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Life's Essential 10 and brain health: A prospective cohort study

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ABSTRACT

Objective: Maintaining brain health while extending life expectancy is an important public health challenge in aging societies. However, the association between cardiovascular health (CVH) and brain health has not been fully established. This study aims to develop a Life's Essential 10 (LE10) framework for assessing CVH and to evaluate the effects of different CVH levels on life expectancy free of stroke and dementia.

Methods: This prospective cohort study included adults aged 37－73 years from the UK Biobank who had no history of stroke or dementia at baseline and had complete data on LE10 metrics and covariates. The LE10 framework developed in this study was based on Life's Essential 8 (LE8), which comprises eight domains, diet, physical activity, nicotine exposure, sleep duration, body mass index, blood lipids, blood pressure, and blood glucose, and additionally incorporated alcohol consumption and sedentary behavior. A total score was calculated by assigning a score to each domain, and participants were categorized as having low, moderate, or high CVH. The primary outcome was life expectancy free of stroke and dementia. Secondary outcomes included the risk of the composite endpoint of

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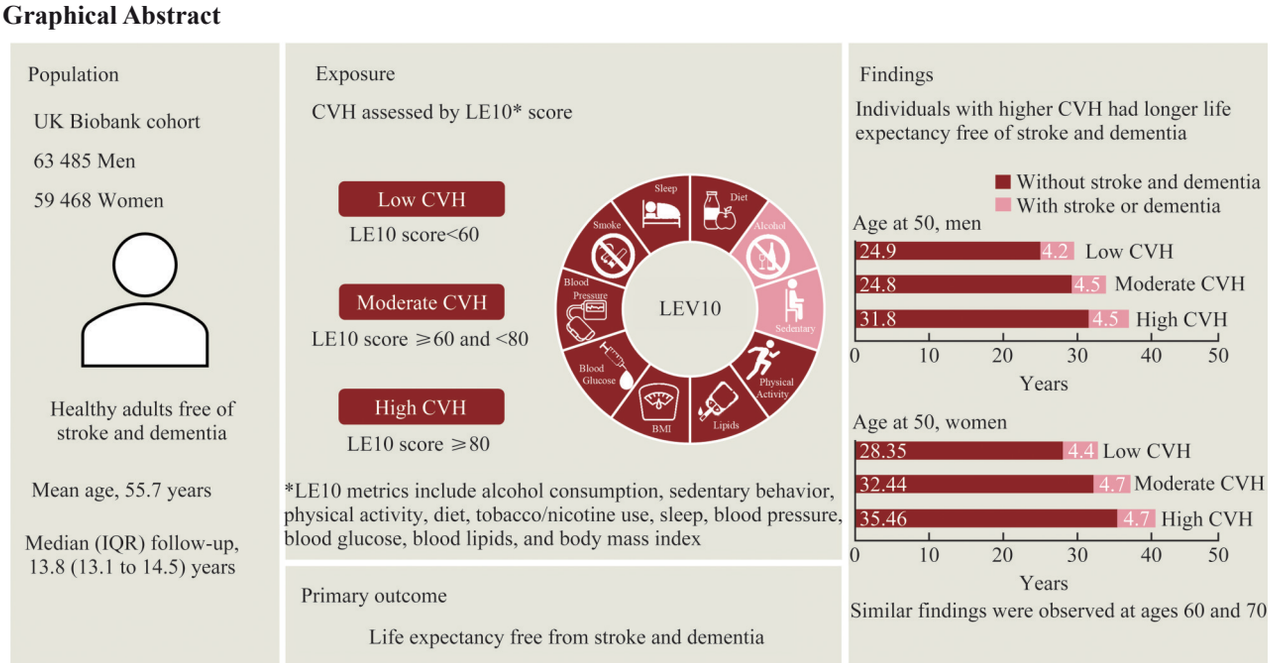
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stroke or dementia, the risk of all-cause mortality, and total life expectancy.

Results: Among 122 953 participants, with a mean age of 55.7 years and 48.4% being women, 13.2%, 60.0%, and 26.8% had low, moderate, and high CVH, respectively. During a median follow-up of 13.8 years, 4 776 composite endpoint events, 3 317 cases of stroke, 1 697 cases of dementia, and 7 825 deaths were recorded. Compared with low CVH, high CVH was associated with a lower risk of the composite endpoint in both men (*HR*=0.59, 95% *CI* 0.52 to 0.67) and women (*HR*=0.50, 95% *CI* 0.42 to 0.59). High CVH was also associated with a lower risk of all-cause mortality in men (*HR*=0.44, 95% *CI* 0.39 to 0.48) and women (*HR*=0.35, 95% *CI* 0.31 to 0.40). At 50 years of age, men with high CVH had a stroke- and dementia-free life expectancy of 31.8 years (95% *CI* 31.1 to 32.5), compared with 24.9 years (95% *CI* 24.5 to 25.2) among those with low CVH. The corresponding estimates for women were 35.5 years (95% *CI* 34.7 to 36.2) and 28.4 years (95% *CI* 27.8 to 28.9), respectively. Analyses of stroke- and dementia-free life expectancy at 60 and 70 years of age and comparisons of total life expectancy across CVH groups consistently showed that higher CVH was associated with longer disease-free survival and total life expectancy.

Conclusion: Higher CVH, as assessed using the LE10 framework, was closely associated with better preservation of brain health and a lower risk of all-cause mortality. Improving the CVH-related behaviors and metabolic factors included in LE10 may contribute to greater longevity and the maintenance of brain health.

Graphical Abstract



Main findings on the association between LE10 CVH and life expectancy with preserved brain health. CVH: Cardiovascular health; IQR: Interquartile range; LE10: Life's Essential 10; BMI: Body mass index.

KEY WORDS cardiovascular health; brain health; stroke; dementia; life expectancy; cardiac rehabilitation

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生命10要素与脑健康：一项前瞻性队列研究

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[摘 要] 目的：在延长寿命的同时维持脑健康，是老龄化社会亟待解决的重要公共卫生问题。心血管健康(cardiovascular health，CVH)与脑健康之间的关联尚未得到充分证实。本研究旨在构建生命10要素(Life’s Essential 10，LE10)CVH评价框架，并评估不同CVH水平对无卒中与痴呆预期寿命的影响。**方法：**本研究为前瞻性队列研究，从英国生物银行数据库中筛选37~73岁、基线时无卒中和痴呆病史，且具备完整的LE10评价指标及协变量数据的成年人作为研究对象。本研究构建的LE10在生命8要素(Life’s Essential 8，LE8；涵盖饮食、体力活动、尼古丁暴露、睡眠时长、体重指数、血脂、血压、血糖8个维度)框架基础上，增加了饮酒和久坐行为2项指标，按各维度赋分后计算总评分，并将研究对象划分为低、中、高3个CVH水平组。研究主要结局指标为无卒中与痴呆的预期寿命；次要结局指标包括卒中/痴呆的复合终点发生风险、全因死亡风险和总预期寿命。**结果：**在122 953名研究对象中(平均年龄为55.7岁，女性占比48.4%)，处于低、中、高CVH水平的研究对象分别占13.2%、60.0%和26.8%。在中位随访13.8年期间，共发生4 776例复合终点事件、3 317例卒中、1 697例痴呆和7 825例死亡。与低CVH水平相比，高CVH水平与较低的复合终点发生风险相关(男性：*HR*=0.59，95% *CI* 0.52~0.67；女性：*HR*=0.50，95% *CI* 0.42~0.59)；高CVH水平还与全因死亡风险降低相关(男性：*HR*=0.44，95% *CI* 0.39~0.48；女性：*HR*=0.35，95% *CI* 0.31~0.40)。预期寿命分析结果显示，50岁时，高CVH水平的男性无卒中与痴呆的预期寿命为31.78(95% *CI* 31.1~32.5)年，而低CVH水平的男性为24.85(95% *CI* 24.5~25.2)年；女性分别为35.46(95% *CI* 34.7~36.2)年和28.35(95% *CI* 27.8~28.9)年。在60岁、70岁年龄节点的无卒中与痴呆预期寿命分析，以及不同CVH水平组的总预期寿命比较中，均观察到CVH水平越高，无病生存期与总预期寿命越长的趋势。**结论：**基于LE10框架评价的较高CVH水平与保持脑健康和较低的全因死亡风险密切相关。积极改善LE10涵盖的各项CVH相关行为与代谢指标，有助于促进长寿和维护脑健康。

[关键词] 心血管健康；脑健康；卒中；痴呆；预期寿命；心脏康复

As global population aging accelerates, maintaining brain health has become a critical public health priority. The American Heart Association (AHA)/American Stroke Association (ASA) related scientific statement proposed that optimal brain health at the clinical level can be defined as the absence of cognitive impairment or dementia, stroke, and other brain diseases, and identified stroke and dementia as important clinical outcomes for monitoring brain health[1-2]. In 2019, stroke and dementia accounted for 87.2% of neurological deaths and 61.7% of neurological disability-adjusted life years globally[3]. In the same year, 57.4 million people were living with dementia, a figure projected to rise to 152.8 million by 2050[4], and the number of people worldwide with stroke reached 101 million[5]. Despite their distinct underlying pathophysiological mechanisms, stroke and dementia are both major adverse brain health outcomes that lead to cognitive impairment, functional dependence, decreased quality of life, and increased disease burden[6-7]. Early identification and tailored prevention are essential to delay onset and reduce the burden of poor brain health.

