

Baseline Depressive Symptoms Predict Subsequent Heart Disease; A 20-Year Cohort

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ABSTRACT

Background: Depression is common among patients with heart disease. Depression is also associated with worse outcomes among patients with heart disease. Fewer studies have shown whether or not baseline depressive symptoms predict subsequent heart disease in general population.

Objectives: This study aimed to investigate whether depressive symptoms at baseline predict risk of developing heart disease during the next 20 years in the United States.

Patients and Methods: The data were extracted from the Health and Retirement Study (HRS), 1992 - 2012. The study was conducted on 8,375 individuals who were older than 50 years at entry, did not have heart disease at baseline, and had data on heart disease over the next 20 years. High depressive symptoms (modified Center for Epidemiologic Studies Depression Scale [CES-D]) were considered as the independent variable. Self-reported data on physician diagnosis of heart disease were measured on a biannual basis. Baseline demographic data (i.e., age and gender), socioeconomic status (i.e., race, marital status, and education level), health behaviors (i.e., drinking, smoking, and exercise), and body mass index were controlled. Cox proportional hazard model was used for data analysis.

Results: Cox proportional hazard model revealed a link between high depressive symptoms at baseline and time to developing heart disease (Hazard ratio = 1.439, 95% CI = 1.253 - 1.652), suggesting that individuals with high depressive symptoms at baseline developed heart disease sooner than others. The association between baseline depressive symptoms and risk of heart disease was significant after controlling for all the covariates.

Conclusions: Individuals with depressive symptomatology are at higher risk of development of heart disease over time. Thus, individuals with depressed mood may need more rigorous evaluation for heart disease.

► Implication for health policy/practice/research/medical education:

As depressed mood contributes to development of heart disease, individuals with depressed mood may need more rigorous evaluation of heart disease.

1. Background

The association between depression and prognosis of cardiovascular disease is well established among patients who have already developed the disease (1). Depression and high depressive symptoms are both associated with an increased risk of cardiovascular morbidity and mortality among patients with Coronary Artery Disease (CAD) (2-7). Reviews and meta-analyses have shown that the effect of depression on outcomes of CAD is relatively consistent

(8-11). Despite availability of strong evidence on the link between depression and outcomes among patients with heart disease, the effect of depression on cardiovascular disease in general population is still not clear (12). Some (13-15), but not all (14, 16) studies have shown positive results. For instance, a prospective cohort of 136,293 community-dwelling postmenopausal women revealed that new antidepressant use was not significantly associated with increased incidence of CAD (16). Another study also failed to find an effect of antidepressant use on the risk of heart failure in patients with CAD (14). Barrick argued that it is premature to describe depression as a cause of

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heart disease (17). Appels also argued that more research is needed before concluding about a causal link between depression and heart disease (18).

2. Objectives

The present study aims to determine whether individuals with high levels of depressive symptoms at baseline are at a higher risk of developing heart disease during the next 20 years in the United States.

3. Patients and Methods

This study used Health and Retirement Study (HRS) data to assess the effect of high depressive symptoms at baseline on development of heart disease in the United States. The HRS is a longitudinal cohort that has enrolled a representative sample of Americans over the age of 50. Since its launch in 1992, the study has interviewed the participants for 20 years every two years. The HRS explores the health transitions that individuals undergo toward the end of their work lives and in the following years. The HRS has collected information about socioeconomic status, physical health, functioning, mental health, and healthcare utilization. University of Michigan Institutional Review Board approved the study. Study design and sampling have been described in details elsewhere (19, 20).

3.1. Participants

The participants of the HRS cohort included individuals who were born between 1931 and 1941 and were 51 to 61 years old. The first interview happened in 1992. Only 8,375 individuals who did not have heart disease at baseline and had data on all waves during the next 20 years were enrolled into the current study.

3.2. Interviews

The data were collected using face-to-face interviews. The interviews were conducted in the participants' houses, and the participants received compensation for taking part in the study.

