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Eight-year total, cognitive-affective, and somatic depressive symptoms trajectories and risks of cardiac events

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In this study, we analyzed pooled data from two prospective population-based cohorts—the Health Retirement Study (HRS) and the English Longitudinal Study of Ageing (ELSA)—to explore the association between trajectories of depressive symptoms and the risk of cardiac events. Depressive symptoms were assessed using the 8-item CES-D scale and categorized into somatic and cognitive-affective subtypes. Trajectories were tracked for four surveys from baseline. Heart disease was identified based on self-reported physician-diagnosed conditions. Hazard ratios and 95% confidence intervals were calculated with Cox proportional risk models that adjusted for potential confounders. In total, 17,787 subjects (59.7% female, median age 63 years) were enrolled at baseline. During a 10-year follow-up, 2409 cases of heart disease were identified. Participants with fluctuating (HR = 1.13, 95% CI: 1.06–1.20), increasing (HR = 1.43, 95% CI: 1.25–1.64), and consistently high (HR = 1.64, 95% CI: 1.45–1.84) depressive symptom trajectories exhibited an increased risk of heart disease compared to those with consistently low depressive symptoms, while a decreasing (HR = 1.07, 95% CI: 0.96–1.19) depressive symptom trajectory did not significantly affect the risk of heart disease. Moreover, the association between heart disease and somatic depressive symptoms was found to be stronger than with cognitive-affective symptoms. These findings suggest a significant link between depressive symptom trajectories and heart disease, with particular emphasis on stronger associations with somatic symptoms. It is recommended that the identification and management of depressive symptoms be incorporated into heart disease prevention strategies.

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INTRODUCTION

Heart disease remains the leading cause of death and disability worldwide [1]. Although the global risk of death from cardiovascular disease has shown a declining trend [2], the absolute number of deaths continues to rise due to population growth, aging, and increased life expectancy. Identification of risk factors for heart disease that are amenable to intervention is essential for the development of strategies to prevent heart disease and its associated morbidity. While many classical risk factors have been identified, such as smoking [3, 4], hypertension [5, 6], and abnormal cholesterol levels [7, 8], these do not fully explain the observed risk. Consequently, there is a growing interest in exploring additional modifiable factors, particularly psychological ones. Among these, depressive symptoms have been identified as a critical area of focus. Depressive symptoms are distinct from clinical depression, which is a mental disorder characterized by persistent low mood and loss of enjoyment that requires a clinical diagnosis. Depressive symptoms are a set of symptoms that may be associated with a depressive disorder but are not sufficient to constitute a complete clinical diagnosis and may significantly contribute to the risk of developing heart disease [9, 10].

This study focuses on depressive symptoms, which are dynamic and may fluctuate over time with varying patterns. However, the relationship between trajectories of change in depressive symptoms over time, such as increasing, fluctuating, and decreasing, and heart disease remains underexplored. Whether getting relief from depressive symptoms has the potential to reduce the risk of heart disease remains an area of uncertainty. Understanding these trajectories could reveal underlying mechanisms that associate depressive symptoms with heart disease, thereby improving causal inferences.

Moreover, depressive symptoms include both cognitive-affective and somatic dimensions [11]. However, the relative contribution of depressive symptoms' different dimensions to heart disease risk remains controversial. Some studies have reported that both somatic and cognitive-affective depressive symptoms are risk factors for cardiac disease progression [12–14], while others have shown that somatic depressive symptoms are more strongly correlated with cardiovascular events than cognitive-affective symptoms [15]. Somatic, but not cognitive-affective, depressive symptoms are associated with myocardial infarction severity and cardiovascular prognosis [16–18]. While these studies have deepened our understanding of how different dimensions of depressive symptoms affect heart disease, they have focused primarily on static analyses of different dimensions of depressive symptoms at a single point in time, and our study seeks to address this limitation by examining the dynamic trajectories of these different dimensions of depressive symptoms over time and their relationship to heart disease.

Utilizing data from the Health and Retirement Study (HRS) and the English Longitudinal Study on Ageing (ELSA), this study aims to