Cardiovascular health (CVH) is closely associated with stroke and dementia[3]. Life’s Essential 8 (LE8) provides a framework for assessing CVH by integrating lifestyle factors associated with cardiovascular well-being[8]. Higher CVH has been linked to a reduced risk of poor brain health-related diseases[9], and may attenuate stroke and dementia risk[10-11]. Furthermore, recent evidence[12] has shown higher CVH to be associated with increased life expectancy free of common non-communicable chronic diseases. However,

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research on the relationship between CVH and life expectancy with preserved brain health remains limited, restricting the evidence base needed to guide targeted prevention strategies and limiting the application of CVH. Additionally, LE8 does not consider sedentary behavior or alcohol consumption, despite their recognition as key risk factors for both cardiovascular and brain diseases[13-14] and inclusion in prevention guidelines[7, 15]. It is crucial to note that sedentary behavior and physical activity are distinct, independent behavioral constructs with different underlying biological mechanisms. Sedentary behavior is not simply a lack of physical activity; in fact, individuals can meet the recommended guidelines for moderate-to-vigorous physical activity but still face elevated health risks due to prolonged sedentary time. For instance, recent study[13] has demonstrated that high amounts of sedentary behavior are significantly associated with an increased risk of incident dementia among older adults, regardless of their physical activity levels. Therefore, separating these 2 indicators in our analysis provides a more precise and scientifically justified evaluation of their independent health impacts.

To address these gaps, this study introduced Life's Essential 10 (LE10), an expanded CVH model that adds sedentary behavior and alcohol consumption into LE8 to support a more comprehensive strategy for brain health management. In this study, brain health was defined as the absence of stroke and dementia, in order to evaluate the association between CVH and poor brain health outcomes from a holistic clinical perspective. We assessed the associations between LE10 and life expectancy with preserved brain health.

1 Materials and methods

1.1 Ethics statement

The UK Biobank study was approved by the North West Multicentre Research Ethics Committee (Approval number: 16/NW/0274). All participants provided written informed consent. In addition, this study was approved by the Ethics Committee of Xiangya Hospital of Central South University (Approval number: 202307141) and registered in the Chinese Clinical Trial Registry (ChiCTR2400083272). We followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines.

1.2 Study design and population

Participants were screened from a prospective cohort of more than 500 000 individuals within the UK Biobank, aged 37 to 73, between 2006 and 2010 across 22 assessment centers in England, Wales, and Scotland[16]. We included participants with complete data on the LE10 metrics. Individuals who were lost to follow-up, pregnant, in poor health, or had a baseline diagnosis of stroke, dementia, or cancer were excluded. Additional exclusions were made for those missing data on covariates. The study protocol is available online[17].

1.3 Assessment of LE10

LE10 metrics, including alcohol consumption, sedentary behavior, physical activity, diet, tobacco/nicotine use, and sleep duration, were collected through questionnaires. Blood pressure was measured by trained nurses, and blood samples were collected to measure non-high-density lipoprotein (non-HDL) cholesterol and blood glucose.

Alcohol consumption was classified into 6 categories: 0 – 100 g/week, >100 – 130 g/week, and >130 g/week subdivided into quartiles based on previous criteria[18] and population distribution[19]. Sedentary behavior was self-reported as daily hours spent in activities like TV watching, computer use, or driving, and scored by deciles[20]. Data collection and scoring methods for LE10 metrics are provided in Supplementary Method 1 (https://doi.org/10.57760/sciencedb.xbyxb.00134).

The standardized LE10 score (range 0 – 100) was derived by weighting each metric using β coefficients from covariate-adjusted Cox regression models, summing, normalizing by total weights, and scaling to 100. Higher scores indicate better CVH.

1.4 Outcomes

The primary outcome was life expectancy free from stroke and dementia. Secondary outcomes included the composite or singular incidence of stroke or dementia, all-cause mortality, and overall life expectancy.

Mortality data were obtained from NHS death registries, and stroke and dementia incidence from

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primary care, hospital records, and death registries. Diagnoses were based on the earliest recorded date, classified using International Classification of Diseases, Tenth Revision (ICD-10) codes (Supplementary Method 1, https://doi.org/10.57760/sciencedb.xbyxb.00134). Follow-up was from enrollment to diagnosis, death, or censoring on 30 November 2022, corresponding to the latest mortality data linkage available at the time of analysis.

1.5 Covariate assessment

Covariates included age, sex, ethnicity, Townsend deprivation index (TDI), education levels, annual household income, and family history[12].

1.6 Statistical analysis

Continuous variables were presented as mean± standard deviation. Categorical variables were presented as frequencies (percentages). Participants were stratified into 3 CVH levels based on their LE10 scores: Low (<60), moderate (60－<80), and high (≥80). The data-driven turning points were initially identified using restricted cubic spline (RCS) regression analysis[21]. To ensure clinical utility and ease of application, these mathematical cut-offs were subsequently rounded to practical integers, conceptually mirroring the classification framework established by the AHA guidelines[8] and restricted cubic spline regression analysis[21] (Supplementary Figure 1, https://doi. org/10. 57760/sciencedb.xbyxb.00134). The LE10 scoring algorithm is detailed in Supplementary Method 2 (https://doi.org/10.57760/sciencedb.xbyxb.00134).

We used Cox proportional hazards regression to estimate hazard ratio (*HR*) for disease incidence and all-cause mortality. Potential confounders, including age, sex at birth, ethnicity, TDI, education level, annual household income, and family history of disease, were adjusted. The proportional hazards assumption was tested by calculating scaled Schoenfeld residuals and no violations were observed. Interactions between CVH and polygenic risk scores (PRS) for stroke and dementia were assessed using relative excess risk due to interaction (RERI) and likelihood ratio tests[22].

Life expectancy was estimated using multistate life tables[23]. Monte Carlo simulations were used to estimate 95% confidence interval (*CI*) via the R package elect[24]. To assess the potential increase in life expectancy by improving LE10 metrics, we estimated overall life expectancy and additional life-years gained from enhancing low-risk CVH metrics. Detailed statistical methods for these calculations are outlined in Supplementary Method 3 (https://doi.org/10.57760/sciencedb.xbyxb.00134).

Subgroup analyses were performed for sex, age, socioeconomic conditions, and family history. Sensitivity analyses were conducted, including landmark analyses excluding events occurring within the first 2 years of follow-up, and multiple imputation of missing data using chained equations[25]. Shapley additive explanations (SHAP) were used to quantify and rank the associations between LE10 metrics and brain health outcomes, leveraging a machine learning approach[26]. Further details are provided in Supplementary Method 4 (https://doi.org/10.57760/sciencedb.xbyxb.00134).

To quantify the incremental predictive value of LE10 to LE8, we calculated concordance index (C-index), continuous net reclassification improvement (NRI), and integrated discrimination improvement (IDI). To address potential overfitting from deriving and evaluating the LE10 score within the same cohort, we performed internal validation using 5-fold cross-validation. The study population was randomly divided into 5 approximately equal-sized folds stratified by outcome status. In each iteration, 4 folds were used to fit the multivariable Cox proportional hazards model, with β coefficients re-estimated in the training set, and the remaining fold was used for validation. This process was repeated until each fold had served once as the validation set. Finally, cross-validated C-index and pooled *HR* were obtained to assess model stability.

All analyses were performed using R version 4.4.2 and Python version 3.9.7, with statistical significance set at $P<0.05$.

