Modifiable Risk Factors explain Socioeconomic Inequalities in Dementia Risk: Evidence from a Population-based Prospective Cohort Study

Running title: Socioeconomic inequalities, lifestyle factors, and dementia risk

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ABSTRACT

Background: Differences in dementia risk across the gradient of socioeconomic status (SES) exist, but their determinants are not well understood.

Objective: This study investigates whether health conditions and lifestyle-related risk factors explain the SES inequalities in dementia risk.

Methods: 6,346 participants from the English Longitudinal Study of Ageing were followed up from 2008/2009 until 2014/2015. We used Cox regression adjusted for age, gender, wealth/education and clustering at the household level to examine the association between SES markers (wealth, education) and time to dementia in a structural equation model including potential mediation or effect modification by a weighted compound score of twelve modifiable risk and protective factors for dementia ('LIfestyle for BRAin health' (LIBRA) score).

Results: During a median follow-up of 6 years, 192 individuals (3.0%) developed dementia. LIBRA scores decreased with increasing wealth and higher educational level. A one-point increase in the LIBRA score was associated with a 13% increase in dementia risk (hazard ratio (HR) = 1.13, 95% confidence interval 1.07-1.19). Higher wealth was associated with a decreased dementia risk (HR = 0.58, 0.39-0.85). Mediation analysis showed that 52% of the risk difference between the highest and lowest wealth tertile was mediated by differences in LIBRA (indirect effect: HR = 0.75, 0.66-0.85). Education was not directly associated with dementia (HR = 1.05, 0.69-1.59), but was a distal risk factor for dementia by explaining differences in wealth and LIBRA scores (indirect effect high education: HR = 0.92, 0.88-0.95).

Conclusion: Socioeconomic differences in dementia risk can be partly explained by differences in modifiable health conditions and lifestyle factors.

INTRODUCTION

Socioeconomic inequalities are a major contributor to the widening health gap, both within and between populations [1]. A recent multi-cohort study and meta-analysis of 1.7 million individuals showed that low socioeconomic status (SES) was associated with a decline of 2.1 years in life expectancy [2]. SES is a broad concept used to determine an individual's social standing and includes prestige- and resource-based measures. Prestige-based measures refer to an individual's relative status in the social hierarchy (e.g. parental educational level, an individual's position within an occupation classification system (e.g. the International Standard Classification of Occupations)), whereas resource-based measures include assets such as wealth, total family income and educational attainment [3].

Socioeconomic disparities have been well described for certain diseases, including different types of cancer and cardiovascular disease [4-6], but are less well understood in dementia. In a meta-analysis of almost 87,000 persons from the United Kingdom, a low educational level was associated with a 76% increased risk of dementia death in women [7]. Educational attainment is a marker of childhood SES, but is also strongly related to intelligence and level of cognitive activity, making it less suited as a 'pure' SES marker in dementia research [8]. In contrast, few studies used resource-based measures of SES. A prospective biracial cohort showed that both prestige- and resource-based measures of SES (educational level, literacy level, family income and perceived financial inadequacy) contribute to disparities in dementia incidence among black and white participants [9], whereas another prospective study of older Mexican Americans showed an association between life-course socioeconomic position (e.g. parental educational level, lifetime occupation) and risk of cognitive impairment and dementia [10]. Recent results from the English Longitudinal Study of Aging (ELSA) showed that wealth was associated with incident dementia even after controlling for education, while education was not an independent predictor of incident dementia [11].

Factors explaining SES inequalities in dementia risk are largely unknown and need further research [12], but include micro- (e.g. differences in risk factors exposure, health literacy, motivation), meso- (e.g. social factors, the built environment) and macro-level (e.g. access to health care, income distribution, wider political forces) factors. Recent studies suggest that there is potential for dementia prevention through lifestyle adaptations, especially if started in midlife [13-19]. Differences in the distribution of modifiable dementia risk factors, treatable by cardiovascular risk management or lifestyle adaptations, might thus partly underlie the gap in dementia risk between poor and rich.

