

## Supplementary Online Content

Aguirre-Acevedo DC, Lopera F, Henao E, et al. Cognitive decline in a Colombian kindred with autosomal dominant Alzheimer disease. *JAMA Neurol*. Published online February 22, 2016. doi:10.1001/jamaneurol.2015.4851.

**eFigure 1.** Flow Diagram for *PSEN* E280A Mutation Carriers

**eFigure 2.** Spaghetti Plot for Longitudinal Assessments of MMSE and CERAD Subtest in *PSENI* E280A Mutation Carriers

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**eTable 1.** Cognitive Decline in MMSE by Risk Factors in *PSENI* E280A Mutation Carriers

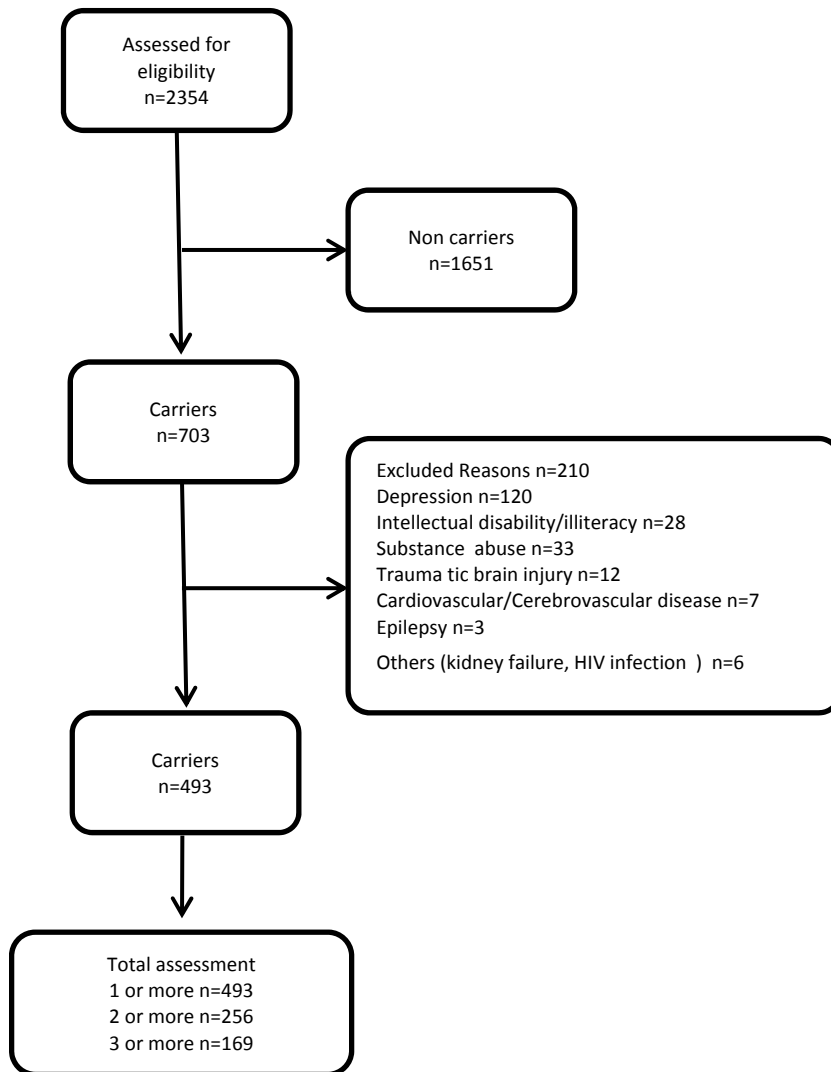
**eTable 2.** Cognitive Decline in CERAD Memory Test by Risk Factors *PSENI* E280A Mutation Carriers

