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The associations of cardiovascular health and all-cause mortality among individuals with depression

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The association between the recently updated cardiovascular health (CVH) assessment algorithm, the Life's Essential 8 (LE8), and all-cause mortality among adults with depression remains unknown. From the National Health and Nutrition Examination Survey (NHANES) spanning 2005–2018, a cohort of 2,935 individuals diagnosed with depression was identified. Their CVH was evaluated through the LE8 score system. The investigation of mortality status utilized connections with the National Death Index up to December 31, 2019. To assess the impact of CVH on mortality risk, Kaplan-Meier survival analysis and Cox proportional hazards models, adjusting for variables related to demographics and socioeconomic status, were applied. Among 2,935 participants, those with higher CVH levels had significantly lower all-cause mortality compared to those with lower CVH levels. Cox regression analyses demonstrated that each 1-point increase in CVH score was associated with a lower risk of all-cause mortality [HR = 0.97, 95%CI:0.96–0.98]. The inverse association between CVH and mortality persisted across different demographic and socioeconomic subgroups. Higher CVH levels were associated with a significantly lower risk of all-cause mortality in individuals with depression. These findings underscore the importance of comprehensive CVH management as part of healthcare strategies for people with depression, suggesting that improving CVH may contribute to longer life expectancy in this vulnerable population.

Keywords Depression, Cardiovascular health, Life's essential 8, Mortality, PHQ-9

Abbreviations

AHA	American Heart Association
BMI	Body mass index
CVH	Cardiovasculardisease
DASH	Dietary Approaches to Stop Hypertension
LE8	Life's Essential 8
LS7	Lifes Simple 7
NCHS	National Center for Health Statistics
NHANES	National Health and Nutrition Examination Survey
non-HDL	Non high density lipoprotein
PHQ 9	Patient Health Questionnaire9
RCS	Restricted cubic spline
SD	Standard deviation
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology

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Background

Depression, characterized by persistent sadness, lack of interest, and a variety of emotional and physical issues, significantly reduces quality of life and increases the risk of various health complications, including mortality[1–3]. As the understanding of mental health's profound impact on overall health outcomes deepens, there is an urgent need to explore how managing concurrent health factors might affect the life quality and longevity of individuals with depression[4].

Improving Cardiovascular Health (CVH) has emerged as a key strategy for enhancing survival and quality of life among vulnerable populations, including those with mental health conditions such as depression[5]. Evidence indicates a clear relationship between modifiable lifestyle factors—such as diet, physical activity, smoking, and alcohol consumption—and cardiovascular disease risk[6–9]. Effective management of these factors offers significant potential for mitigating the cardiovascular risks associated with depression, highlighting the importance of a multifaceted approach to health risk management in individuals with depression[10].

The American Heart Association (AHA) has played a crucial role in defining and promoting CVH through initiatives such as "Life's Simple 7" (LS7) and more recently, "Life's Essential 8" (LE8). These frameworks classify key lifestyle and health metrics, including diet, exercise, exposure to tobacco/nicotine, sleep quality, body mass index (BMI), blood lipids, blood glucose, and blood pressure[11]. For individuals with depression, integrating comprehensive CVH management strategies, including the LE8 criteria, may offer a pathway to significantly improve health outcomes[12,13]. Notably, individuals with depression often experience under-recognition or undertreatment of their cardiovascular needs compared to those without depression[14,15]. This may stem from various factors, such as inadequate screening of cardiovascular risk factors during mental health appointments, reduced adherence to treatment plans due to depressive symptoms, or diminished access to preventive care. Such gaps in care can heighten the risk for adverse cardiovascular outcomes, underscoring the importance of a holistic approach that simultaneously addresses mental health and cardiovascular risk management[16,17]. Individuals with depression are at an increased risk of developing cardiovascular diseases due to factors such as inflammation, autonomic dysfunction, and unhealthy lifestyle behaviors commonly associated with depression[18,19]. Despite the known benefits of optimal CVH in reducing mortality risk in the general population, it remains unclear whether these benefits extend to individuals with depression, who may face unique challenges in managing their health. Addressing this gap is crucial because tailored interventions that improve CVH could potentially mitigate the elevated mortality risk observed in this vulnerable group. Emerging evidence has illustrated the inverse association between CVH and depression, underscoring the importance of managing CVH levels in individuals with depression[20,21]. However, current research predominantly consists of cross-sectional studies that have established an association between CVH and the prevalence of depression, leaving a gap in understanding whether controlling CVH levels could reduce all-cause mortality rates among individuals with depression. Therefore, investigating the prospective relationship between CVH and mortality in individuals with depression is essential to inform integrated healthcare strategies that could enhance both mental and physical health outcomes.