Therefore, this study aimed to investigate whether modifiable health conditions and lifestyle factors explain wealth inequalities in dementia incidence. In addition, we explored whether education might be part of this pathway.

MATERIALS AND METHODS

Study design and participants

ELSA is a multi-centre panel study representing the English population aged 50 and over with bi-annual waves [20], collecting data on health, economics, lifestyle, psychology and social wellbeing. More details have been published elsewhere [21].

For this study, Wave 4 (2008/2009; $n = 9,886$) was considered the baseline because it covered a large number of modifiable risk and protective factors for dementia. If possible, identical information from other waves (in most cases Wave 3 (2006/2007) or Wave 5 (2010/2011); Supplementary Table 1) was used if data on wealth, educational level and lifestyle factors were missing. The last assessment was Wave 7 (2014/15) yielding a maximum follow-up period of 7 years. After exclusion of (prevalent) dementia cases at Wave 4 ($n = 209$), and persons with fewer than eleven 'LIfestyle for BRAin health' (LIBRA) factors at Wave 4 ($n = 1,374$), loss to follow-up (e.g. removal, withdrawal, lost contact, moved abroad, death, etc.; n

= 1,940), invalid sampling weight (*n* = 12) or missing education data (*n* = 5), the analysis

sample included 6,346 individuals.

The National Health Service Multicentre Research and Ethics Committee and the University

College London Research Ethics Committee approved the study according to the guidelines

of the Helsinki Declaration. All participants provided written informed consent.

Measures

Dementia ascertainment

The diagnosis of dementia was based on a combined algorithm of (1) physician-diagnosed

dementia or Alzheimer's disease self-reported by the participant or their informant during the

computer-assisted personal interview; or (2) an average score of ≥3.38 on the shortened

version of the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) [22-

25]. This questionnaire uses informant reports to measure the change in cognitive abilities

(e.g. memory) based on the pre-morbid level of functioning [26]. Each item was scored on a 1

(much improved) to 5 (much worse) range. The validity of this scale was previously

examined, and the threshold used has both high specificity (0.84) and sensitivity (0.82) [25,

27].

Socioeconomic status indicators

Self-reported household wealth was considered a resource-based indicator of SES at Wave 4,

calculated by summing wealth from the total value of a respondent's home (minus outstanding

mortgage payments), physical wealth (e.g. jewellery, artwork), business assets (e.g.

investments), and financial assets such as cash and savings (minus debts and loans). The

overall measure of wealth was divided into tertiles (low, medium, high).

Educational level was used as a prestige-based marker of SES at Wave 4. This variable indicating the highest level of education achieved was regrouped into 3 categories: low (no formal qualifications), medium (ordinary (O-)level or secondary education (equivalent to (junior) high school)) or high (advanced (A-)level or above (college/university)).

Health- and lifestyle factors

Health- and lifestyle factors were captured by a poly-environmental risk score called the LIBRA index [14]. LIBRA was developed after triangulation of results from a systematic literature review on risk and protective factors for dementia and an expert consensus study and consists of twelve modifiable risk and protective factors for dementia [14]. Risk factors are coronary heart disease, (type-2) diabetes, hypercholesterolemia, hypertension, depression, obesity, smoking, physical inactivity and renal disease. Protective factors are low-to-moderate alcohol use, high cognitive activity and a healthy diet. A weight was assigned to each factor, based on the factor's relative risk [14]. Weights were then standardised and summed to yield the final LIBRA score (range: -5.9 to +12.7). Higher scores have been shown to predict cognitive decline and higher dementia risk in previous (population- and patient-based) cohort studies [28-31].

In ELSA, information was available for all LIBRA factors at Wave 4, except for renal dysfunction, based on clinical data from nurse visits or self-reported information (observed range from -5.9 to 11.6; Supplementary Table 2). Each measure was dichotomized according to established cut-offs (Supplementary Table 2) before assigning the weights.