**eTable 3.** Cognitive Decline in CERAD Language and Praxis Test by Risk Factors in *PSENI* E280A Mutation Carriers

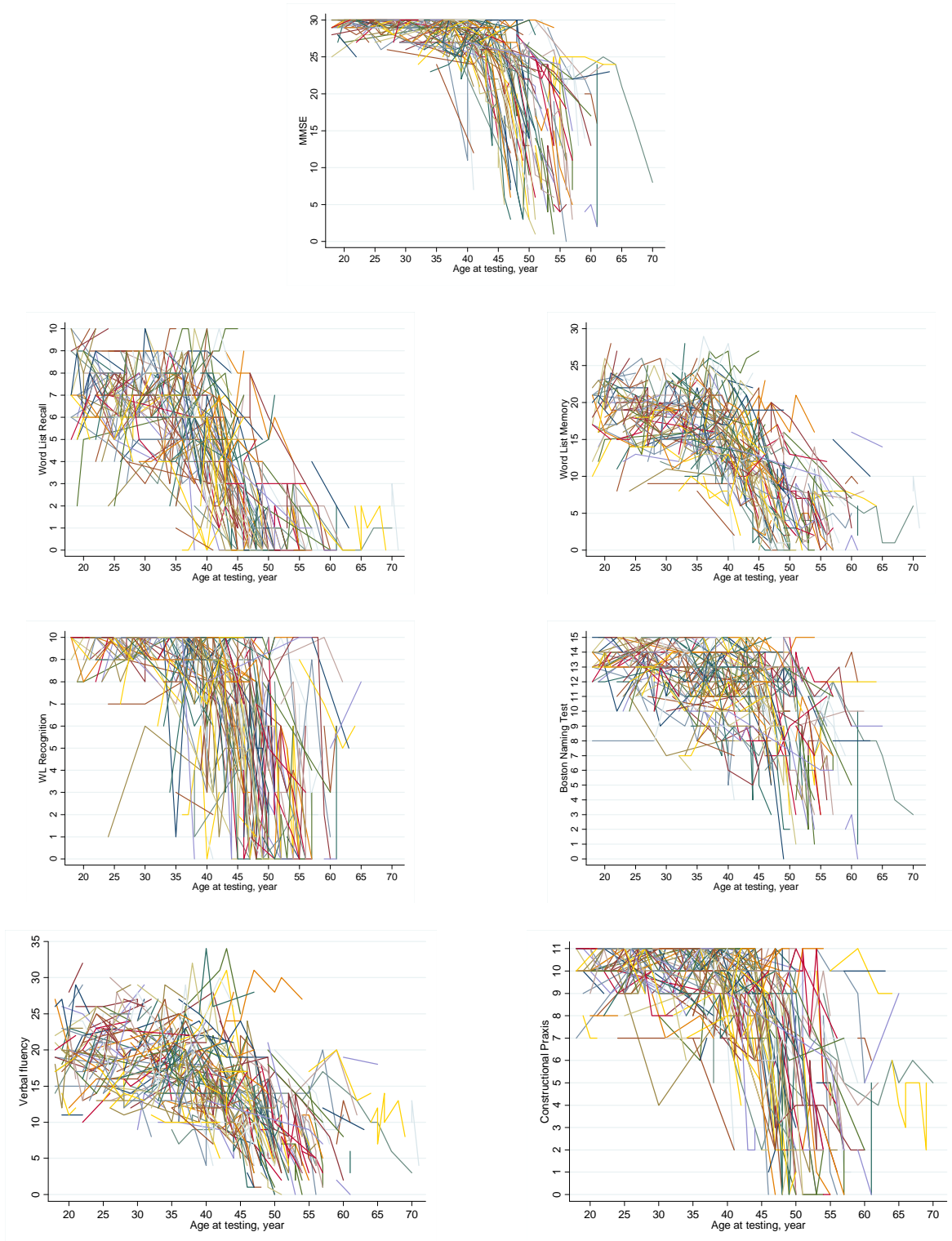
**eTable 4.** Cognitive Decline in CERADts, MMSE, and CERAD Subtest in 256 *PSENI* E280A Mutation Carriers With Two or More Assessments

This supplementary material has been provided by the authors to give readers additional information about their work.

