Associations of socioeconomic status and healthy lifestyle with incident dementia and cognitive decline: two prospective cohort studies

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eClinicalMedicine
2024;76: 102831

Published Online xxx

https://doi.org/10.1016/j.eclinm.2024.102831

Summary

Background Little is known about the complex associations of socioeconomic status (SES) and healthy lifestyle with cognitive dysfunction.

Methods Using data from the Health and Retirement Study (HRS) [2008–2020] and the English Longitudinal Study of Ageing (ELSA) [2004–2018], SES was constructed by latent class analysis using education level, total household income and wealth. Overall healthy lifestyle was derived using information on never smoking, low to moderate alcohol consumption (drinks/day: (0, 1] for women and (0, 2] for men), top tertile of physical activity, and active social contact.

Findings A total of 12,437 and 6565 participants from the HRS and ELSA were included (40.8% and 46.0% men and mean age 69.3 years and 65.1 years, respectively). Compared with participants of high SES, those of low SES had higher risk of incident dementia (hazard ratio 3.17, 95% confidence interval 2.72–3.69 in the HRS; 1.43, 1.09–1.86 in the ELSA), and the proportions mediated by overall lifestyle were 10.4% (7.3%–14.6%) and 2.7% (0.5%–14.0%), respectively. Compared with participants of high SES and favorable lifestyle, those with low SES and unfavorable lifestyle had a higher risk of incident dementia (4.27, 3.40–5.38 in the HRS; 2.02, 1.25–3.27 in the ELSA) and accelerated rate of global cognitive decline (β = −0.058 SD/year; 95% CI: −0.073, −0.043 in the HRS; β = −0.049 SD/year; 95% CI: −0.063, −0.035 in the ELSA).

Interpretation Unhealthy lifestyle only mediated a small proportion of the socioeconomic inequality in dementia risk in both US and UK older adults.

Funding This work was supported by grants from the National Natural Science Foundation of China (82088102 and 82370819), the National Key R&D Program of China (2023YFC2506700), the Shanghai Municipal Government (22Y31900300), the Shanghai Clinical Research Center for Metabolic Diseases (19MC1910100), the Innovative Research Team of High-Level Local Universities in Shanghai, the Special Project for Clinical Research in Health Industry of Shanghai Municipal Health Commission (202340084), and Ruijin Hospital Youth Incubation Project (KY20240805). Y.X. is supported by the National Top Young Talents program.

Keywords: Socioeconomic status; Lifestyle; Dementia; Cognitive decline; Mediation analysis

Introduction

Dementia is among the leading causes of disability and mortality in older people and a pressing public health concern given global population ageing.[1] Owing to the absence of curative strategies, targeting the high-risk subgroup with lifestyle intervention is of significant

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Research in context

Evidence before this study

We searched PubMed and Web of Science for articles published in English using the keywords "socioeconomic status", "SES", "education", "income", "wealth", "lifestyle", "cognitive decline", "cognitive impairment", and "dementia" from inception up to December 17, 2023. As of December, 2023, we identified several relevant studies focused on the interaction or modification effect between SES, using composite score or individual metrics, and modifiable risk factors for cognitive impairment, only few explored the role of behavioral risk factors with mediation analysis rarely conducted. Therefore, the extent to which dementia burden could be counteracted by healthy lifestyles in people with different SES status remains unclear.

Added value of this study

Using data from two nationally representative cohorts, we found that lower SES was associated with higher risk of incident dementia, with only 1.7%–18.4% mediated by lifestyle factors. Compared with participants of high SES and favorable lifestyle, those with low SES and unfavorable lifestyle had a higher risk of incident dementia and an accelerated rate of cognitive decline. These findings support the important role of healthy lifestyles in reducing dementia burden, however, the low mediation proportion also indicated that substantial reductions of the socioeconomic inequity in brain health could not be achieved through promoting healthy lifestyles alone, and other measures to tackle the social determinants of health are still needed.

Implications of all the available evidence

Our study could aid in current research through helping answer to what extent lifestyle interventions could tackle the socioeconomic inequality in dementia burden, and the design of future public health strategies may also be tailored based on this evidence. Meanwhile, future prospective or interventional studies with more complete lifestyle factors are warranted to confirm our findings on the reduction of the socioeconomic inequity in brain health.

importance to help reduce dementia burden. Socioeconomic status (SES) is a complex concept reflecting a person's overall status in society, and the related socioeconomic inequality has been substantially reported in different diseases including dementia.[2] Mounting evidence supports the mediation effects of lifestyle factors between SES and health outcomes and that healthy lifestyles could alleviate the socioeconomic inequities in health.[3] However, one recent study reported that unhealthy lifestyles only mediated a small proportion of the socioeconomic inequality for cardiovascular disease and mortality,[4] whether it is also the case for dementia remains unknown.

The contribution of individual or several lifestyle factors in the association between socioeconomic level and cognitive dysfunction has been long suggested, however, important knowledge gaps remain, especially about the proportion mediated by an overall lifestyle. First, available studies investigated the interaction between SES and risk factors on dementia incidence, focusing primarily on modifiable risk factors identified by frameworks such as the Lifestyle for BRAin health (LIBRA) score,[5,6] which comprises both biological and behavioral risk factors. Unlike biological factors (e.g., blood pressure, blood glucose), which are heavily influenced by the accessibility of health services, behavioral factors (e.g., smoking, physical activity) are more dependent on personal choices and thus more suitable for individual-level prevention strategies. However, the exact role of behavioral risk factors in the context of SES-related dementia incidence has not been comprehensively explored, with mediation analysis rarely conducted. Second, certain behavioral factors, such as social contact, are also important for cognitive outcomes, yet have not been included. Third, previous studies tended to use single variables (e.g., education, occupation) or sum of these variables to represent socioeconomic level, which cannot comprehensively reflect the whole picture.[7,8]

To fill these research gaps, we conducted a prospective analysis among older adults (≥50 years old) using data from two nationally representative cohorts (the Health Retirement Study [HRS] and the English Longitudinal Study of Ageing [ELSA]) to explore whether overall lifestyle mediates the association between SES (derived from latent class analysis using education, total household income and wealth) and incident dementia and also to investigate the joint associations of SES and lifestyle with dementia incidence and cognitive decline. Our study could aid in current research through helping answer to what extent lifestyle intervention could tackle the socioeconomic inequality in dementia burden, and the design of future public health strategies may also be tailored based on this evidence.