Statistical analyses

Independent samples *t*-tests and χ^2-tests tested differences in demographics, SES and LIBRA factors between individuals with and without incident dementia. Structural equation

modelling for continuous-time survival analysis (Cox proportional hazard regression) examined the associations between SES, LIBRA and time to dementia, resulting in hazard ratios (HR) and their 95% confidence interval (CI). The proportional hazard assumption was assessed based on the Schoenfeld residuals. To study mediation by lifestyle factors of the association between SES and incident dementia, the total effect of wealth was decomposed into direct and indirect (mediated) effects [32]. In all analyses, dementia was treated as the failure event. Survival time was used on the time axis and was calculated from the date of Wave 4 interview to date of dementia diagnosis (as reported by the participant or calculated as the midpoint between waves) or study exit (date of death or date of the last interview, whichever came first). Since participants could come from the same household, we used a sandwich estimator to allow clustering at the household level [33]. In addition, a sampling weight (baseline cross-sectional weight) was used in order to back-weight estimates from the analysis sample to the total sample to minimise selection bias. All analyses were adjusted for age, gender and wealth or education. Analyses were conducted in Stata 15.1 (StataCorp, College Station, TX, USA) and Mplus 8 (Muthén & Muthén).

RESULTS

Sample characteristics

During the median follow-up of 6 years (interquartile range 0.33), 192 individuals (3.0%) developed dementia (incidence rate 52.0, 95% CI, 45.0-60.4) per 10 000 person-years). The mean age was 64.9 years (standard deviation (SD) 8.6, range 50-94), and 3536 (55.7%) were female. Baseline characteristics are summarised by dementia status in Table 1.

--- Please insert Table 1 ---

SES, lifestyle and dementia

LIBRA scores were lower in the highest wealth tertile (n = 2,274; mean LIBRA score -1.37, SD 2.79) in comparison with the lowest wealth tertile (n = 1,882; mean LIBRA score 1.58, SD 3.13; $p < 0.001$; Supplementary Figure 1), indicating higher risk. Likewise, individuals with medium (n = 1,766; mean LIBRA score -0.18, SD 3.06) or high (n = 2,168; mean LIBRA score -1.35, SD 2.87) education had lower LIBRA scores in comparison with individuals with low education (n = 2,412; mean LIBRA score 1.18, SD 3.05); $p < 0.001$). The incidence of dementia, was 77.0 (62.0-96.8), 45.2 (34.8-59.8) and 36.1 (27.3-48.7) per 10,000 person-years in the lowest, medium and highest wealth tertile, respectively. In line with previous findings, education was not associated with dementia risk (high education: HR = 1.05, 0.69-1.59). A one-point increase in LIBRA was, on average, associated with a 13% increase in dementia risk (HR = 1.13, 1.07-1.19; Figure 1). The association between LIBRA and dementia risk was stronger for people aged 50-70 years (HR = 1.20, 1.06-1.36) than for those aged 70 years and older: HR = 1.11, 1.05-1.17). Higher wealth was associated with a decreased risk of dementia (total effect; highest versus lowest wealth tertile: HR = 0.58, 0.39-0.85; Figure 2).

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Mediation analysis

LIBRA significantly mediated the association between wealth and incident dementia (Figure 3). Mediation analysis showed an effect for the indirect path from wealth to dementia via LIBRA (highest versus lowest wealth tertile: HR = 0.75, 0.66-0.85). Further calculations showed that differences in lifestyle factors explained 52.2% of the difference between the

highest and lowest wealth tertile on dementia risk. There was no interaction of LIBRA with wealth, suggesting that lifestyle was similarly related to dementia risk across wealth strata. In contrast, there was no direct (residual) effect of wealth on dementia (highest versus lowest wealth tertile: HR = 0.77, 0.51-1.16). Stronger but directionally similar mediation results were found in those aged 50 to 69 years (indirect path of wealth on dementia via LIBRA (lowest versus highest tertile): HR = 0.64, 0.47-0.86) than those aged ≥70 years (HR = 0.81, 0.72-0.91). Additional analyses for reversed causation did not show an association between LIBRA and dementia via wealth. That is, while there was a direct effect of LIBRA on wealth, there was no direct effect of wealth on dementia and no indirect effect of LIBRA on dementia via wealth.