**eFigure 1. Flow Diagram for *PSEN* E280A Mutation Carriers**

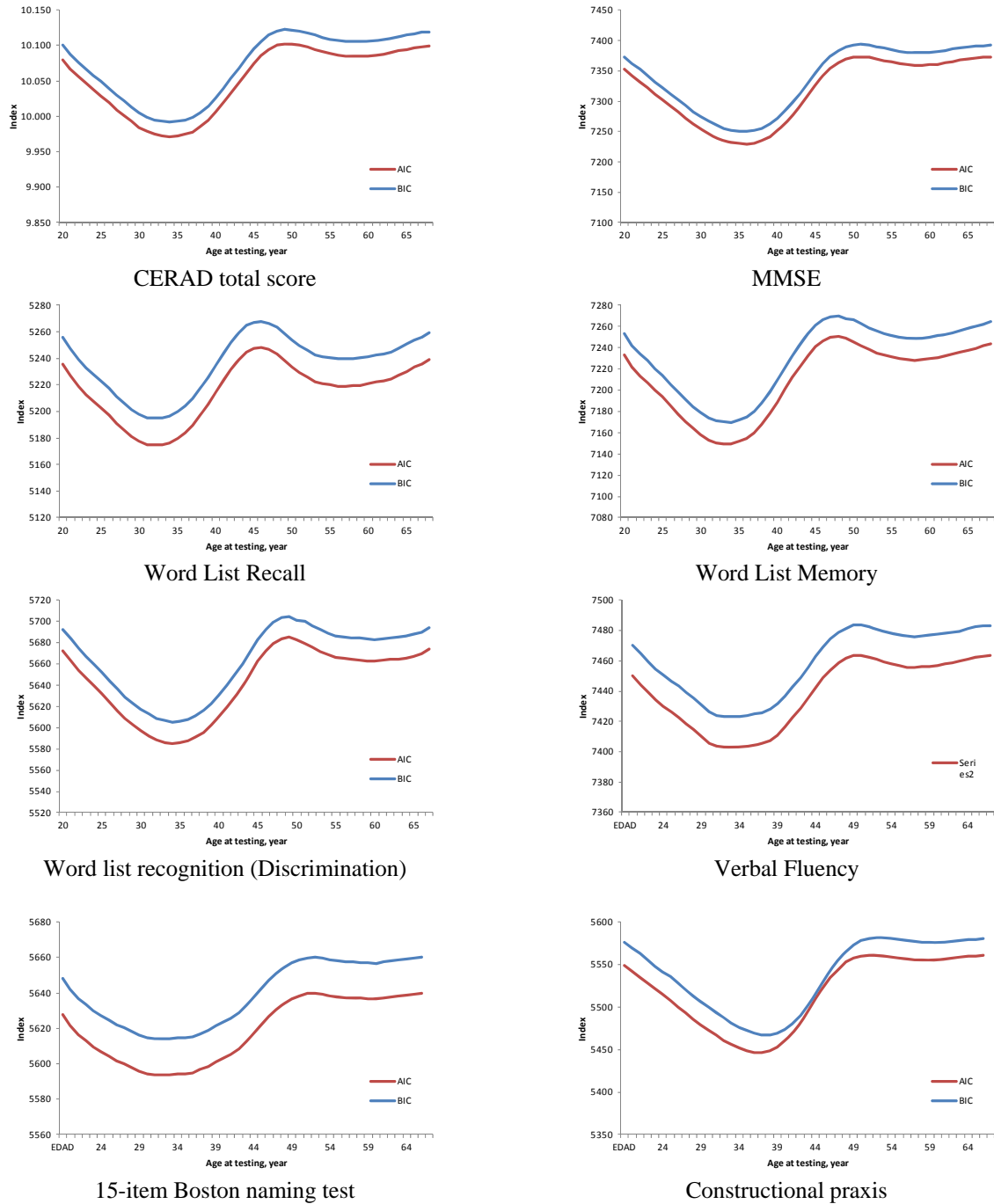


**eFigure 2. Spaghetti Plot for Longitudinal Assessments of MMSE and CERAD Subtest in *PSEN1* E280A Mutation Carriers**

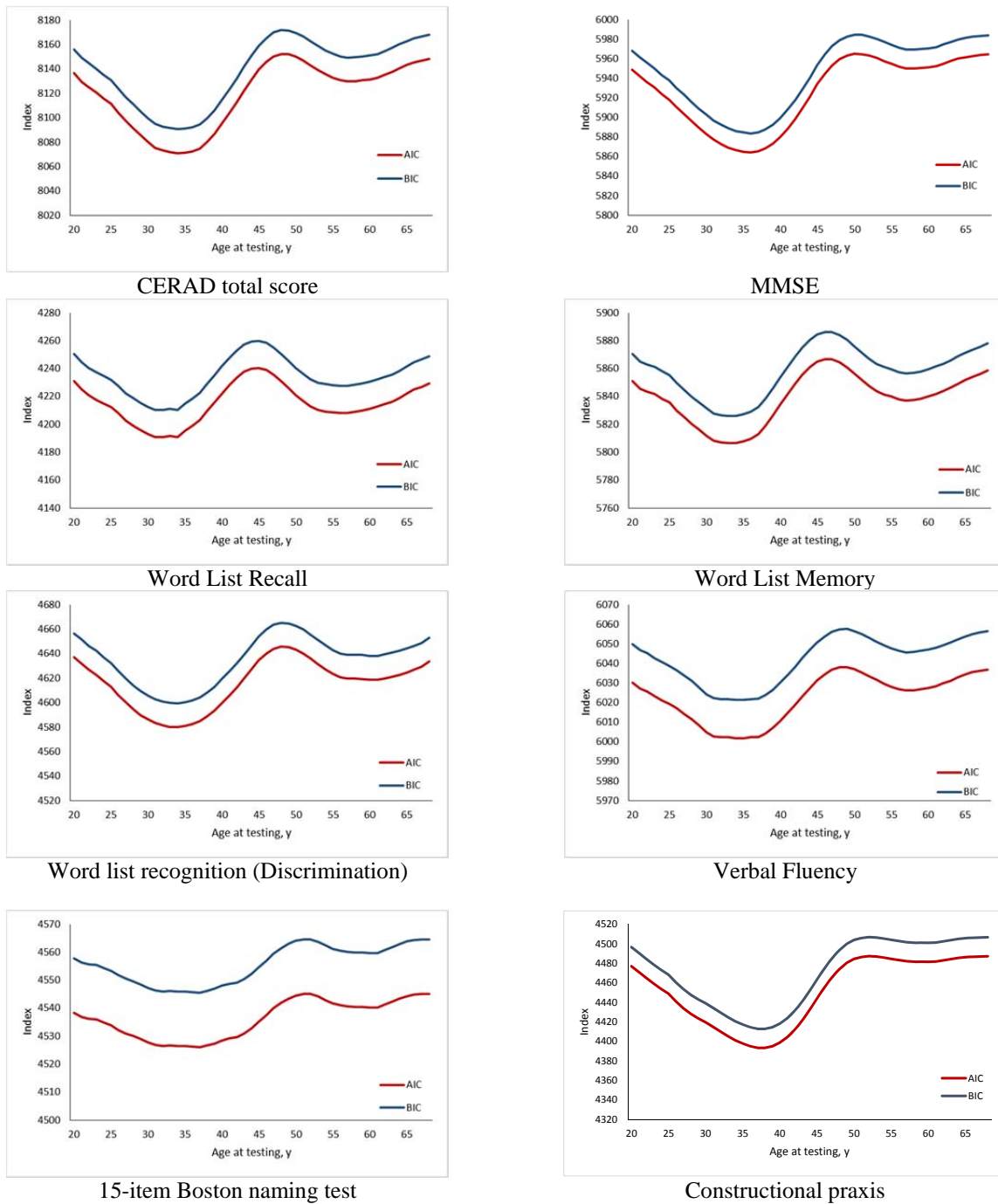


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**eFigure 3. Akaike and Bayesian Goodness-of-Fit