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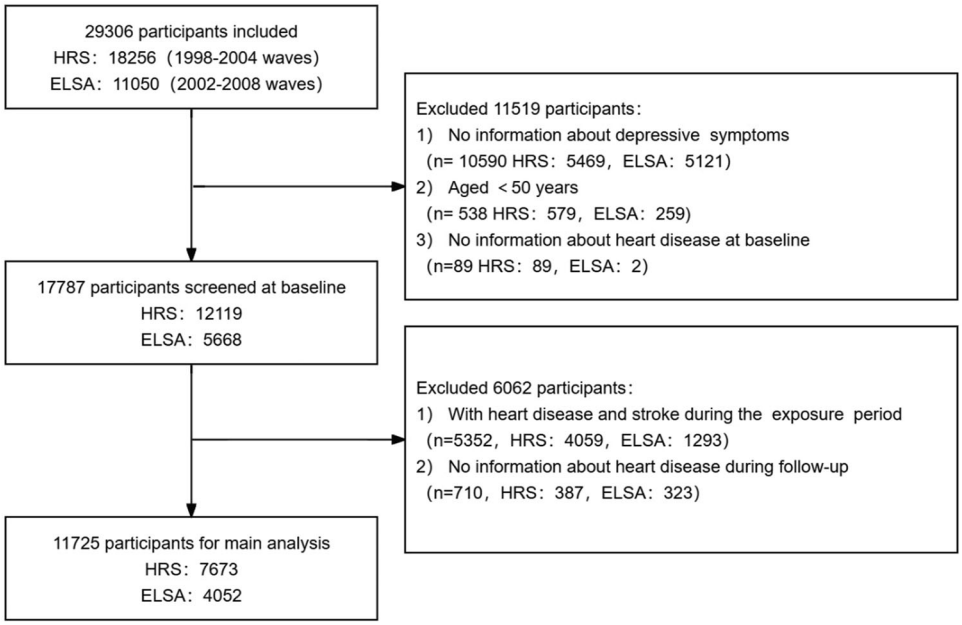

Fig. 1 Flow chart for the study population. The flowchart illustrates the inclusion and exclusion process for this study population.

provide the first estimates of the 8-year trajectories of total, cognitive-affective, and somatic depressive symptoms and their association with heart disease over a subsequent 10-year follow-up period. We hypothesize that individuals with high levels of depressive symptoms across multiple time points will be at greater risk for developing heart disease and that both cognitive-affective and somatic depressive symptom trajectories will be correlated with heart disease risk.

METHODS

Study population

The present study utilizes data from two important longitudinal datasets, the HRS and the ELSA, which are representative of the national aging population in the United States and the United Kingdom, respectively. Both datasets are based on adults over the age of 50 who are interviewed every two years using standardized questionnaires and similar measurement tools to assess economic, physical, and mental health aspects, thus establishing strong comparability between the two cohorts in terms of depressive symptoms and their trajectories over time, and in terms of assessments of heart disease.

We pooled data from waves 4 to 12 of the HRS (1998–2014), and waves 1 to 9 of the ELSA (2002–2018). Wave 4 in HRS (1998) and Wave 1 in ELSA (2002) were considered as baseline. The dynamic trajectory of depressive symptoms was assessed from these baseline points through the next three survey waves: up to Wave 7 for HRS and Wave 4 for ELSA. Subsequent surveys tracked heart disease outcomes until the final waves—Wave 12 for HRS and Wave 9 for ELSA.

Exclusion criteria for this analysis included (1) age less than 50 years, (2) lack of a complete trajectory of depressive symptoms during the exposure period, (3) presence of heart disease and stroke before and during the exposure period, and (4) missing information on heart disease during follow-up. Participants younger than 50 years were excluded to focus the analysis on an aging population, which is more susceptible to the onset of new heart disease and depressive symptoms due to age-related physiological and social changes. Additionally, individuals with pre-existing heart disease or stroke were excluded to ensure that our analysis more accurately assesses the impact of depressive symptoms on the incidence of new heart disease events. A detailed flowchart of the sample selection process is shown in Fig. 1.

Primary exposures

Depressive symptoms were assessed using a modified version of the Centre for Epidemiological Studies Depression Scale (CES-D) validated 8-item scale [19], and it has been found to be reliable in assessing depressive symptoms in older adults [20]. At the biennial follow-up survey, participants were asked whether they had experienced each of the eight symptoms in the past week. By summing the number of "yes" responses to each of the eight items (with two positive items reverse scored), a total score ranging from 0–8. Previous validation studies have shown that a score of 3 or higher is effective in differentiating clinically significant depressive symptoms in the elderly population, and therefore we chose this threshold to identify significant total depressive symptoms [21, 22]. Two domains of depressive symptoms were identified: cognitive-affective and somatic. The cognitive-affective domain, comprising symptoms such as 'Feeling depressed,' 'Feeling lonely,' and 'Feeling sad,' reflects core emotional disturbances associated with depression. In contrast, the somatic domain includes 'Everything was an effort,' 'Restless sleep,' and 'Could not get going,' which are indicative of the physical expressions of depressive states commonly experienced by the elderly [23]. The bifactorial model of depressive symptoms, which was validated in a previous study using confirmatory factor analysis (CFA), effectively differentiates between two distinct domains: cognitive-affective and somatic symptoms. This two-factor models had sufficient discriminant validity [24]. Scores for both cognitive-affective and somatic domains were dichotomized using the upper tertiles as cut-offs, with CES-D $\geq$ 2 indicating significant symptoms for each domain [25].