Methods

Study design and participants

We used data from the HRS waves 9 to 15 (2008–2020) and the ELSA waves 2 to 9 (2004–2018). The detailed study design of these two cohorts has been described elsewhere.[9,10] Briefly, they are sister studies with similar survey protocols and randomly sampled community-dwelling adults aged older than 50 years living in the US and the UK, respectively with follow-up resurveys performed biennially. To ensure comparable cognitive function, available measurements of required variables, and sufficient sample size across two cohorts, this study analyzed data from waves 9 to 15 (2008–2020) of the HRS and waves 2 to 9 (2004–2018) of the ELSA. The HRS was approved by the Institutional Review Board at the University of Michigan and the National Institute on Aging (HUM00061128) and the ELSA was approved by the London Multicenter Research Ethics Committee (MREC/01/2/91). All participants provided written informed consent. This study was conducted following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.[11]

The flow chart for participants' selection of the present study is shown in ESM Fig. S1. The HRS sample comprised 17,217 participants recruited at baseline (HRS wave 9 [2008]), of which 4780 were excluded for the following reasons: younger than 50 years (n = 355), prevalent dementia or unavailable cognitive status (n = 1524), unavailable measurement of socioeconomic status (n = 3) or lifestyle factors (n = 2898) at baseline. The ELSA sample included 9432 participants recruited at baseline (ELSA wave 2 [2004]), of which 2867 were excluded for the following reasons: younger than 50 years (n = 261), prevalent dementia or unavailable cognitive status (n = 256), unavailable measurement of socioeconomic status (n = 821) or lifestyle factors (n = 1529) at baseline. Hence, 19,002 participants (12,437 from the HRS and 6565 from the ELSA) were finally included in our study.

Socioeconomic status

Previous studies investigating the associations between SES and health outcomes tend to encompass education, income, and occupation as indicators. Given that participants in the current study were mostly retirees, we used total household wealth instead of occupation.[12] Therefore, an overall SES metric was derived using latent class analysis based on education level, total household income and wealth (Table 1, Appendix p 1). The latent class analysis can use multiple observed categorical variables to characterize a multidimensional discrete latent variable. As shown in ESM Table S1, results from model fit evaluation suggested three latent classes, which respectively represented a high, medium, and low SES according to the item-response probabilities (Table 2).

In addition, we defined the SES status in two other ways for sensitivity analyses: (a) summed socioeconomic scores: by assigning 0, 1, and 2 points to each low, medium, and high level socioeconomic factor and summing them up to get a total socioeconomic score, then categorizing as low (0–1), medium (2–4), and high (5–6) level; and (b) adapted SES: derived using latent class analysis based on education level, total household income, total household wealth, marital status, and retirement status.

Socioeconomic indicators	Harmonized values	Measurements in two cohorts	
		HRS	ELSA
Education level	Primary	Less than upper secondary education	
	Secondary	Upper secondary & vocational training	
	Tertiary	Tertiary education	
Total household income	Tertile 1 (low)	The sum of respondent and spouse earnings, pensions and annuities, disability pensions, unemployment and workers compensation, other government transfers, household capital income, and other income in local currencies.	
	Tertile 2 (medium)		
	Tertile 3 (high)		
Total household wealth	Tertile 1 (low)	The sum of net value of primary residence, business, non-housing financial, and other assets minus all debts in local currencies.	
	Tertile 2 (medium)		
	Tertile 3 (high)		

Table 1: **Measurements of socioeconomic indicators in the Health Retirement Study (HRS) and the English Longitudinal Study of Aging (ELSA).**

Healthy lifestyle factors

Multiple lifestyle factors have been reported to be associated with cognitive dysfunction. We used four lifestyle factors shown to be important during middle- and later-life to lower dementia risk, as reported by previous studies and endorsed by both the World Health Organization and the Lancet commission for dementia prevention, including smoking status, alcohol consumption, physical activity, and social contact.[13,14] Diet was not included given the concern that it may not be related to cognitive dysfunction based on recent studies.[15,16] Information on lifestyle was obtained through structured questionnaires. Detailed harmonization strategies are shown in the Appendix (pp 2 and 3).

Each lifestyle factor would be assigned 1 point for a healthy level and 0 point for an unhealthy level. Thus, the total lifestyle score was the sum of these four factors (ranged from 0 to 4), with higher scores indicating healthier lifestyles, and was further categorized into unfavorable (0–1), intermediate (2), and favorable (3–4) level. Furthermore, given that this additive method is based on the assumption that the association between different behavioral factors and incident dementia were identical, which may not be true, we also constructed a weighted lifestyle score, with each factor weighted by its association with incident dementia (appendix p 4). In addition, we calculated a composite modifiable risk score including body mass index (BMI), blood pressure, total cholesterol, hemoglobin A1c (HbA1c), smoking status, alcohol consumption, physical activity, social contact, and also depressive status in a sensitivity analysis (Appendix p 4).