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Testing the role of education as a distal risk factor

While education was not associated with dementia risk once wealth was adjusted for (Supplementary Figure 2), we tested whether it is a distal risk factor via its associations with wealth and LIBRA. Mediation analysis showed that education indeed had no direct effect on dementia risk. However, high education was associated with higher wealth. In addition, there was an indirect path from education to dementia risk via wealth and LIBRA scores (indirect effect medium education: HR = 0.96, 0.94-0.98; indirect effect high education: HR = 0.92, 0.88-0.95; Supplementary Figure 3). Additionally, there was an indirect path from education to dementia via LIBRA (indirect effect medium education: HR = 0.89, 0.85-0.94; indirect effect high education: HR = 0.80, 0.73-0.88; Supplementary Figure 3). Taken together, higher education related to a lower dementia risk by its direct association with better lifestyle on the

one hand, and by its association with higher midlife SES that in turns is associated with better lifestyle on the other hand.

Sensitivity analyses

The group with less than eleven LIBRA factors (n =1,374) was on average older, with more dementia cases, (192/6,346 versus 52/588), less educated, had lower wealth, had higher number of health conditions (excluding obesity, hypercholesterolemia and hypertension) and lifestyle factors (excluding healthy diet). Those lost to follow-up (*n* =1,940) were on average older, were more often male, were less educated, had lower wealth and had higher number of health conditions (excluding obesity) and lifestyle factors. Multiple imputation was used to impute missing values for the eleven LIBRA factors and educational level. Multivariate imputation by chained equations was carried out using all non-missing data on risk and protective factors and socio-demographic covariates (age, sex and wealth) [34]. Ten imputed datasets were created, and the results combined using Rubin's rules [35]. After multiple imputation, the analysis sample consisted of 6,920 individuals, of which 238 (3.4%) developed incident dementia. In line with the primary Cox proportional hazard regression analyses adjusted for age, gender and wealth or education (and taking clustering at the household level into account), a one-point increase in LIBRA was, on average, associated with a 15% increase in dementia risk (HR = 1.15, 1.10-1.20), education was not associated with dementia risk (medium education: HR = 0.76, 0.53-1.10; high education: HR = 0.85, 0.58-1.25; in comparison with low education), and higher wealth was associated with a decreased risk of dementia (medium wealth: HR = 0.64, 0.46-0.90; high wealth: HR = 0.69, 0.48-0.98; in comparison with low wealth).

DISCUSSION

In this prospective cohort study, participants with lower wealth had a higher risk for dementia, which was to a large degree due to modifiable risk factors. In contrast, higher education had no direct effect on dementia risk, but showed lower risk by its relationship with higher wealth and better lifestyle/health. These findings suggest that improving the health and managing risk in those with both less wealth and low educational level might have an effect on dementia prevention by narrowing the gap in dementia risk between poor and rich.

The observed association between a less healthy lifestyle and dementia risk are in line with the results from previous studies that found an association between LIBRA measured in midlife and late life and incident dementia [30, 31]. In line with the few other studies that have examined the association between SES and dementia-related outcomes [7, 9, 10], we found that higher wealth, as a resource-based indicator of SES, was associated with decreased dementia risk. Only a few studies investigated the exact mechanisms underlying this association. A retrospective case-control study from Japan showed that diabetes minimally mediated the association between SES and dementia [36]. In contrast, we found mediation, in which more than 50% of the differences in dementia risk between the low and high wealth groups could be attributed to modifiable health conditions and lifestyle factors.

