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Associations of "Life's Essential 8" cardiovascular health with dementia risk, cognition, and neuroimaging markers of brain health

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Key Points

Question

Is cardiovascular health (CVH), as measured by the American Heart Association's Life's Essential 8 (LE8) score, associated with dementia, cognition, and neuroimaging outcomes, and do these associations differ by apolipoprotein E (APOE) genotypes?

Findings

In this cohort study of 316,669 adults from the UK Biobank, healthier LE8 profiles were associated with reduced risk of incident dementia (mainly driven by vascular dementia), better cognitive performance, and better neuroimaging markers of brain health. These associations were more pronounced among APOE-ε4 noncarriers.

Meaning

These findings suggested that promoting adherence to optimal CVH levels, as measured by the LE8 score, should be encouraged to maintain neurocognitive brain health.

ABSTRACT

Importance: The American Heart Association (AHA)'s Life's Essential 8 (LE8) score, a recently updated metric for promoting cardiovascular health (CVH), has addressed the limitations of the original metrics (Life's Simple 7) and is able to quantify CVH.

Objective: To evaluate the associations of LE8 score with the risk of incident dementia and its subtypes, cognition, and neuroimaging outcomes and to determine whether these associations differ among apolipoprotein E (APOE)-ε4 genotypes.

Design, Setting, and Participants: UK Biobank participants without prior cardiovascular disease nor dementia at baseline (2006–2010) were enrolled in this prospective cohort study. Data analysis was conducted from December 20, 2022, to February 15, 2023.

Exposures: A modified version of the LE8 score was created (range: 0–100) and categorized into poor (0–49), intermediate (50–79), and optimal (80–100) CVH.

Main Outcomes and Measures: The outcomes included incident dementia (all-cause, vascular [VaD], and Alzheimer's disease ascertained through hospital inpatient and death records), cognitive test scores (fluid intelligence and numeric memory), and neuroimaging markers (total brain volume [BV], white matter hyperintensity [WMH], and hippocampal volume). Adjusted Cox proportional hazard and multivariable linear regression models were used.

Results: A subsample of 316,669 participants (mean [SD] age, 56.3 [8.1] years) were included. Higher LE8 scores were associated with reduced risk of all-cause dementia and VaD, the adjusted hazard ratios (HRs) in the optimal CVH versus the poor CVH group were 0.56 (95% confidence interval [CI], 0.48–0.64) and 0.29 (95% CI, 0.22–0.38), respectively. A 10-point increment in LE8 was associated with higher fluid intelligence (β, 0.088; 95% CI, 0.073–0.102) and numeric memory (β, 0.054; 95% CI, 0.043–0.065), and was also associated with lower WMH volume (β, −0.673; 95% CI, from −0.751 to −0.596) and larger BV (β, 77.93; 95% CI, 62.03–93.84) and hippocampal volume (β, 0.197; 95% CI, 0.106–0.288). These associations were more evident in APOE-ε4 noncarriers.

Conclusions and Relevance: Individuals with a higher LE8 score experienced less

dementia events (driven especially by incident VaD) and were associated with better neurocognitive brain health profiles. CVH optimization may be beneficial to the maintenance of brain health.

Keywords: Cardiovascular health; Cognition; Dementia; Life's Essential 8; Magnetic resonance imaging

INTRODUCTION

With the rapid increase in the prevalence and absence of effective treatments, dementia remains a global challenge for public health and social care [1]. Therefore, considering modifiable risk factors as primary interventions for reducing the risk of dementia and maintaining cognitive capacity is critical [2,3]. Increasing evidence [4–7] indicated individual or multidomain lifestyle/cardiovascular risk factors play a role in cognitive decline or dementia.

The Life's Simple 7 (LS7) score [8], initially proposed by the American Heart Association (AHA) in 2010, defined ideal cardiovascular health (CVH) as presence of seven modifiable health factors, including four health behaviors (smoking, body mass index, physical activity, and diet) and three biological factors (total cholesterol, blood pressure, and fasting blood glucose). Extensive subsequent evidence has linked this metric to brain health [9,10]. The AHA recently introduced an updated approach that addressed the limitations of LS7, namely, "Life's Essential 8" (LE8), which is a more comprehensive measurement and sensitive scoring system to inter-individual differences by assessing CVH in a broader and more granular manner than the original score [11]. LE8 incorporated sleep as an additional health metric, which has also been proven to contribute to cognitive decline and possibly increase the risk of dementia, including Alzheimer's disease (AD) [12]. Increasing longitudinal studies have investigated the associations between LS7 and dementia in American cohorts [13,14] and some European countries [15], including the UK [16]. Beyond these clinical endpoints, few studies have evaluated whether enhanced CVH is associated with enhanced brain health, as measured by cognitive performance tests [17,18] and neuroimaging markers [19,20]. By contrast, no studies have yet explored the longitudinal associations between the newly launched LE8 score and multiple neurocognitive outcomes in European populations.