2 Results

2.1 Demographics and characteristics

A total of 122 953 participants (48.4% women) with complete LE10 data were included after excluding those lost to follow-up (*n*=398), pregnant or in poor health (*n*=5 408), with prevalent stroke or dementia (*n*= 13 080), or missing covariates (*n*=13 868; Supplementary

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Figure 2, https://doi.org/10.57760/sciencedb.xbyxb.00134). The age was (55.7±8.1) years, and LE10 score was 72.5±10.9. CVH was classified as low in 13.2%, moderate in 60.0%, and high in 26.8%. Higher LE10 CVH scores were more common in younger individuals, women, and those with higher education and income. Participant characteristics are detailed in Table 1 and Supplementary Tables 1−3 (https://doi.org/10.57760/sciencedb.xbyxb.00134).

Over a median of 13.8 years (interquartile range 13.1 to 14.5; 1 658 965 person-years) a total of 4 776 (3.88%) composite events of stroke or dementia were recorded (3 038 men, 1 738 women), equating to 2.9 events per 1 000 person-years; 3 317 (2.70%) initial stroke events (2 166 men, 1 151 women) and 1 697 (1.38%) initial dementia events (1 044 men, 653 women) corresponding to 2.0 and 1.0 events per 1 000 person-years, respectively. Additionally, there were 7 825 deaths (6.36%) reported during the follow-up period (5 253 men, 2 572 women) equating to 4.7 events per 1 000 person-years.

2.2 Associations of LE10 CVH with brain health

Restricted cubic spline analysis consistently demonstrates that prolonged daily sedentary time and excessive weekly alcohol consumption correlate with elevated risks of composite incidence of stroke or dementia, stroke incidence, dementia incidence, and all-cause mortality, with statistically significant overall and non-linear dose-response relationships (all overall and non-linear P<0.001; Supplementary Figures 3 and 4, https://doi.org/10.57760/sciencedb.xbyxb.00134). Higher alcohol consumption and sedentary behavior scores were associated with reduced composite incidence risks compared to low scores, with *HRs* of 0.88 (95% *CI* 0.80 to 0.96) and 0.75 (0.69 to 0.82), respectively (Supplementary Table 4, https://doi.org/10.57760/sciencedb.xbyxb.00134). This trend extended to individual incidence of either stroke or dementia (Supplementary Tables 5 and 6, https://doi.org/10.57760/sciencedb.xbyxb.00134).

In men, composite incidence decreased from 5.2 (4.9 to 5.6) per 1 000 person-years in low CVH to 3.4 (3.3 to 3.6) in moderate CVH and 2.2 (2.0 to 2.4) in high CVH. Corresponding adjusted *HRs* were 0.74 (0.68 to 0.80) for moderate CVH and 0.59 (0.52 to 0.67) for high CVH, compared to low CVH (all P<0.001; Table 2). Among women, composite incidence declined from 3.9 (3.4 to 4.4) per 1 000 person-years in low CVH to 2.5 (2.3 to 2.6) in moderate CVH and 1.2 (1.1 to 1.4) in high CVH. The adjusted *HRs* were 0.70 (0.61 to 0.80) for moderate CVH and 0.50 (0.42 to 0.59) for high CVH (all P<0.001; Table 2).

Stroke incidence rates per 1 000 person-year were 1.5 (1.3 to 1.7) versus 3.8 (3.5 to 4.2) among men with high versus low CVH, and 0.8 (0.7 to 0.9) versus 2.7 (2.3 to 3.1) among women. The corresponding dementia incidence rates were 0.8 (0.6 to 0.9) versus 1.6 (1.4 to 1.8) among men, and 0.5 (0.4 to 0.6) versus 1.3 (1.0 to 1.6) among women.

Participants with the most low-risk CVH metrics had the lowest composite and disease-specific incidence risks (Supplementary Figure 5, https://doi.org/10.57760/sciencedb.xbyxb.00134). Kaplan-Meier analyses revealed participants with high CVH demonstrated the highest survival probabilities free of disease incidence throughout the follow-up (Figure 1A−1C).

2.3 Association between LE10 CVH and all-cause mortality

Restricted cubic spline analysis demonstrated an inverse association between LE10 score and all-cause mortality (Supplementary Figure 1, https://doi.org/10.57760/sciencedb.xbyxb.00134). Participants with high CVH had the lowest all-cause mortality risk (men: *HR*=0.44, 95% *CI* 0.39 to 0.48, P<0.001; women: *HR*=0.35, 95% *CI* 0.31 to 0.40, P<0.001) compared to those with low CVH (Table 2, Figure 1D). Additionally, participants with the highest number of low-risk CVH metrics had the lowest all-cause mortality (Supplementary Figure 5, https://doi.org/10.57760/sciencedb.xbyxb.00134).

High or moderate alcohol consumption scores were associated with lower all-cause mortality, compared to low scores, with *HRs* of 0.65 (0.61 to 0.70) and 0.76 (0.69 to 0.83), respectively. Lower sedentary time was also associated with reduced mortality risk, with *HRs* of 0.78 (0.73 to 0.83) and 0.91 (0.86 to 0.97) for high and moderate sedentary behavior scores, respectively (Supplementary Table 7, https://doi.org/10.57760/sciencedb.xbyxb.00134).

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Table 1 Baseline characteristics of participants categorized by CVH level

Variables	Total (*n*=122 953)	Low CVH (*n*=16 218)	Moderate CVH (*n*=73 776)	High CVH (*n*=32 959)
Age/Years	55.7±8.1	57.5±7.5	56.4±7.9	53.3±8.1
Sex/[No.(%)]				
Male	63 485(51.6)	11 549(71.2)	40 200(54.5)	11 736(35.6)
Female	59 468(48.4)	4 669(28.8)	33 576(45.5)	21 223(64.4)
Race and ethnicity/[No.(%)]				
White	118 707(96.5)	15 745(97.1)	71 093(96.4)	31 869(96.7)
Asian	1 849(1.5)	169(1.0)	1 130(1.5)	550(1.7)
Black	1 089(0.9)	151(0.9)	735(1.0)	203(0.6)
Mixed	597(0.5)	76(0.5)	365(0.5)	156(0.5)
Other ethnicity	711(0.6)	77(0.5)	453(0.6)	181(0.5)
Townsend deprivation index	−1.7±2.9	−1.2±3.1	−1.7±2.9	−1.9±2.7
Education levels/[No.(%)]				
College or above	48 473(39.4)	4 469(27.6)	26 974(36.6)	17 030(51.7)
High school or equivalent	61 164(49.8)	8 960(55.2)	38 017(51.5)	14 187(43.0)
Less than high school	13 316(10.8)	2 789(17.2)	8 785(11.9)	1 742(5.3)
Annual household income/[No.(%)]				
<18 000 £	20 717(16.8)	3 678(22.7)	13 193(17.9)	3 846(11.7)
18 000−30 999 £	29 718(24.2)	4 121(25.4)	18 652(25.3)	6 945(21.1)
31 000−51 999 £	34 207(27.8)	4 332(26.7)	20 481(27.7)	9 394(28.5)
52 000−100 000 £	29 977(24.4)	3 324(20.5)	17 084(23.2)	9 569(29.0)
>100 000 £	8 334(6.8)	763(4.7)	4 366(5.9)	3 205(9.7)
Family history/[No.(%)]				
No	74 224(60.4)	9 638(59.4)	44 230(59.9)	20 356(61.8)
Yes	48 729(39.6)	6 580(40.6)	29 546(40.1)	12 603(38.2)
LE10 score				
Total score	72.5±10.9	53.6±5.3	70.9±5.5	85.4±4.1
Alcohol consumption score	87.8±26.0	63.9±40.3	88.7±23.9	97.6±8.5
Sedentary score	59.2±28.8	38.1±25.3	55.9±27.7	77.0±22.4
Physical activity score	77.9±35.3	48.9±43.3	77.7±34.8	92.7±19.2
Tobacco/nicotine exposure score	65.3±38.6	32.2±33.1	62.1±38.4	88.7±24.5
Healthy diet score	57.0±17.2	48.4±15.7	55.8±16.6	63.7±16.8
Sleep health score	90.4±17.3	82.1±22.7	90.1±17.2	95.1±11.9
Body mass index score	71.3±27.0	47.7±27.3	68.7±25.6	88.8±17.0
Blood lipid score	75.0±25.1	64.4±25.2	72.3±25.0	86.2±20.9
Blood glucose score	92.8±17.6	80.5±26.2	93.0±17.0	98.4±8.3
Blood pressure score	48.1±28.0	30.2±22.0	44.1±25.5	65.9±27.0

Data are presented as mean±standard deviation for continuous variables or frequencies (percentages) for categorical variables. CVH levels (low: <60, moderate: 60−<80, high: ≥80) were defined using LE10 score cut-offs derived from restricted cubic spline analysis and adapted for clinical utility. CVH: Cardiovascular health; LE10: Life's Essential 10.