Low SES has been identified as one of the key barriers in facilitating healthy behaviour in midlife in order to prevent dementia in late-life [37]. Several mechanisms can account for this observation. Low SES has been associated with low health literacy [38], less access to health resources and proper medical care [39], poor health behaviours and health outcomes [38, 40-44], of which some are related to increased risk of cognitive decline or dementia [14, 18, 45]. Higher education, a prestige-based indicator of high SES [8], is associated with better health choices and mixed results for dementia risk [11, 39, 46]. In line with recent research in ELSA [11], education was not directly associated with dementia risk. This seems in line with results

from the Whitehall II study, which showed that low midlife occupation rather than low childhood education was associated with increased dementia risk [47]. Using mediation analysis, we were able to show that education is a distal risk factor for dementia in our sample that explains differences in wealth and lifestyle factors. Hence, strategies to improve access to (higher) education might also reduce dementia risk, especially in resource poor settings where education is not a universal good [18]. However, educational attainment also reflects inborn intelligence and predisposes individuals differently to engagement in stimulating mental activities during the life-course, thereby building up cognitive reserve that acts in return as a buffer against dementia risk [48]. Through this confounding, it might be a suboptimal indicator of SES in dementia research.

Because uptake of advice and health recommendations tends to be greater among more educated and affluent people, one of the main challenges of behaviour change programs to mitigate dementia risk will be to design them in order to reduce rather than increase social inequalities [49]. Additionally, focusing on the individual level alone might lead to excessive victim-blaming. A strong common political focus is needed, including a national and global policy on the promotion of healthy brain behaviour. In line with this, health services should be available for all layers of society based on an individual's need (universal proportionalism) [50].

Our study has several strengths, including an extended follow-up period in a large representative sample of the British population. Some important limitations have to be considered, too. First, participants with missing data (34% of the total sample) were excluded from the analysis. Exclusion of these individuals has probably led to an underestimation of the observed associations. Our sensitivity analyses, including multiple imputation showed similar results as the primary analyses. Second, as an inevitable part of all longitudinal studies, not all participants who entered the study returned for the follow-up measurements. This might have

led to some selection of a healthier sample and therefore may result in an underestimation of the "true" association. Third, the ascertainment of dementia diagnosis, wealth and some LIBRA factors was based on self-report, which could have led to response bias or non-differential exposure misclassification. In order to reduce these forms of bias, we only included self-reported information when objective measurements (e.g. from nurse visits) were not available. Worldwide, dementia is underdiagnosed in the general population [51]. So, physician diagnoses (even if they are accurately reported) will underestimate dementia incidence. Fourth, possible interactions between risk and protective factors were not taken into account in the LIBRA score. Fifth, the observed associations may have been confounded by factors like childhood/parental SES, occupational experiences and SES mobility.

Despite these limitations, our study does have important implications and provides valuable input for public health policies. Targeting lifestyle factors in tailored health education programs might eventually lead to a reduction in socioeconomic inequalities in (brain) health. Effective public health programs in dementia prevention and care must take the needs and resources of this vulnerable group into consideration before deciding on the most appropriate preventative measures at the individual, societal and political level.

In conclusion, socioeconomic differences in dementia risk can be partly explained by differences in modifiable health conditions and lifestyle factors.

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CONFLICT OF INTEREST

The authors have no conflict of interest to report.

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Table 1. Baseline characteristics of ELSA Wave 4 participants by incident dementia status