Therefore, this study aimed to investigate the association between the LE8 score and incident dementia and its subtypes, neuroimaging markers, and cognition in UK Biobank (UKB), one of the largest population-based cohorts worldwide. Apolipoprotein E (APOE) genotype ε4 allele is the most important genetic risk factor for AD and dementia [21]. It could increase dementia risk through multiple mechanisms

that also are the potential pathways through which CVH or its components are linked with cognition [13,21,22]. Thus, the effect modification of APOE-ε4 allele status on the association between LE8 scores and the aforementioned neurodegenerative outcomes was further examined in the present study.

METHODS

Study Participants

Data from UKB were used, an ongoing large-scale population-based cohort of over 500,000 participants aged 37–73 who attended one of 22 assessment centers across the UK between 2006 and 2010 [23]. At the baseline visit, the participants underwent a touch-screen questionnaire, had physical measurements and cognitive assessments taken, and provided biological samples. Between August 5, 2014, and October 14, 2016, a subset of participants was invited to attend the first wave of neuroimaging assessments and underwent brain MRI [24]. The reporting of analyses and results followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.

This study explored three subsets of the UKB population: a dementia risk subset, a cognition subset, and a separate neuroimaging subset. The analytical samples for each subset varied in accordance with the number of participants with available data, ranging from approximately 26,000 participants for neuroimaging outcomes to approximately 320,000 participants for dementia incidence. An overview of the study design is presented in **eFigure 1**.

LE8 Score

The updated AHA LE8 metrics included four health behaviors (diet, physical activity, smoking, and sleep) and four health factors (BMI, non-HDL-C, Hb1Ac, and blood pressure). However, an adapted version of diet using the available dietary data from UKB was employed in this study. Instead of using the DASH-style eating pattern as proposed by the AHA, a previously published [25] diet score was used as a surrogate measure of diet quality, which has been reported to be associated with the risk of

cardiovascular disease in the UKB population [26]. The detailed definitions and scoring for the aforementioned component metrics of LE8 are provided in **eTable 1**. Each component was scored from 0 to 100 points, with higher scores indicating healthier CVH [27]. The overall LE8 score was calculated as the mean of the eight metrics, ranging from 0 (lowest) to 100 (highest) and then treated as a continuous score and categorized as poor for scores ranging from 0 to 49, intermediate for scores ranging from 50 to 79, and optimal for scores ranging from 80 to 100 as suggested in the literature [28].

APOE genotype information

The detailed genetic information of the genotyping, imputation, and quality control performed by UKB was reported previously [29]. Given that APOE-ε4 genotype has a recognized association with susceptibility to AD, the APOE genotype was determined by two APOE SNPs rs429358 and rs7412, and the participants were categorized into APOE-ε4 carriers (one or two ε4 alleles) and APOE-ε4 noncarriers (no ε4 allele) [30].

Outcomes

Incident dementia

The primary outcome of the study included incident dementia and its two major component endpoints, AD and vascular dementia (VaD). Dementia cases were ascertained using a combination of primary/secondary diagnosis (hospital inpatient records) or underlying/contributory cause of death (death register) in accordance with the International Classification of Diseases coding system or self-report **(eTable 2)**. The participants' follow-up time in years was calculated from the date of attendance until the date of dementia diagnosis, date of loss to follow-up, death date, or the last date with available information (September 30, 2021), whichever came first.

Cognitive Performance

Two baseline cognitive assessments were administered to the UKB participants via a computerized touch screen interface, and they were described in detail elsewhere [31]. In the fluid intelligence test, the participants were asked to complete as many verbal and

numerical reasoning questions as they could within 2 min. The total number of correct answers given (range: 0–13) was used as the outcome measure. Numeric short-term memory was assessed via digit span test, where the participants were required to try to remember progressively longer numbers and enter them once the number had disappeared from the screen. The maximum number of digits remembered (range: 0–12) was used as the outcome measure. Overall, higher scores indicated better cognitive performance. In the analyses, cognitive data were standardized to Z-scores as described previously [32].