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2.4 Association between CVH and overall life expectancy

At age 50, men with low, moderate, and high CVH were projected to live 29.1 (28.7 to 29.5), 33.3 (32.9 to 33.7), and 36.2 (35.5 to 36.9) years, respectively; women, 32.8 (32.2 to 33.4), 37.1 (36.5 to 37.7), and 40.1 (39.4 to 40.9) years, respectively. High CVH was associated with longer life expectancy compared to low CVH, with an increase of 7.1 (7.1 to 7.2) years in men and 7.3 (7.3 to 7.4) years in women. Similar trends were observed at ages 60 and 70 (Supplementary Table 8, https://doi.org/10.57760/sciencedb.xbyxb.00134).

Life expectancy increased with the number of low-risk LE10 metrics (Supplementary Table 9, https://doi.org/10.57760/sciencedb. xbyxb. 00134). Among men, it increased from 27.0 (26.3 to 27.6) years in those with 0−1 low-risk metrics to 38.9 (38.1 to 39.7) years in those with all 10 (Supplementary Figure 6A, https://doi.org/10.57760/sciencedb. xbyxb. 00134), while for women, it rose from 30.1 (29.4 to 30.9) years to 42.2 (41.4 to 43.1) years (Supplementary Figure 6B, https://doi.org/10.57760/sciencedb. xbyxb. 00134). Achieving complete low-risk LE10 metrics was associated with gains of 12.0 years in men (Supplementary Figure 6C, https://doi.org/10.57760/sciencedb. xbyxb. 00134) and 12.1 years in women (Supplementary Figure 6D, https://doi.org/10.57760/sciencedb.xbyxb.00134).

2.5 Association between CVH and life expectancy with preserved brain health

At age 50, men with low, moderate, and high CVH were estimated to live 24.9 (24.5 to 25.2), 28.8 (28.4 to 29.2), and 31.8 (31.1 to 32.5) years free of stroke and dementia, respectively. Women were estimated to live 28.4 (27.8 to 28.9), 32.4 (31.9 to 33.0), and 35.5 (34.7 to 36.2) years, respectively (Figure 2A). Estimates of life expectancy free of stroke and free of dementia are presented separately in Figures 2B and 2C, respectively. Life expectancy with preserved brain health increased with the addition of further low-risk metrics (Supplementary Table 11, https://doi.org/10.57760/sciencedb.xbyxb.00134). Participants with all 10 low-risk CVH metrics had a life expectancy with preserved brain health of 33.7 (33.0 to 34.5) years for men and 37.5 (36.7 to 38.3) years for women, while participants with 0 − 1 low-risk metric were 22.2 (21.7 to 22.7) years for men and 25.6 (25.0 to 26.3) years for women (Figure 3A and 3B). Improving all 10 metrics to low-risk status at age 50 was associated with disease-free life-years gained of 11.5 (11.5 to 11.5) years for men and 11.8 (11.8 to 11.9) for women (Figure 3C and 3D). Similar trends were observed for stroke or dementia individually (Supplementary Figures 7 and 8; Supplementary Tables 10 and 11; https://doi.org/10.57760/sciencedb.xbyxb.00134).

At age 50, men with the highest alcohol consumption scores gained 2.6 (2.6 to 2.6) years free of stroke and dementia compared to those with the lowest scores (Supplementary Figure 9, https://doi.org/10.57760/sciencedb.xbyxb.00134); women gained 2.7 (2.6 to 2.7) years (Supplementary Figure 10, https://doi.org/10.57760/sciencedb.xbyxb.00134). Comparable trends were observed for sedentary behavior (Supplementary Figures 9 and 10, https://doi.org/10.57760/sciencedb.xbyxb.00134).

2.6 Subgroup and sensitivity analysis

In subgroup analyses, the inverse association between LE10 and composite disease incidence (Supplementary Figure 11, https://doi.org/10.57760/sciencedb.xbyxb.00134), individual incidence of stroke or dementia (Supplementary Figures 12 and 13, https://doi.org/10.57760/sciencedb. xbyxb. 00134) and all-cause mortality (Supplementary Figure 14, https://doi.org/10.57760/sciencedb.xbyxb.00134) remained consistent. Similar patterns were observed for life expectancy stratified by socioeconomic factors and by family history (Supplementary Figure 15−18, https://doi.org/10.57760/sciencedb.xbyxb.00134).

Sensitivity analyses incorporating multiple imputation and 2-year landmark analyses supported the robustness of the findings with consistent results across analyses for outcomes including disease incidence and mortality (Multiple imputation: Supplementary Figure 19; Landmark analysis: Supplementary Figure 20; https://doi. org/10.57760/sciencedb. xbyxb. 00134), and overall and disease-free life expectancy (Multiple imputation: Supplementary Figure 21; Landmark analysis: Supplementary Figure 22; https://doi.org/10.57760/sciencedb.xbyxb.00134).

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Table 2 Association between CVH levels estimated by the LE10 score and mortality and disease incidence

Variables	Men				
	No. of cases/ total No.	Events per 1 000 person-years	Rate difference per 1 000 person-years	*HR* (95% *CI*)*	*P*
Composite incidence of stroke or dementia					
Low CVH	817/11 549	5.2(4.9, 5.6)	0(reference)	1(reference)	NA
Moderate CVH	1 872/40 200	3.4(3.3, 3.6)	−1.8(−2.2, −1.4)	0.74(0.68, 0.80)	<0.001
High CVH	349/11 736	2.2(2.0, 2.4)	−3.0(−3.5, −2.6)	0.59(0.52, 0.67)	<0.001
Stroke incidence					
Low CVH	605/11 549	3.8(3.5, 4.2)	0(reference)	1(reference)	NA
Moderate CVH	1 319/40 200	2.4(2.3, 2.5)	−1.4(−1.8, −1.1)	0.70(0.63, 0.77)	<0.001
High CVH	242/11 736	1.5(1.3, 1.7)	−2.3(−2.7, −2.0)	0.53(0.46, 0.62)	<0.001
Dementia incidence					
Low CVH	258/11 549	1.6(1.4, 1.8)	0(reference)	1(reference)	NA
Moderate CVH	663/40 200	1.2(1.1, 1.3)	−0.4(−0.6, −0.2)	0.84(0.73, 0.97)	0.021
High CVH	123/11 736	0.8(0.6, 0.9)	−0.9(−1.1, −0.6)	0.73(0.59, 0.91)	0.004
All−cause mortality					
Low CVH	1 546/11 549	10.1(9.6, 10.7)	0(reference)	1(reference)	NA
Moderate CVH	3 198/40 200	5.9(5.7, 6.1)	−4.2(−4.8, −3.7)	0.65(0.61, 0.69)	<0.001
High CVH	509/11 736	3.2(2.9, 3.5)	−7.0(−7.5, −6.4)	0.44(0.39, 0.48)	<0.001
Variables	Women				
	No. of cases/ total No.	Events per 1 000 person-years	Rate difference per 1 000 person-years	*HR* (95% *CI*)	*P*
Composite incidence of stroke or dementia					
Low CVH	246/4 669	3.9(3.4, 4.4)	0(reference)	1(reference)	NA
Moderate CVH	1 131/33 576	2.5(2.3, 2.6)	−1.4(−1.9, −0.9)	0.70(0.61, 0.80)	<0.001
High CVH	361/21 223	1.2(1.1, 1.4)	−2.6(−3.1, −2.1)	0.50(0.42, 0.59)	<0.001
Stroke incidence					
Low CVH	171/4 669	2.7(2.3, 3.1)	0(reference)	1(reference)	NA
Moderate CVH	752/33 576	1.6(1.5, 1.8)	−1.1(−1.5, −0.6)	0.66(0.56, 0.78)	<0.001
High CVH	228/21 223	0.8(0.7, 0.9)	−1.9(−2.3, −1.5)	0.43(0.35, 0.52)	<0.001
Dementia incidence					
Low CVH	82/4 669	1.3(1.0, 1.6)	0(reference)	1(reference)	NA
Moderate CVH	425/33 576	0.9(0.8, 1.0)	−0.4(−0.7, −0.1)	0.79(0.62, 1.00)	0.050
High CVH	146/21 223	0.5(0.4, 0.6)	−0.8(−1.1, −0.5)	0.69(0.52, 0.91)	0.008
All−cause mortality					
Low CVH	454/4 669	7.3(6.6, 8.0)	0(reference)	1(reference)	NA
Moderate CVH	1 588/33 576	3.5(3.3, 3.7)	−3.8(−4.5, −3.1)	0.50(0.45, 0.56)	<0.001
High CVH	530/21 223	1.8(1.7, 2.0)	−5.5(−6.2, −4.8)	0.35(0.31, 0.40)	<0.001

**HRs* were estimated for all-cause mortality and disease incidence through Cox regression models. Models were adjusted for age, birth sex, race and ethnicity, Townsend deprivation index, education level, annual household income, and family history. *CI*: Confidence interval; NA: Not applicable.