We constructed five trajectories of depressive symptoms (persistently low, decreasing, fluctuating, increasing, and persistently high) [21] based on changes in CES-D scores in waves 4–7 of the HRS and waves 1–4 of the ELSA. Persistently low was defined as no elevation of depressive symptoms at any of the four time points. Decreasing was defined as (1) elevated depressive symptoms at time point 1 only, followed by decreasing depressive symptoms at the next 3 time points, or (2) elevated depressive symptoms at the first 2 time points, followed by decreasing depressive symptoms consistently over the next 2 time points. Increasing was defined as depressive symptoms not elevated only at time point 1 and elevated at all subsequent time points; or (2) depressive symptoms not elevated at the first 2 time points but consistently elevated at both subsequent time points. Persistently high was defined as elevated depressive symptoms at all 4 time points throughout the assessment period. Fluctuating encompassed other depressive symptom trajectories that did not fit the above categorization (Supplementary Table 1). Respondents with persistent low depressive symptoms served as a reference group for the other depressive symptoms trajectories. The somatic depressive symptoms trajectories and cognitive-affective depressive symptoms trajectories were also categorized in this way.

Heart disease outcomes

Heart disease was assessed at waves 8–12 in HRS and waves 5–9 in ELSA. In both HRS and ELSA, heart disease was determined on the basis of self-reported physician diagnosis based on self-reported diagnosis during the follow-up period. At each wave of both cohorts' participants were asked "Has your doctor ever told you that you have a heart condition (including angina, heart attack, congestive heart failure and other heart problems)?" Heart disease was considered to have occurred if the participant self-reported a diagnosed heart condition during the follow-up period. In the next wave, participants were asked to confirm the presence or absence of heart disease if they had reported having a heart disease in the previous wave. If a participant disputed a self-reported heart condition in previous waves, it was retrospectively corrected. Regarding self-reported heart disease, ELSA researchers confirmed 77.5% of self-reported coronary heart disease (defined as angina and heart attack) [26]. Self-reported health conditions in the HRS is strongly consistent with medical record data, and previous studies using the HRS have shown that self-reported health conditions measures have good external validity [27].

Covariates

Covariates were carefully selected based on their potential confounding effects on the relationship between depressive symptoms and the risk of heart disease. These include self-reported demographic and socio-economic variables such as age, sex (male or female), highest level of education (less than high school, high school graduate/general educational development (GED), some colleges or 4-year colleges and above, other), marital status (married/partnered, separated/divorced/widowed, or unmarried). Additionally, self-reported measures of health behavior and conditions were considered, including drinking status (ever drank, never drank), and smoking status (ever smoked, never smoked). Also included were self-reported, physician-diagnosed health conditions such as diabetes and high blood pressure. Including these covariates helps control for their confounding influence when assessing the direct impact of depressive symptoms trajectories on heart disease.

Ethical approval

Both the HRS and the ELSA were conducted in strict accordance with the ethical principles of the Declaration of Helsinki. The HRS was approved by the Institute for Social Research and Survey Research Center of the University of Michigan. Written informed consent was obtained from all participants or their guardians. The ELSA received ethical approval for all waves from the London Multicentre Research Ethics Committee, with informed consent obtained from all participants.

Statistical analysis

The baseline demographics of the study population was statistically described according to different trajectories of depressive symptoms. Continuous variables were expressed using mean [standard deviation (SD)] or median [interquartile range (IQR)], and categorical variables were expressed as frequency (percentage).

To estimate the association between different trajectories of depressive symptoms and the risk of developing heart disease, Cox proportional risk models were used to calculate hazard ratios (HR) and their 95% confidence intervals (95% CI), providing a measure of the relative risk over time. The 'time' variable was defined by the duration until the first occurrence of heart disease or the end of follow-up, whichever occurred first. Follow-up time ended at the last survey completed by each participant. Three models were fitted for Cox regression using the persistent low trajectory of depressive symptoms as a reference. Model 1 was unadjusted, with depressive symptoms trajectories being the only variable. Progressing to model 2, we additionally adjusted for the potential demographic confounders of age, gender, education level, and marital status. In Model 3, we extended the adjustments to include health behaviors (smoking, alcohol consumption) and health conditions (hypertension, diabetes), building upon the adjustments made in Model 2. The proportional risk assumptions of these Cox regression models were confirmed by Schoenfeld residuals. Missing data for covariates were handled using chained-equation multiple imputation via the R package 'mice'. We conducted five rounds of imputation to generate five datasets, setting the maximum number of iterations to 50 for each. The first complete dataset from these was selected and merged to form a complete analyzed dataset.

We performed three sensitivity analyses using HRS data to assess the robustness of our findings. These analyses were sequentially repeated, each time increasing the number of follow-up years by extending the cardiac event endpoint to waves 13, 14, and 15, respectively. Model 3 was used for all analyses, and sections containing missing values were removed.