Neuroimaging Measures

Details of the magnetic resonance imaging (MRI) neuroimaging research protocol used by the UKB are available elsewhere [33]. In brief, a subset of the UKB participants underwent structural brain MRI scans using a Siemens Skyra 3T scanner with a 32-channel head coil in accordance with standard protocols [34]. The outcomes of interest were total brain volume (BV), hippocampal volume, and white matter hyperintensity (WMH) volume, which were ascertained using the T1- and T2-weighted fluid-attenuated inversion recovery volumes on structural brain MRI [24]. All neuroimaging data were naturally log-transformed to approximate normality and standardized by subtracting the mean and dividing by the SD.

Detailed information of covariates and statistical analyses was available in Supplement.

RESULTS

Characteristics of Study Participants

The main sample included 316,669 participants with a mean (SD) age of 56.3 (8.1) years; 164,667 (52%) were women and 282,949 (89.6%) were White **(eTable 4)**. About one quarter of the subjects (28.5%) were carriers of an APOE ε4 allele. Overall, the participants with optimal CVH were more likely to be younger, women, White, less deprived, more educated, and higher income earners than those with poor CVH. The

participants with poor CVH were more likely to have depression and ≥ 1 prevalent comorbidity, to drink alcohol daily or almost daily, and self-report more time spent in sedentary activities. More importantly, the participants with better CVH had better cognitive performance in fluid intelligence and numeric memory and higher levels of BV and hippocampal volume but lower WMH.

Dementia Outcomes

Over 3,912,364 person–years (median [interquartile range] length of follow-up, 12.6 [11.9–13.3] years), 4,238 all-cause incident dementia cases developed, including 1,797 AD cases and 939 VaD cases. The incidence rate per 1,000 person–years of dementia outcomes decreased with the increase in CVH **(Table 1)**. Dementia risk also decreased monotonically across the LE8 categories. Compared with those of participants with poor CVH, the hazard ratios (HRs) of participants with optimal CVH were 0.42 (95% confidence interval [CI], 0.37–0.49) for incident all-cause dementia, 0.67 (95% CI, 0.52–0.85) for incident AD, and 0.19 (95% CI, 0.14–0.24) for incident VaD (model 1). After further adjustment (model 2), the optimal CVH group was still associated with a substantially lower risk of all-cause dementia (HR, 0.86; 95% CI, 0.83–0.89; *P* for trend < 0.001) and VaD (HR, 0.70; 95% CI, 0.65–0.75; *P* for trend < 0.001), except for AD (HR, 0.96; 95% CI, 0.91–1.01; *P* for trend = 0.313). **eTable 5** shows the associations between individual lifestyle and the biological components of the LE8 score and dementia outcomes.

The associations of continuous LE8 score with dementia are shown in **Figure 1**. An L-shaped association could be observed between the LE8 score and all-cause dementia and VaD (all *P* for non-linear < 0.001), though the observed risk for AD was dose–response (*P* for non-linear = 0.249). In addition, the estimated PAFs of non-adherence to optimal CVH were 9.50% (5.46%, 13.37%) for all-cause dementia and 35.3% (24.8%, 44.4%) for VaD **(Table 1)**. Similar results were observed when analyses were performed using a 4-year landmark (**eTable 6 and eFigure 2**).

Cognitive Outcomes

The individuals with intermediate profiles had 15.2% (β = 0.152; SE, 0.058; $P = 0.009$) higher fluid intelligence and 14.1% (β = 0.141; SE, 0.042; $P = 0.001$) higher numeric memory than those with poor LE8 profiles. Moreover, those with optimal profiles had 29.6% (β = 0.296; SE, 0.059; $P < 0.001$) higher fluid intelligence and 21.1% (β = 0.211; SE, 0.043; $P < 0.001$) higher numeric memory than those with poor LE8 profiles (**Table 2**, model 2).

Neuroimaging Outcomes

A 10-point increment in the LE8 scores was associated with 77.933 cm^3 (95% CI, 62.030–93.836 cm^3) larger BV and 0.197 cm^3 (95% CI, 0.106–0.288 cm^3) larger hippocampal volume (β, 0.197; SE, 0.046; $P < 0.001$) but 0.673 cm^3 (95% CI, from −0.751 cm^3 to −0.596 cm^3) lower WMH (**Table 3**, model 2).