Index for Model and Change Point Selection in CERAD Total Score, MMSE, and CERAD Subtest in *PSEN1* E280A Mutation Carriers**

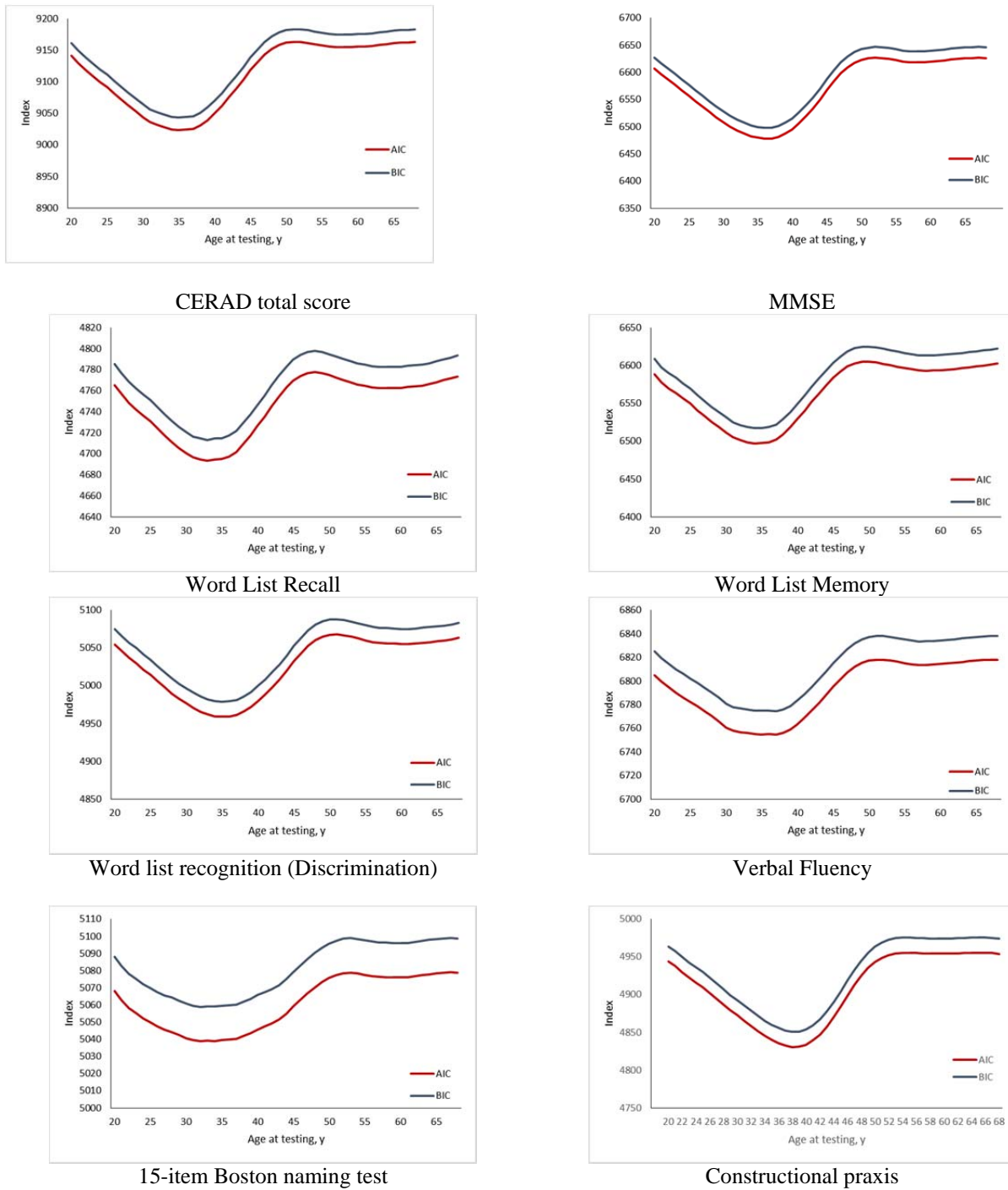


**eFigure 4. Akaike and Bayesian Goodness-of-Fit Index for Model and Change Point Selection in CERAD Total Score, MMSE, and CERAD Subtest in *PSEN1* E280A Mutation Carriers With Two or More Assessments**



