**Supplementary Material**

**Modifiable Risk Factors Explain Socioeconomic Inequalities in Dementia Risk: Evidence from a Population-Based Prospective Cohort Study**

**Supplementary Table 1**. Strategies to reduce missing values (if information at ELSA Wave 4 was missing).

|  |  |
| --- | --- |
| **Variable** | **Strategies to reduce missing values** |
| Wealth | * Look at identical information from ELSA Wave 3 and Wave 5 * Look at identical information from ELSA Waves 2, 6, 1, 7 |
| Educational level | * Look at identical information from ELSA Wave 5-7 (when information before Wave 4 was not available) |
| Diabetes | * Look at ELSA Wave 1-3 for ever reported diabetes * Look at ELSA Wave 5-7 for never reported diabetes |
| Heart disease | * Look at ELSA Wave 3 for ever reported heart disease * Look at ELSA Wave 5-7 for never reported heart disease |
| Physical inactivity | * Look at identical information from ELSA Wave 3 and Wave 5 |
| Smoking | * Look at identical information from ELSA Wave 3 and Wave 5 |
| Hypertension | * Look at self-report at ELSA Wave 4 if objective measures were unavailable * Look at identical information from ELSA Wave 3 and Wave 5 |
| Hypercholesterolemia | * Look at self-report at ELSA Wave 4 if objective measures were unavailable * Look at identical information from ELSA Wave 3 and Wave 5 |
| Low-to-moderate alcohol use | * Look at identical information from ELSA Wave 3 and Wave 5 |
| Depression | * Look at self-report at ELSA Wave 4 if CES-D data was unavailable * Look at identical information from ELSA Wave 3 and Wave 5 |
| High cognitive activity | * Look at identical information from ELSA Wave 3 and Wave 5 |
| Obesity | * Look at identical information from ELSA Wave 2 and Wave 6 (objective nurse data available) |
| Healthy diet | * Look at identical information from ELSA Wave 3 and Wave 5 |

**Supplementary Table 2**. LIBRA operationalization and weights in ELSA

|  |  |  |
| --- | --- | --- |
| **Factor** | **Operationalization** | **Weight** |
| Heart disease | Physician’s diagnosis of angina pectoris or myocardial infarction. | +1.0 |
| Diabetes (type-2)\* | Blood glycated hemoglobin level ≥ 48 mmol/mol (6.5%) according to the WHO guidelines [1]. | +1.3 |
| Hypercholesterolemia\* | Total cholesterol level of ≥5.0 mmol/L and low-density lipoprotein of ≥3.0 mmol/L, following the guidelines of the National Health Service UK [2]. | +1.4 |
| Hypertension\* | Mean systolic blood pressure ≥140 mm Hg or mean diastolic blood pressure ≥90 mm Hg [3]. | +1.6 |
| Depression\* | Total score on the 8-item Centre of Epidemiological Studies Depression (CES-D) scale of 3 or greater (range: 0-8) [4,5]. | +2.1 |
| Obesity | Established cut-offs according to the WHO guidelines [6].Waist circumference (men: > 102 cm; women: > 88 cm) and waist-to-hip ratio (men: >90; women: >85) were only used if data on body mass index (BMI ≥ 30) was missing. | +1.6 |
| Smoking | Self-reported current smokers or non-smokers. | +1.5 |
| Low-to-moderate alcohol use | Self-reported frequency of any alcohol consumed in the past 12 months. Low-to-moderate alcohol use was defined as 1-14 glasses per week according to recent UK alcohol guidelines [7]. | -1.0 |
| Physical inactivity | Self-reported engagement in vigorous, moderate or mild physical activity during leisure time (more than once per week, once per week, one to three times per month, hardly ever). Participants were dichotomized into physically active (≥1/week) or physically inactive (1-3 times/month, hardly ever/never). | +1.1 |
| High cognitive activity | Self-reported engagement in intellectual and social activities undertaken in the last 12 months (e.g., read the newspaper on a daily basis, have a hobby, take a holiday, using the internet, being a member of any organizations, clubs or societies). Engagement in seven or more of these activities was considered as cognitively active (distribution-based cut-off). | -3.2 |
| Healthy diet | Reported amount of fruits and vegetables consumed by the participant the previous day. A healthy diet was defined as consuming five or more portions of fruits and vegetables on a daily basis [8]. | -1.7 |
|  |  |  |
| Total observed LIBRA range |  | -5.9 to +11.6 |

ELSA, English Longitudinal Study of Ageing; LIBRA, LIfestyle for BRAin health; UK, United Kingdom; WHO, World Health Organization.