Effect Modification by APOE-ε4 Allele Status and Other Factors

Significant interactions were observed when exploring the potential effect modification of different APOE-ε4 allele statuses in LE8-dementia associations by using the model 2 (**Figure 2**). The associations of LE8 profiles with the risk of developing all-cause dementia and VaD remained significant across subgroups, although they were more profound in APOE-ε4 noncarriers than in carriers ($HR_{\text{all-cause dementia}}$ = 0.39 vs. 0.71 and HR_{VaD} = 0.18 vs. 0.41 in the optimal group, all P for interaction < 0.001). By contrast, for AD, a significant association was only observed among APOE-ε4 noncarriers (P for interaction < 0.001).

However, APOE genotype did not significantly modify the associations of LE8 profiles with cognitive measures and most of neuroimaging markers (**Tables 2** and **3**). Only interactions of APOE-ε4 allele status with total BV were observed (**Table 3**), and the estimates of the association between a 10-point increment in the LE8 scores and BV were stronger among APOE-ε4 noncarriers (P for interaction = 0.025).

Subgroup analyses were further conducted in accordance with other potential modifying factors, and the results are shown in **eTables 7–9**. While similar associations were observed across subgroups, the associations between LE8 profiles and all-cause

dementia were stronger among younger adults (< 65 years), those with deprivation ≥ one comorbidity, and those without a family history of dementia (all *P* for interaction < 0.05; **eTable 7**). Other associations among the different dementia subtypes are shown in **eTables 8** and **9**.

Original LE7 and New LE8 Scores

The Spearman's correlation between the new LE8 score and the previous LS7 score was 0.801 (*P* value < 0.001), as shown in **eFigure 3**. The results remained similar when the LE7 scores were used (**eTable 10**).

DISCUSSION

By using a large, well-characterized, prospective cohort in the UK, associations were found between LE8 scores (AHA's recently updated CVH metrics) and multiple measures of neurocognitive brain health after multiple adjustment. Individuals with a higher LE8 score had a decreased risk of all-cause dementia and VaD. They also had better cognitive performance in fluid intelligence and numeric memory and were associated with larger BV and hippocampal volume but lower WMH volume. This association was most pronounced in VaD, and the results of PAFs suggested that 35.3% of VaD events could have been avoided if individuals had optimal LE8 profile. Moreover, an interaction was observed between LE8 score and APOE-ε4 genotype for dementia diagnoses and BV, and the associations were more significant among APOE-ε4 noncarriers.

To the best of the authors' knowledge, this research was the first to report the association of AHA's updated LE8 metrics and multiple neurocognitive outcomes in a European population. Previous studies have assessed the associations between the older CVH metrics, LS7, and cognitive aging across diverse population groups [9]. However, the limitations of LS7 definitions have been revealed, which includes less sensitivity to inter- and intra-individual differences, inability to be used to assess dose–response effects, and possible inability to reflect the full scope of health behavior and practices in the current situation [11,35]. The present study adopted LE8, an updated and modified

metrics with a new scaling system; it could better address intra-individual changes and inter-individual differences and includes more comprehensive data on lifestyle factors (sleep), hence considered as an improved tool to assess CVH [11]. By using LE8 as the updated CVH metrics, the findings were found to be consistent with the current knowledge that ideal CVH could reduce dementia risk [13–15,36]. While existing evidence concerning the relationship between CVH and dementia was limited to all-cause dementia, the present study extended prior studies by examining the relationship between CVH and dementia subtypes by using LE8 as the novel definition of CVH. Similar to those of a Chinese study among older adults [37], the results of the present study demonstrated that ideal CVH was associated with a lower risk of dementia and VaD but not AD. The heterogeneous pathophysiology of different dementia subtypes linking to CVH needs further research to be completely unraveled. In addition, higher LE8 was found to be associated with better task performance for fluid intelligence and numeric memory, the reliable proxies of overall cognitive status [38,39]. These findings were consistent with previous cross-sectional [17,18] and longitudinal findings [40]. They were also in line with a UKB study by Falcone *et al.* [19], who reported that higher LS7 was associated with lower WMH and larger BV, and another study in New York by Glodzik *et al.* [41], who suggested that elevated Framingham cardiovascular risk was correlated with reduced hippocampal response. These findings supported the potential role of favorable behavioral CVH profile in maintaining brain health.

