

**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) <sup>1</sup> | 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) <sup>2</sup> | 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 <sup>3</sup> | 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 <sup>4</sup> | 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 <sup>2</sup> ), 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 <sup>2</sup> ), 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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|              |             |          |           |              |                  | $\epsilon$ 4 (beta coefficient model)   |                 |                 |         |         |              |      |
|              |             |          |           |              |                  | age, education, sex, systolic BP, BMI, Total cholesterol, physical activity, APOE $\epsilon$ 4; Cut-off Score $\geq$ 10 | 81.0            | 61.0            | 9.0     | 99.0    | 61.6         |      |
|              |             |          |           |              |                  | age, education, sex, systolic BP, BMI, total cholesterol, physical activity, APOE $\epsilon$ 4; Cut-off Score $\geq$ 11 | 67.0            | 72.0            | 10.0    | 98.0    | 71.2         |      |
|              |             |          |           |              |                  | education, sex, systolic BP, BMI, total cholesterol, physical activity, APOE $\epsilon$ 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.

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