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**eFigure 5. Akaike and Bayesian Goodness-of-Fit Index for Model and Change Point Selection in CERAD Total Score, MMSE, and CERAD Subtest in *PSEN1* E280A Mutation Carriers With CDR of 0**



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**eTable 1. Cognitive Decline in MMSE by Risk Factors in PSEN1 E280A Mutation Carriers**

	Before 36 years old	(95% CI)	After 36 years old	(95% CI)
<b>Sex</b>				
Female	0.06	(-0.02 to 0.15)	-0.68	(-0.75 to -0.61)
Male	0.00	(-0.19 to 0.20)	-0.57	(-0.73 to -0.41)
<b>Education<sup>†</sup></b>				
High (greater than or equal 7)	0.02	(-0.03 to 0.07)	-0.70	(-0.80 to -0.60)
Low (less than 7)	0.02	(-0.10 to 0.14)	-0.65	(-0.72 to -0.57)
<b>Socioeconomic status</b>				
Middle/High	0.06	(-0.03 to 0.14)	-0.74	(-0.87 to -0.60)
Low	0.01	(-0.23 to 0.25)	-0.60	(-0.84 to -0.36)
<b>Residence area</b>				
Urban	0.07	(0.00 to 0.13)	-0.68	(-0.82 to -0.54)
Rural	-0.05	(-0.27 to 0.17)	-0.53	(-0.79 to -0.27)
<b>Occupation type</b>				
Non-Manual	0.04	(-0.28 to 0.36)	-0.60	(-0.80 to -0.41)
Manual	0.04	(-0.34 to 0.41)	-0.64	(-1.15 to -0.12)
<b>Marital status</b>				
Single	0.16	(-0.07 to 0.40)	-0.83	(-1.04 to -0.61)
Married	0.07	(-0.02 to 0.16)	-0.55	(-0.62 to -0.48)
<b>HTA</b>				
Present	0.12	(-0.40 to 0.64)	-0.49	(-0.70 to -0.28)
Absent	0.09	(-0.35 to 0.53)	-0.61	(-0.75 to -0.48)
<b>Dyslipidemia</b>				
Present	0.26	(-0.18 to 0.70)	-0.38	(-0.60 to -0.15)
Absent	0.08	(0.00 to 0.16)	-0.63	(-0.70 to -0.55)
<b>Diabetes</b>				
Present	1.11	(-0.27 to 2.48)	-1.02	(-1.51 to -0.52)
Absent	0.09	(0.01 to 0.16)	-0.58	(-0.65 to -0.51)
<b>Tobacco use</b>				
Present	0.11	(-0.08 to 0.30)	-0.67	(-0.75 to -0.59)
Absent	0.08	(-0.01 to 0.16)	-0.53	(-0.62 to -0.45)
<b>Alcohol use</b>				
Present	0.01	(-0.29 to 0.31)	-0.72	(-0.93 to -0.50)
Absent	0.09	(-0.12 to 0.31)	-0.55	(-0.69 to -0.42)
<b>APOE ε4</b>				
Present	-0.03	(-0.47 to 0.41)	-0.79	(-1.16 to -0.41)
Absent	0.09	(-0.10 to 0.28)	-0.93	(-1.06 to -0.79)

Adjusted coefficients by other factors; CI: Confidence interval; HTA: Hypertension