Statistical analysis procedures were all performed using R software (version 4.3.2). Statistical tests were performed using two-sided tests, and differences were considered statistically significant at $P < 0.05$.

RESULTS

Our study investigated the relationship between the trajectory of depressive symptoms and the occurrence of heart disease in 2409 participants over a 10-year follow-up period. The findings shed light on the impact of different dimensions and multiple trajectories of depressive symptoms on heart disease.

Table 1 describes the demographic and health characteristics of the 17,787 pooled sample grouped at baseline according to the overall depressive symptom trajectory. The median age of the participants was 63.0 years, with a majority being female (59.7%), had a high school or GED (52.0%). Lifestyle factors showed 59.4% were former smokers, and 35.5% had never consumed alcohol. Most notably, 57.8% exhibited a consistently low trajectory of depressive symptoms throughout the study period. Participants with a consistently low trajectory of depressive symptoms were more likely to be married or in a partnership (76.2%). In contrast, the majority of participants (50.6%) with a persistently high trajectory of depressive symptoms had less than high school education, and 55.3% of participants with a persistently high trajectory of depressive symptoms had high blood pressure and 17.2% had diabetes.

Table 2 and Figs. 2–4 shows the longitudinal associations of overall depressive symptom trajectories, somatic depressive symptom trajectories, and cognitive-affective depressive symptom trajectories with heart disease for the pooled sample. In Model 3, i.e., after adjusting for age, gender, marital status, education level, health behaviors, and health conditions, individuals with consistently high depressive symptoms had a higher risk for incident heart disease compared with those with consistently low depressive symptoms (reference) (HR = 1.64, 95% CI: 1.45–1.84). Similarly, individuals with increasing (HR = 1.43, 95% CI: 1.25–1.64) and fluctuating (HR = 1.13, 95% CI: 1.06–1.20) depressive symptoms also had a higher risk, compared with the reference group. However, the effect estimates for incident heart disease were not significantly different for individuals with decreasing depressive symptoms (HR = 1.07, 95% CI: 0.96–1.19), when compared with the reference group.

The somatic depressive symptoms trajectories resulted in a stronger risk of heart disease than the total depressive symptoms trajectories. Using participants with consistently low somatic depressive symptoms as a reference, individuals with consistently high somatic depressive symptoms had a significantly higher risk for incident heart disease in model 3 (HR = 1.93, 95% CI: 1.70–2.19). The risks of heart disease for individuals with fluctuating somatic depressive symptoms and increasing somatic depressive symptoms were 1.33 (95% CI: 1.25–1.41) and 1.31 (95% CI: 1.14–1.50), respectively. Similarly, the association between decreasing somatic depressive symptoms and heart disease was not statistically significant (HR = 0.94, 95% CI: 0.84–1.05).

The pattern of association between cognitive-affective depressive symptoms trajectories and the risk of developing heart disease was similar to that observed with total depressive symptoms trajectories and somatic depressive symptoms. In contrast, while cognitive-affective symptoms trajectories are linked to an increased risk of heart disease, they had less impact on heart disease development compared to the effects of total and somatic depressive symptoms trajectories. After adjusting for demographic characteristics and health behaviors and conditions (model 3), the association between decreasing depressive

Table 1. Baseline characteristics of participants for baseline depressive symptom trajectory analyses.

Variables		Depressive symptoms trajectory group				
	Overall sample	Consistently low	Decreasing	Fluctuating	Increasing	Consistently high
Number (%)	17787	10277 (57.8)	1238 (7.0)	4499 (25.3)	788 (4.4)	985 (5.5)
Age, M (QR), years	63. 0[57.0; 70.0]	62.0 [57.0; 70.0]	62.0 [56.0; 70.0]	63.0 [57.0; 71.0]	66.0 [58.0; 73.0]	63.0 [57.0; 71.0]
Sex, n (%)						
Male	7174 (40.3)	4757 (46.3)	431 (34.8)	1502 (33.4)	237 (30.1)	247 (25.1)
Female	10613 (59.7)	5520 (53.7)	807 (65.2)	2997 (66.6)	551 (69.9)	738 (74.9)
Education, n (%)						
Below high school	4818 (27.1)	2136 (20.8)	408 (33.0)	1491 (33.1)	285 (36.2)	498 (50.6)
High school	9250 (52.0)	5545 (54.0)	621 (50.2)	2273 (50.5)	399 (50.6)	412 (41.8)
College or above	3219 (18.1)	2309 (22.5)	183 (14.8)	605 (13.4)	76 (9.6)	46 (4.7)
Other	500 (2.8)	287 (2.8)	26 (2.1)	130 (2.9)	28 (3.6)	29 (2.9)
Marital status, n (%)						
Married or partnered	12551 (70.6)	7828 (76.2)	750 (60.6)	2963 (65.9)	505 (64.1)	505 (51.3)
Separated/divorced/ Widowed	4629 (26.0)	2115 (20.6)	449 (36.3)	1377 (30.6)	257 (32.6)	431 (43.8)
Never married	607 (3.4)	334 (3.2)	39 (3.2)	159 (3.5)	26 (3.3)	49 (5.0)
Smoking status, n (%)						
Never smokers	7227 (40.6)	4336 (42.2)	504 (40.7)	1754 (39.0)	277 (35.2)	356 (36.1)
Ever smokers	10560 (59.4)	5941 (57.8)	734 (59.3)	2745 (61.0)	511 (64.8)	629 (63.9)
Drinking status, n (%)						
Never drinkers	6307 (35.5)	3159 (30.7)	457 (36.9)	1802 (40.1)	365 (46.3)	524 (53.2)
Ever drinkers	11480 (64.5)	7118 (69.3)	781 (63.1)	2697 (59.9)	423 (53.7)	461 (46.8)
Hypertension (yes/no), *n* (%)	7379 (41.5)	3829 (37.3)	553 (44.7)	2057 (45.7)	395 (50.1)	545 (55.3)
Diabetes (yes/no), *n* (%)	1796 (10.1)	812 (7.9)	139 (11.2)	572 (12.7)	104 (13.2)	169 (17.2)