The objective of the present study is to utilize the LE8 score, defined by a comprehensive strategy, to measure CVH and data from the National Health and Nutrition Examination Survey (NHANES), to investigate whether CVH is associated with all-cause mortality among individuals with depression and if it can be employed as a method for managing and controlling mortality rates in daily life.

Methods

Study population

Initiated by the National Center for Health Statistics (NCHS), the NHANES serves as a nationally representative study aimed at assessing the health and nutrition of American residents[22]. NHANES employs a complex, multistage probability sampling design to select participants who are representative of the civilian, non-institutionalized U.S. population. This design includes stratification, clustering, and oversampling of certain subgroups (e.g., persons aged 60 and over, African Americans, Hispanics) to ensure adequate representation and improve the reliability and precision of estimates for these groups[23]. The NHANES website offers detailed descriptions of its design and methodologies. This study utilizes data spanning from 2005 to 2018 from NHANES, along with additional insights from the NHANES Linked Mortality File, which connects participant data to the National Death Index until the end of 2019. Exclusion criteria were: (1) 297 participants with missing mortality data; (2) 2,947 participants not in 20–80 years old age range; (3) 803 individuals pregnant or breastfeeding; (4) 26,441 participants without depression or missing data on depression. Ultimately, the study incorporated 2,935 participants for analysis (Fig. 1). Written informed consent was obtained from all individuals involved, ensuring the research complied with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for reporting.

Depression

The Patient Health Questionnaire-9 (PHQ-9), an established tool with nine items, evaluates the severity of depression using a scale from 0 (none) to 3 (nearly every day), allowing for a cumulative score between 0 and 27[24]. Achieving a score of 10 or more on the PHQ-9 signals the presence of depressive symptoms[25]. Depression intensity is classified into moderate (scores of 10–14) and moderately severe to severe (scores of 15 or higher) categories[25].

Cardiovascular Health

The LE8 scoring system is a complex algorithm for measuring CVH, which integrates eight key components: dietary patterns, exercise intensity, smoking, sleep quality, BMI, non-HDL cholesterol, blood glucose levels,
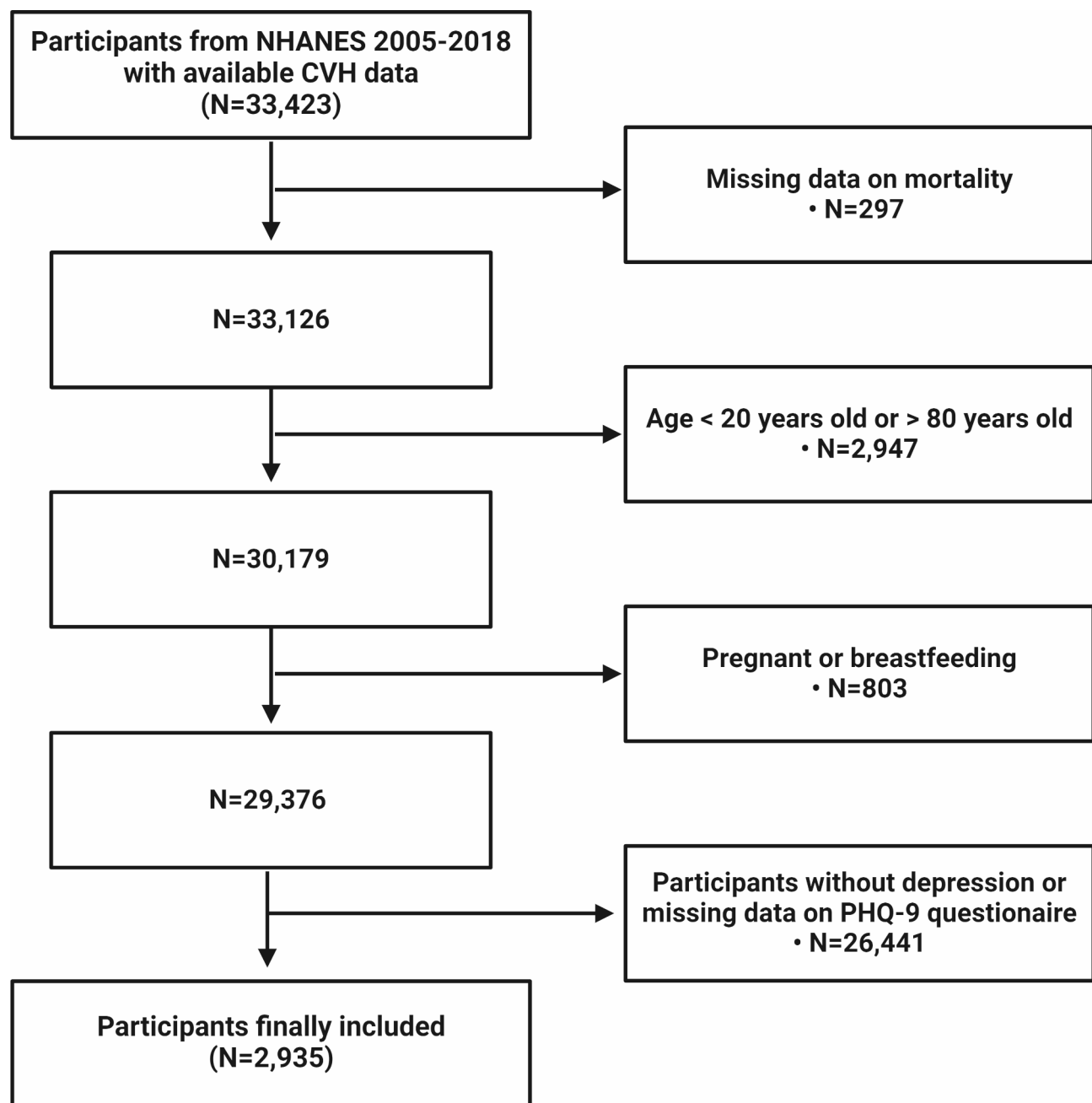
Fig. 1. Flow Chart of Participant Selection. NHANES, National Health and Nutrition Examination Survey; PHQ-9, Patient Health Questionnaire-9; CVH, Cardiovascular Health. This flow chart summarizes the inclusion and exclusion criteria leading to a final sample of participants with depression (PHQ-9 ≥ 10) who had complete data for mortality follow-up, key demographic/socioeconomic information, and LE8 cardiovascular health metrics.