Variable	Incident dementia status		
	Yes (*n* = 192)	No (*n* = 6,154)	*p*
Demographics			
Age, mean (SD)	77.3 (8.6)	64.5 (8.3)	< 0.001
Female, n (%)	124 (64.6)	3,412 (55.4)	0.012
Educational level, n (%)			< 0.001
Low	112 (58.3)	2,300 (37.4)	
Medium	38 (19.8)	1,728 (28.1)	
High	42 (21.9)	2,126 (34.6)	
Wealth, n (%)			< 0.001
Low	84 (43.8)	1,798 (29.2)	
Medium	57 (29.7)	2,133 (34.7)	
High	51 (26.6)	2,223 (36.1)	
Health- and lifestyle factors			
Heart disease, n (%)	41 (21.4)	538 (8.7)	< 0.001
Diabetes, n (%)	44 (22.9)	926 (15.1)	0.003
Hypercholesterolemia, n (%)	69 (35.9)	3,222 (52.4)	< 0.001
Hypertension, n (%)	86 (44.8)	1,979 (32.2)	< 0.001
Depression, n (%)	70 (36.5)	1,135 (18.4)	< 0.001
Obesity, n (%)	61 (31.8)	2,005 (32.6)	0.814
Smoking, n (%)	17 (8.9)	782 (12.7)	0.113
Low-to-moderate alcohol use, n (%)	72 (37.5)	3,508 (57.0)	< 0.001
Physical inactivity, n (%)	113 (58.9)	1,480 (24.1)	< 0.001
High cognitive activity, n (%)	33 (17.2)	2,747 (44.6)	< 0.001
Healthy diet, n (%)	105 (54.7)	3,687 (59.9)	0.146
LIBRA score, mean (SD)[*]	1.9 (2.8)	-0.1 (3.2)	< 0.001

SD=standard deviation. LIBRA=LIfestyle for BRAin health; *P* values are presented for the comparison of individuals with and without dementia at follow-up (independent samples *t*-tests and χ^2-tests).

[*] LIBRA score theoretical range: -5.9 to 11.6; observed range: -5.9 to 10.3

Figure 1. The cumulative hazard of dementia over time in study by LIBRA score tertiles
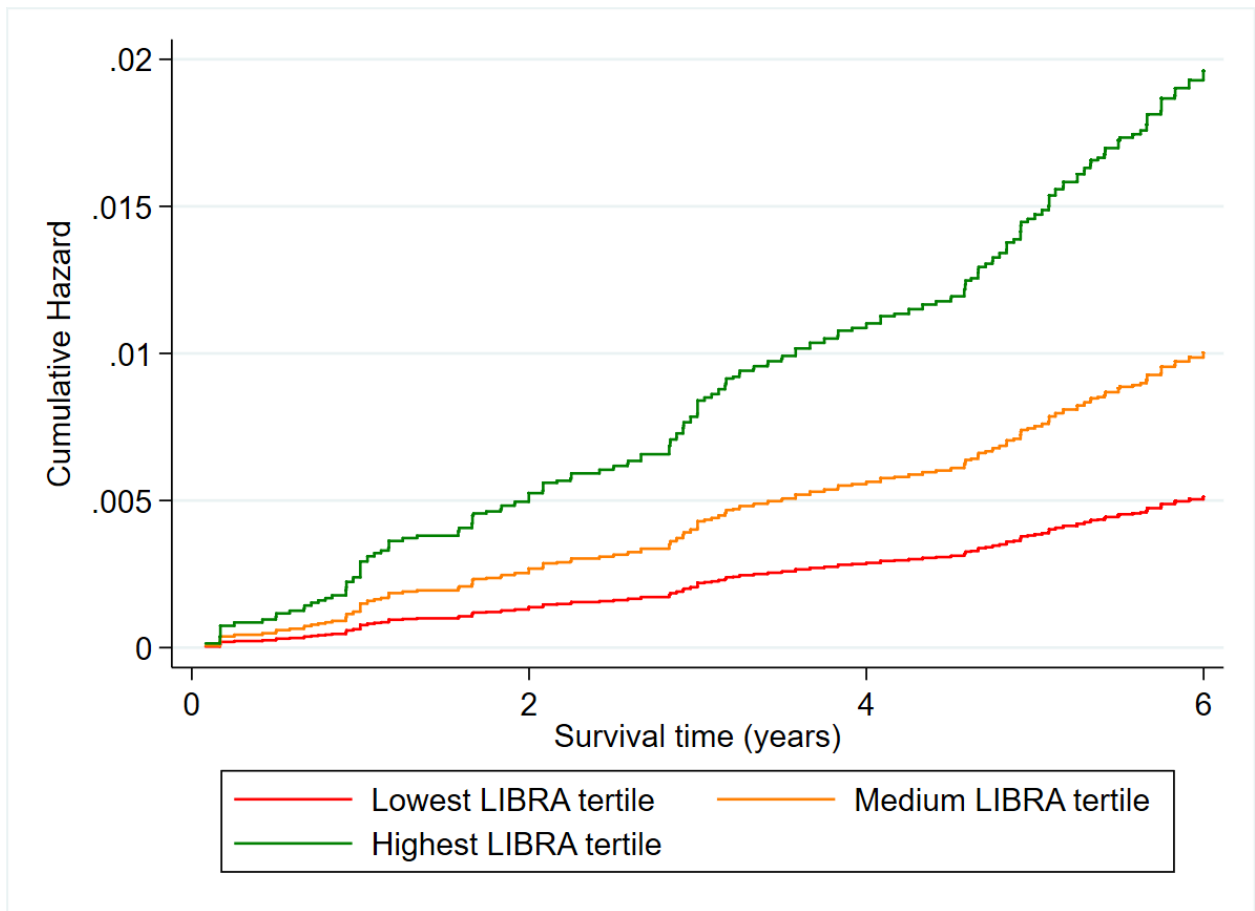
Model adjusted for age, gender, education and clustering at the household level
LIBRA=LIfestyle for BRAin health