A total of 17,787 participants were included in the Baseline.
Quantitative data are shown as median and quartiles and categorical variables are presented as counts and percentages.
This table presents the baseline characteristics of the participants included in the analysis of depressive symptom trajectories. It summarizes variables such as age, gender, socioeconomic status, and initial depressive symptom scores, providing an overview of the participants' demographic profiles at the start of the study.

symptoms and heart disease remained statistically non-significant (HR = 1.03, 95% CI: 0.92–1.14). Fluctuating depressive symptoms were associated with a 10% higher risk of heart disease (HR = 1.10, 95% CI: 1.04–1.18), and increasing depressive symptoms were associated with a 31% higher risk of heart disease (HR = 1.31, 95% CI: 1.13–1.51). Persistent high level of depressive symptoms trajectories remained the strongest positive association with heart disease (HR = 1.64, 95% CI: 1.43–1.87).

Sensitivity analyses were consistent with the main analysis results. When follow-up years were extended to 12, 14, and 16 years, using persistently low depressive symptoms as a reference, no statistically significant association was found between decreasing depressive symptoms and the risk of heart disease. In contrast, fluctuating, increasing, and persistently high depressive symptoms all demonstrated a significant correlation with heart disease risk, with persistently high depressive symptoms associated with the highest risk. Similarly, somatic depressive symptoms trajectories also increased the risk of heart disease more than the overall depressive symptoms trajectories and the cognitive-affective depressive symptoms trajectories. (The results of sensitivity analyses are presented in the Supplementary Material).

DISCUSSION

In this study of middle-aged and older adults in the United States and the United Kingdom, we analyzed the relationship between heart disease and long-term depressive symptom trajectories: persistently low, decreasing, fluctuating, increasing, and persistently high. Our findings indicate that there was no significant correlation between heart disease risk and the decreasing trajectory among the five trajectories, whether total, somatic, or cognitive-affective. In contrast, trajectories characterized by increasing, fluctuating, and persistently high depressive symptoms were identified as risk factors for heart disease, with the persistently high trajectories showing the strongest correlations.

Furthermore, somatic symptom trajectories—whether fluctuating, increasing, or persistently high—demonstrated greater predictive power for heart disease risk compared to the overall and cognitive-affective symptom trajectories. These conclusions remain robust after adjusting for multiple potential confounders and covariates that could influence the relationship between depressive symptom trajectories and heart disease risk. Moreover, the robustness of the results persists across varying durations of follow-up. To our knowledge, it is the first study to measure the relationship between somatic depressive symptoms trajectories and cognitive-affective symptoms trajectories and heart disease.

Depressive symptoms can be long-lasting and dynamic, so repeated measures of depressive symptoms mapping the trajectory of the illness are more useful in predicting the impact of depressive symptoms on long-term heart health. By analysing different trajectories of depressive symptoms, the present study found that persistently high levels of total depressive symptoms

Table 2. Cox proportional hazard ratios for the association of depressive symptom trajectories with heart disease over a 10-year follow-up period.

