

Supplementary Table 1. Characteristic of midlife risk models for the general population

Study sample	Sample size	Outcomes	Follow-up	Baseline age	Number of events	Model	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)	AUC
Kaiser Permanente Medical Care Program of Northern California (KPNC) ¹	9480	dementia	mean 36.9 years	40–55 (mean 46.1)	2767	CAIDE score (age, education, sex, cholesterol, BMI, systolic blood pressure)						0.74
						CAIDE score (age, education, sex, cholesterol, BMI, systolic blood pressure) for Asian					0.81	
						CAIDE score (age, education, sex, cholesterol, BMI, systolic blood pressure) for Black					0.75	
						CAIDE score (age, education, sex, cholesterol, BMI, systolic blood pressure) for White					0.74	
						CAIDE score, central obesity (Logistic Analysis)					0.75	
						CAIDE score, depressed mood (Logistic Analysis)					0.75	
						CAIDE score, diabetes mellitus (Logistic Analysis)					0.75	
						CAIDE score, head trauma (Logistic Analysis)					0.75	
CAIDE score, poor lung function (Logistic Analysis)						0.75						

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						CAIDE score, smoking (Logistic Analysis)						0.75
						CAIDE score, central obesity (Cox Analysis)						0.67
						CAIDE score, depressed mood (Cox Analysis)						0.67
						CAIDE score, diabetes mellitus (Cox Analysis)						0.67
						CAIDE score, head trauma (Cox Analysis)						0.67
						CAIDE score, poor lung function (Cox Analysis)						0.67
						CAIDE score, smoking (Cox Analysis)						0.67
National Finnish population study (FINRISK) ²	7114	dementia and AD	Mean 16.1 years	47.9 ±13.2 years	407 dementia, 319 AD	sex, total cholesterol, systolic blood pressure, BMI, education level and number of APOE ε 4 alleles, NT-proBNP (dementia, 18 years)						0.65
						sex, total cholesterol, systolic blood pressure, BMI, education level and number of APOE ε 4 alleles, NT-proBNP (dementia, 10 years)						0.69
						sex, total cholesterol, systolic blood pressure, BMI, education level and number of APOE ε 4 alleles, hs-TNI (dementia, 18 years)						0.65

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						sex, total cholesterol, systolic blood pressure, BMI, education level and number of APOE ε 4 alleles, hs-TNI (dementia, 10 years)						0.70
						sex, total cholesterol, systolic blood pressure, BMI, education level and number of APOE ε 4 alleles, NT-proBNP, hs-TNI (dementia, 18 years)						0.65
						sex, total cholesterol, systolic blood pressure, BMI, education level and number of APOE ε 4 alleles, NT-proBNP, hs-TNI (dementia, 10 years)						0.69
						sex, total cholesterol, systolic blood pressure, BMI, education level and number of APOE ε 4 alleles, NT-proBNP (AD, 18 years)						0.67
						sex, total cholesterol, systolic blood pressure, BMI, education level and number of APOE ε 4 alleles, NT-proBNP (AD, 10 years)						0.72
Finnish Twin Cohort (FTC) study ³	2602	dementia	mean 27.8 years	mean age of 46.7 years	265	age, education, work status, nature of work, work environment, physicality of work	69.0	70.0	19.0	96.0	70.0	0.77
	1086	dementia	mean 39.1 years	32-38 years, mean 34.7 years	46 (diagnosed by TELE)	age, education, work status, nature of work, work environment, physicality of work						0.66

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	1086	dementia	mean 39.1 years	32-38 years, mean 34.7 years	34 (diagnosed by TICS)	age, education, work status, nature of work, work environment, physicality of work						0.72
Cardiovascular Risk Factors, Aging, and Dementia (CAIDE) Study ⁴	1409	dementia	20 years	39 - 64 midlife exam (mean 50.4); 65 - 80 late life exam	61	age, education, sex, systolic BP (Cut-off 140mmHg), BMI (Cut-off 30kg/m ²), total cholesterol (Cut-off 6.5 mmol/L), physical inactivity (risk score model)						0.77
						age, education, sex, systolic BP (Cut-off 140mmHg), BMI (Cut-off 30kg/m ²), total cholesterol (Cut-off 6.5 mmol/L), physical inactivity (beta coefficient model)					0.78	
						age, education, sex, systolic BP, BMI, total cholesterol, physical activity; Cut-off Score ≥9	77.0	63.0	9.0	98.0	63.5	
						age, education, sex, systolic BP, BMI, total cholesterol, physical activity; Cut-off Score ≥10	63.0	75.0	10.0	98.0	74.0	
						education, sex, systolic BP, BMI, total cholesterol, physical inactivity						0.76
						age, education, sex, systolic BP, BMI, total cholesterol, physical activity, APOE ε 4 (risk score model)						0.78
						age, education, sex, systolic BP, BMI, total cholesterol, physical activity, APOE						0.79

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Study sample	Sample size	Outcomes	Follow-up	Baseline age	Number of events	Model	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)	AUC
						ε 4 (beta coefficient model)						
						age, education, sex, systolic BP, BMI, Total cholesterol, physical activity, APOE ε 4; Cut-off Score ≥ 10	81.0	61.0	9.0	99.0	61.6	
						age, education, sex, systolic BP, BMI, total cholesterol, physical activity, APOE ε 4; Cut-off Score ≥ 11	67.0	72.0	10.0	98.0	71.2	
						education, sex, systolic BP, BMI, total cholesterol, physical activity, APOE ε 4						0.76

Abbreviations: AD: Alzheimer disease; BP: blood pressure; BMI: body mass index; CAIDE: Cardiovascular Risk Factors, Aging and Dementia Study; hs-TnI: high-sensitivity cardiac troponin I; NT-proBNP: N-terminal pro-brain natriuretic peptide; TELE: telephone assessment for dementia; TICS: Telephone Interview for Cognitive Status.

1. Exalto LG, Quesenberry CP, Barnes D, *et al.* Midlife risk score for the prediction of dementia four decades later. *Alzheimer's and Dementia* 2014; 10(5): 562-70.
2. Tynkkynen J, Hernesniemi JA, Laatikainen T, *et al.* High-sensitivity cardiac troponin I and NT-proBNP as predictors of incident dementia and Alzheimer's disease: the FINRISK Study. *J Neurol* 2017; 264(3): 503-11.
3. Vuoksimaa E, Rinne JO, Lindgren N, *et al.* Middle age self-report risk score predicts cognitive functioning and dementia in 20-40 years. *Alzheimers Dement (Amst)* 2016; 4: 118-25.
4. Kivipelto M, Ngandu T, Laatikainen T, *et al.* Risk score for the prediction of dementia risk in 20 years among middle aged people: a longitudinal, population-based study. *Lancet Neurol* 2006; 5(9): 735-41.