Genetic risk levels did not alter the protective association between higher CVH and reduced incidence of both stroke and dementia. This inverse relationship remained consistent across 3 genetic risk strata (Supplementary Tables 12 and 13, https://doi.org/10.57760/sciencedb.xbyxb.00134).

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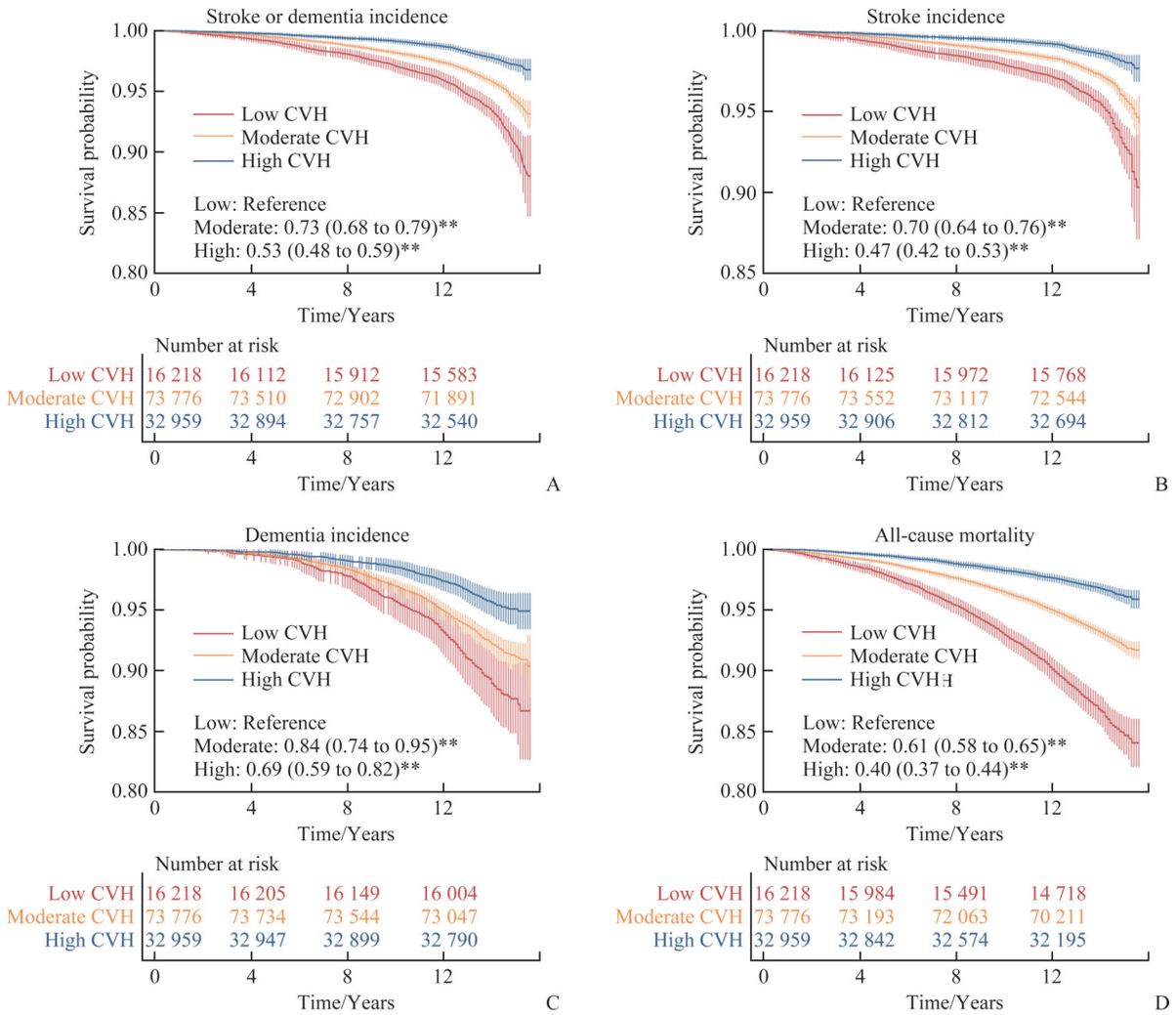


Figure 1 Kaplan-Meier curves for composite and individual incidence of stroke and dementia and all-cause mortality by CVH level

A: Composite incidence of stroke or dementia. B: Stroke incidence. C: Dementia incidence. D: All-cause mortality. Curves were stratified by CVH level: Low (red), moderate (orange), and high (blue). Number at risk is presented below the Kaplan-Meier curves at specified time points. Shaded areas represent 95% confidence intervals. **P<0.01. CVH: Cardiovascular health.

2.7 Discriminative performance and internal validation

For all-cause mortality, the C-index for LE8 was 0.731 (0.725 to 0.736), whereas for LE10 was 0.736 (0.730 to 0.741), representing an increase of 0.005 (P< 0.001). For composite incidence of stroke or dementia, the C-index was 0.739 (0.732 to 0.746) for LE8 and 0.742 (0.735 to 0.749) for LE10, representing an increase of 0.003 (P<0.001).

Additionally, the LE10 yielded a statistically significant improvement in continuous NRI across all outcomes, including all-cause mortality (0.026, 95% *CI* 0.007 to 0.043, P<0.001), the composite outcome of stroke and dementia incidence (0.070, 95% *CI* 0.045 to 0.089, P<0.001), stroke incidence (0.073, 95% *CI* 0.037 to 0.095, P<0.001), and dementia incidence (0.052, 95% *CI* 0.012 to 0.095, P=0.020). Similarly, the IDI showed significant improvements for all-cause mortality (P<0.001), the composite of stroke and dementia incidence (P<0.001), and stroke incidence (P<0.001). However, the IDI improvement for dementia incidence alone did not reach statistical significance (P=0.119).

Internal validation using 5-fold cross-validation showed stable model discrimination across all outcomes

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(Supplementary Table 14, https://doi.org/10.57760/sciencedb.xbyxb.00134). The cross-validated C-indices were 0.724±0.005 for the composite incidence of stroke and dementia, 0.696±0.004 for stroke, 0.784±0.007 for dementia, and 0.727±0.008 for all-cause mortality. Furthermore, moderate and high CVH levels consistently predicted significantly lower risks for all outcomes compared to low CVH (all P<0.001).

2.8 Online platform

To facilitate the application of the LE10 model, we developed *MyLifeEssential* (https://brain.mylifeessential.com), a web-based risk assessment tool. Users input demographic and LE10 data to generate aggregate and individualized LE10 scores, alongside personalized incidence risk estimates for stroke and dementia. The platform also projects potential risk reductions achievable by improving CVH metrics. Prioritizing data security, the tool operates without collecting personally identifiable information (PII). All inputs are processed transiently for real-time calculations and are never stored or shared, as detailed in the confidentiality statement provided prior to use (Supplementary Figure 23, https://doi.org/10.57760/sciencedb.xbyxb.00134).