	Model 1		Model 2		Model 3	
	HR (95% CI)	***P*-value**	**HR (95% CI)**	***P*-value**	**HR (95% CI)**	***P*-value**
Consistently low	Reference		Reference		Reference	
Total depressive symptom trajectory						
Decreasing	1.04 (0.94–1.16)	0.459	1.10 (0.99–1.22)	0.084	1.07 (0.96–1.19)	0.224
Fluctuating	1.13 (1.07–1.21)	<0.001	1.18 (1.11–1.26)	<0.001	1.13 (1.06–1.20)	<0.001
Increasing	1.46 (1.28–1.67)	<0.001	1.53 (1.33–1.75)	<0.001	1.43 (1.25–1.64)	<0.001
Consistently high	1.65 (1.47–1.85)	<0.001	1.76 (1.57–1.98)	<0.001	1.64 (1.45–1.84)	<0.001
Somatic trajectory of depressive symptom						
Decreasing	0.92 (0.83–1.03)	0.161	0.98 (0.87–1.09)	0.671	0.94 (0.84–1.05)	0.259
Fluctuating	1.33 (1.25–1.41)	<0.001	1.39 (1.31–1.48)	<0.001	1.33 (1.25–1.41)	<0.001
Increasing	1.38 (1.20–1.59)	<0.001	1.41 (1.23–1.62)	<0.001	1.31 (1.14–1.50)	<0.001
Consistently high	1.93 (1.71–2.18)	<0.001	2.10 (1.85–2.38)	<0.001	1.93 (1.70–2.19)	<0.001
Cognitive-affective trajectory of depressive symptom						
Decreasing	1.00 (0.90–1.12)	0.938	1.06 (0.95–1.18)	0.290	1.03 (0.92–1.14)	0.627
Fluctuating	1.10 (1.03–1.17)	0.005	1.14 (1.07–1.21)	<0.001	1.10 (1.04–1.18)	0.002
Increasing	1.32 (1.15–1.53)	<0.001	1.38 (1.19–1.59)	<0.001	1.31 (1.13–1.51)	<0.001
Consistently high	1.65 (1.45–1.88)	<0.001	1.72 (1.51–1.97)	<0.001	1.64 (1.43–1.87)	<0.001

A total of 11,725 participants were included in the analysis.
Results of the Cox regression model are reported as HR and 95% CI.
Consistently low depressive symptoms are used as the reference category.
Model 1 was unadjusted.
Model 2 additionally adjusts for sociodemographics (age and sex, education, marital status).
Model 3 additionally adjusts for health behaviors and conditions (smoking, alcohol consumption, hypertension and diabetes).
This table displays the Cox proportional hazard ratios, which quantify the association between different trajectories of depressive symptoms and the incidence of heart disease during a 10-year follow-up period. The table includes hazard ratios, 95% confidence intervals, and *p*-values, providing a comprehensive statistical overview of how depressive symptoms relate to heart disease risk over time.

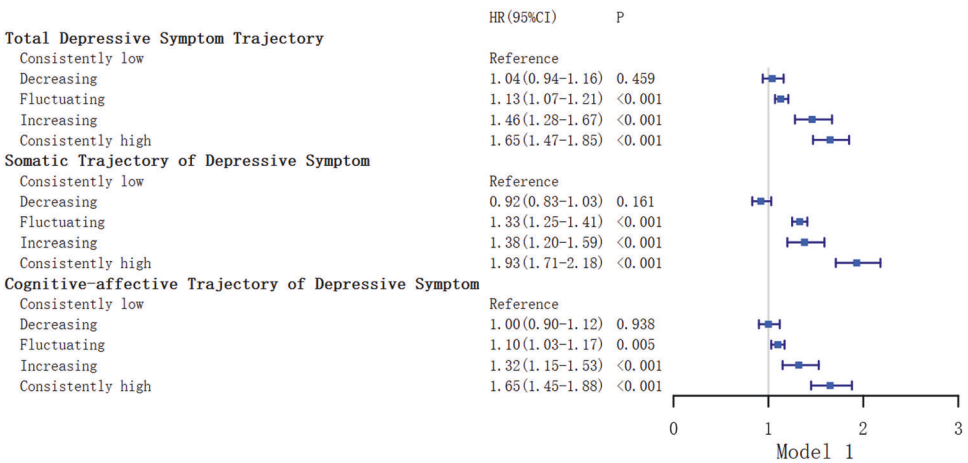

Fig. 2 Forest plot visualization of Model 1 results from Table 2. This forest plot visually represents the hazard ratios (HRs) and 95% confidence intervals (CIs) for each variable in Model 1 from Table 2. Each horizontal line corresponds to a different variable, with the square indicating the point estimate (HR) and the horizontal line representing the 95% confidence interval. The vertical dashed line denotes the null value (HR = 1), indicating no effect of the variable.

were most strongly associated with the risk of heart disease, possibly due to cumulative cardiovascular damage over time. In contrast, the association between the group with decreasing trajectory of depressive symptoms and heart disease was not statistically significant [28]. This result suggests that with sufficient recovery time (i.e., a sustained period of low depressive symptoms), there may not be an increased risk of adverse outcomes such as heart disease, even in people who experience high depressive symptoms. It has been found that improving depressive symptoms by administering psychotherapy leads to a reduced risk of new-onset cardiovascular disease [29]. This may suggest that reducing or mitigating the progression of depressive states is a potential way to reduce the risk of heart disease, and intervening in the trajectory of depressive symptoms may be an effective heart disease prevention strategy.