3.3. Measures

3.3.1. Demographic Data

The data on race, ethnicity, age, gender, education level, and marital status were used. The respondents' race was asked if they considered themselves White or Caucasian, Black or African-American, American-Indian, Asian, or something else. Besides, ethnicity included Hispanic or Latino.

3.3.2. Depressive Symptomatology

A modified nine-item version of the Center for Epidemiologic Studies Depression Scale (CES-D) was used to measure depressive symptoms (21). The participants reported whether they had felt (a) depressed, (b) everything was an effort, (c) sleep was restless, (d) happy, (e) lonely, (f) that they enjoyed life, (g) sad, (h) that they could not get going, and (i) that they had a lot of energy during the past week. Factor analysis studies have identified the following three subscales for this measure: somatic (items 2, 3, 8, and 9), lack of positive affect (items 4 and 6), and dysphoria (items 1, 5, and 7) (22). In this scale, higher scores reflected

negative affect, and scores 4 and above represented high depressive symptoms. The measure displayed acceptable internal consistency ($\alpha = 0.80 - 0.83$) (23).

3.3.3. Heart Disease

The participants reported if a doctor had ever told them that they had any heart conditions, including heart attacks, angina, congestive heart failure, or coronary heart disease. If the respondents reported "yes" in the previous wave of data and "no" in the current wave, their response was coded as "no" (24).

3.3.4. Smoking

Two items were used to measure smoking behavior at baseline. In the first item, ever smoking and in the second item, current smoking was asked. Using both items, the individuals were categorized into never smokers, previous smokers, and current smokers.

3.3.5. Exercise

Three items were used to measure physical activity and exercise. Cronbach's alpha of the measure was 0.792.

3.4. Statistical Note

Due to the complex sample design, Stata 13.0 (Stata Corp., College Station, TX) was used for data analysis. Taylor series linearization was used for estimation of standard errors. Thus, stratified and clustered nature of the data was considered for data analysis. P values less than 0.05 were considered to be statistically significant. The data were downloaded from the HRS website, Institute for Social Research (ISR), University of Michigan (<http://hrsonline.isr.umich.edu/>).

Cox proportional hazard model was used to determine whether the association between high depressive symptoms and time to developing heart disease is significant after controlling the effects of baseline demographic data, socioeconomic status, health behaviors, and Body Mass Index (BMI). Covariates included age, gender, race, ethnicity, education level, marital status, smoking, physical activity, drinking, and BMI. Hazard Ratios (HR) with 95% CI were reported. HRs greater than 1 suggests higher risk of developing heart disease at each time point.

The possible multi-collinearity between the covariates was also tested. With considering correlation coefficients of larger than 0.4 as indicator of collinearity, no sign of multi-collinearity between the predictors was found. Additionally, Kaplan–Meier curves were used to depict how risk of developing heart disease over time varied based on race, gender, smoking, and depressive symptoms.

4. Results

In this study, most of the participants were female (54%) and White and non-Hispanic (95%). Besides, 42% were never smokers, 38% were past smokers, and 19% were current smokers. In addition, 68% reported drinking alcohol. About 8% had high depressive symptoms and 42% developed new CAD during the 20-year follow-up (Table 1).

Kaplan–Meier curves showed that the risk of developing heart disease was higher among males compared to females

Table 1. Proportion of the Socioeconomic Status, Behaviors, and Outcome among the Participants

	%	Linearize d Std.	95% Confidence Interval, (n = 8,375)	
Socioeconomics				
Gender				
Male	45.49	0.008	43.96	47.01
Female	54.51	0.008	52.99	56.04
Race				
White	95.13	0.005	94.14	96.12
Black	4.87	0.005	3.88	5.86
Ethnicity				
Non-Hispanic	95.42	0.008	93.81	97.03
Hispanic	4.58	0.008	2.97	6.19
Behaviors				
Smoking				
Never	42.42	0.011	40.15	44.69
Current	38.27	0.01	36.21	40.33
Drinking				
No	19.31	0.009	17.44	21.17
Yes	32.41	0.014	29.55	35.28
Yes	67.59	0.014	64.27	70.45
Predictor				
Depressive symptoms				
Low	92.41	0.005	91.43	93.4
High	7.59	0.005	6.6	8.57
Outcome				
New heart disease				
No	57.8	0.012	55.38	60.23
Yes	42.2	0.012	39.77	44.62