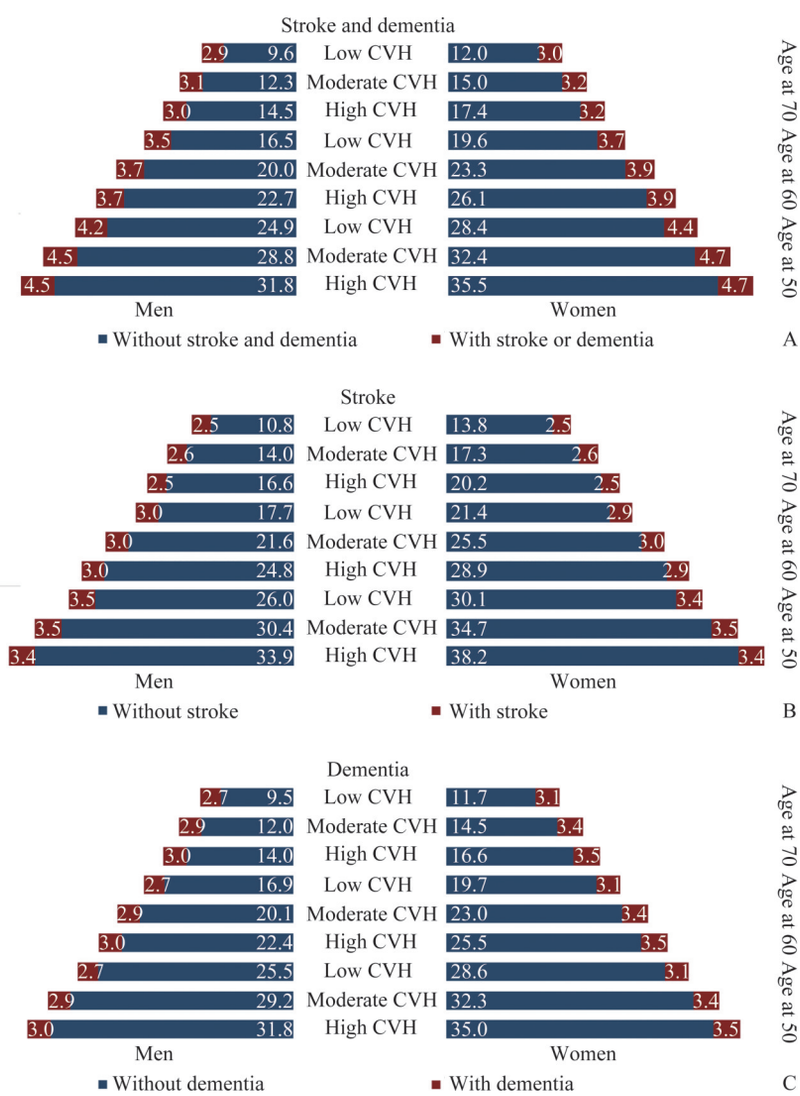


Figure 2 Life expectancy without and with stroke and/or dementia

A–C: Life expectancy without and with stroke and/or dementia by CVH levels in men and women at ages 50, 60, and 70, including composite stroke and dementia outcomes (A), stroke-specific estimates (B), and dementia-specific estimates (C). Years lived without disease (blue bars) and with disease (red bars) are shown side-by-side for each subgroup. LE10: Life's Essential 10; Ref: Reference.

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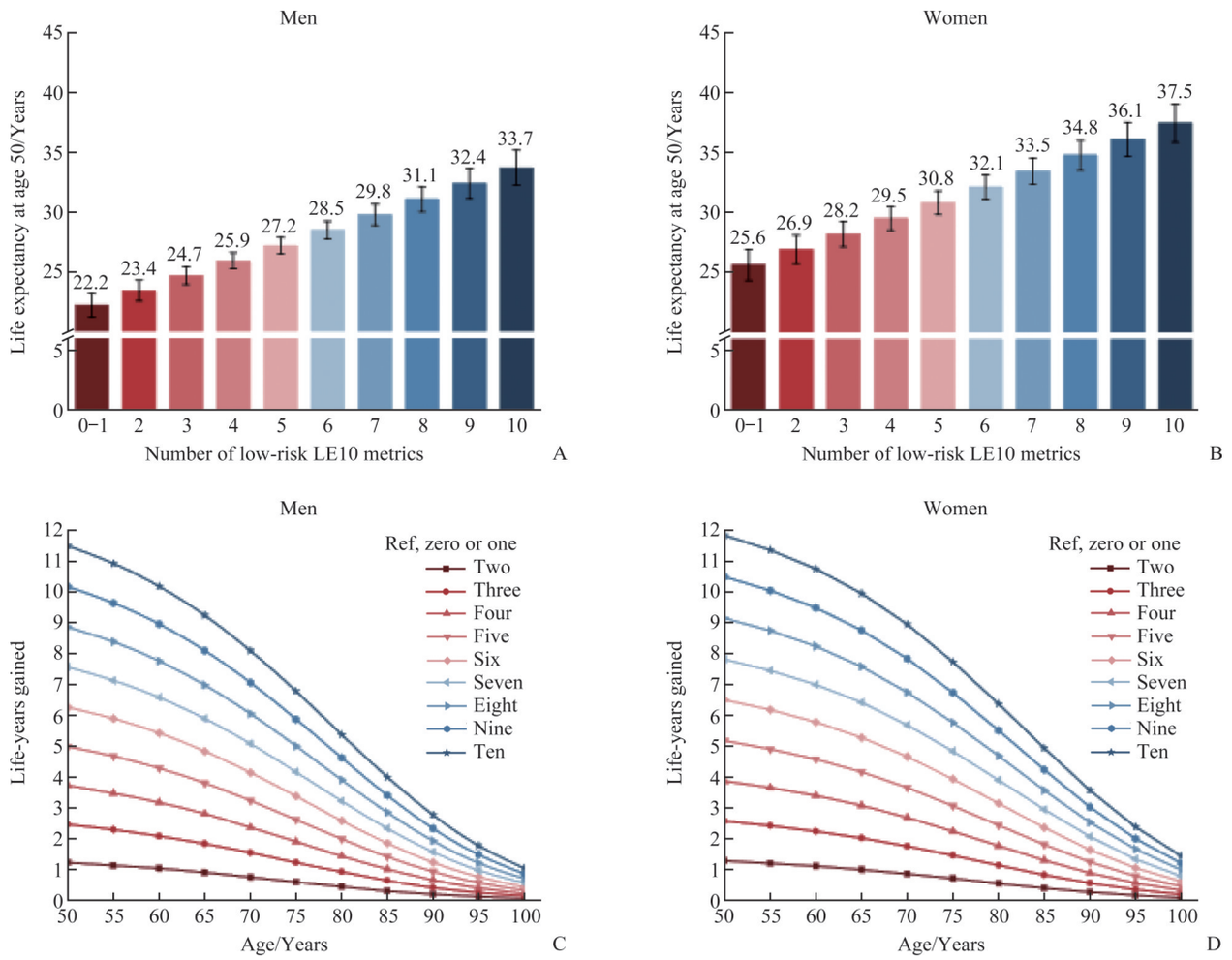


Figure 3 Life expectancy without and with stroke and/or dementia, and life-years gained across CVH levels and numbers of low-risk LE10 metrics

A and B: Estimated life expectancy free of stroke and dementia at age 50 by the number of low-risk LE10 metrics in men (A) and women (B). C and D: Life-years gained free of stroke and dementia compared with participants with 0−1 low-risk metrics in men (C) and women (D). Curves represent incremental gains in disease-free life expectancy associated with achieving a greater number of low-risk metrics. Low-risk CVH metrics were defined as: Physical activity score ≥80; smoke score ≥80; healthy diet score ≥80; sleep score ≥80; body mass index score ≥70; blood lipid score ≥60; blood glucose score ≥60; blood pressure score ≥75; alcohol consumption score ≥90; sedentary score ≥80. Estimates are based on multistate life table.

3 Discussion

This study developed the LE10-based CVH by incorporating sedentary behavior and alcohol consumption into the LE8 framework. To the best of our knowledge, this is the first study to demonstrate that a higher LE10 score is associated with more favorable brain health outcomes.

A growing body of research has independently linked CVH to increased lifespan[27-28], reduced risk of stroke[10], and lower incidence of dementia[29]. In this study, we found that individuals with optimal CVH profiles not only lived significantly longer but also experienced delayed onset of stroke and dementia compared with those with suboptimal CVH. The results of this study showed that higher CVH was inversely associated with the risk of stroke incidence, dementia incidence, and composite incidence of stroke or dementia. These consistent findings suggest that the association observed for the composite outcome was unlikely to be driven solely by either stroke or dementia, but may reflect a broader and relatively consistent

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relationship between optimal CVH and reduced risk of brain health-related adverse outcomes. These results underscore the clinical importance of evaluating and managing CVH and extend its implications for promoting healthy aging and preserving brain health.

