

# Lifestyle for Brain Health (LIBRA)

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# Lifestyle for Brain Health (LIBRA): a new model for dementia prevention

Olga J. G. Schiepers<sup>1</sup>, Sebastian Köhler<sup>1</sup>, Kay Deckers<sup>1</sup>, Kate Irving<sup>2,†</sup>, Catherine A. O'Donnell<sup>3</sup>, Marjan van den Akker<sup>4</sup>, Frans R. J. Verhey<sup>1</sup>, Stephanie J. B. Vos<sup>1</sup>, Marjolein E. de Vugt<sup>1</sup> and Martin P. J. van Boxtel<sup>1</sup>

<sup>1</sup>School for Mental Health and Neuroscience, Alzheimer Center Limburg, Maastricht University, Maastricht, The Netherlands

<sup>2</sup>School of Nursing and Human Sciences, Dublin City University, Dublin, Ireland

<sup>3</sup>General Practice and Primary Care, Institute of Health and Wellbeing, University of Glasgow, Glasgow, UK

<sup>4</sup>Department of General Practice, Maastricht University, Maastricht, The Netherlands

Correspondence to: M. P. J. van Boxtel, E-mail: martin.vanboxtel@maastrichtuniversity.nl

<sup>†</sup>On behalf of the In-MINDD project team.

**Objective:** Modifiable risk factors for dementia were recently identified and compiled in a systematic review. The 'Lifestyle for Brain Health' (LIBRA) score, reflecting someone's potential for dementia prevention, was studied in a large longitudinal population-based sample with respect to predicting cognitive change over an observation period of up to 16 years.

**Methods:** Lifestyle for Brain Health was calculated at baseline for 949 participants aged 50–81 years from the Maastricht Ageing Study. The predictive value of LIBRA for incident dementia and cognitive impairment was examined by using Cox proportional hazard models and by testing its relation with cognitive decline.

**Results:** Lifestyle for Brain Health predicted future risk of dementia, as well as risk of cognitive impairment. A one-point increase in LIBRA score related to 19% higher risk for dementia and 9% higher risk for cognitive impairment. LIBRA predicted rate of decline in processing speed, but not memory or executive functioning.

**Conclusions:** Lifestyle for Brain Health (LIBRA) may help in identifying and monitoring risk status in dementia-prevention programmes, by targeting modifiable, lifestyle-related risk factors. Copyright © 2017 John Wiley & Sons, Ltd.

**Key words:** dementia; prevention; lifestyle; ageing; cognitive function

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## Introduction

Dementia is a worldwide public health problem (Mathers and Loncar, 2006) as the number of people with dementia rises rapidly (Ferri *et al.*, 2005). No curative treatment for dementia exists, and the need for new prevention strategies is high.

Primary prevention requires identification of risk and protective factors that are potentially modifiable. Early primary prevention may be particularly relevant for risk factors known to have a larger impact on dementia risk when occurring during midlife, for

example, as in hypertension (Qiu *et al.*, 2005) and obesity (Fitzpatrick *et al.*, 2009).

In a recent systematic review, modifiable risk and protective factors for dementia were compiled (Deckers *et al.*, 2015). Identified risk factors were depression, diabetes, physical inactivity, (midlife) hypertension, (midlife) obesity, smoking, high cholesterol, coronary heart disease, renal dysfunction, and low unsaturated fat intake, whereas high cognitive activity, low/moderate alcohol consumption, and Mediterranean diet were qualified as protective factors.

Several studies developed prediction models to calculate individual dementia risk. While some developed risk indices specifically for Alzheimer's disease (AD) (Reitz *et al.*, 2010; Jessen *et al.*, 2011), others presented risk scores for dementia (Kivipelto *et al.*, 2006; Barnes *et al.*, 2009). All studies employed a highly data-driven approach by using single cohort studies each prone to sampling variation and type I and type II errors, which yield a restricted number of factors. This limitation was overcome in a recent study by Anstey *et al.* (2013), who introduced a risk assessment tool for AD, based on literature review. Another drawback, however, is that these risk indices comprise both modifiable and non-modifiable factors (e.g. age, sex, and apolipoprotein E genotype). Although including the latter might increase predictive accuracy, such factors are not amenable to change, cannot be targeted in routine care, and do not indicate individual 'room for improvement'.