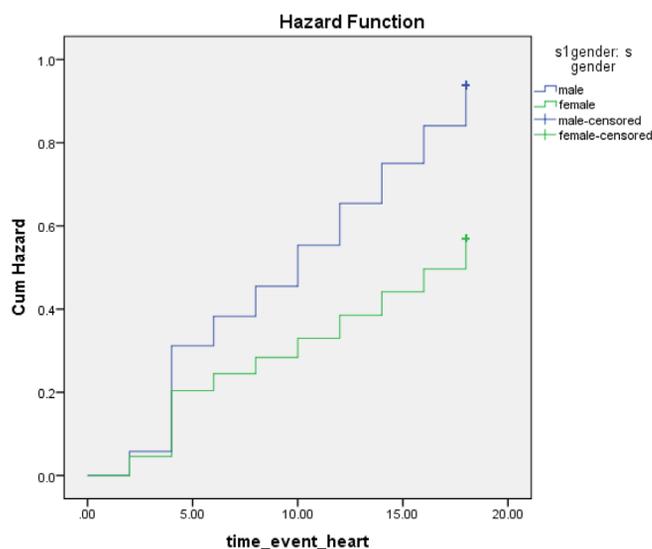
(Figure 1), among African-Americans compared to Whites (Figure 2), among smokers compared to non-smokers (Figure 3), and among the individuals with high depressive symptoms (Figure 4). Moreover, Cox proportional hazard model confirmed that the association between high level of depressive symptoms and time to development of heart

disease was statistically significant (HR = 1.439, 95% CI = 1.253 - 1.652) after controlling for demographic data, socioeconomic status, health behaviors, and BMI (Table 2).

5. Discussion

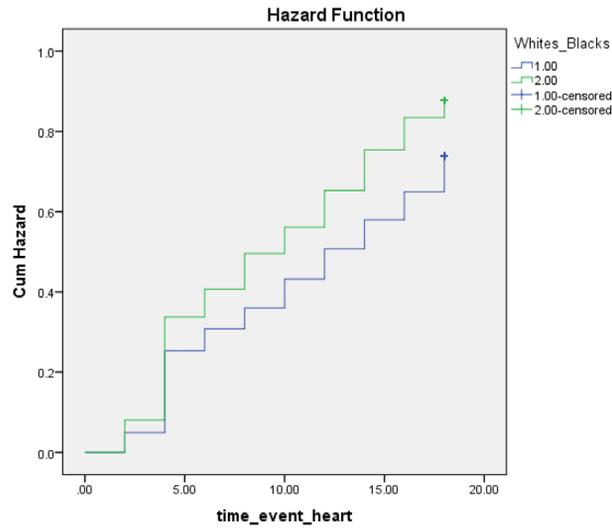
The results of the current longitudinal study showed that high

Figure 1. Kaplan-Meier Graph Showing Hazard of Developing Heart Disease Over 20 Years Based on Gender



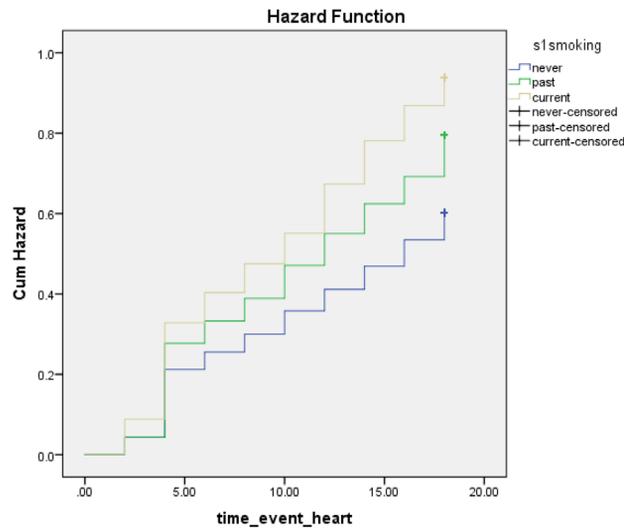
Male = Blue, Female = Green

Figure 2. Kaplan-Meier Graph Showing Hazard of Developing Heart Disease Over 20 Years Based on Race (n = 8,375)