and blood pressure. Extensive information on scoring for CVH factors is available in Table S1 and referenced articles[12,26,27]. Individual CVH factors are scored on a 0 to 100 scale, with the overall CVH score being the average of these eight scores. The American Heart Association defines CVH levels as high (80–100), moderate (50–79), and low (0–49) based on these scores[11].

Outcome definition
Data from the NHANES were aligned with records from the National Death Index up to December 31, 2019, using a probabilistic algorithm to verify mortality status. The causes of death were identified according to the International Classification of Diseases, Tenth Revision. All-cause mortality encompassed deaths from any cause. As mortality data were obtained through this linkage, loss to follow-up regarding mortality status was minimized, ensuring comprehensive outcome data for the participants included in our analysis[28].

Covariates

Similar to previous studies, since most of the important covariate information is already included in the calculation of the CVH, among the covariates we mainly included demographically relevant covariates[12,26,28]. Information on demography including age, sex, race, family income to poverty ratio (PIR), educational level were collected through standard survey.

Statistical analysis

The proportion of missing data for variables used in the statistical models ranged from 0 to 21.3%. Missing data were addressed using the random forest imputation method via the 'missForest' package in R[29], which is suitable for handling mixed-type data and has been shown to perform well in various scenarios[30]. This method allows for the estimation of missing values based on observed data without substantially biasing the results. CVH was classified into low (< 50), moderate (50–79), and high (80–100) according to the LE8 score methods (**Table S1**). Kaplan-Meier survival plots quantified the overall mortality for each CVH group (low, moderate, high). Cox regression models were deployed to investigate the association between CVH and mortality from all causes. Three models were utilized as follows: Model 1 was unadjusted for covariates; Model 2 was including age, sex, and race; Model 3 further augmented Model 2 by integrating socioeconomic factors (education level and PIR) and total PHQ-9 score. Subgroup analyses and tests for interaction examined the consistency of the association between CVH and mortality across diverse groups, including sex (male/female), age (< 60/≥60 years), family income to poverty ratio (PIR; <1.3, 1.3–3.0, > 3.0), education level (less than high school, high school, more than high school) and depression severity (moderate: PHQ-9 scores of 10–14; moderately severe to severe: PHQ-9 scores of ≥ 15). A restricted cubic spline (RCS) analysis was performed to explore the dose-response relationship between CVH and all-cause mortality[31]. These statistical analyses were executed in R (version 4.3.0), using two-tailed tests, with a significance threshold set at P values < 0.05.

Results

Table 1 demonstrates the baseline characteristics of the 2,935 individuals diagnosed with depression (57.27% moderate, 42.73% moderately severe to severe) classified according to the level of CVH, with 38.40% of the participants having a low level of CVH, 56.01% of the participants having a moderate level of CVH and only 5.59% of the participants reaching a high level of CVH. Individuals with higher levels of CVH tended to be younger, female, have higher socioeconomic status (educational level and PIR), and lower PHQ-9 scores.