Cognitive function

Both cohorts conducted a battery of cognitive tests in each wave, including orientation, memory, and executive function tests, with higher scores indicating better cognitive function. Orientation and memory function

Characteristics	HRS				ELSA			
	Total population	High SES[a]	Medium SES[a]	Low SES[a]	Total population	High SES[a]	Medium SES[a]	Low SES[a]
Sample size, n	12,437	3249	6182	3006	6565	1621	2992	1952
Age at baseline, years	69.3 (9.7)	67.3 (9.2)	69.4 (9.5)	71.2 (10.1)	65.1 (9.4)	62.0 (8.1)	64.2 (8.9)	69.1 (9.9)
Men	5076 (40.8%)	1625 (50.0%)	2526 (40.9%)	925 (30.8%)	3021 (46.0%)	863 (53.2%)	1430 (47.8%)	728 (37.3%)
Married	7873 (63.3%)	2701 (83.1%)	4153 (67.2%)	1019 (33.9%)	4560 (69.5%)	1407 (86.8%)	2280 (76.2%)	873 (44.7%)
Education level								
Primary	2159 (17.4%)	0 (0%)	587 (9.5%)	1572 (52.3%)	2581 (39.3%)	165 (10.2%)	854 (28.5%)	1562 (80.0%)
Secondary	7504 (60.3%)	1107 (34.1%)	5084 (82.2%)	1313 (43.7%)	3022 (46.0%)	661 (40.8%)	2006 (67.0%)	355 (18.2%)
Tertiary	2774 (22.3%)	2142 (65.9%)	511 (8.3%)	121 (4.0%)	962 (14.7%)	795 (49.0%)	132 (4.4%)	35 (1.8%)
Total household wealth								
Low	4146 (33.3%)	122 (3.8%)	1309 (21.2%)	2715 (90.3%)	2189 (33.3%)	28 (1.7%)	553 (18.5%)	1608 (82.4%)
Medium	4146 (33.3%)	385 (11.8%)	3470 (56.1%)	291 (9.7%)	2188 (33.3%)	134 (8.3%)	1710 (57.2%)	344 (17.6%)
High	4145 (33.3%)	2742 (84.4%)	1403 (22.7%)	0 (0%)	2188 (33.3%)	1459 (90.0%)	729 (24.4%)	0 (0%)
Total household income								
Low	4146 (33.3%)	118 (3.6%)	1273 (20.6%)	2755 (91.7%)	2189 (33.3%)	45 (2.8%)	559 (18.7%)	1585 (81.2%)
Medium	4146 (33.3%)	318 (9.8%)	3577 (57.9%)	251 (8.3%)	2188 (33.3%)	120 (7.4%)	1701 (56.9%)	367 (18.8%)
High	4145 (33.3%)	2813 (86.6%)	1332 (21.5%)	0 (0%)	2188 (33.3%)	1456 (89.8%)	732 (24.5%)	0 (0%)
Still employed	4713 (38.4%)	1629 (50.8%)	2327 (38.1%)	757 (25.5%)	3250 (49.5%)	969 (59.8%)	1569 (52.5%)	712 (36.5%)
Body mass index, kg/m^2	29.3 (6.2)	28.3 (5.3)	29.6 (6.0)	30.0 (7.1)	27.9 (4.8)	27.1 (4.2)	28.0 (4.8)	28.5 (5.3)
Systolic blood pressure, mmHg	131.0 (20.1)	128.0 (18.8)	131.1 (19.8)	134.1 (21.6)	135.6 (19.0)	133.1 (17.8)	135.3 (18.8)	138.4 (19.9)
Diastolic blood pressure, mmHg	79.1 (11.4)	78.8 (10.8)	79.2 (11.5)	79.4 (12.0)	75.7 (11.3)	76.5 (11.0)	75.7 (11.2)	74.9 (11.7)
Hemoglobin A1c, %	5.9 (0.9)	5.7 (0.7)	5.9 (0.9)	6.1 (1.2)	5.6 (0.7)	5.5 (0.6)	5.6 (0.7)	5.7 (0.8)
No depressive symptom	10660 (87.7%)	3021 (94.8%)	5383 (88.9%)	2256 (77.4%)	5621 (85.9%)	1517 (93.9%)	2599 (87.1%)	1505 (77.5%)
Healthy lifestyle								
Never smoking	5400 (43.4%)	1573 (48.4%)	2625 (42.5%)	1202 (40.0%)	2406 (36.6%)	687 (42.4%)	1098 (36.7%)	621 (31.8%)
Low to moderate alcohol consumption	4905 (39.4%)	1785 (54.9%)	2427 (39.3%)	693 (23.1%)	3073 (46.8%)	572 (35.3%)	1455 (48.6%)	1046 (53.6%)
Top tertile of physical activity	4145 (33.3%)	1630 (50.2%)	1977 (32.0%)	538 (17.9%)	2188 (33.3%)	811 (50.0%)	1007 (33.7%)	370 (19.0%)
Active social contact	10,562 (84.9%)	2838 (87.3%)	5346 (86.5%)	2378 (79.1%)	5727 (87.2%)	1464 (90.3%)	2660 (88.9%)	1603 (82.1%)
Comorbidities								
Hypertension	8512 (68.5%)	1952 (60.1%)	4272 (69.1%)	2288 (76.2%)	3699 (56.3%)	783 (48.3%)	1628 (54.4%)	1288 (66.0%)
Diabetes	2822 (22.7%)	493 (15.2%)	1368 (22.1%)	961 (32.0%)	561 (8.5%)	87 (5.4%)	252 (8.4%)	222 (11.4%)
Heart disease	3015 (24.3%)	614 (18.9%)	1527 (24.7%)	874 (29.1%)	1092 (16.6%)	196 (12.1%)	470 (15.7%)	426 (21.8%)
Stroke	920 (7.4%)	160 (4.9%)	429 (6.9%)	331 (11.0%)	241 (3.7%)	25 (1.5%)	90 (3.0%)	126 (6.5%)
Lung disease	1174 (9.5%)	158 (4.9%)	559 (9.1%)	457 (15.2%)	386 (5.9%)	33 (2.0%)	168 (5.6%)	185 (9.5%)
Cancer	1937 (15.6%)	528 (16.3%)	950 (15.4%)	459 (15.3%)	441 (6.7%)	113 (7.0%)	201 (6.7%)	127 (6.5%)

Values are mean (standard deviation) for continuous variables and number (percentage) for categorical variables. [a]SES was generated through latent class analysis using information on education level, total household wealth, and total household income.

