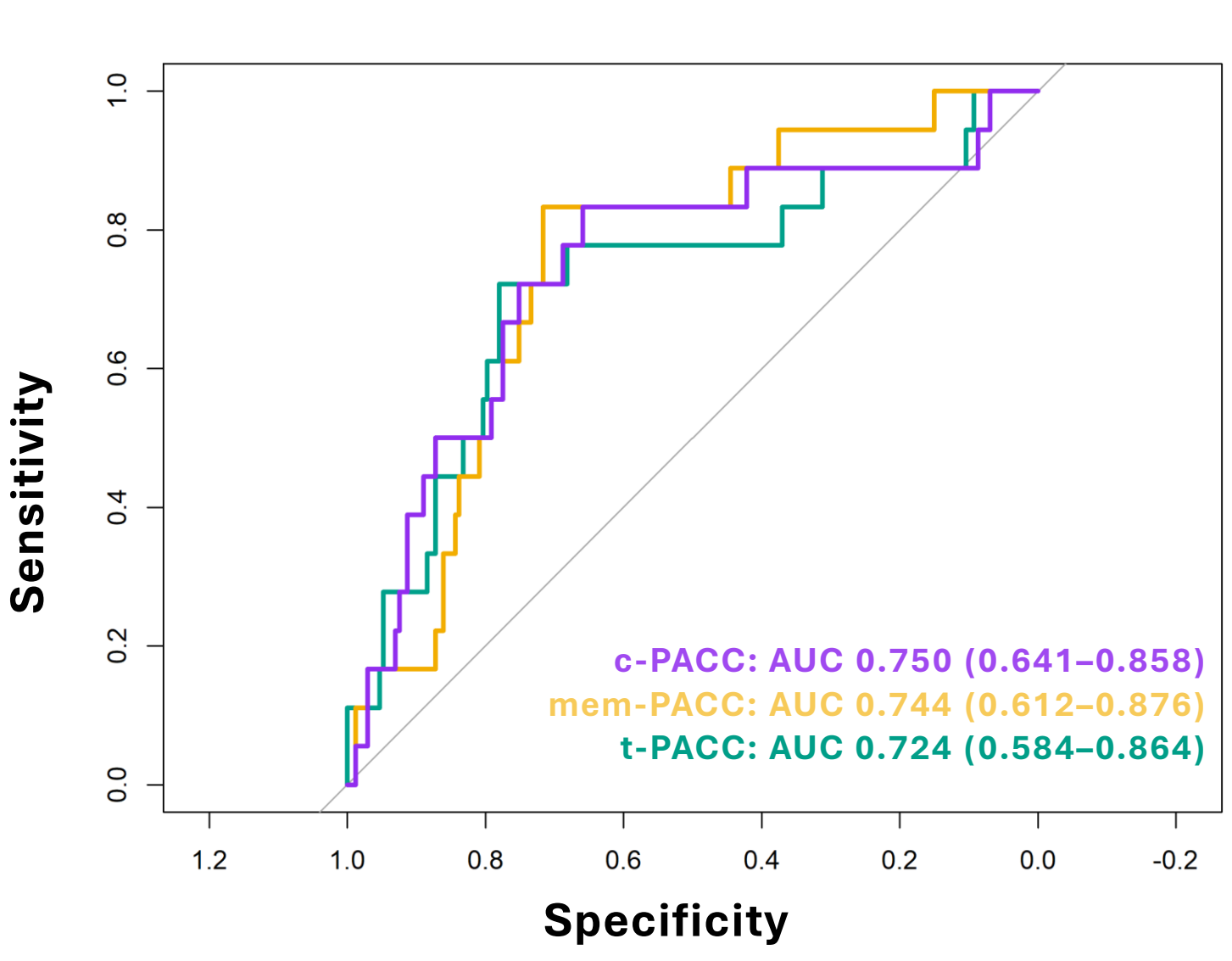
M3



Odds Ratio for ADNPC (95% CI)

- Outcome:** Alzheimer’s disease neuropathological change (ADNPC; plasma p-tau217 > 0.42) [9]
- Models**
 - M1:** t-PACC + covariates
 - M2:** mem-PACC + covariates
 - M3:** c-PACC + covariates
- Clustering based on familial relationships (monozygotic + dizygotic twin family id)
- Covariate odds ratios for ADNPC are from **M1**
- Continuous covariates were scaled
- * = predictor association with ADNPC was statistically significant in the GEE model (Benjamin-Hochberg-adjusted p-value < 0.05)

Receiver Operating Characteristic analysis (N = 191)



Sensitivity

Specificity

c-PACC: AUC 0.750 (0.641–0.858)
mem-PACC: AUC 0.744 (0.612–0.876)
t-PACC: AUC 0.724 (0.584–0.864)

- Outcome:** Cognitive impairment based on the Consortium to Establish a Registry for Alzheimer’s Disease neuropsychological battery (CERAD-nb)
- Clustering based on familial relationships (monozygotic + dizygotic twin family id)
- No covariates