Over the course of a median follow-up period of 7.4 years (range: 4.1–10.7 years), 330 participants (11.24%) with depression were recorded to have died. Participants with depression at high CVH levels had significantly lower all-cause mortality than participants with depression at lower CVH levels (Fig. 2). Table 2 demonstrates the correlation between CVH and all-cause mortality among participants with depression. In model not adjusted for any covariates, each unit increase in CVH in participants with depression was associated with a 3% lower risk of all-cause mortality [HR = 0.97, 95%CI:0.96–0.98]. Moderate and high CVH levels were associated with a 48% [HR = 0.52, 95%CI:0.39–0.70] and 78% [HR = 0.22, 95%CI:0.08–0.65] lower risk of mortality risk, respectively, when compared to low CVH levels. This inverse association remained significant after adjusting for demographic and socioeconomic status variables. After adjusting for all covariates, each unit increase in CVH among participants with depression was correlated with a 3% **lower** mortality risk [HR = 0.97, 95%CI:0.96–0.98]. Participants with moderate levels of CVH and participants with high levels of CVH had a 37% [HR = 0.63, 95%CI:0.46–0.87] and 63% [HR = 0.37, 95%CI:0.11–1.10] **lower** mortality risk, respectively, compared to those with the bottom CVH group, although this inverse association was not statistically significant among participants with high levels of CVH, which was likely due to the small number of participants with high levels of CVH who recorded a death (n = 5), and the test for trend remained significant (P for trend < 0.001). Figure 3 shows that the total CVH score is linearly associated with all-cause mortality risk, with a nonlinearity P-value of 0.866, suggesting that as the total CVH score increased, the all-cause risk decreased linearly.

To verify whether the association between CVH and all-cause mortality is robust in different populations with depression, subgroup analyses based on sex, age, education level, PIR and depression severity differences were investigated (Fig. 4). The results showed that the inverse association between CVH and all-cause mortality remained significant in all subgroups (all P for interaction > 0.05).

Discussion

In this prospective study involving 2,935 nationally representative participants with depression, we found an inverse association between CVH and all-cause mortality after adjusting for all covariates. Our findings suggest that maintaining optimal CVH may be associated with a lower mortality risk among individuals with depression. This provides prospective evidence supporting the importance of managing cardiovascular health to potentially extend life expectancy in this population. These results emphasize the need for an integrated healthcare approach that combines mental health management with cardiovascular disease prevention and intervention strategies.

Based on the NHANES sample of U.S. adults, three recent cross-sectional studies have investigated the association between CVH levels and the prevalence of depression in the general U.S. adult population[20,21,32]. The results of Shen et al. demonstrated a significant inverse non-linear association between CVH, as measured by the LE8 score, and depression, which remained stable across subgroups, with participants with high levels of CVH (80–100) serving as a reference, and participants with low levels of CVH (0–49) having an OR of 4.71 for depression prevalence[20]. Similar inverse associations were observed in the other two studies, although due to the differences in sample size and study methodology effect values[21,32]. However, these studies could not establish temporal relationships due to their cross-sectional design. Our results contribute prospective evidence on the association between higher levels of CVH and lower mortality in individuals with depression. This suggests that

Characteristics	Low (LE8 < 50)	Moderate(50 ≤ LE8 < 80)	High (LE8 ≥ 80)	P-value
No. of participants in sample	1127	1644	164	
Age, y (SD)	52.13 ± 13.38	46.63 ± 15.83	37.26 ± 13.95	< 0.001
Sex, %				
Male	38.95	38.50	33.54	
Female	61.05	61.50	66.46	
Race/ethnicity, %				< 0.001
Mexican American	12.07	17.52	17.07	
Others	10.20	14.60	10.37	
Non-Hispanic White	48.54	38.93	42.07	
Non-Hispanic Black	23.43	20.38	15.24	
Other Hispanic	5.77	8.58	15.24	
PIR	1.49 ± 1.15	1.77 ± 1.39	2.56 ± 1.65	< 0.001
Education level, %				< 0.001
Less than high school	39.04	33.11	14.63	
High school	26.71	23.37	20.12	
More than high school	34.25	43.52	65.24	
PHQ-9 score	15.29 ± 5.30	14.81 ± 5.57	13.77 ± 4.05	< 0.001
Severity of depression, %				0.013
Moderate	54.13	58.82	63.41	
Severe	45.87	41.18	36.59	
AHA LE8 score (SD)				
Mean total CVH score	39.85 ± 7.32	61.54 ± 7.90	86.01 ± 4.89	< 0.001
Mean DASH diet score	25.68 ± 26.30	41.16 ± 30.96	65.46 ± 30.69	< 0.001
Mean physical activity score	6.68 ± 22.40	35.23 ± 44.39	85.91 ± 29.24	< 0.001
Mean tobacco/nicotine exposure score	40.02 ± 38.35	58.97 ± 40.22	88.99 ± 22.55	< 0.001
Mean sleep health score	56.84 ± 33.34	74.27 ± 29.28	87.56 ± 19.91	< 0.001
Mean body mass index score	34.55 ± 30.98	59.16 ± 34.64	84.97 ± 21.27	< 0.001
Mean blood lipid score	46.18 ± 29.99	69.09 ± 29.55	87.68 ± 19.24	< 0.001
Mean blood glucose score	62.20 ± 31.57	84.39 ± 24.70	97.20 ± 11.91	< 0.001
Mean blood pressure score	46.63 ± 31.46	70.10 ± 31.18	90.34 ± 17.52	< 0.001