Here, we report on a new prediction model for dementia that differs from previous risk indices by focusing exclusively on modifiable risk factors, increasing its potential application in the development of tailored interventions and primary prevention. We evaluate this model in a large population-based study containing extensive information about risk and protective factors for dementia and cognitive decline.

## Methods

The study was part of the Innovative Midlife Intervention for Dementia Deterrence project (In-MINDD), aimed at decreasing dementia risk and/or delaying its onset by means of lifestyle interventions in midlife (O'Donnell *et al.*, 2015).

### Study population

We used data from the Maastricht Ageing Study (MAAS), a 12-year longitudinal study into the determinants and consequences of cognitive ageing (Jolles *et al.*, 1995; Van Boxtel *et al.*, 1998). Participants were randomly drawn from a register of family practices (Metsemakers *et al.*, 1992). Exclusion criteria were chronic neurological pathology, psychiatric disorders, mental retardation, and psychotropic drug use. MAAS consists of 1823 individuals, aged 24 to 81 years at baseline, comprising four independent but demographically identical panels, each stratified for age, sex, and level of occupational achievement. Between 1993 and 1995 (baseline), all participants completed a general health and lifestyle questionnaire and

underwent extensive medical and neuropsychological examination. Follow-up examinations took place after 6 and 12 years.

Only participants aged 50 years or older ( $n = 955$ ) at baseline were included. Data were incomplete for six participants, so the final study sample comprised 949 individuals. During the 12-year follow-up period, 432 participants dropped out of the study for various reasons, including death, illness, or refusal to participate (Van Beijsterveldt *et al.*, 2002). Only legally competent persons with a Mini-Mental State Examination score  $>24$  could participate. The Ethics Committee of Maastricht University Medical Centre approved the study, and all participants gave informed consent.

### Dementia diagnosis

Dementia status was based on Diagnostic and Statistical Manual of Mental Disorders, 4th Edition criteria (DSM-4; American Psychiatric Association, 2000) in all participants up to 16 years after the start of the study, using both the International Classification of Primary Care coded information from individual patient records and medical and cognitive data obtained in MAAS. A total of 62 incident cases of dementia were identified by the consensus committee (neuropsychiatrist and neuropsychologist). A valid risk score was lacking for one participant who was later diagnosed with dementia; the final study sample ( $n = 949$ ) comprised 61 (6.4%) dementia cases.

### Cognitive functioning

*Cognitive tests.* The Visual Verbal Word Learning Task was used to assess verbal memory (Van der Elst *et al.*, 2005). Delayed recall was the outcome measure used in the present study.

The Stroop Colour–Word Interference Test was used to assess executive functioning (Van der Elst *et al.*, 2006b). The outcome parameter was the difference in time needed to complete subtask 3 and subtasks 1 and 2, which is a measure of interference susceptibility.

The Letter–Digit Substitution Test was used to assess information processing speed (Van der Elst *et al.*, 2006a). The total number of correct substitutions completed within 90 s was recorded.

*Incident cognitive impairment.* After excluding cases with incident dementia ( $n = 61$ ), means and SDs of test results were calculated for age categories (i.e. 50–60 years, 60–70 years, and 70+ years) at baseline,

6- and 12-year follow-up. Participants scoring 1.5 SD below the mean on any of the three cognitive tests mentioned in the preceding texts were classified as cognitively impaired. Individuals showing cognitive impairment at baseline ( $n = 142$ ) were excluded from this part of the statistical analysis. Incident cognitive impairment at 6- or 12-year follow-up was recorded, resulting in 91 (12.2%) cases out of a total sample of 746 participants.

*Cognitive decline.* Cognitive decline was measured in 746 participants, after excluding all cases of incident dementia ( $n = 61$ ) and cognitive impairment at baseline ( $n = 142$ ). Individual course of cognitive functioning across all three measurements (baseline and 6- and 12-year follow-up) was assessed on each cognitive test.