**eTable 2. Cognitive Decline in CERAD Memory Test by Risk Factors *PSEN1* E280A Mutation Carriers**

	Word list recall				Word list memory				Word list Recognition			
	Before 32 years old	(95% CI)	After 32 years old	(95% CI)	Before 34 years old	(95% CI)	After 34 years old	(95% CI)	Before 34 years old	(95% CI)	After 34 years old	(95% CI)
<b>Sex</b>												
Female	-0.02	(-0.06 to 0.02)	-0.23	(-0.26 to -0.21)	-0.01	(-0.09 to 0.07)	-0.58	(-0.64 to -0.51)	0.01	(-0.03 to 0.05)	-0.30	(-0.34 to -0.27)
Male	0.00	(-0.10 to 0.09)	-0.25	(-0.31 to -0.18)	0.06	(-0.12 to 0.25)	-0.59	(-0.75 to -0.44)	0.01	(-0.09 to 0.10)	-0.28	(-0.37 to -0.20)
<b>Education†</b>												
High (greater than or equal 7)	-0.02	(-0.06 to 0.02)	-0.39	(-0.44 to -0.34)	0.02	(-0.06 to 0.10)	-0.81	(-0.93 to -0.70)	0.00	(-0.04 to 0.03)	-0.35	(-0.40 to -0.30)
Low (less than 7)	-0.05	(-0.10 to 0.00)	-0.21	(-0.24 to -0.18)	0.04	(-0.07 to 0.14)	-0.51	(-0.57 to -0.45)	0.01	(-0.05 to 0.07)	-0.27	(-0.31 to -0.23)
<b>Socioeconomic status</b>												
Middle/High	-0.02	(-0.06 to 0.01)	-0.28	(-0.35 to -0.21)	0.07	(-0.02 to 0.15)	-0.72	(-0.84 to -0.59)	0.01	(-0.04 to 0.05)	-0.35	(-0.41 to -0.28)
Low	-0.02	(-0.15 to 0.10)	-0.23	(-0.34 to -0.11)	-0.03	(-0.26 to 0.20)	-0.52	(-0.75 to -0.29)	0.00	(-0.12 to 0.12)	-0.26	(-0.38 to -0.14)
<b>Residence area</b>												
Urban	-0.02	(-0.04 to 0.01)	-0.25	(-0.32 to -0.18)	0.02	(-0.04 to 0.08)	-0.62	(-0.75 to -0.49)	0.02	(-0.01 to 0.06)	-0.33	(-0.40 to -0.26)
Rural	-0.01	(-0.11 to 0.10)	-0.20	(-0.32 to -0.08)	0.02	(-0.18 to 0.23)	-0.48	(-0.72 to -0.24)	-0.04	(-0.14 to 0.07)	-0.21	(-0.34 to -0.07)
<b>Occupation type</b>												
Non-Manual	0.00	(-0.12 to 0.11)	-0.22	(-0.30 to -0.13)	0.02	(-0.26 to 0.30)	-0.54	(-0.71 to -0.37)	0.01	(-0.14 to 0.17)	-0.20	(-0.29 to -0.12)
Manual	-0.01	(-0.18 to 0.15)	-0.24	(-0.44 to -0.04)	0.02	(-0.30 to 0.35)	-0.58	(-1.03 to -0.13)	0.01	(-0.16 to 0.17)	-0.30	(-0.54 to -0.05)
<b>Marital status</b>												
Single	0.04	(-0.08 to 0.16)	-0.23	(-0.31 to -0.14)	0.14	(-0.09 to 0.36)	-0.58	(-0.79 to -0.38)	0.06	(-0.06 to 0.18)	-0.31	(-0.43 to -0.19)
Married	0.03	(-0.02 to 0.08)	-0.20	(-0.23 to -0.17)	0.14	(0.04 to 0.23)	-0.48	(-0.55 to -0.42)	0.03	(-0.02 to 0.09)	-0.26	(-0.30 to -0.22)
<b>HTA</b>												
Present	-0.01	(-0.45 to 0.24)	-0.22	(-0.31 to -0.13)	0.14	(-0.42 to 0.70)	-0.48	(-0.69 to -0.28)	0.00	(-0.31 to 0.31)	-0.25	(-0.37 to -0.14)
Absent	0.03	(-0.26 to 0.33)	-0.20	(-0.25 to -0.14)	0.13	(-0.35 to 0.61)	-0.50	(-0.64 to -0.37)	0.04	(-0.22 to 0.30)	-0.27	(-0.35 to -0.20)
<b>Dyslipidemia</b>												
Present	-0.05	(-0.28 to 0.18)	-0.25	(-0.34 to -0.15)	0.09	(-0.35 to 0.53)	-0.42	(-0.63 to -0.21)	0.07	(-0.16 to 0.30)	-0.23	(-0.35 to -0.11)
Absent	0.00	(-0.01 to	-0.19	(-0.22 to -	0.13	(0.05 to	-0.51	(-0.58 to -	0.04	(-0.01 to	-0.28	(-0.32 to -



	4	0.08)		0.16)		0.22)		0.44)		0.09)		0.24)
<b>Diabetes</b>												
Present	0.46	(-0.50 to 1.41)	-0.37	(-0.56 to -0.17)	0.40	(-1.02 to 1.83)	-0.91	(-1.34 to -0.47)	0.39	(-0.36 to 1.15)	-0.46	(-0.71 to -0.22)
Absent	0.04	(-0.01 to 0.08)	-0.20	(-0.23 to -0.17)	0.13	(0.05 to 0.21)	-0.49	(-0.56 to -0.43)	0.04	(-0.01 to 0.09)	-0.27	(-0.30 to -0.23)
<b>Tobacco use</b>												
Present	0.00	(-0.09 to 0.09)	-0.19	(-0.22 to -0.16)	0.06	(-0.13 to 0.25)	-0.52	(-0.60 to -0.44)	0.02	(-0.08 to 0.13)	-0.29	(-0.34 to -0.25)
Absent	0.04	(0.00 to 0.09)	-0.21	(-0.24 to -0.17)	0.14	(0.05 to 0.22)	-0.48	(-0.56 to -0.41)	0.04	(-0.01 to 0.09)	-0.26	(-0.30 to -0.21)
<b>Alcohol use</b>												
Present	-0.04	(-0.19 to 0.12)	-0.21	(-0.30 to -0.13)	0.12	(-0.17 to 0.41)	-0.62	(-0.82 to -0.41)	0.02	(-0.13 to 0.18)	-0.27	(-0.39 to -0.16)
Absent	0.04	(-0.07 to 0.15)	-0.20	(-0.26 to -0.14)	0.13	(-0.07 to 0.34)	-0.47	(-0.61 to -0.34)	0.04	(-0.06 to 0.15)	-0.27	(-0.35 to -0.19)
<b>APOE ε4</b>												
Present	-0.11	(-0.35 to 0.12)	-0.22	(-0.36 to -0.08)	0.25	(-0.64 to 1.14)	-0.76	(-1.06 to -0.46)	-0.04	(-0.32 to 0.25)	-0.33	(-0.51 to -0.14)
Absent	-0.05	(-0.14 to 0.05)	-0.30	(-0.35 to -0.25)	0.02	(-0.17 to 0.21)	-0.67	(-0.78 to -0.57)	0.03	(-0.09 to 0.16)	-0.34	(-0.40 to -0.27)