Figure 2. The cumulative hazard of dementia over time in study by wealth tertiles

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

Figure 3. Mediation analysis for the relationship between wealth and dementia as mediated

by LIBRA

Indirect effect of wealth on dementia via LIBRA
Highest wealth tertile: HR = 0.75, 0.66-0.85
Medium wealth tertile: HR = 0.84, 0.78-0.90

LIfestyle for BRAin Health (LIBRA)

Direct effect wealth on LIBRA
Highest wealth tertile: B -2.358, SE 0.105
Medium wealth tertile: B -1.448, SE 0.101

Direct effect of LIBRA on dementia
HR = 1.13, 1.07-1.19

Wealth

Dementia

Direct effect wealth on dementia
Highest wealth tertile: HR = 0.77, 0.51-1.16
Medium wealth tertile; HR = 0.72, 0.49-1.05

B=unstandardized regression coefficient. HR=hazard ratio. SE=standard error

Supplementary material

Table 1. Strategies to reduce missing values

Table 2. LIBRA operationalization and weights in ELSA

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

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

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

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

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 haemoglobin 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 dichotomised 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 organisations, 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.

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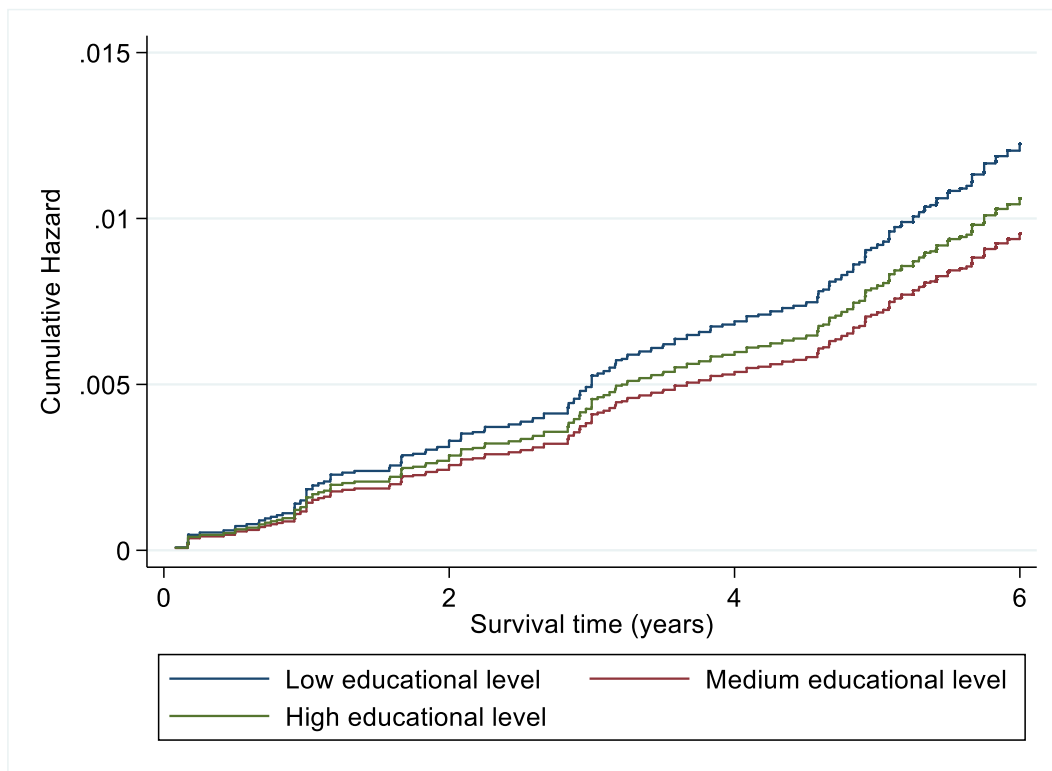8. National Health Service. *5 A Day.* London: NHS;2009.