#### Education

In order to use education as an independent variable in the risk-prediction models, educational level was categorized into 'low' (<8 years of formal education) or 'average/high' ( $\geq 8$  years) (Anstey *et al.*, 2013).

#### Risk-prediction model

*Inventory of modifiable risk factors.* Information was available on 11 of the 13 factors identified (Table 2). Alcohol consumption measured in standard units per week was categorized into 'low/moderate' (<14 units/week) or 'other'. The latter category included both non-drinkers as well as individuals drinking at least 14 units of alcohol per week. Physical activity was recorded as 'average number of hours up and about per day'. Participants in the lowest tertile were classified as physically inactive. Participants reporting high cholesterol levels and/or using cholesterol-lowering medication at baseline were classified as having high cholesterol. Current smoking was recorded as 'yes' or 'no'. Obesity corresponded to a body mass index of 30 or higher. Participants with high blood pressure (i.e. mean systolic blood pressure  $\geq 140$  mm Hg or mean diastolic blood pressure  $\geq 90$  mm Hg) and/or using antihypertensive medication were classified as hypertensive. Cardiovascular disease was defined as 'currently suffering from heart disease or vascular disorders'. Diabetes was defined as 'currently suffering from diabetes'. Renal dysfunction was defined as 'currently suffering from renal disease'.

Depressive state was measured with the Dutch version of the depression subscale of the Symptom Checklist 90 (Arrindell and Ettema, 1986).

Participants scoring within the highest quartile were classified as having clinically relevant depressive symptoms. Cognitive activity was measured by calculating the average number of hours per week spent on reading or mental exercise (e.g. gaming). Sum scores in the highest tertile indicated high cognitive activity.

Direct or indirect (proxy) measures were lacking for two variables: unsaturated fat intake and Mediterranean diet and were not included in the overall risk score.

*Risk score.* A model incorporating the risk and protective factors for dementia mentioned in the preceding texts was created, based on 11 measured risk factors. Using the relative risks (RRs) of all factors (Deckers *et al.*, 2015), a risk index (Lifestyle for Brain Health, LIBRA) was calculated according to a previously reported approach (Kivipelto *et al.*, 2006; Anstey *et al.*, 2013). First, the natural logarithm of the RR was calculated for each factor. Second, these were standardized by taking the lowest natural logarithm (RR) as a reference value, that is,  $-0.30$  for low/moderate alcohol consumption, and dividing all other values by this value (Table 1). Finally, individual total risk scores represent the sum of the scores assigned to the separate risk factors.

Because these variables have been included in other risk indices, we also calculated a 'modified' LIBRA score that also incorporates these factors to study change in predictive accuracy. Three risk-prediction models were constructed: model (1) LIBRA score (measured modifiable factors); model (2) LIBRA score + education; and model (3) LIBRA score + education, age, and sex. The original algorithm was modified by adding standardized scores for 'age for men', 'age for women', and 'years of education', based on the beta weights reported by Anstey *et al.* (2013).

Continuous risk scores, as well as subgroups based on quintiles, were analysed to determine if dementia risk increased in a linear fashion across cutoffs of the risk score. Individual risk scores were calculated if data were available for at least 9 out of 11 risk factors for model 1 ( $n = 949$ ), 10 out of 12 risk factors for model 2 ( $n = 948$ ), and 11 out of 13 risk factors for model 3 ( $n = 948$ ).