\*The self-reported doctor’s diagnoses of diabetes, hypercholesterolemia, hypertension or depression were taken into account when objective measurements were not available.

**REFERENCES**

[1] World Health Organization (2011) *Use of Glycated Haemoglobin (HbA1c) in the Diagnosis of Diabetes Mellitus: Abbreviated Report of a WHO Consultation.* World Health Organization, Geneva.

[2] National Health Service. High cholesterol. http://www.nhs.uk/Conditions/Cholesterol/Pages/Introduction.aspx. Accessed 27-09-2016.

[3] Guidelines Subcommittee (1999) 1999 World Health Organization-International Society of Hypertension Guidelines for the Management of Hypertension. *J Hypertens* **17**, 151-183.

[4] Radloff LS (1977) The CES-D Scale: A Self-Report Depression Scale for Research in the General Population. *Appl Psychol Measure* **1**, 385-401.

[5] Turvey CL, Wallace RB, Herzog R (1999) A revised CES-D measure of depressive symptoms and a DSM-based measure of major depressive episodes in the elderly. *Int Psychogeriatr* **11**, 139-148.

[6] World Health Organization (2008) *Waist circumference and waist–hip ratio: Report of a WHO expert consultation.* World Health Organization.

[7] Department of Health (2016) *Alcohol guidelines review — report from the guidelines development group to the UK Chief Medical Officers.* Department of Health.

[8] National Health Service (2009) *5 A Day.* NHS, London.

**Supplementary Figure 1**. Estimated (marginal) LIBRA score means per wealth stratum



LIBRA, LIfestyle for BRAin health

Model corrected for age, gender, education, and clustering at the household level.

**Supplementary Figure 2**. The cumulative hazard of dementia over time in study by educational level



Model adjusted for age, gender, wealth, and clustering at the household level

**Supplementary Figure 3.** Mediation analysis for the relationship between wealth, education, LIBRA, and dementia

**Indirect effect of education on dementia via wealth and LIBRA**

Medium education on medium wealth tertile: HR = 1.00, 95%CI 0.99-1.00

Medium education on highest wealth tertile: HR = 0.96, 95%CI 0.95-0.98

High education on medium wealth tertile: HR = 1.00, 95%CI 1.00-1.00

High education on highest wealth tertile: HR = 0.92, 95%CI 0.88-0.95

**Indirect effect of wealth on dementia via LIBRA**

Medium wealth tertile: HR = 0.84, 95%CI 0.78-0.90

Highest wealth tertile: HR = 0.75, 95%CI 0.66-0.85

**Direct effect of wealth on LIBRA**

Medium wealth tertile: B = -1.448, SE = 0.101

Highest wealth tertile: B = -2.358, SE = 0.105

**Wealth**

**LIfestyle for BRAin Health (LIBRA)**

**Direct effect of wealth on dementia**

Medium wealth tertile; HR = 0.72, 95%CI 0.49-1.05

Highest wealth tertile: HR = 0.77, 95%CI 0.51-1.16

**Direct effect LIBRA on dementia**

HR = 1.13, 95%CI 1.07-1.19

**Indirect effect of education on dementia via LIBRA**

Medium education: HR = 0.89, 95%CI 0.85-0.94

High education: HR = 0.80, 95%CI 0.73-0.88

**Direct effect of education on wealth**

Medium education on medium wealth tertile: HR = 1.03, 95%CI 0.99-1.06

Medium education on highest wealth tertile: HR = 1.14, 95%CI 1.11-1.18

High education on medium wealth tertile: HR = 0.87, 95%CI 0.84-0.90

High education on highest wealth tertile: HR = 1.35, 95%CI 1.31-1.39

**Indirect effect of education on dementia via wealth**

Medium education on medium wealth tertile: HR = 0.99, 95%CI 0.98-1.00

Medium education on highest wealth tertile: HR = 0.96, 95%CI 0.91-1.02

High education on medium wealth tertile: HR = 1.01, 95%CI 0.99-1.02

High education on highest wealth tertile: HR = 0.92, 95%CI 0.82-1.05

**Direct effect of education on LIBRA**

Medium education: B = -0.945, SE = 0.099

Highest education: B = -1.804, SE = 0.097

**Education**

**Dementia**

**Direct effect of education on dementia**

Medium education: HR = 0.85, 95%CI 0.58-1.26

High education: HR = 1.05, 95%CI 0.69-1.59