Previous evidence[30-31] demonstrated higher CVH, as measured by LE8, is associated with a reduced risk of noncommunicable diseases. However, LE8 does not account for alcohol consumption or sedentary behavior, despite both being evidence-based predictors of stroke and dementia. LE10 addresses this gap and aligns with international guidelines, including the AHA's 2024 guideline for the primary prevention of stroke[15] and 2024 report of the Lancet standing commission for dementia prevention[7], which emphasize achieving core CVH metrics and reducing alcohol intake and sedentary behavior. Moderate to high alcohol consumption is associated with a higher risk of stroke and dementia[32-33]. Furthermore, sedentary time is associated with a 44.0% greater incidence of stroke and greater dementia risk, especially when total sedentary time exceeds 10 hours per day[13, 34]. In our study, both alcohol consumption and sedentary time were associated with the composite incidence of stroke or dementia, and with longer life expectancy. SHAP analysis confirmed their significant contributions (Supplementary Figure 24, https://doi.org/10.57760/sciencedb.xbyxb.00134).

The inclusion of alcohol consumption and sedentary behavior in the LE10 framework is strongly supported by well-established biological and molecular mechanisms linking these risk factors to stroke, dementia, and reduced life expectancy. Excessive alcohol intake contributes to cerebrovascular pathology through multiple pathways, including sustained hypertension, dysregulated lipid metabolism, chronic systemic inflammation, and endothelial dysfunction[35-36]. These alterations not only increase stroke risk but also promote neurotoxicity, white matter degradation, and cortical atrophy, accelerating cognitive decline and dementia onset[37-38]. Similarly, heightened sedentary behavior induces adverse physiological changes such as insulin resistance, disrupted glucose homeostasis, elevated inflammatory cytokine production, and impaired cerebral perfusion[39]. These factors synergistically promote vascular injury and neurodegeneration, contributing to both increased stroke susceptibility and progressive cognitive impairment[40].

Although the incremental improvement in predictive discrimination (i.e., the C-index) from LE8 to LE10 observed in our study was modest, this reflects a well-recognized phenomenon in epidemiological modeling: It is methodologically challenging to achieve large absolute increases in discrimination when adding variables to an already robust baseline model like LE8. Therefore, we emphasize that the primary clinical value of transitioning to LE10 lies in guiding holistic risk modification rather than purely enhancing risk prediction. By integrating alcohol consumption and sedentary behavior—both highly prevalent and modifiable independent risk factors for cardiovascular and brain health—LE10 provides a more comprehensive framework for primary prevention. Crucially, capturing these 2 additional metrics introduces negligible operational or financial burden to the healthcare system. Unlike physiological biomarkers, they require no laboratory tests, physical examinations, or specialized equipment, and can be efficiently assessed through routine verbal inquiries or simple self-reported questionnaires during standard clinical encounters. Consequently, LE10 facilitates more integrated and streamlined behavioral counseling in primary care without adding practical complexity.

Nevertheless, several limitations merit consideration. First, despite our adjustment for multiple confounders and the consistent findings from the 2-year landmark analysis, residual confounding (e. g., unmeasured socioeconomic trajectory or psychosocial stress) and reverse causality remain plausible alternative explanations that cannot be entirely excluded. Second, individuals with high CVH may differ in other health-related or socioeconomic attributes, which potentially introduces residual confounding. Third, CVH metrics and lifestyle factors were measured exclusively at baseline. Given the dynamic nature of lifestyle behaviors, our inability to account for longitudinal changes over the follow-up period is a notable limitation. Such reliance on baseline data may lead to non-differential misclassification, which typically biases the results toward the null and potentially attenuates the true strength of the observed associations. Future studies incorporating repeated measurements of CVH metrics and lifestyle behaviors are warranted to better capture

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their dynamic changes over time and to further refine the assessment of their associations with health outcomes. Fourth, the study cohort may not be fully representative of the general population. Because our sample was predominantly of European ancestry and generally healthier than average, the absolute life expectancy estimates may not generalize to more diverse or higher-risk populations. Future studies in diverse, multi-ethnic, and higher-risk cohorts are warranted to validate these findings and improve generalizability. Nonetheless, the relative comparisons between CVH categories should be internally valid. Fifth, *MyLifeEssential* online tool only serves as a theoretical derivation model based on a single cohort and is strictly intended as an academic demonstration platform rather than a mature tool for clinical medical decision-making. Future multi-center external validation studies are essential and planned before recommending its broader clinical application. Finally, assessments of lifestyle factors, particularly alcohol consumption and sedentary behavior, were self-reported in the UK Biobank and may be prone to measurement or reporting bias.

In conclusion, LE10 represents a novel tool for comprehensive CVH assessment. Higher LE10 CVH was strongly associated with lower risks of composite stroke or dementia, and reduced all-cause mortality, suggesting that improving CVH may serve as a practical clinical and public health strategy to prevent major chronic neurological diseases and to promote healthy longevity and brain health. Additionally, we developed *MyLifeEssential* online platform as a research demonstration and health education tool to visualize the associations of LE10 CVH with related health outcomes and life expectancy.

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Contributions: DU Yang Research design, data acquisition, analysis, and interpretation, paper writing and revision; YANG Feiran, YE Qing, Jeffrey W. Ripley-Gonzalez. HE Liwen, and GAO Siyao Data acquisition, analysis, and interpretation, paper writing and revision; LIU Fangkun, Ray W. Squires and Thomas P. Olson Research design and paper revision; WU Xinyin Research design and data analysis; DUN Yaoshan Research design, data acquisition, analysis, and interpretation, paper writing and revision, and funding acquisition; XIA Jian and LIU Suixin Research design, project administration. The final version of the manuscript has been approved and read by all authors.

Conflict of interest: The authors declare that they have no conflicts of interest to disclose.

Data availability statement: All data are available through application to the UK Biobank. The relevant code is accessible on GitHub (https://github.com/YSDun/LE10-for-stroke-and-dementia.git).

References

[1] Lazar RM, Howard VJ, Kernan WN, et al. A primary care agenda for brain health: a scientific statement from the American Heart Association[J/OL]. Stroke, 2021, 52(6): e295-e308[2026-04-01]. https://doi.org/10.1161/str.0000000000000367.

[2] Gorelick PB, Furie KL, Iadecola C, et al. Defining optimal brain health in adults: a presidential advisory from the American Heart Association/American Stroke Association [J/OL]. Stroke, 2017, 48(10): e284-e303[2026-04-01]. https://doi.org/10.1161/str.0000000000000148.

[3] Avan A, Hachinski V. Stroke and dementia, leading causes of neurological disability and death, potential for prevention[J]. Alzheimers Dement, 2021, 17(6): 1072-1076. https://doi.org/10.1002/alz.12340.

[4] GBD 2019 Dementia Forecasting Collaborators. Estimation of the global prevalence of dementia in 2019 and forecasted prevalence in 2050: an analysis for the Global Burden of Disease Study 2019[J/OL]. Lancet Public Health, 2022, 7(2): e105-e125[2026-04-01]. https://doi.org/10.1016/s2468-2667(21)00249-8.

[5] GBD 2019 Stroke Collaborators. Global, regional, and national burden of stroke and its risk factors, 1990—2019: a systematic analysis for the Global Burden of Disease Study 2019[J]. Lancet Neurol, 2021, 20(10): 795-820. https://doi.org/10.1016/S1474-4422(21)00252-0.

[6] Feigin VL, Owolabi MO, Feigin VL, et al. Pragmatic solutions to reduce the global burden of stroke: a World Stroke Organization-Lancet Neurology Commission[J]. Lancet Neurol, 2023, 22(12): 1160-1206. https://doi.org/10.1016/S1474-4422(23)00277-6.

[7] Livingston G, Huntley J, Liu KY, et al. Dementia prevention, intervention, and care: 2024 report of the Lancet standing Commission[J]. Lancet, 2024, 404(10452): 572-628. https://doi.org/10.1016/S0140-6736(24)01296-0.

[8] Lloyd-Jones DM, Allen NB, Anderson CAM, et al. Life's

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essential 8: updating and enhancing the American Heart Association's construct of cardiovascular health: a presidential advisory from the American Heart Association[J/OL]. Circulation, 2022, 146(5): e18-e43[2026-04-01]. https://doi.org/10.1161/cir.0000000000001078.

[9] Clocchiatti-Tuozzo S, Rivier CA, Renedo D, et al. Life's essential 8 and poor brain health outcomes in middle-aged adults[J/OL]. Neurology, 2024, 103(10): e209990[2026-04-01]. https://doi.org/10.1212/wnl.0000000000209990.

[10] Liu Y, Qin X, Jiang J, et al. Life's essential 8 trajectories and risk of stroke: a prospective cohort study[J]. Stroke, 2024, 55(11): 2611-2621. https://doi.org/10.1161/STROKEAHA.124.046352.