The potential biological mechanisms that may underlie this finding may be that it has been found [30] in the presence of persistent depressive symptoms, both the somatic and cognitive-affective symptom dimensions may influence heart health by affecting an individual's behavioral patterns [31]. Cognitive-

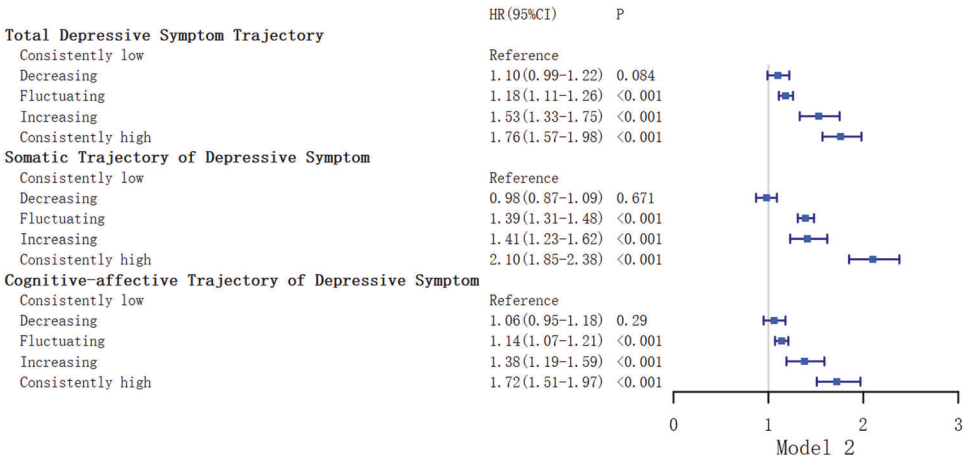

Fig. 3 Forest plot visualization of Model 2 results from Table 2. This forest plot visually represents the hazard ratios (HRs) and 95% confidence intervals (CIs) for each variable in Model 2 from Table 2. Each horizontal line corresponds to a different variable, with the square indicating the point estimate (HR) and the horizontal line representing the 95% confidence interval. The vertical dashed line denotes the null value (HR = 1), indicating no effect of the variable.

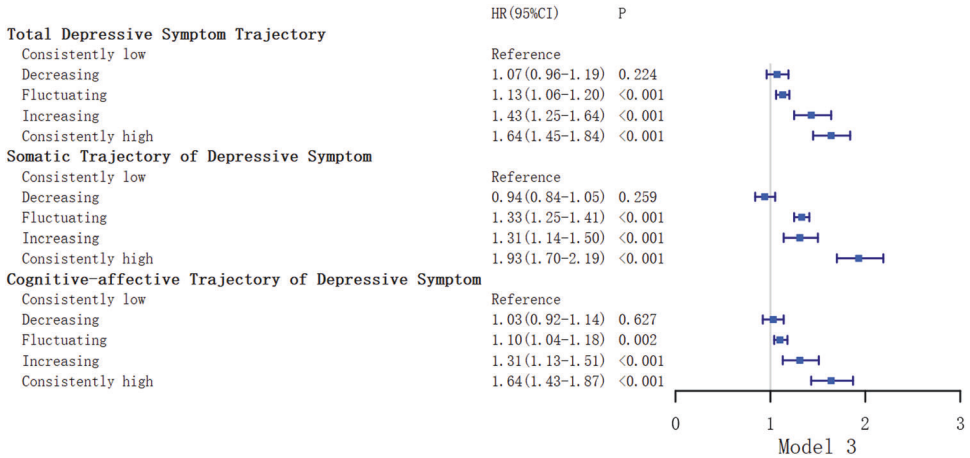

Fig. 4 Forest plot visualization of Model 3 results from Table 2. This forest plot visually represents the hazard ratios (HRs) and 95% confidence intervals (CIs) for each variable in Model 3 from Table 2. Each horizontal line corresponds to a different variable, with the square indicating the point estimate (HR) and the horizontal line representing the 95% confidence interval. The vertical dashed line denotes the null value (HR = 1), indicating no effect of the variable.

affective depressive symptoms (e.g., mood disorders, anxiety, and emotional stress) involve changes in mood, socialization, and other areas. These changes are thought to be associated with an increased risk of heart disease. Emotional factors play an important role in heart health [32], and prolonged depression may lead to imbalanced hormone levels in the body, affecting cardiovascular function. In addition, cognitive- affective depressive symptoms may contribute to heart disease through multiple biopsychosocial pathways. These symptoms can lead to poor health behaviors, resulting in individuals being unable to effectively manage their health and exhibiting poor lifestyles, such as reduced physical activity, unhealthy eating habits, and non-compliance with medical advice. In addition, depressive symptoms may cause feelings of loneliness and decreased socialization, all of which may increase the risk of heart disease [33]. At the same time, lack of well-being and socialization opportunities may lead to reduced physical activity, decreased treatment adherence, and worsened dietary habits, all of which may further increase the risk of heart disease.