The interaction of favorable lifestyle and genetic risk on cognitive aging remains inconsistent. This study also provided evidence for the joint effects of LE8 and APOE genotype on incident dementia diagnosis. For dementia and VaD, higher LE8 score was found to be associated with lower dementia risk regardless of APOE status, though the effect was modestly stronger among ε4 noncarriers. These results were in line with those of other studies [4,42], which showed a cluster of lifestyle factors to be related to decreased dementia risk among APOE-ε4 carriers or participants with high polygenic risk scores. For AD, however, the CVH gradients in dementia risk persisted only among noncarriers, as also observed in other studies [13,14,43]. Additional research is needed to further understand the relevant mechanisms underlying the modification effects of

APOE-ε4 allele across dementia subtypes. The results of this study also showed that the protective associations of LE8 with cognition and neuroimaging markers of brain health were attenuated in APOE-ε4 allele carriers. This phenomenon could be explained by that the benefits of ideal CVH may be offset and masked by the accumulated detrimental effects in ε4 carriers [13].

The strength of this study refers to the population-based longitudinal design in a large and well-characterized cohort of middle-aged and older adults that integrated comprehensive CVH metric assessments, cognitive measures, structural brain MRI data, detailed information on related covariates, and individual genotype dataset for investigating CVH–gene interactions. In addition, the linear and nonlinear associations were assessed, thus addressing the limitations of most previous studies using LS7 as CVH metrics. However, some limitations of this study must be mentioned. First, the healthy lifestyle metrics were self-reported at baseline, which are subject to some recall and misclassification bias. In addition, the lack of some health factors used in LE8 in the UKB at follow-ups hindered the assessment of the effects of longitudinal change in LE8 on brain health. However, potential reverse causation was limited using a 2-year landmark analysis in the main analyses and a 4-year landmark analysis in the sensitivity analyses, and robust results were yielded. Future studies with repeatedly measured CVH are required to evaluate the longitudinal evolution of LE8 or interventions to improve the influence of LE8 scores on brain aging. Moreover, given that some diet information was unavailable in the UKB, a modified version of the diet score was used, which is different from the original AHA LE8 score. However, these differences were mitigated using similar or proxy dietary variables. Furthermore, the UKB is not representative of the general population of the UK, attributable to its relatively high education and high socioeconomic position, and the known "healthy volunteer selection bias," which all limited the generalization of the findings. Finally, the nature of the observational study design prevented concluding the causality between CVH and dementia risk.

CONCLUSION

This study provides evidence that intermediate to optimal CVH profiles measured by new AHA LE8 metrics was associated with slower progression of brain aging, which was assessed by several markers, including neuroimaging markers of cerebral small vessel disease, cognition, and subtypes of dementia. Moreover, a significant interaction was found between LE8 and APOE-ε4 genotype for dementia diagnosis and BV, with the associations being more pronounced in APOE-ε4 noncarriers. These results indicated a potential beneficial role of promoting LE8 scores as a feasible and effective approach for maintaining neurocognitive brain health.

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Ethical approval: The UKB received ethical approval from the National Health Service National Research Ethics Service (Ref: 11/NW/0382). All participants provided written informed consent. This work was conducted under the UKB application number 55794.

Data availability: The data of this study can be requested from the UK Biobank (https://www.ukbiobank.ac.uk/).

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TABLES

Table 1. HRs (95% CIs) of incident dementia according to Life's Essential 8 cardiovascular health scores.