[11] Dai Y, Liu Y, Pan Y, et al. Associations of cardiovascular health assessed by life's crucial 9 with incident cardiovascular disease and dementia: a prospective cohort study[J]. J Prev Alzheimers Dis, 2025, 12(8): 100273. https://doi.org/10.1016/j.tjpad.2025.100273.

[12] Wang X, Ma H, Li X, et al. Association of cardiovascular health with life expectancy free of cardiovascular disease, diabetes, cancer, and dementia in UK adults[J]. JAMA Intern Med, 2023, 183(4): 340-349. https://doi.org/10.1001/jamainternmed.2023.0015.

[13] Raichlen DA, Aslan DH, Sayre MK, et al. Sedentary behavior and incident dementia among older adults[J]. JAMA, 2023, 330(10): 934. https://doi.org/10.1001/jama.2023.15231.

[14] Popa-Wagner A, Dumitrascu DI, Capitanescu B, et al. Dietary habits, lifestyle factors and neurodegenerative diseases[J]. Neural Regen Res, 2020, 15(3): 394-400. https://doi.org/10.4103/1673-5374.266045.

[15] Bushnell C, Kernan WN, Sharrief AZ, et al. 2024 guideline for the primary prevention of stroke: a guideline from the American heart association/American stroke association[J/OL]. Stroke, 2024, 55(12): e344-e424[2026-04-01]. https://doi.org/10.1161/str.0000000000000475.

[16] Palmer LJ. UK Biobank: bank on it[J]. Lancet, 2007, 369(9578): 1980-1982. https://doi.org/10.1016/S0140-6736(07)60924-6.

[17] Sudlow C, Gallacher J, Allen N, et al. UK biobank: an open access resource for identifying the causes of a wide range of complex diseases of middle and old age[J/OL]. PLoS Med, 2015, 12(3): e1001779[2026-04-01]. https://doi.org/10.1371/journal.pmed.1001779.

[18] Wood AM, Kaptoge S, Butterworth AS, et al. Risk thresholds for alcohol consumption: combined analysis of individual-participant data for 599 912 current drinkers in 83 prospective studies[J]. Lancet, 2018, 391(10129): 1513-1523. https://doi.org/10.1016/S0140-6736(18)30134-X.

[19] Karimi R, Mallah N, Nedjat S, et al. Association between alcohol consumption and chronic pain: a systematic review and meta-analysis[J]. Br J Anaesth, 2022, 129(3): 355-365. https://doi.org/10.1016/j.bja.2022.03.010.

[20] Joensuu L, Koivunen K, Tynkkynen NP, et al. Genetic liability to sedentary behaviour and cardiovascular disease incidence in the FinnGen and HUNT cohorts[J]. Br J Sports Med, 2025, 59(11): 783-790. https://doi.org/10.1136/bjsports-2024-109491.

[21] Zhang J, Chen G, Habudele Z, et al. Relation of Life's Essential 8 to the genetic predisposition for cardiovascular outcomes and all-cause mortality: results from a national prospective cohort[J]. Eur J Prev Cardiol, 2023, 30(15): 1676-1685. https://doi.org/10.1093/eurjpc/zwad179.

[22] Knol MJ, VanderWeele TJ, Groenwold RH, et al. Estimating measures of interaction on an additive scale for preventive exposures[J]. Eur J Epidemiol, 2011, 26(6): 433-438. https://doi.org/10.1007/s10654-011-9554-9.

[23] Dhana K, Franco OH, Ritz EM, et al. Healthy lifestyle and life expectancy with and without Alzheimer's dementia: population based cohort study[J/OL]. BMJ, 2022, 377: e068390[2026-04-01]. https://doi.org/10.1136/bmj-2021-068390.

[24] van den Hout A, Sum Chan M, Matthews F. Estimation of life expectancies using continuous-time multi-state models[J]. Comput Meth Programs Biomed, 2019, 178: 11-18. https://doi.org/10.1016/j.cmpb.2019.06.004.

[25] White IR, Royston P, Wood AM. Multiple imputation using chained equations: Issues and guidance for practice[J]. Stat Med, 2011, 30(4): 377-399. https://doi.org/10.1002/sim.4067.

[26] Feng H, Yang L, Ai S, et al. Association between accelerometer-measured amplitude of rest-activity rhythm and future health risk: a prospective cohort study of the UK Biobank[J/OL]. Lancet Healthy Longev, 2023, 4(5): e200-e210[2026-04-01]. https://doi.org/10.1016/S2666-7568(23)00056-9.

[27] Ma H, Wang X, Xue Q, et al. Cardiovascular health and life expectancy among adults in the United States[J]. Circulation, 2023, 147(15): 1137-1146. https://doi.org/10.1161/CIRCULATIONAHA.122.062457.

[28] Xu C, Zhang P, Cao Z. Cardiovascular health and healthy longevity in people with and without cardiometabolic disease: a prospective cohort study[J]. eClinicalMedicine, 2022, 45: 101329. https://doi.org/10.1016/j.eclinm.2022.101329.

[29] Beydoun HA, Beydoun MA, Meirelles O, et al. Cardiovascular health, infection burden, and incident dementia in the UK Biobank[J]. Alzheimers Dement, 2023, 19(10): 4475-4487. https://doi.org/10.1002/alz.13405.

[30] Prugger C, Perier MC, Sabia S, et al. Association between changes in cardiovascular health and the risk of multimorbidity: community-based cohort studies in the UK and Finland[J]. Lancet Reg Health Eur, 2024, 42: 100922. https://doi.org/10.1016/j.lanepe.2024.100922.

[31] Walker J, Won D, Guo J, et al. Cumulative Life's Essential 8 scores and cardiovascular disease risk[J]. JAMA Cardiol, 2025, 10(7): 649. https://doi.org/10.1001/jamacardio.2025.0630.

[32] Smyth A, O'Donnell M, Rangarajan S, et al. Alcohol intake as a risk factor for acute stroke: the INTERSTROKE study[J/OL]. Neurology, 2023, 100(2): e142-e153[2026-04-01]. https://doi.org/10.1212/wnl.0000000000201388.

[33] Zheng L, Liao W, Luo S, et al. Association between alcohol consumption and incidence of dementia in current drinkers: linear and non-linear Mendelian randomization analysis[J].

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eClinicalMedicine, 2024, 76: 102810. https://doi.org/10.1016/j.eclinm.2024.102810.

[34] Hooker SP, Diaz KM, Blair SN, et al. Association of accelerometer-measured sedentary time and physical activity with risk of stroke among US adults[J/OL]. JAMA Netw Open, 2022, 5(6): e2215385[2026-04-01]. https://doi.org/10.1001/jamanetworkopen.2022.15385.

[35] Bukiya AN, Vaithianathan T, Kuntamallappanavar G, et al. Smooth muscle cholesterol enables BK β1 subunit-mediated channel inhibition and subsequent vasoconstriction evoked by alcohol[J]. Arterioscler Thromb Vasc Biol, 2011, 31(11): 2410-2423. https://doi.org/10.1161/atvbaha.111.233965.

[36] Muneer PMA, Alikunju S, Szlachetka AM, et al. The mechanisms of cerebral vascular dysfunction and neuroinflammation by MMP-mediated degradation of VEGFR-2 in alcohol ingestion[J]. Arterioscler Thromb Vasc Biol, 2012, 32(5): 1167-1177. https://doi.org/10.1161/atvbaha.112.247668.

[37] Rehm J, Hasan OSM, Black SE, et al. Alcohol use and dementia: a systematic scoping review[J]. Alzheimers Res Ther, 2019, 11(1): 1-11. https://doi.org/10.1186/s13195-018-0453-0.

[38] 尹晴, 杨利. 脑梗死相关认知障碍机制[J]. 中南大学学报(医学版), 2024, 49(10): 1692-1699. https://doi.org/10.11817/j.issn.1672-7347.2024.240213.
YIN Qing, YANG Li. Mechanisms of cognitive impairment associated with cerebral infarction[J]. Journal of Central South University. Medical Science, 2024, 49(10): 1692-1699. https://doi.org/10.11817/j.issn.1672-7347.2024.240213.

[39] Pinto AJ, Bergouignan A, Dempsey PC, et al. Physiology of sedentary behavior[J]. Physiol Rev, 2023, 103(4): 2561-2622. https://doi.org/10.1152/physrev.00022.2022.

[40] Dichgans M, Leys D. Vascular cognitive impairment[J]. Circ Res, 2017, 120(3): 573-591. https://doi.org/10.1161/circresaha.116.308426.

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