Table 1. Baseline characteristics of participants with CVH categories from LE8 score. Mean (SD) for continuous variables: The *P* value was calculated by the weighted linear regression model. Percentages for categorical variables: The *P* value was calculated by the weighted chi-square test. CVH is categorized into 3 grades, low: LE8 score < 50, moderate:50 ≤ LE8 score < 80, high: LE8 score ≥ 80. Abbreviation: AHA, American Heart Association; LE8, Life's Essential 8; CVH, cardiovascular health; DASH, Dietary Approaches to Stop Hypertension; PHQ-9, Patient Health Questionnaire-9; PIR, The ration of family income to poverty.

interventions aimed at improving CVH could have significant implications for reducing mortality in this group. From a clinical perspective, integrating CVH improvement strategies into mental health care could enhance overall health outcomes. For example, encouraging physical activity, healthy dietary habits, and smoking cessation not only benefits cardiovascular health but may also alleviate depressive symptoms[33–36]. Moreover, our findings have important public health implications. Given the high prevalence of depression and its substantial impact on morbidity and mortality, public health initiatives that promote CVH could play a crucial role in improving life expectancy and quality of life for individuals with depression. Future research should focus on developing and testing integrated intervention programs that address both mental health and cardiovascular risk factors.

Such an integrated approach has also been applied to populations with other chronic conditions. Studies have investigated the association between CVH and all-cause mortality in participants with diabetes and cancer, finding that higher CVH levels are linked with reduced mortality risk[37–39]. In addition, evidence from 341,331 participants in UK Biobank also suggests that high levels of CVH are linked with a lower risk of premature death and longer life expectancy[40].