	Life's essential 8 cardiovascular health scores			*P* for trend	HR per 11 points higher LE8 scores
	Poor (0–49 points)	Intermediate (50–79 points)	Optimal (80–100 points)		
All-cause dementia					
Event (%)	269 (3.2)	3,235 (1.5)	734 (0.8)		
Incidence rate per 1,000 person-years (95% CI)	2.66 (2.36–2.99)	1.20 (1.16–1.24)	0.65 (0.61–0.70)		
Unadjusted	1.00 (Ref.)	0.44 (0.39–0.49)	0.23 (0.20–0.27)	<0.001	0.68 (0.66–0.70)
Model 1	1.00 (Ref.)	0.52 (0.46–0.58)	0.42 (0.37–0.49)	<0.001	0.80 (0.78–0.83)
Model 2	1.00 (Ref.)	0.62 (0.55–0.71)	0.56 (0.48–0.64)	<0.001	0.86 (0.83–0.89)
PAF*, %	-	-	9.50 (5.46–13.37)		
Alzheimer's disease					
Event (%)	82 (1.0)	1,361 (0.6)	354 (0.4)		
Incidence rate per 1,000 person-years (95% CI)	0.78 (0.63–0.97)	0.51 (0.48–0.53)	0.31 (0.28–0.35)		
Unadjusted	1.00 (Ref.)	0.63 (0.50–0.78)	0.38 (0.30–0.49)	<0.001	0.76 (0.73–0.79)
Model 1	1.00 (Ref.)	0.72 (0.58–0.90)	0.67 (0.52–0.85)	0.005	0.91 (0.86–0.95)
Model 2	1.00 (Ref.)	0.84 (0.67–1.05)	0.84 (0.65–1.07)	0.313	0.96 (0.91–1.01)
PAF, %	-	-	1.04 (-4.44, 6.23)		
Vascular dementia					
Event (%)	113 (1.4)	708 (0.3)	118 (0.1)		
Incidence rate per 1,000 person-years (95% CI)	1.10 (0.92–1.32)	0.26 (0.24–0.28)	0.11 (0.09-0.13)		
Unadjusted	1.00 (Ref.)	0.23 (0.19–0.28)	0.09 (0.07–0.12)	<0.001	0.53 (0.50–0.56)

Model 1	1.00 (Ref.)	0.28 (0.23–0.34)	0.19 (0.14–0.24)	<0.001	0.62 (0.58–0.66)
Model 2	1.00 (Ref.)	0.38 (0.31–0.46)	0.29 (0.22–0.38)	<0.001	0.70 (0.65–0.75)
PAF, %	-	-	35.3 (24.8–44.4)		

* PAFs based on Model 2 were calculated to theoretically estimate the proportion of each dementia outcome in this study population that could have been prevented if the population had optimal LE8 scores (80-100 points).

Model 1: adjusted for age (continuous, years), sex (men/women), ethnicity (White/others), and socio-economic status (quintiles of Townsend deprivation index).

Model 2: adjusted for model 1 plus education (university or college degree/others), household income (<18,000, 18,000–30,999, 31,000–51,999, 52,000–100,000, or >100,000 £), alcohol consumption frequency (never or occasional, 1–2 times per week, 3–4 times per week, or daily or almost daily), sedentary time (continuous, hours), family history of dementia (yes/no), Charlson comorbidity index (o or ≥1), and depression.

Abbreviations: LE8, Life's Essential 8; HR, hazard ratio; CI, confidence interval; PAF, population attributable fraction.

Table 2. Multivariable linear regression estimates for the association of Life's Essential 8 cardiovascular health scores with fluid intelligence score and numeric memory among 75,566 UK Biobank participants.

LE8 profile	Overall (n=75,566)			APOE carriers (n=17,841)			APOE noncarriers (n=46,088)			*P* for interaction
	β (95% CI)	*SE*	*P* value	β (95% CI)	*SE*	*P* value	β (95% CI)	*SE*	*P* value	
Fluid intelligence										0.678
Poor	Ref.			Ref.			Ref.			
Intermediate	0.152 (0.038, 0.266)	0.058	0.009	0.230 (-0.028, 0.487)	0.131	0.080	0.137 (-0.012, 0286)	0.076	0.072	
Optimal	0.296 (0.181, 0.412)	0.059	<0.001	0.350 (0.090, 0.611)	0.133	0.008	0.282 (0.131, 0.433)	0.077	<0.001	
Per 10 points increment	0.088 (0.073, 0.102)	0.008	<0.001	0.081 (0.050, 0.112)	0.016	<0.001	0.084 (0.065, 0.103)	0.010	<0.001	
Numeric memory										0.672
Poor	Ref.			Ref.			Ref.			
Intermediate	0.141 (0.058, 0.224)	0.042	0.001	0.193 (0.006, 0.0379)	0.095	0.043	0.146 (0.037, 0.255)	0.055	0.009	
Optimal	0.211 (0.127, 0.296)	0.043	<0.001	0.270 (0.081, 0.459)	0.096	0.005	0.221 (0.111, 0.332)	0.056	<0.001	
Per 10 points increment	0.054 (0.043, 0.065)	0.006	<0.001	0.052 (0.029, 0.074)	0.011	<0.001	0.060 (0.046, 0.074)	0.007	<0.001	

Abbreviations: LE8, Life's Essential 8; CI, confidence interval; APOE, apolipoprotein E.

Table 3. Multivariable linear regression estimates for the association of Life's Essential 8 cardiovascular health scores with total brain volume, hippocampal volume, and white matter hyperintensity volume among 26,409 UK Biobank participants.