#### Statistical analyses

Chi-squared tests and independent samples *t*-tests were used to examine differences in risk factors and demographic variables between participants with incident dementia and others. Cox proportional hazard

Table 1 Algorithm for calculating individual Lifestyle for Brain Health (LIBRA) score<sup>a</sup>

Modifiable risk factor	Relative risk (RR)	Ln (RR)/beta weight	Score	Available in MAAS
Low/moderate alcohol consumption	0.74	-0.30 (reference)	-1.0	+
Coronary heart disease	1.36	0.31	+1.0	+
Physical inactivity	1.39	0.33	+1.1	+
Renal dysfunction	1.39	0.33	+1.1	+
Diabetes	1.47	0.39	+1.3	+
High cholesterol	1.54	0.43	+1.4	+
Smoking	1.59	0.46	+1.5	+
Obesity	1.60	0.47	+1.6	+
Hypertension	1.61	0.48	+1.6	+
Mediterranean diet	0.60	0.51	-1.7 <sup>c</sup>	-
Depression	1.85	0.62	+2.1	+
High cognitive activity	0.38	-0.97	-3.2	+
Low unsaturated fat intake <sup>b</sup>	—	—	—	-

Note: Ln, natural logarithm; MAAS, Maastricht Ageing Study.

<sup>a</sup>LIBRA score represents the sum of the scores assigned to the individual risk factors.

<sup>b</sup>RR not available from meta-analyses.

<sup>c</sup>[Correction added on 30 July 2018, after first online publication: Changes have been made in Table 1, row "Mediterranean diet", column "Score", "+1.7" should be "-1.7"].

models were used to assess whether individual risk scores (models 1–3) predicted dementia risk as well as incident cognitive impairment during follow-up, with time since baseline as the time axis. The analyses were corrected for age, sex, and education in model 1 and age and sex in model 2. Area under the Receiver Operator Characteristic curve (AUC) was calculated to examine predictive accuracy.

Linear mixed models were used to assess whether risk scores predicted the individual course of cognitive decline. The association between risk scores and individual course of cognitive decline was estimated by the two-way interaction between time (measured in years since baseline, i.e. 0, 6, and 12 years) and risk score, which represents the rate of change in cognitive performance as a function of risk score. The analyses were corrected for age, age<sup>2</sup>, sex, and education in model 1 and age, age<sup>2</sup>, and sex in model 2. All statistical analyses were performed by using IBM SPSS STATISTICS version 20 (New York, NY, USA).

## Results

Dementia incidence rate for the present study sample was 6.7 cases per 1000 person-years (95% CI: 5.0, 8.3), which is comparable to the incidence rates reported for the Dutch population, aged 60+ years (i.e. 5.8–11.1 cases per 1000 persons/year) (Schrijvers *et al.*, 2012).

Table 2 shows the characteristics of the study population. Individuals diagnosed with dementia were older than those without dementia ( $p < 0.001$ ). In addition, participants later diagnosed with dementia were more likely to show hypertension at baseline

( $p < 0.001$ ). Likewise, a larger percentage of individuals who were diagnosed with dementia suffered from diabetes at baseline ( $p = 0.051$ ).

### Dementia risk

*Model 1: LIBRA score based on modifiable risk factors only.* The LIBRA scores ranged from -4.2 (protective) to 9.2 (risk) with a mean of 1.5 and a standard deviation of 2.5 (Table 2). Individual risk scores differed significantly between participants with dementia and others, LIBRA scores being higher for those with dementia (mean difference (95% CI) = -0.82 (-1.48; -0.16),  $p = 0.014$ ).

After correction for age, sex, and education, the LIBRA scores predicted dementia risk in Cox regression (Table 3). When risk was categorized into quintiles, hazard ratios (HRs) for the second to fifth quintiles (lowest quintile is reference) were 0.39, 2.38, 2.59, and 2.74 (Figure 1). Quintiles 3–5 predicted a higher dementia risk as compared to the lowest quintile ( $p = 0.037$ ,  $p = 0.023$ , and  $p = 0.021$  respectively). The AUC for the unadjusted continuous LIBRA score was 0.60 (95% CI 0.53; 0.67) ( $p = 0.012$ ).

*Models 2 and 3: LIBRA score based on modifiable and non-modifiable factors.* Modified risk scores ranged from -4.2 to 11.9 (mean 2.7, SD 2.8) for model 2 and -4.2 to 21.2 (mean 5.3, SD 4.6) for model 3 (Table 2). They differed between participants with dementia and others (mean difference (95% CI) = -0.89 (-1.61; -0.17),  $p = 0.015$  for model 2 and -4.10 (-5.27; -2.94),  $p < 0.001$  for model 3).