Importantly, integrating mental health and cardiovascular care may create a "virtuous cycle" wherein improvements in one domain facilitate gains in the other[41,42]. For instance, effective depression management can foster increased motivation for healthy behaviors—such as regular physical activity, balanced nutrition, and consistent medication adherence—that in turn enhance CVH. Meanwhile, better cardiovascular health may help stabilize mood and potentially reduce the physiological stress responses that exacerbate depressive symptoms[17]. Collaborative or stepped-care interventions focusing on both mental health and cardiovascular risk factors have demonstrated promising results, highlighting the potential synergy of combined treatment approaches[43]. Such interventions could not only lower the elevated mortality risk among individuals with depression but also
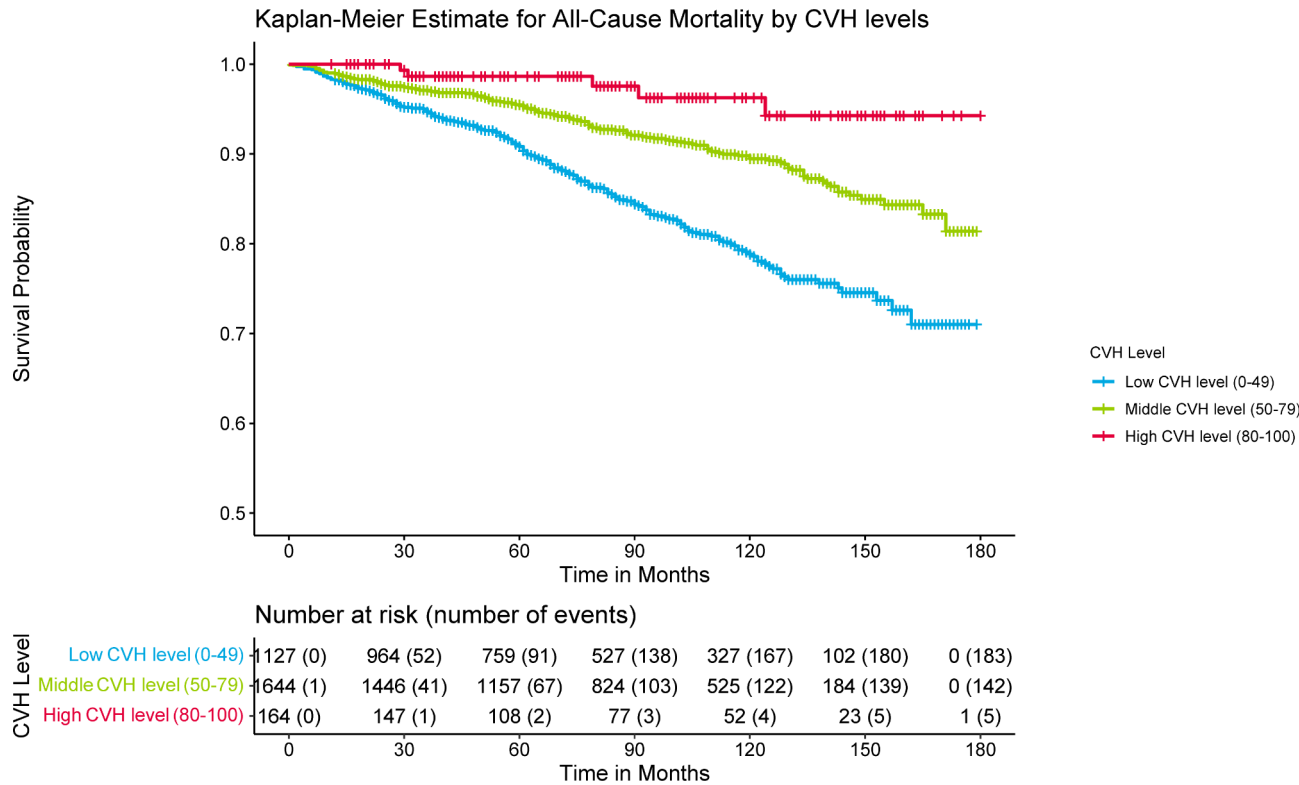
Fig. 2. Kaplan–Meier Curves for All-Cause Mortality by CVH Level. CVH, Cardiovascular Health; LE8, Life's Essential 8; HR, Hazard Ratio.CVH levels were defined as low (0 49), middle (50 79), and high (80 100) based on LE8 scoring. Eachcurve represents all cause mortality among participants categorized by CVH level.

Variables	Model 1 [HR (95% CI), P]	Model 2 [HR (95% CI), P]	Model 3 [HR (95% CI), P]
Total CVH score	0.97 (0.96, 0.98) < 0.001	0.98 (0.97, 0.99) < 0.001	0.97 (0.96, 0.98) < 0.001
CVH categories			
Low (LE8 < 50)	Ref.	Ref.	Ref.
Moderate (50 ≤ LE8 < 80)	0.52 (0.39, 0.70) < 0.001	0.66 (0.49, 0.90) 0.008	0.63 (0.46, 0.87) 0.001
High (LE8 ≥ 80)	0.22 (0.08, 0.65) 0.006	0.40 (0.14, 1.17) 0.095	0.37 (0.11, 1.10) 0.072
P for trend	< 0.001	< 0.001	< 0.001

Table 2. The associations between the life's essential 8 Cardiovascular Health (CVH) score and all-cause mortality among individuals with depression. Model 1 was unadjusted for covariates; Model 2 enhanced Model 1 by including age and race; and Model 3 further augmented Model 2 by integrating education level, family income-to-poverty ratio and PHQ-9 symptom scores. Abbreviation: CVH, cardiovascular health; DASH, Dietary Approaches to Stop Hypertension. *Tests for linear trends across three categories of cardiovascular health metrics scores were performed by modeling the median value within each category as a continuous variable.

improve their overall quality of life, underscoring the critical need for continued research and policy initiatives aimed at developing and disseminating integrated care models.