Figure 1. Estimated (marginal) LIBRA score means per wealth stratum
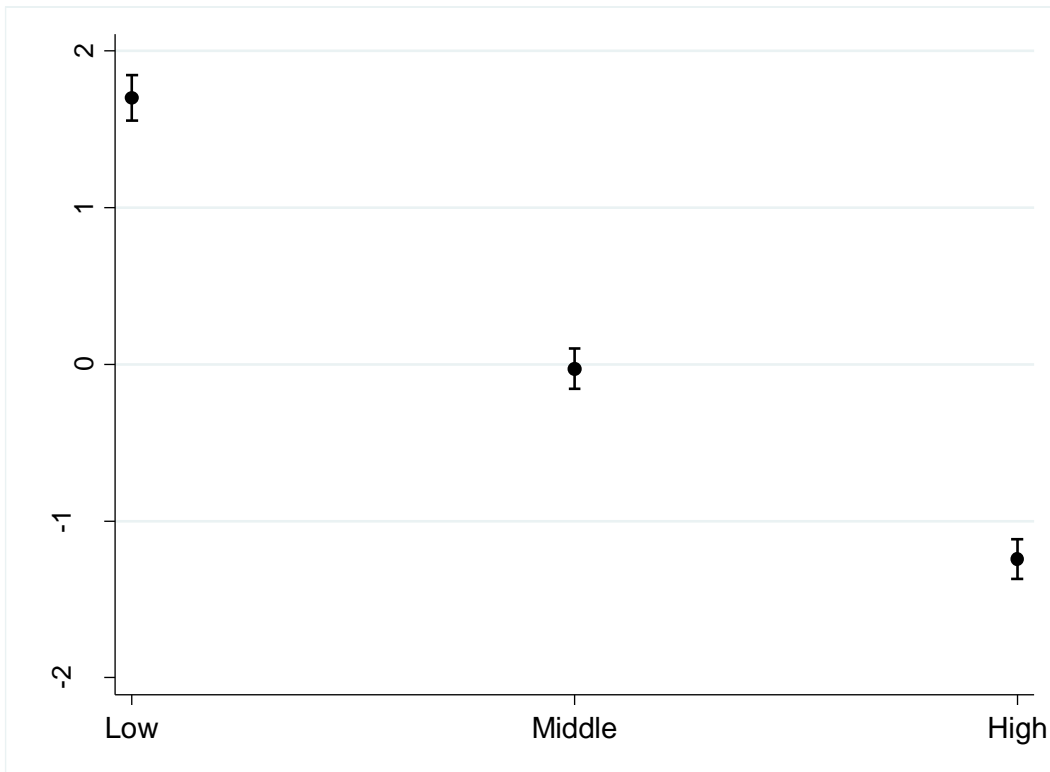
LIBRA=LIfestyle for BRAin health
Model corrected for age, gender, education and clustering at the household level.

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

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

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)

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 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

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

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