Table 2 Characteristics of the study population according to dementia status

Variable	Total study sample	Dementia	No dementia	<i>p</i> -value <sup>a</sup>
<i>n</i>	949	61 (6.4%)	888 (93.6%)	
Age	65.0 (8.7)	72.5 (6.3)	64.5 (8.6)	<0.001
Female sex	466 (49.1%)	28 (45.9%)	438 (49.3%)	0.605
Low level of education	200 (21.1%)	16 (26.2%)	184 (20.7%)	0.298
Low/moderate alcohol consumption	516 (54.7%)	26 (42.6%)	490 (55.2%)	0.109
Cardiovascular disease	173 (18.2%)	12 (19.7%)	161 (18.1%)	0.763
Physical inactivity	365 (38.6%)	25 (41.0%)	340 (38.3%)	0.774
Renal dysfunction	50 (5.3%)	3 (4.9%)	47 (5.3%)	0.899
Diabetes	66 (7.0%)	8 (13.1%)	58 (6.5%)	0.051
High cholesterol	139 (14.6%)	8 (13.1%)	131 (14.8%)	0.726
Smoking	217 (22.9%)	9 (14.8%)	208 (23.4%)	0.115
Obesity	223 (23.5%)	14 (23.0%)	209 (23.5%)	0.910
Hypertension	545 (57.4%)	50 (82.0%)	495 (55.7%)	<0.001
Depression	233 (24.6%)	17 (27.9%)	216 (24.3%)	0.389
High cognitive activity	331 (34.9%)	17 (27.9%)	314 (35.4%)	0.364
Risk score Model 1 <sup>b</sup>	1.6 (−4.2 to 9.2)	2.7 (−4.2 to 8.8)	1.5 (−4.2 to 9.2)	0.014
Model 2	2.7 (−4.2 to 11.9)	3.6 (−4.2 to 11.5)	2.7 (−4.2 to 11.9)	0.015
Model 3	4.6 (−4.2 to 21.1)	9.2 (−0.1 to 21.1)	4.3 (−4.2 to 18.1)	<0.001

Note: Values are presented as *n* (%), mean (SD), or median (range).

<sup>a</sup>*p*-value for the difference between participants with dementia and non-demented individuals.

<sup>b</sup>Model 1, Lifestyle for Brain Health (LIBRA) score (modifiable risk factors only); model 2, LIBRA score + education; model 3, LIBRA score + education, age, and sex.

Adding weights for education and adjusting analyses for age and sex in model 2, individual risk scores predicted dementia risk in survival analysis (Table 3). When the risk score was categorized into quintiles, the HRs for the second to fifth quintiles (lowest quintile is reference) were 0.98, 2.19, 2.40, and 1.96 (model 2) and 4.63, 8.32, 21.92, and 40.74 (model 3) (Figure 1). For model 2, only quintile 4 predicted a higher dementia risk as compared to the lowest quintile ( $p = 0.041$ ). The AUC for unadjusted continuous risk score was 0.59 (95% CI 0.52; 0.66,  $p = 0.018$ ). When adding weights for education, age, and sex, risk score predicted dementia risk in model 3 (Table 3). When the score was categorized into quintiles, the HRs for the second to fifth quintiles (lowest quintile is reference) were 4.63, 8.32, 21.92, and 40.74. For model 3, quintiles 3 to 5 predicted a higher dementia risk as compared to the lowest quintile ( $p = 0.045$ ,  $p = 0.003$ , and  $p < 0.001$  respectively). The AUC was 0.59 for model 2 (0.52; 0.66) ( $p = 0.018$ ) and 0.75 (0.69; 0.80) ( $p < 0.001$ ) for model 3. The AUC for the unadjusted continuous risk score was 0.75 (95% CI 0.69; 0.80,  $p < 0.001$ ).