The level of CVH assessed by LE8 as a combined strategy (healthy behavioral lifestyle and biophenotyping) is what gives it its strengths over other metrics and is key to understanding the replication mechanism by which maintaining higher levels of CVH in individuals with depression reduces the risk of death. The quality of dietary intake, which is part of the assessment of CVH, has not only been linked to cardiovascular risk, but has also been shown to be an important factor in the management of stress and the maintenance of mental health[44,45]. Physical activity is closely related to brain structure and may activate brain function as well as improve cardiorespiratory fitness in depressed patients, thereby reducing cardiovascular risk[46]. Smoking, a traditional risk factor for cardiovascular disease, has also been suggested to increase susceptibility to depression and anxiety[47]. Alcohol abuse is also an important risk factor for cardiovascular and depression, and a multi-cohort study based in four European countries has shown that alcohol abuse is an important cause of reduced life expectancy in
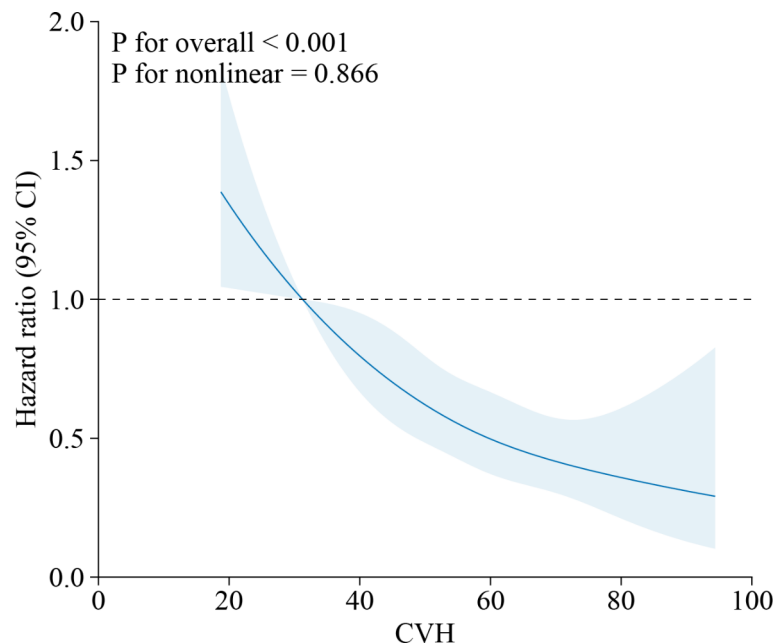
Fig. 3. Dose–Response Relationship Between Total LE8 Scores and All-Cause Mortality. CVH, Cardiovascular Health; PHQ 9, Patient Health Questionnaire 9; CI, Confidence Interval. The solid line represents the estimated hazard ratio for all cause mortality with res tricted cubic splinemodeling, and the shaded region indicates the 95% CI. The model is adjusted for age, sex, race, education level,PIR, and PHQ 9 total scores.

depressed patients[48]. Sleep disorders have long been recognized as a complication of depression, with several longitudinal studies demonstrating that sleep disorders are associated with higher cardiovascular risk as well as all-cause mortality[49,50]. Unhealthy biological phenotypes such as obesity, hypertension, hyperlipidemia, and hyperglycemia are also important factors in depression and increased risk of death[51–54].

Strengths of our study include the use of nationally representative data to provide a comprehensive understanding of the association between CVH levels and all-cause mortality in individuals with depression. In addition, the LE8 score, as a comprehensive measure to evaluate CVH levels, provides a holistic view of cardiovascular health using multiple cardiovascular health indicators. We must also acknowledge some limitations of this study. First, the diagnosis of depression relies on self-report, which may introduce a potential participant selection bias. Another limitation is that we only investigated the association of CVH with all-cause mortality and not specific pre-existing deaths, due to the insufficient statistical size of 0 cardiovascular deaths among participants with high levels of CVH among approximately 3,000 participants with depression, which will need to be supplemented by larger prospective studies in the future. Finally, because CVH levels change over time, relying on a single measurement at baseline may not fully encapsulate the ongoing impact of CVH changes on health.