Table 2: **Baseline characteristics of participants from the Health Retirement Study (HRS) and the English Longitudinal Study of Aging (ELSA) according to socioeconomic status (SES).**

in these two cohorts were evaluated by using identical tests. Orientation was assessed by the date-naming test and memory was determined by immediate and delayed recall tests. The executive function was assessed by the serial seven test and the counting-backward test in the HRS, while by the animal-naming fluency test in the ELSA. Detailed information are shown in the Appendix (p 5).

The z scores were calculated to allow direct comparisons across different cognitive tests. Specifically, we standardized the follow-up score by subtracting the mean of the baseline score and then dividing it by the baseline standard deviation (SD). The global cognitive z score was estimated by averaging the z scores from these three cognitive domain tests and then standardizing it to baseline using the mean and SD of the global cognitive z score. Therefore, a unit of z score would mean the one SD above the mean baseline score.

Incident dementia

Incident algorithm-predicted dementia (hereafter referred to as "dementia") was ascertained using either a self-reported physician diagnosis or an alternative approach.[17] For the HRS, we used a cognition summary score, comprising the domains of memory and executive function, ranging from 0 to 27, with a cutoff point of 6 or less defined as dementia.[18] For the ELSA, incident dementia was determined as a combination of cognitive impairment (impairment in two or more domains of cognitive function) and functional impairment.[19] Detailed information is shown in the Appendix (pp 6 and 7). HRS wave 9 and ELSA wave 2 were used as the start time of follow-up, and participants were followed until incident dementia, death, lost to follow-up, or the end of the study period (wave 15 for the HRS, wave 9 for the ELSA).

Covariates
Structured questionnaires were administered by trained researchers in both cohorts. Sociodemographic factors included age, sex, and marital status (married or not). BMI was calculated as body weight divided by the square of height (kg/m^2). Blood pressure level was measured three times by nurses with the means used, and hypertension was defined as a systolic blood pressure of ≥140 mmHg and/or a diastolic blood pressure of ≥90 mmHg, self-reported doctor-diagnosed hypertension, or use of blood pressure-lowering medications. Blood sample collection and measurement of HbA1c and total cholesterol in the HRS and ELSA were performed, and diabetes was defined as HbA1c ≥6.5% (47.5 mmol/mol), self-reported doctor-diagnosed diabetes, or current use of blood glucose-lowering medications. Other information including self-reported doctor-diagnosed heart disease, stroke, lung disease, and cancer was also collected. Once the candidate covariates were decided, we used a directed acyclic graph (ESM Fig. S2) based on previous evidence to choose the minimally sufficient adjustment set (MSAS). According to the directed acyclic graph, only age and sex were confounders and thus included in the MSAS; all the other candidate covariates were likely to be mediators between SES and dementia incidence (Appendix p 13).

Statistical analysis
No priori statistical protocol was developed for current study. Considering the evident heterogeneity regarding participants' characteristics between the HRS and ELSA, a cohort-specific analysis was performed. Baseline characteristics are presented as mean (SD) for continuous variables and frequency (percentage) for categorical variables. Cox proportional hazard model was used to estimate the hazard ratio (HR) and 95% confidence interval (CI) of dementia incidence related to SES and lifestyle. The proportional hazard assumption was assessed by visual inspection of the scaled Schoenfeld residual plot and no significant deviation was observed, with the MSAS (age and sex) adjusted. Then, total lifestyle score was added into the model. The difference method was used to calculate the mediation proportion by the mediator (overall lifestyle) for the association between SES and incident dementia, which compares estimates from models with and without the mediator of interest, and constructs the related 95% confident interval using the Δ method.[20]

To investigate the joint associations between SES and lifestyle with incident dementia and cognitive decline, we firstly quantified the multiplicative and additive interactions regarding dementia incidence by adding a product term of SES and lifestyle category into the model. The HR of the product term was the measure of multiplicative interaction and the relative excess risk due to interaction (RERI) was used as the estimation of additive interaction.[21] Then, we classified participants into nine groups according to their SES (low, medium, and high) and lifestyle (unfavorable, intermediate, and favorable) status and estimated the corresponding HRs of incident dementia and coefficients of cognitive decline in different groups compared with those with high SES and favorable lifestyle.

To check for any possible effect modification, age- and sex-specific analyses were performed by stratifying age (50–65 *vs* > 65 years) and sex (male *vs* female). In addition, several sensitivity analyses were conducted to test the robustness of the main findings. First, we repeated all analyses by substituting SES with individual socioeconomic factors (education, total household income and wealth) and also substituting overall lifestyle score with individual lifestyle factors (smoking, alcohol consumption, physical activity, and social contact). Second, we used alternative SES definitions such as the summed socioeconomic scores and the adapted latent class derived SES. Third, a weighted healthy lifestyle score was constructed to account for varied magnitudes of the associations between different lifestyle factors and incident dementia. Fourth, we repeated the mediation analyses using a composite modifiable risk score. Fifth, we excluded incident dementia cases that occurred within the first five years of follow-up to reduce potential reverse causation. Sixth, we used multiple imputation (MI) to impute all missing independent variables to test the influence of missing variables, with a wide range of predictive variables included to strength the plausibility of the missing at random (MAR) assumption (ESM Table 2). Seventh, participants with prevalent diabetes, heart disease, stroke, lung disease, and cancer at baseline were excluded because both SES and lifestyle could be influenced by major chronic diseases. Eighth, we adapted the definition of dementia case in the HRS, with incident dementia determined as a combination of cognitive impairment (ascertained as the sum of memory and executive function lower than 11, similar to criteria used for defining cognitive impairment no dementia[18]) and functional impairment.