#### Risk of incident cognitive impairment

**Model 1.** After exclusion of participants with cognitive impairment at baseline, LIBRA scores ranged from −4.2 to 9.1 (mean 1.3, SD 2.5). Individual risk scores did not differ between participants with

cognitive impairment and those without ((95% CI) = −0.56 (−1.14; 0.01),  $p = 0.054$ ). After correction, LIBRA scores predicted cognitive impairment in survival analysis (Table 3). When risk was categorized into quintiles, the HRs for the second to fifth quintiles (lowest quintile is reference) were 1.91, 2.81, 2.58, and 1.67. Quintiles 3 and 4 predicted a higher risk of cognitive impairment as compared to the lowest quintile ( $p = 0.002$  and  $p = 0.008$  respectively). The AUC was 0.56 (95% CI 0.50; 0.62) ( $p = 0.056$ ).

**Models 2 and 3.** Individual risk scores ranged from −4.2 to 10.5 (mean 2.5, SD 2.7) for model 2 and −4.2 to 18.1 (mean 4.8, SD 4.4) for model 3. Risk scores differed between participants with cognitive impairment and those without for model 2 (mean difference (95% CI) = −0.65 (−1.24; −0.06),  $p = 0.030$ ), but not for model 3 (−0.58 (−1.49; 0.32),  $p = 0.207$ ).

Adding weights for education and adjusting analyses for age and sex in model 2, individual risk scores predicted risk for cognitive impairment (Table 3). When risk score was categorized into quintiles, the HRs for the second to fifth quintiles (lowest quintile is reference) were 1.75, 2.75, 2.63, and 1.92, suggesting that quintiles 3 and 4 predicted a higher risk of cognitive impairment as compared to the lowest quintile ( $p = 0.004$  and  $p = 0.006$  respectively). The AUC for the unadjusted continuous risk scores was 0.57 (95% CI 0.51; 0.63,  $p = 0.031$ ).

Table 3 Predictive value of risk score for individual risk of dementia and incident cognitive impairment using Cox proportional hazard models

Outcome measure	Risk score	HR (95% CI)	p-value
Dementia	Model 1 <sup>a</sup>	1.19 (1.08; 1.32)	0.001
	Model 2	1.15 (1.05; 1.26)	0.002
	Model 3	1.25 (1.19; 1.32)	<0.001
Incident cognitive impairment	Model 1	1.09 (1.004; 1.18)	0.039
	Model 2	1.09 (1.01; 1.17)	0.022
	Model 3	1.05 (1.002; 1.11)	0.040

Note: HR, hazard ratio.

<sup>a</sup>Model 1, Lifestyle for Brain Health (LIBRA) score (modifiable risk factors only), adjusted for age, gender, and education; model 2, LIBRA score + score for education, adjusted for age and gender; model 3, LIBRA score + scores for education, age, and sex and no covariate adjustment.

When adding weights for education, age, and sex in model 3, individual risk scores predicted risk for cognitive impairment (Table 3). The HRs ranged from 1.30 to 1.50, 1.58, and 2.05 when comparing quintiles 2 to 5 with quintile 1 (reference). For model 3, only the fifth quintile predicted a higher risk of cognitive impairment as compared to the lowest quintile ( $p = 0.045$ ). The AUC for the unadjusted continuous risk scores was 0.55 (95% CI 0.48; 0.61,  $p = 0.173$ ).

Risk of cognitive decline

In model 1, linear mixed models did not reveal an association between LIBRA scores and individual course of cognitive decline on the domains of verbal memory and executive functioning (Table 4). In contrast, information processing speed showed a significant association with LIBRA scores (Table 4).

Linear mixed models revealed an association between modified risk scores and individual course of cognitive decline on the domains of verbal memory

and executive functioning for model 3, but not for model 2 (Table 4). Information processing speed showed an association with risk scores for both models (Table 4).

Discussion

The present study introduces a prediction model for late-life risk of dementia, based on modifiable risk factors (LIBRA). We tested it in a large population-based dataset with a follow-up period of up to 16 years for dementia and 12 years for incident cognitive impairment and individual course of cognitive decline.