Conclusion

This study found that maintaining ideal CVH levels was associated with a lower risk of all-cause mortality among U.S. adults with depression. These findings suggest that managing CVH levels from the perspective of LE8 scores is important for maintaining health and prolonging life in individuals with depression. Larger prospective studies are essential to elucidate the association between CVH and different cause-specific deaths in populations with depression.
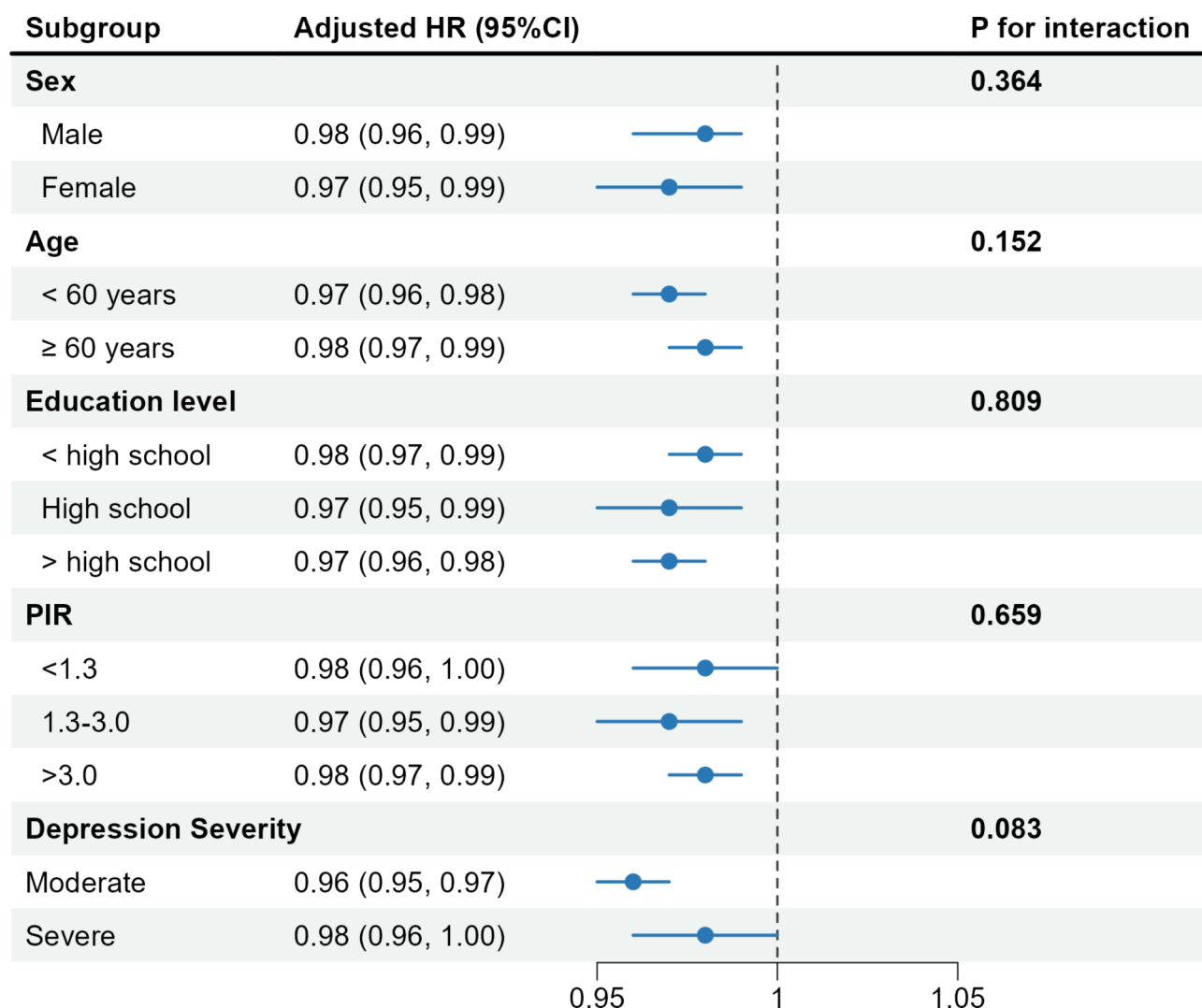
Subgroup	Adjusted HR (95%CI)		P for interaction
Sex			**0.364**
Male	0.98 (0.96, 0.99)		
Female	0.97 (0.95, 0.99)		
Age			**0.152**
< 60 years	0.97 (0.96, 0.98)		
≥ 60 years	0.98 (0.97, 0.99)		
Education level			**0.809**
< high school	0.98 (0.97, 0.99)		
High school	0.97 (0.95, 0.99)		
> high school	0.97 (0.96, 0.98)		
PIR			**0.659**
<1.3	0.98 (0.96, 1.00)		
1.3-3.0	0.97 (0.95, 0.99)		
>3.0	0.98 (0.97, 0.99)		
Depression Severity			**0.083**
Moderate	0.96 (0.95, 0.97)		
Severe	0.98 (0.96, 1.00)		

0.95   1   1.05

Fig. 4. Subgroup Analyses of the Association Between CVH and All-Cause Mortality. HR, Hazard Ratio; CI, Confidence Interval; PIR, Ratio of Family Income to Poverty; CVH,Cardiovascular Health.Subgroups were defined by sex (male/female), age (<60/≥60), education (<high school, high school, >highschool), PIR (<1.3, school), PIR (<1.3, 1.31.3−−3.0, >3.0) and depression severity (moderate/severe). Hazard ratios (95% CI) are from the 3.0, >3.0) and depression severity (moderate/severe). Hazard ratios (95% CI) are from the model adjusted for age, sex, race, education level, PIR, and PHQmodel adjusted for age, sex, race, education level, PIR, and PHQ--9 total scores. P9 total scores. P--values for interaction are shown values for interaction are shown on the right.on the right.

Data availability
NHANES data are publicly available at https://www.cdc.gov/nchs/nhanes/index.htm. We intend to provide rele vant code on written reasonable request.

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Competing interests
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