Data were handled and analyzed with SPSS Statistics version 25.0.0.1 (IBM Corp., Armonk, NY, USA) and R, CRAN version 4.3.1. All analyses were performed at the significance level of 0.05 (2-tailed).

Role of the funding source
The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the

manuscript. YX and YB had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Baseline characteristics

Table 2 shows baseline characteristics of participants from the HRS and ELSA. Among 12,437 participants from the HRS (mean age 69.3 years, 40.8% men), 3249 (26.1%) were of high SES, 6182 (49.7%) of medium SES, and 3006 (24.2%) of low SES. Among 6565 participants from the ELSA (mean age 65.1 years, 46.0% men), 1621 (24.7%) were of high SES, 2992 (45.6%) of medium SES, and 1952 (29.7%) of low SES. Participants with higher SES were more likely to be men, married, still employed, and to have a higher level of education, wealth, and income, and to have a lower level of BMI, blood pressure, and HbA1c, and a lower prevalence of depression and comorbidities. Healthy levels of smoking, alcohol consumption (only in the HRS), physical activity, and social contact were also more prevalent among those with higher SES.

Mediation analysis of lifestyle on the association of SES with incident dementia

During a mean follow-up of 9.9 years in the HRS and 9.2 years in the ELSA, 1575 and 494 incident dementia cases were recorded, respectively. After adjusting for baseline age, sex, and lifestyle factors, comparing to participants with high SES, the hazards ratios for incident dementia of those with medium and low SES were 1.32 (95% CI 1.13–1.54) and 2.81 (2.40–3.28) in the HRS, 1.24 (0.95–1.62) and 1.41 (1.08–1.84) in the ELSA (Table 3). When comparing low and medium SES with high SES, the proportion for dementia risk mediated by healthy lifestyle was 18.4% (8.2%–36.4%) and 10.4% (7.3%–14.6%) in the HRS, 1.7% (0%–55.5%) and 2.7% (0.5%–14.0%) in the ELSA (Table 3).

Results from the subgroup analysis revealed that when low SES was compared with high SES, the hazard ratio regarding dementia incidence was higher in male than female (3.38 [2.68–4.27] *vs* 2.45 [1.99–3.01] in the HRS), and higher in midlife than late-life (5.26 [3.59–7.72] *vs* 2.48 [2.09–2.93] in the HRS; 2.23 [1.30–3.84] *vs* 1.18 [0.88–1.59] in the ELSA). However, the mediation proportions were largely robust, except that the corresponding proportions increased in the midlife subgroups (ESM Table S3).

Joint analysis of SES and lifestyle with dementia incidence and cognitive decline

No significant interaction was found between SES and lifestyle on incident dementia in both cohorts, with insignificant interaction terms found, except that the additive interaction observed in the HRS was evident (RERI 1.03 [0.25–2.23]). These indicated that the association with lifestyle factors did not vary substantially across SES levels. Keeping a favorable lifestyle was associated with a lower risk of incident dementia among participants with various SES subgroups in both cohorts, whereas the associations were relatively stronger among those within medium SES level (Fig. 1). To be specific, in the HRS, the hazard ratios for participants with favorable lifestyle (having three to four healthy lifestyle factors) compared with unfavorable lifestyle (having no or one healthy lifestyle factor) for incident dementia were 0.83 (0.58–1.20) among high SES, 0.67 (0.54–0.82) among medium SES, and 0.68 (0.54–0.87) among low SES, while these patterns were not observed in the ELSA (ESM Table S4). When being treated as a continuous variable, per one increment of total healthy lifestyle score was associated with 6%–16% lower risks of incident dementia among different SES subgroups (ESM Table S4).

When SES and lifestyle were combined to explore their joint association on incident dementia and cognitive decline, there was a monotonic association with lower SES level and increasingly unhealthy lifestyle (Figs. 2 and 3). Compared to participants with high SES and favorable lifestyle, those with low SES and unfavorable lifestyle had

	Total no. of participants	No. of dementia cases/person-years	Incidence rate per 1000 person-years	Hazard ratio (95% CI)		Mediation proportion (%) (95% CI)
				Unadjusted for lifestyle score	Adjusted for lifestyle score	
HRS						
High SES	3249	253/31,405	8.1	1 (Reference)	1 (Reference)	
Medium SES	6182	673/54,191	12.4	1.40 (1.21, 1.63)	1.32 (1.13, 1.54)	18.4 (8.2–36.4)
Low SES	3006	649/22,185	29.3	3.17 (2.72, 3.69)	2.81 (2.40, 3.28)	10.4 (7.3–14.6)
ELSA						
High SES	1621	86/16,376	5.3	1 (Reference)	1 (Reference)	
Medium SES	2992	209/26,183	8.0	1.25 (0.95, 1.63)	1.24 (0.95, 1.62)	1.7 (0–55.5)
Low SES	1952	199/14,421	13.8	1.43 (1.09, 1.86)	1.41 (1.08, 1.84)	2.7 (0.5–14.0)

SES was generated through latent class analysis using information on education level, total household wealth, and total household income. All models adjusted for age and sex. The healthy lifestyle score consisted of never smoking, low to moderate alcohol consumption, top tertile of physical activity, and active social contact.