Lifestyle for Brain Health comprising only modifiable risk factors and corrected for age, sex, and education predicted future risk of dementia and cognitive impairment with similar predictive values, independent of age, sex, and education: a one-point increase in LIBRA scores related to a 19% higher risk for dementia and a 9% higher risk for cognitive

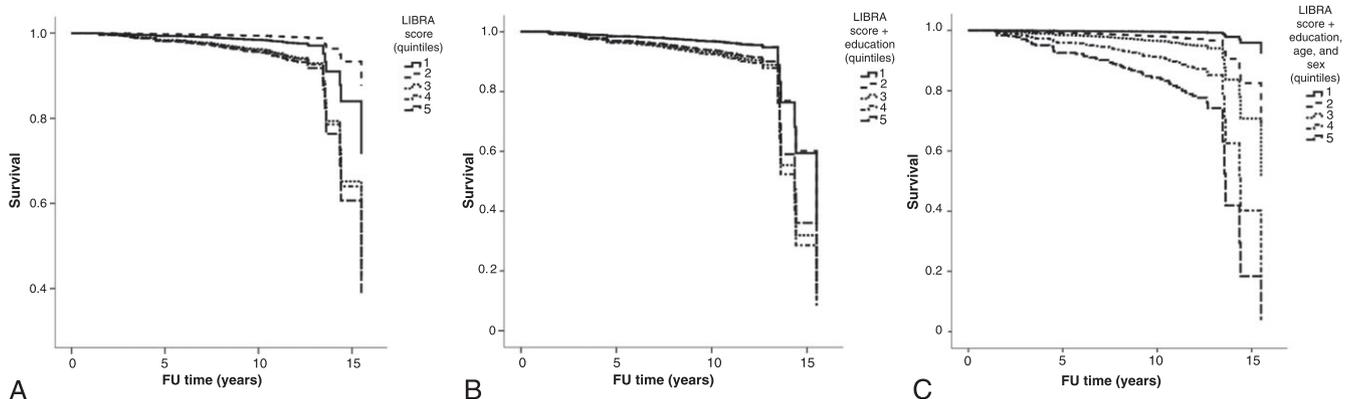


Figure 1 Survival probability for dementia. The predictive value of Lifestyle for Brain Health scores (depicted in quintiles) for dementia risk as assessed by means of Cox proportional hazard models.

Table 4 Predictive value of risk score for cognitive decline

Cognitive domain		Regression coefficient for risk score * time (95% CI)	p-value
Verbal memory (delayed word recall)	Model 1 <sup>b</sup>	-0.01 (-0.06; 0.04)	0.806
	Model 2	-0.02 (-0.07; 0.02)	0.350
	Model 3	-0.05 (-0.08; -0.02)	0.002
Executive functioning <sup>a</sup>	Model 1	0.28 (-0.25; 0.81)	0.303
	Model 2	0.21 (-0.28; 0.69)	0.403
	Model 3	0.72 (0.38; 1.06)	<0.001
Information processing speed	Model 1	-0.15 (-0.28; -0.02)	0.022
	Model 2	-0.17 (-0.29; -0.05)	0.005
	Model 3	-0.31 (-0.39; -0.22)	<0.001

<sup>a</sup>Positive regression coefficients indicate cognitive decline over time, as test results reflect the time needed to complete the test.

<sup>b</sup>Model 1, Lifestyle for Brain Health (LIBRA) score (modifiable risk factors only), adjusted for age, gender, and education; model 2, LIBRA score + score for education, adjusted for age and gender; model 3, LIBRA score + scores for education, age, and sex and no covariate adjustment.

impairment. Including age and sex along with these modifiable factors increased the predictive accuracy for dementia, although it remained comparable for incident cognitive impairment in all three models. Individual course of cognitive decline on the domains of verbal memory and executive functioning was only significantly predicted when age and sex were included, whereas decline in information processing speed was predicted in all models tested. Age is the most important risk factor for dementia, so it was not surprising that model 3 had the highest predictive value for dementia (AUC 0.75). Other risk indices like the Cardiovascular Risk Factors, Aging, and Incidence of Dementia score (CAIDE) including non-modifiable factors such as age, gender, and apolipoprotein E genotype report an AUC of 0.77–0.78 (Kivipelto *et al.*, 2006). Therefore, LIBRA may be regarded as a model for dementia *prevention*, whereas model 3 (i.e. LIBRA + education, age, and sex) can be considered a risk-prediction model.