LE8 profile	Overall (n=26,409)			APOE carriers (n=6,245)			APOE noncarriers (n=16,250)			*P* for interaction
	β (95% CI)	*SE*	*P* value	β (95% CI)	*SE*	*P* value	β (95% CI)	*SE*	*P* value	
Total brain volume										**0.025**
Poor	Ref.			Ref.			Ref.			
Intermediate	297.963 (150.143-445.783)	75.416	<0.001	206.194 (-135.067, 547.455)	174.082	0.236	370.257 (183.283, 557.231)	95.390	<0.001	
Optimal	399.884 (250.375-549.394)	76.278	<0.001	256.939 (-87.065, 600.942)	175.481	0.143	504.154 (314.961, 693.346)	96.522	<0.001	
Per 10 points increment	77.933 (62.030, 93.836)	8.114	<0.001	52.046 (18.489, 85.602)	17.118	0.002	95.046 (74.966, 115.126)	10.244	<0.001	
Hippocampal volume										0.485
Poor	Ref.			Ref.			Ref.			
Intermediate	1.414 (0.571, 2.258)	0.431	0.001	2.231 (0.275, 4.186)	0.998	0.025	1.212 (0.142, 2.282)	0.546	0.026	
Optimal	1.597 (0.743, 2.450)	0.435	<0.001	2.252 (0.280, 4.224)	1.006	0.025	1.389 (0.306, 2.471)	0.552	0.012	
Per 10 points increment	0.197 (0.106, 0.288)	0.046	<0.001	0.190 (-0.003, 0.382)	0.098	0.053	0.161 (0.046, 0.276)	0.059	0.006	
White matter hyperintensity volume										0.211
Poor	Ref.			Ref.			Ref.			
Intermediate	-2.870 (-3.591, -2.150)	0.368	<0.001	-4.549 (-6.167, -2.932)	0.825	<0.001	-1.848 (-2.764, -0.932)	0.467	<0.001	
Optimal	-3.729 (-4.458, -3.000)	0.372	<0.001	-5.478 (-7.109, -3.848)	0.832	<0.001	-2.712 (-3.639, -1.785)	0.473	<0.001	
Per 10 points increment	-0.673 (-0.751, -0.596)	0.039	<0.001	-0.656 (-0.815, -0.497)	0.081	<0.001	-0.681 (-0.779, -0.583)	0.050	<0.001	

Abbreviations: LE8, Life's Essential 8; CI, confidence interval; APOE, apolipoprotein E.

FIGURE LEGENDS

Figure 1. Association of Life's Essential 8 cardiovascular health scores with incident dementia with a 2-years landmark analyses (n=316,669).

Abbreviations: LE8, Life's Essential 8; CI, confidence interval.

Figure 2. Association of Life's Essential 8 cardiovascular health scores with incident dementia stratified by APOE genotype.

Abbreviations: LE8, Life's Essential 8; HR, hazard ratio; CI, confidence interval; APOE, apolipoprotein E.