Somatic depressive symptoms have a stronger predictive power. It involves a range of physical discomforts, such as depletion of a lot of energy, sleep disturbances, and behavioral delays. These somatic symptoms may increase the risk of heart disease through several pathways. Firstly, somatic complaints may lead to adverse lifestyle changes such as physical inactivity [34–36], poor diet [37, 38], smoking [39–41], and alcohol abuse [42–44], which are important influences on heart health. Secondly, persistent somatic symptoms may trigger a stress response, leading to a highly stressed cardiovascular system that exhibits an imbalance in the autonomic nervous system [45], in particular a disruption of the balance between sympathetic and parasympathetic nerves. Excessive activation of the sympathetic nervous system can lead to an increase in heart rate and blood pressure [46], and in the long term, this state increases the risk of cardiovascular disease. It has also been found that the somatic depressive symptoms are associated with dysregulated levels of inflammation in the body. Inflammatory markers such as C-reactive protein (CRP) [11, 47, 48] and interleukin-6 (IL-6) [49, 50] are inflammatory factors that can damage the walls of blood vessels and contribute to the development of atherosclerosis [51, 52], which can increase the risk of heart disease [53]. There is also the possibility that hypothalamic-pituitary-adrenal (HPA) axis hyperactivity may be a key pathophysiological mechanism for depressive symptoms [54, 55]. Multiple factors

may collectively mediate the risk that somatic depressive symptoms promote the development of heart disease.

The strength of this study is the large sample size, pooling two large cohorts from nationally representative, prospective study designs in the United States and the United Kingdom, which enhances the generalizability of the results. Secondly, repeated measures and long-term assessments of depressive symptoms dynamically mapped the trajectories of depressive symptoms, capturing the nuances of how depressive symptoms trajectories differentially affect heart disease risk, and finding that reducing depressive symptoms was not associated with increased risk of heart disease. The correlation between somatic and cognitive-affective depressive symptoms and heart disease, respectively, was also analyzed, leading to the hypothesis that increased intervention for somatic depressive symptoms may be more effective in preventing heart disease. Additionally, participants were not selected on the basis of mental health issues and are therefore more representative of the general population. There are a number of limitations to our study. Although we used a more appropriate classification of somatic symptoms for the 8-item CES-D, this may be inconsistent with the definition of somatic depressive symptoms in the literature and the types of items characterizing this symptom cluster in different depression scales [56]. Secondly, the study population was over 50 years of age in the United States and the United Kingdom, and the results may not be generalizable to other populations. Given that the data collection relies on self-reported questionnaires, which subjects may not accurately recall or may report in socially desirable ways, there is a risk of recall bias, which can affect the accuracy of responses. And the results of this study should be interpreted with caution as they may be subject to the effects of confounding variables not accounted for in the analysis. In addition, the nature of observational studies limits the identification of causal relationships.

Based on the results of the current study, we recommend that the identification and management of depressive symptoms be incorporated into heart disease prevention strategies. This includes assessing the psychological status of all patients during routine health checkups, especially those who exhibit somatic depressive symptoms that require special attention. A comprehensive intervention plan that includes medication, psychotherapy, and other supportive interventions is essential, tailored to each patient's individual situation. At the same time, a comprehensive mental health and heart health assessment should be conducted regularly, and the treatment plan should be adjusted according to the results of the assessment to effectively reduce or alleviate depressive symptoms and thus reduce the risk of heart disease.

CONCLUSION

We found significant associations between different trajectories (fluctuating, increasing, and persistently high depressive symptoms) and the increased risk of heart disease. However, a trajectory with depressive symptoms that started high but decreased over time was not associated with higher heart disease risk. The somatic symptoms have a stronger association with heart disease incident. Further studies are needed to explore the underlying overall and trajectory-specific mechanisms of these associations.

DATA AVAILABILITY

The databases used in this study are available at https://hrs.isr.umich.edu and www.elsa-project.ac.uk, respectively.

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AUTHOR CONTRIBUTIONS

XL: Formal analysis, Writing—original draft. CL: Methodology, Software, Writing—review & editing. HL: Software, Writing—review & editing. XQ: Visualization, Writing—review & editing. CW: Writing—review & editing. CJ: Supervision, Project administration. FJ*: Conceptualization, funding acquisition, Supervision, Writing—review & editing, Final approval of the paper.

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COMPETING INTERESTS

The authors declare no competing interests.

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