Adjusted coefficients by othe factors; CI: Confidence interval; HTA: Hypertension

**eTable 3. Cognitive Decline in CERAD Language and Praxis Test by Risk Factors in PSEN1 E280A Mutation Carriers**

	Verbal fluency				15-item Boston naming test				Constructional praxis			
	Before 34 years old	(95% CI)	After 34 years old	(95% CI)	Before 34 years old	(95% CI)	After 34 years old	(95% CI)	Before 38 years	(95% CI)	After 38 years	(95% CI)
<b>Sex</b>												
Female	0.14	(0.04 to 0.23)	-0.46	(-0.53 to -0.39)	0.05	(0.01 to 0.09)	-0.20	(-0.23 to -0.17)	0.00	(-0.03 to 0.04)	-0.31	(-0.34 to -0.27)
Male	0.06	(-0.16 to 0.28)	-0.45	(-0.62 to -0.29)	-0.04	(-0.14 to 0.07)	-0.15	(-0.22 to -0.08)	0.00	(-0.08 to 0.09)	-0.27	(-0.35 to -0.18)
<b>Education†</b>												
High (greater than or equal 7)	0.13	(0.04 to 0.22)	-0.77	(-0.94 to -0.60)	0.01	(-0.02 to 0.04)	-0.28	(-0.36 to -0.21)	0.00	(-0.03 to 0.03)	-0.33	(-0.40 to -0.27)
Low (less than 7)	-0.02	(-0.11 to 0.07)	-0.49	(-0.56 to -0.42)	-0.05	(-0.10 to 0.00)	-0.19	(-0.23 to -0.16)	0.01	(-0.04 to 0.06)	-0.29	(-0.33 to -0.25)
<b>Socioeconomic status</b>												
Middle/High	0.16	(0.06 to 0.25)	-0.61	(-0.76 to -0.46)	0.03	(-0.01 to 0.07)	-0.25	(-0.32 to -0.18)	0.01	(-0.04 to 0.05)	-0.33	(-0.38 to -0.27)
Low	0.04	(-0.24 to 0.32)	-0.41	(-0.68 to -0.15)	-0.01	(-0.14 to 0.12)	-0.16	(-0.28 to -0.04)	-0.01	(-0.11 to 0.09)	-0.28	(-0.39 to -0.17)
<b>Residence area</b>												
Urban	0.13	(0.06 to 0.20)	-0.49	(-0.65 to -0.33)	0.03	(0.00 to 0.05)	-0.19	(-0.27 to -0.11)	0.00	(-0.03 to 0.04)	-0.31	(-0.37 to -0.25)
Rural	0.03	(-0.22 to 0.27)	-0.39	(-0.67 to -0.11)	-0.02	(-0.14 to 0.10)	-0.18	(-0.31 to -0.05)	-0.01	(-0.11 to 0.08)	-0.24	(-0.36 to -0.12)
<b>Occupation type</b>												
Non-Manual	0.11	(-0.19 to 0.42)	-0.34	(-0.54 to -0.14)	0.01	(-0.12 to 0.14)	-0.10	(-0.19 to 0.00)	-0.01	(-0.20 to 0.18)	-0.27	(-0.36 to -0.18)
Manual	0.10	(-0.29 to 0.49)	-0.47	(-0.98 to 0.04)	0.01	(-0.18 to 0.20)	-0.19	(-0.41 to 0.04)	0.00	(-0.17 to 0.17)	-0.29	(-0.57 to -0.01)
<b>Marital status</b>												
Single	0.17	(-0.10 to 0.44)	-0.42	(-0.64 to -0.19)	0.07	(-0.06 to 0.20)	-0.20	(-0.29 to -0.11)	0.02	(-0.08 to 0.12)	-0.39	(-0.50 to -0.27)
Married	0.22	(0.11 to 0.33)	-0.38	(-0.46 to -0.31)	0.03	(-0.02 to 0.08)	-0.15	(-0.18 to -0.12)	0.00	(-0.04 to 0.04)	-0.28	(-0.31 to -0.24)
<b>HTA</b>												
Present	0.40	(-0.27 to 1.07)	-0.43	(-0.66 to -0.21)	-0.01	(-0.33 to 0.31)	-0.10	(-0.19 to 0.00)	0.05	(-0.16 to 0.26)	-0.30	(-0.41 to -0.19)
Absent	0.19	(-0.39 to 0.77)	-0.38	(-0.53 to -0.23)	0.05	(-0.23 to 0.32)	-0.17	(-0.24 to -0.11)	0.00	(-0.17 to 0.17)	-0.29	(-0.36 to -0.22)
<b>Dyslipidemia</b>												
Present	0.17	(-0.35 to 0.68)	-0.34	(-0.58 to -0.10)	0.15	(-0.09 to 0.38)	-0.09	(-0.19 to 0.01)	0.16	(-0.03 to 0.35)	-0.22	(-0.34 to -0.10)
Absent	0.20	(0.10 to 0.29)	-0.39	(-0.47 to -0.32)	0.04	(0.00 to 0.08)	-0.17	(-0.20 to -0.14)	0.00	(-0.04 to 0.03)	-0.31	(-0.34 to -0.27)
<b>Diabetes</b>												
Present	-0.10	(-1.83 to 1.63)	-0.34	(-0.83 to 0.14)	0.04	(-0.82 to 0.90)	-0.17	(-0.38 to 0.05)	0.29	(-0.22 to 0.79)	-0.33	(-0.58 to -0.07)
Absent	0.20	(0.11 to 0.29)	-0.39	(-0.46 to -0.31)	0.04	(0.00 to 0.09)	-0.16	(-0.19 to -0.13)	0.00	(-0.03 to 0.04)	-0.29	(-0.33 to -0.25)
<b>Tobacco use</b>												
Present	0.23	(0.02 to 0.44)	-0.46	(-0.54 to -0.37)	0.10	(0.01 to 0.20)	-0.19	(-0.22 to -0.15)	0.04	(-0.06 to 0.13)	-0.33	(-0.37 to -0.29)
Absent	0.19	(0.09 to 0.28)	-0.34	(-0.43 to -0.26)	0.03	(-0.01 to 0.08)	-0.14	(-0.18 to -0.11)	0.00	(-0.04 to 0.03)	-0.26	(-0.30 to -0.21)
<b>Alcohol use</b>												
Present	0.27	(-0.07 to 0.62)	-0.52	(-0.75 to -0.30)	0.05	(-0.12 to 0.21)	-0.20	(-0.29 to -0.11)	-0.02	(-0.15 to 0.11)	-0.36	(-0.47 to -0.25)
Absent	0.19	(-0.06 to 0.44)	-0.36	(-0.50 to -0.21)	0.04	(-0.08 to 0.17)	-0.15	(-0.21 to -0.09)	0.01	(-0.08 to 0.10)	-0.27	(-0.34 to -0.19)

