

Supplementary Material

A Comparison of Operational Definitions for Mild Cognitive Impairment

Supplementary Table 1. Predictive accuracy of different cutoffs (z-scores) of the base rate approach [1] with regard to 1) incident all-cause dementia, 2) incident AD dementia, and 3) an AD biomarker signature (CSF Ab42/Tau). About 10% of the normative controls in [1] had deviant test scores on a number of CERAD subtests for each of the cutoffs examined. Impairment thresholds of 1.28 SD (in four or more subtests) and 1.0 SD (in five or more subtests) rank highest in terms of predictive accuracy.

Cutoffs for impairment [1]		MCI at baseline	PPV		NPV		Sensitivity		Specificity		J	Accuracy		Hazard ratio	
z-scores	CERAD tests impaired out of 10	%	%	95% CI	%	95% CI	%	95% CI	%	95% CI	%	value	95% CI	value	95% CI
(1) Predictive accuracy regarding incident all-cause dementia within three years															
≤ -0.67	≥ 6	48.4	42.6	[39.0, 46.3]	89.6	[86.1, 92.3]	79.3	[71.8, 85.6]	62.5	[57.6, 67.2]	41.8	66.9	[62.8, 70.7]	4.6	[3.1, 7.0]
≤ -1.00	≥ 5	45.5	44.1	[40.2, 48.1]	89.1	[85.8, 91.8]	77.2	[69.6, 83.8]	65.6	[60.8, 70.2]	42.9	68.6	[64.6, 72.5]	5.4	[3.6, 8.0]
≤ -1.28	≥ 4	47.1	44.5	[40.8, 48.3]	90.5	[87.2, 93.1]	80.7	[73.3, 86.8]	64.7	[59.8, 69.3]	45.3	68.8	[64.8, 72.6]	5.9	[3.7, 8.9]
≤ -1.48	≥ 3	52.7	41.5	[38.3, 44.8]	91.3	[87.7, 93.9]	84.1	[77.2, 89.7]	58.4	[53.4, 63.2]	42.5	65.1	[60.9, 69.0]	6.0	[3.8, 9.4]
≤ -1.96	≥ 2	49.6	43.0	[39.5, 46.5]	90.8	[87.3, 93.3]	82.1	[74.8, 87.9]	61.7	[56.9, 66.5]	43.8	67.0	[63.0, 70.9]	5.6	[3.7, 8.7]
≤ -2.32	≥ 1	53.9	39.87	[36.8, 43.1]	90.3	[86.5, 93.1]	82.8	[75.6, 88.5]	56.2	[51.2, 61.0]	38.93	63.1	[58.9, 67.1]	5.3	[3.4, 8.2]
(2) Predictive accuracy regarding incident AD dementia within three years															
≤ -0.67	≥ 6	48.4	31.1	[28.2, 34.1]	95.1	[92.3, 97.0]	85.6	[77.0, 91.9]	59.8	[55.2, 64.4]	45.4	64.3	[60.2, 68.3]	6.7	[3.8, 11.9]
≤ -1.00	≥ 5	45.5	31.5	[28.4, 34.8]	94.4	[91.6, 96.3]	82.5	[73.4, 89.5]	62.3	[57.7, 66.7]	44.7	65.8	[61.7, 69.7]	7.1	[4.2, 12.1]
≤ -1.28	≥ 4	47.1	32.3	[29.4, 35.4]	95.9	[93.3, 97.6]	87.6	[79.4, 93.4]	61.4	[56.8, 65.9]	49.0	66.0	[61.9, 69.9]	9.5	[5.2, 17.5]
≤ -1.48	≥ 3	52.7	28.9	[26.4, 31.6]	95.5	[92.5, 97.3]	87.6	[79.4, 93.4]	54.7	[50.0, 59.3]	42.3	60.4	[56.2, 64.5]	7.6	[4.1, 14.0]
≤ -1.96	≥ 2	49.6	30.0	[27.2, 32.9]	95.0	[92.1, 96.9]	85.6	[77.0, 91.9]	57.9	[53.3, 62.5]	43.5	62.7	[58.6, 66.8]	6.9	[3.9, 12.1]
≤ -2.32	≥ 1	53.9	27.6	[25.1, 30.2]	94.6	[91.4, 96.6]	85.6	[77.0, 91.9]	52.7	[48.0, 57.4]	38.3	58.4	[54.2, 62.6]	6.4	[3.6, 11.4]
(3) Predictive accuracy regarding AD biomarker Odds ratio															
≤ -0.67	≥ 6	48.4	55.8	[51.1, 60.5]	65.0	[59.2, 70.4]	65.9	[58.1, 73.0]	54.9	[47.6, 62.1]	20.8	60.0	54.7, 65.1	2.4	[1.5, 3.7]
≤ -1.00	≥ 5	45.5	59.4	[54.3, 64.2]	67.6	[62.1, 72.7]	66.5	[58.8, 73.6]	60.6	[53.4, 67.6]	27.1	63.3	58.1, 68.3	3.1	[2.0, 5.0]
≤ -1.28	≥ 4	47.1	59.1	[54.4, 63.7]	69.1	[63.3, 74.4]	70.1	[62.5, 76.9]	58.0	[50.7, 65.1]	28.1	63.6	58.4, 68.6	3.1	[1.9, 5.0]
≤ -1.48	≥ 3	52.7	56.4	[52.0, 60.7]	67.8	[61.5, 73.5]	71.3	[63.8, 78.0]	52.3	[45.0, 59.6]	23.6	61.1	55.9, 66.2	2.7	[1.7, 4.3]
≤ -1.96	≥ 2	49.6	56.8	[51.9, 61.5]	65.5	[59.8, 70.7]	65.3	[57.5, 72.5]	57.0	[49.7, 64.1]	22.3	60.8	55.6, 65.9	2.8	[1.7, 4.5]
≤ -2.32	≥ 1	53.9	54.1	[49.7, 58.4]	64.2	[58.1, 70.0]	67.7	[60.0, 74.7]	50.3	[43.0, 57.5]	17.9	58.3	53.1, 63.5	2.4	[1.5, 3.8]

PPV, positive predictive value, NPV, negative predictive value, CI, confidence interval, J, Youden's index, Highest values are highlighted in bold, Sample size: $n = 360$.

[1] Mistridis P, Egli SC, Iverson GL, Berres M, Willmes K, Welsh-Bohmer KA, Monsch AU (2015) Considering the base rates of low performance in cognitively healthy older adults improves the accuracy to identify neurocognitive impairment with the Consortium to Establish a Registry for Alzheimer's Disease-Neuropsychological Assessment Battery (CERAD-NAB). *Eur Arch Psychiatry Clin Neurosci* **265**, 407–417.