Thus, modifiable risk factors may reduce an individual's risk of dementia in later life. The risk factors included (modifiable and non-modifiable) are readily identifiable and measured in primary care settings. Indeed, many already are targeted in chronic disease prevention programmes and are known to be prevalent in the general population (Australian Institute of Health and Welfare, 2012; Linardakis *et al.*, 2013).

Modifiable risk factors might account for a third (Norton *et al.*, 2014) up to half of all AD cases worldwide (Barnes and Yaffe, 2011). A risk factor reduction of 10 to 25% might prevent up to 3 million cases of AD worldwide (Barnes and Yaffe, 2011). Recent policy statements have suggested the need to bring dementia prevention into wider health policy and healthcare delivery (Royal Society for Public Health Vision, 2014) (Public Health England and UK Health Forum, 2014).

### Strengths and limitations

Lifestyle for Brain Health was derived from a recent study which identified putative modifiable risk factors through an extensive systematic literature review, rather than analysis of a single cohort study. The advantage of our methodology is that it is evidence-based, using effect sizes for each risk factor that were derived from meta-analyses, which can be considered more reliable and less susceptible to mere sampling variation than those obtained in single cohort studies.

Furthermore, LIBRA is suitable for use in population-based settings, as it does not incorporate clinical measures that require diagnostic workup. In addition, LIBRA is not only a useful predictive instrument but it might also be used to assess risk of cognitive impairment and cognitive decline in the general population. Other advantages include the long follow-up time, which allowed for risk factor assessment at a time point well before the onset of cognitive deterioration.

This study also has limitations. First, two risk factors were lacking in MAAS, so it was not possible to evaluate a risk-prediction model comprising all 13 modifiable factors. Second, although data were available on most risk factors, some variables could only be included via proxy measures, for example, physical activity, or self-reported data about disease, for example, renal dysfunction. This may result in lower predictive accuracy of LIBRA. Therefore, further validation in other external datasets is important, preferably by controlling for competing risks. Third, we identified 61 (6.4%) dementia cases at follow-up, on a total of 949 participants. Therefore, the study does not allow subgroup analysis on different types of dementia.

Finally, it is important to note that our risk-prediction algorithm assumes additivity of risk factor effects and possible interactions between risk factors were not modeled in our algorithm.

## Conclusion

We presented a risk-prediction model for dementia based on modifiable risk factors. LIBRA predicted individual risk of dementia over a follow-up period of up to 16 years and cognitive impairment and decline in information processing speed over a period of 12 years. By focusing on modifiable risk factors, LIBRA may contribute to new prevention strategies for dementia, for example, by raising awareness for a window of opportunity at middle age to reduce dementia risk and by prioritizing lifestyle changes with the largest impact on brain health in both research and clinical practices. Also, the LIBRA score may be useful as a composite score to study (or control for) differences in health and lifestyle factors in epidemiological studies and for stratifying participants into different levels of dementia risk.

Additional studies should test the predictive accuracy of LIBRA in the general population. In addition, future research might point out whether incorporating other risk factors, such as those we were not able to include in the present study, or taking into account potential interactions between risk factors will improve its predictive accuracy.

## Conflict of interest

None declared.

### Key points

- Recent epidemiological evidence shows that a substantial part of dementia risk is related to modifiable risk factors, which are open to early intervention.
- The steady rise in dementia prevalence and absence of effective treatment requires a more proactive public health approach.
- The recently developed LIBRA score reflects the personalized 'room for improvement' in the individual dementia risk profile.
- Outcome of this longitudinal observational study demonstrates that personal LIBRA scores indeed are related to dementia outcome.

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