Table 3: **Associations of socioeconomic status (SES) with incident dementia and the corresponding mediation proportion attributed to lifestyle.**

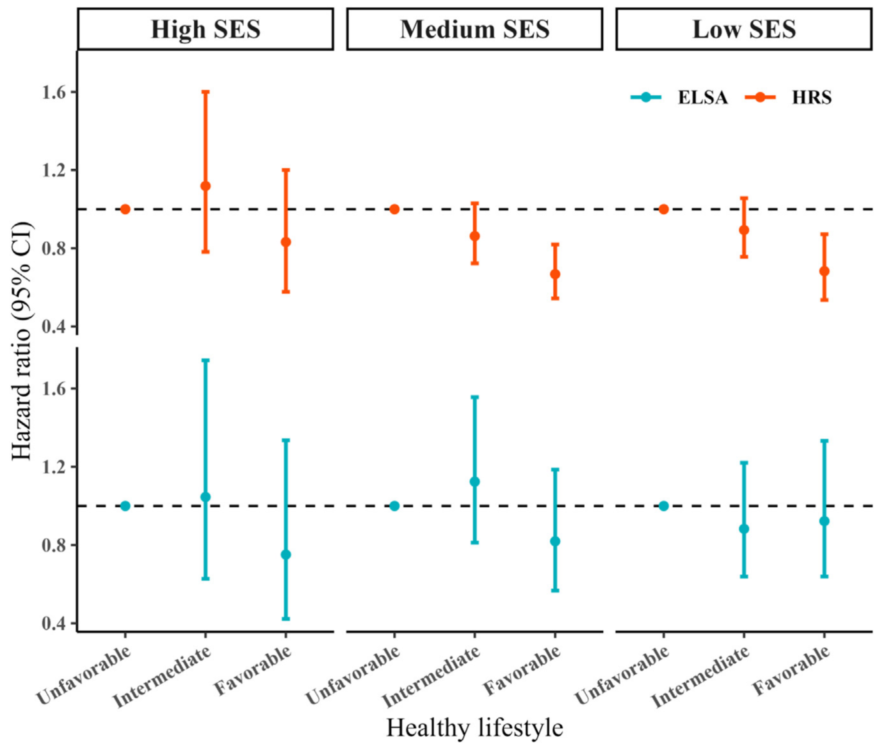

Fig. 1: Associations of healthy lifestyle with incident dementia by socioeconomic status (SES) SES was generated through latent class analysis using information on education level, total household wealth, and total household income. All models adjusted for age and sex. The healthy lifestyle score consisted of never smoking, low to moderate alcohol consumption, top tertile of physical activity, and active social contact, and further categorized as unfavorable (0–1), intermediate (2), and favorable (3–4) level.

a higher risk of developing dementia, with HR 4.27 (3.40–5.38) in the HRS and 2.02 (1.25–3.27) in the ELSA, as well as an accelerated cognitive decline, with the difference in annual changing rate of global cognition –0.058 SD/year (95% CI –0.073, –0.043) in the HRS and –0.049 SD/year (–0.063, –0.035) in the ELSA. Results remain consistent for different cognitive domains in both cohorts (ESM Table S5).

Sensitivity analysis

Several sensitivity analyses were performed to test the robustness of the mediation results. Regarding individual socioeconomic factors when comparing low with high status, the hazard ratios were higher for education (2.18 [1.83–2.60]), total household wealth (1.27 [1.10–1.47]), and total household income (1.57 [1.34–1.85]) in the HRS, but only for total household

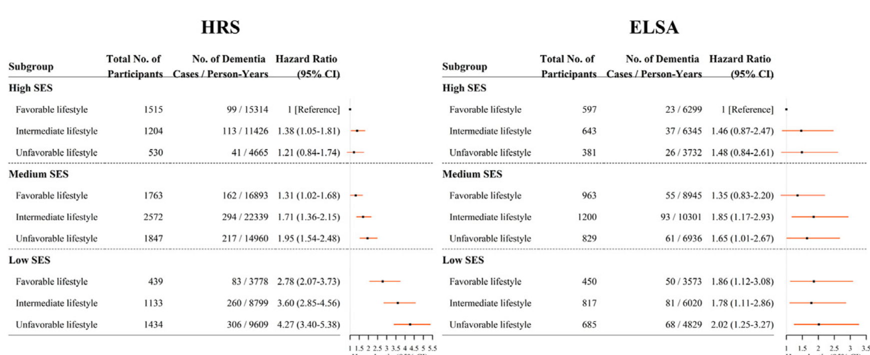

Fig. 2: Joint associations of socioeconomic status (SES) and healthy lifestyle with incident dementia. SES was generated through latent class analysis using information on education level, total household wealth, and total household income. All models adjusted for age and sex. The healthy lifestyle score consisted of never smoking, low to moderate alcohol consumption, top tertile of physical activity, and active social contact, and further categorized as unfavorable (0–1), intermediate (2), and favorable (3–4) level.