Figures

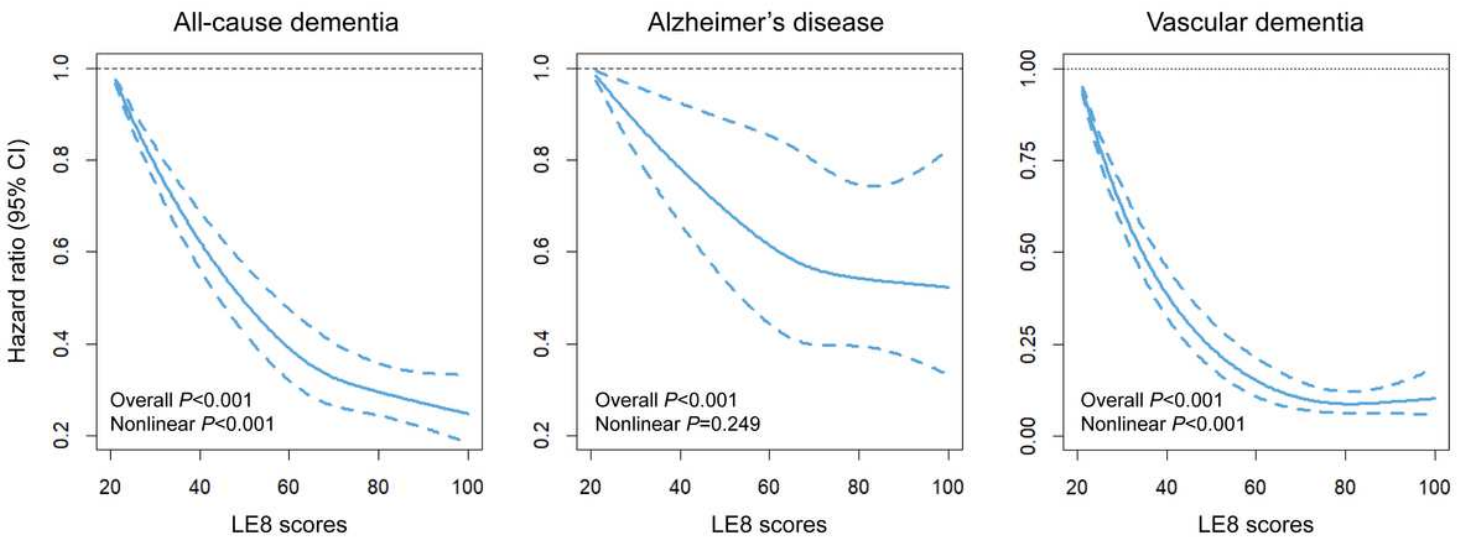

Figure 1

Association of Life's Essential 8 cardiovascular health scores with incident dementia with a 2-years landmark analyses (n=316,669).

Abbreviations: LE8, Life's Essential 8; CI, confidence interval.

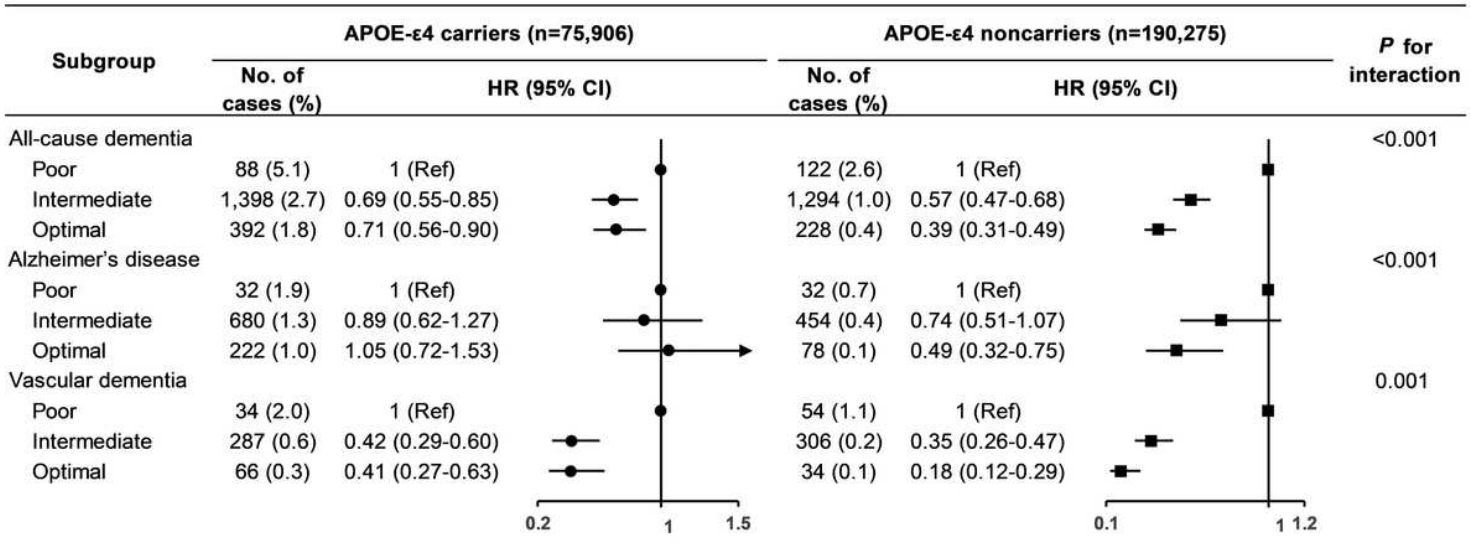

Figure 2

Association of Life's Essential 8 cardiovascular health scores with incident dementia stratified by APOE genotype.

Abbreviations: LE8, Life's Essential 8; HR, hazard ratio; CI, confidence interval; APOE, apolipoprotein E.