<i>APOE ε4</i>												
Present	- 0.08	(-0.70 to 0.54)	-0.52	(-0.86 to - 0.18)	- 0.12	(-0.38 to 0.13)	-0.16	(-0.33 to 0.01)	- 0.02	(-0.21 to 0.16)	-0.38	(-0.57 to - 0.18)
Absent	0.06	(-0.19 to 0.32)	-0.48	(-0.60 to - 0.35)	- 0.03	(-0.14 to 0.08)	-0.24	(-0.30 to - 0.18)	0.05	(-0.03 to 0.13)	-0.47	(-0.54 to - 0.39)

Adjusted coefficients by other factors; CI: Confidence interval; HTA: Hypertension, diabetes, tobacco and alcohol use.

**eTable 4. Cognitive Decline in CERADts, MMSE, and CERAD Subtest in 256 PSEN1 E280A Mutation Carriers With Two or More Assessments**

	Coefficients					
	Mean	(95% CI)	Before CP	(95% CI)	After CP	(95% CI)
CERADts	75,0	(80,72 to 89,24)	0,02	(-0,30 to 0,34)	-2,20	(-2,41 to -1,99)
MMSE	29,8	(28,76 to 30,85)	0,05	(-0,04 to 0,15)	-0,74	(-0,82 to -0,66)
WLR	7,6	(6,95 to 8,19)	-0,01	(-0,07 to 0,05)	-0,25	(-0,28 to -0,22)
WLM	20,4	(18,90 to 21,90)	-0,07	(-0,18 to 0,05)	-0,61	(-0,68 to -0,55)
WLRd	9,8	(9,26 to 10,32)	0,02	(-0,05 to 0,08)	-0,31	(-0,34 to -0,27)
VF	22,4	(20,43 to 24,30)	0,1	(-0,04 to 0,24)	-0,49	(-0,56 to -0,41)
BNT	13,8	(13,06 to 14,52)	-0,02	(-0,08 to 0,03)	-0,19	(-0,23 to -0,16)
CPT	10,6	(9,82 to 11,33)	0,02	(-0,02 to 0,06)	-0,34	(-0,38 to -0,30)

CI: Confidence interval; MMSE: Minimal state examination, CERADts: Total score of CERAD; WLR: Word list recall; WLM: Word list memory, WLRd: Word list recognition (Discrimination); VF: Verbal fluency; BNT: 15-item Boston naming test; CPT: Constructional praxis. †Adjusted by sex, education, socioeconomic status, residence area, occupation type, marital status, hypertension, dyslipidemia