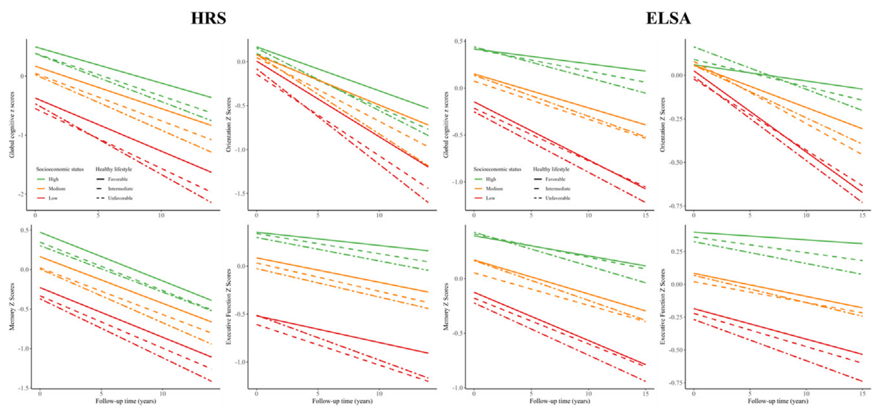

Fig. 3: Joint associations of socioeconomic status (SES) and healthy lifestyle with cognitive decline. SES was generated through latent class analysis using information on education level, total household wealth, and total household income. All models adjusted for age and sex. The healthy lifestyle score consisted of never smoking, low to moderate alcohol consumption, top tertile of physical activity, and active social contact, and further categorized as unfavorable (0–1), intermediate (2), and favorable (3–4) level.

wealth (1.62 [1.24–2.11]) in the ELSA, and the proportion mediated by lifestyles ranged from less than 1% for total household income in the ELSA to 19.8% for total household wealth in the HRS (ESM Table S6). In addition, the proportion mediated by individual lifestyle factors when compared low to high SES for dementia risk ranged from less than 1% for smoking and social contact in both cohorts to 24.3% for physical activity in the ELSA (ESM Table S7).

When socioeconomic level was determined using alternative methods, the hazard ratios for incident dementia comparing low with high status were 2.99 (2.54–3.51) in the HRS and 1.42 (1.07–1.88) in the ELSA using the summed socioeconomic score, and 2.54 (2.18–2.97) in the HRS and 1.26 (0.99–1.61) in the ELSA using the adapted SES (additionally including marital and retirement status), and related mediation proportion remain robust. Similar patterns were observed using weighted lifestyle score. When lifestyle score was replaced by a composite modifiable risk score, the corresponding mediation proportion became larger: when comparing low and medium SES with high SES, the proportion for dementia risk mediated by modifiable risk factors was 12.5% (8.5%–18.0%) and 20.3% (8.2%–41.9%) in the HRS, 7.5% (2.0%–23.9%) and 4.3% (0.1%–80.1%) in the ELSA. In addition, results from all other sensitivity analyses were largely consistent (ESM Table S8).

Discussion

In these two large US and UK cohorts, lower SES was associated with higher risk of incident dementia, with only 1.7%–18.4% mediated by lifestyle factors. Furthermore, compared with participants of high SES and favorable lifestyle, those with low SES and unfavorable lifestyle had a higher risk of incident dementia and an accelerated rate of cognitive decline.

Socioeconomic inequality in brain health is increasingly discussed. One recent meta-analysis including 39 prospective studies found that low SES was associated with a 40% increased risk of all-cause dementia.[2] However, due to the lack of a standardized definition, these included articles applied different SES designs and criteria, with less than half had a relatively comprehensive SES indicator (education, income, and occupation). In addition, given that cognitive dysfunction is an ageing-related disease with most patients already retired, simply using dichotomized occupation factors (whether retired) might not be appropriate. Results from former meta-analyses found that only low levels of education and income, but not occupation, were substantially related to an elevated combined risk of cognitive impairment and dementia,[2] and that job-related factors, such as mental work, work complexity, and job strain, may be related to cognitive decline and incident dementia.[22] Meanwhile, different components of SES are not exchangeable, thus, using the sum of these indicators cannot comprehensively reflect the socioeconomic level of individuals.[7,8] Here we derived SES from latent class analysis using education, total household income and wealth. Also, sensitivity analyses using traditional summed score and adapted definition by additionally including marital and retirement status remain robust. Our analysis confirmed the socioeconomic disparity in dementia risk and further extended the findings to individual SES factors. In the HRS cohort, low levels of education, wealth, and income were respectively related to a 4.5%, 19.8%, and 7.8% increased risk of dementia. Therefore, exploring the possible methods to reduce socioeconomic inequality in dementia burden is urgently needed, especially for those with disadvantageous wealth level.

Lifestyle factors have attracted much attention as potential targets for dementia prevention. However, evidence regarding the contribution of healthy lifestyle to socioeconomic inequality in health was mostly about cardiovascular diseases,[3] with dementia much less reported. Results from the Toyama Dementia Survey and the Leipzig Research Centre for Civilization Diseases (LIFE) Adult Study found that the associations of SES with incident dementia or cognitive function could be partially attributed to lifestyle factors.[6,23] By now, firm conclusions cannot be made about how much an overall lifestyle mediates the association between SES and dementia. First, available studies used single or different combinations of related socioeconomic factors, which might reflect different socioeconomic domains and should not be simply replaced by others. Second, most studies investigated the interaction effect between SES and lifestyle factors, only few explored the mediation effects.[5,6] Third, the characteristics of study populations (e.g., age, race composition, regions, health status), study design (cross sectional or longitudinal, and follow-up duration), data collection methods, and statistical methods (such as adjustment for covariates) also varied widely.

Embedded in two nationally representative cohorts with repeated cognitive and functional assessments over a long follow-up duration, our study concluded that lower SES was associated with higher risk of incident dementia, with 1.7%–18.4% mediated by lifestyle factors. Although comparing with previous studies is difficult given the discrepancies in the variable calculation and statistical design, our findings are, generally, consistent with the LIFE-Adult Study reporting that healthy lifestyle can attenuate socioeconomic inequalities in dementia incidence.[24] Results from joint analysis also revealed that keeping a favorable lifestyle was associated with a lower risk of incident dementia and a slower rate of cognitive decline in different SES subgroups, which can be further confirmed by the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) Trial, which reported that multidomain lifestyle intervention (comprising nutrition, exercise, cognitive training, and management of vascular risk factors) had beneficial effects on cognition regardless of participants' baseline socioeconomic status.[25] These findings support the important role of healthy lifestyles in reducing dementia burden, however, the low mediation proportion also indicated that substantial reductions of the socioeconomic inequality in brain health could not be achieved through promoting healthy lifestyles alone, and other measures to tackle the social determinants of health are still needed. For instance, population-level interventions that focus on improving the risk profile of communities by directly changing societal conditions, such as acting through fiscal (e.g., removing primary school fees) or availability (e.g., cleaner fuel replacement programs for cooking stoves),[26] may be more effective in reducing socioeconomic disparities in brain health.

We also investigated the mediation role of individual lifestyle factors between SES and dementia and found that the mediation effects were mostly derived from alcohol consumption, physical activity, and social contact, while smoking and social contact accounted for the least. Social contact could enhance cognitive reserve or encourages beneficial behaviors, and former meta-analysis found that good social engagement was only modestly protective for incident dementia in long-term studies (≥10 years).[27] Also, the modified definition criteria used here for social contact might be insufficient to capture the whole picture of individual's social engagement status. Regarding the small mediation effect observed for smoking status, this may partly due to the reason that smokers are at a higher risk of premature death before the age at which they might have developed dementia, introducing some bias and uncertainty in the association between smoking and risk of dementia. Considering that the mean age at baseline was larger than 65 for the included participants, this may further dilute the protective effect derived from late-life smoking cessation. Although the importance of smoking control for cardiovascular health is undisputable, the quality of evidence about tobacco cessation for dementia prevention is still low.[13] Besides, lifespan health promotion to reduce dementia risk suggests different health effects during different life courses for different risk factors.[28] This should also be considered here as previous studies found that a substantial proportion of the relationship between education and dementia risk was mediated through mid-life vascular risk factors.[29] Therefore, future work should seek to identify the etiologic windows over the life course when lifestyle intervention may be effective.

It is noteworthy that alcohol consumption accounted for a large proportion of mediation effects. In the HRS, the prevalence of low to moderate alcohol consumption was higher with higher SES level, which is not the case in the ELSA where the prevalence became lower with higher SES. The problem of harmful alcohol drinking in the UK is referred to as a middle-class phenomenon, reported by multiple studies,[4,30] that people in better health, with higher income or higher educational attainment, and socially more active are more likely to drink at harmful levels. This discrepancy in the distribution of alcohol consumption may partly explain the inconsistent findings observed between these two cohorts since low to moderate alcohol consumption was associated with lower dementia risk found among the US and UK people.[31,32]

Major strengths of this study are the large sample size with long follow-up from two well established nationally representative cohorts. The large sample size allowed us to perform the joint and subgroup analyses with sufficient statistical power. In addition, we constructed an overall SES variable and healthy lifestyle score to comprehensively evaluate the complex relations of SES and lifestyle factors with incident dementia. We also conducted a series of sensitivity analyses to show the robustness of the findings, and evaluated individual socioeconomic and lifestyle factors. Nevertheless, we also acknowledge several limitations. First, the majority of the included participants were of White ethnicity, restricting generalization to other ethnicities. Second, information on socioeconomic level and lifestyle was mainly self-reported, thus measurement errors were inevitable. Third, isolated tasks were used to assess cognitive function, which may lack sensitivity in detecting subtle cognitive changes and could also bias the definition of dementia cases. Although our sensitivity analysis by using adapted ascertainment for incident dementia generated robust results, the related bias cannot be fully eliminated. Also, there was discordance in both test items for executive function and corresponding results between the two cohorts, which could undermine the consistency of our results. Fourth, given that those excluded from the analysis because of missing values were more likely to be of lower SES as found during the nonresponse analysis, we additionally conducted a missing completely at random (MCAR) test using the Little's method and found that the MCAR assumption was not plausible, therefore, we tried to strengthen the plausibility of the MAR assumption by including sufficient predictive variables in the MI imputation. However, since statistical procedure cannot completely eliminate the potential impact caused by missingness, the socioeconomic inequality in dementia burden might not be fully captured and our results should be interpreted with caution. Fifth, owing to the nature of post hoc subgroup analyses, sample size in each subgroup was not calculated before data collection. Especially, the number of participants and events might be insufficient in the ELSA study, and the results should be cautiously interpreted. Sixth, since only baseline lifestyle was used here, the related mediation effect might be underestimated. Seventh, other possible lifestyle factors, such as sleep and diet, were not included in current study, which may have underestimated the mediation effect of total lifestyles. Future studies with more comprehensive lifestyle measurements are warranted to validate our findings.

In conclusion, lower SES was significantly related to a higher dementia risk, with only a small proportion mediated by unhealthy lifestyle. Nevertheless, keeping a favorable lifestyle was associated with a lower risk of incident dementia and a slower rate of cognitive decline regardless of the SES levels. Our findings support the important role of healthy lifestyles in helping to lower the risk of cognitive dysfunction. Moreover, other measures, in addition to lifestyle interventions, are also needed to achieve the substantial reduction of the socioeconomic inequality in brain health.

Contributors
KW, YX and YB are responsible for the study concept and design. KW composed the statistical dataset, performed the statistical analyses, and wrote the manuscript. YX and YB had full access to all the data in the study and had final responsibility for the decision to submit for publication. All authors contributed to interpreting the data and critically revising the manuscript.

Data sharing statement
The original HRS dataset is available at https://hrs.isr.umich.edu/. The original ELSA dataset is available at https://www.elsa-project.ac.uk/. The full dataset used in this analysis is available from the corresponding author upon reasonable request.

Declaration of interests
No potential conflicts of interest relevant to this article were reported.

Acknowledgements
We thank the staff and the participants of the HRS and ELSA study.

Appendix A. Supplementary data
Supplementary data related to this article can be found at https://doi.org/10.1016/j.eclinm.2024.102831.

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