Whites = Blue, Blacks = Green

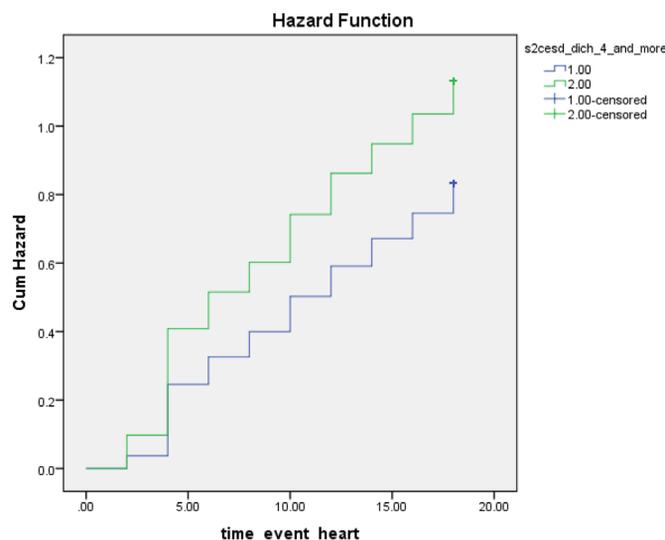
Figure 3. Kaplan-Meier Graph Showing Hazard of Developing Heart Disease Over 20 Years Based on Smoking Status at Baseline



Never Smoker = Blue, Past Smoker = Green, Current Smoker = Yellow

level of depressive symptoms at baseline was associated with CAD over a 20-year period. Our results suggested that this link remained significant after controlling for demographic data, socioeconomic characteristics, BMI, and health behaviors (i.e. exercise and smoking). These findings were in line with those studies that have shown that individuals who experience negative emotions, such as depression, were at an increased

risk of CAD (12, 25, 26). In a cohort of 7,709 patients with confirmed CAD but without a diagnosis of heart failure or depression, a subsequent diagnosis of depression was associated with 50% increase in the risk of heart failure (14). The Nurses' Health Study analysis also suggested that antidepressant use tripled the risk of sudden cardiac death in healthy women (15). Similarly, the Women's Ischemia Syndrome Evaluation

Figure 4. Kaplan-Meier Graph Showing Hazard of Developing Heart Disease Over 20 Years Based on Level of Depressive Symptoms at Baseline (n = 8,375)

Low Depressive Symptoms = Blue, High Depressive Symptoms = Green

Table 2. The Summary of Cox Proportional Hazard Models among the Participants (n = 8,375)

	HR	SE	Sig.	95% Confidence Interval	
High depressive symptoms	1.439	0.071	< 0.001	1.253	1.652
Female gender	0.568	0.048	< 0.001	0.517	0.625
Age	1.043	0.004	< 0.001	1.034	1.051
Blacks	0.973	0.074	0.716	0.842	1.125
Hispanics	0.668	0.100	< 0.001	0.549	0.812
Education	0.969	0.008	< 0.001	0.954	0.984
Marital status					
1	2.182	0.356	0.028	1.086	4.383
2	1.537	0.133	0.001	1.184	1.995
BMI	1.022	0.004	< 0.001	1.014	1.030
Exercise	1.029	0.007	< 0.001	1.015	1.043
Smoking					
Past smoker	1.184	0.052	< 0.001	1.070	1.310
Current smoker	1.494	0.059	< 0.001	1.329	1.678
Drinking	0.837	0.047	< 0.001	0.764	0.918

revealed doubling of the risk of cardiovascular disease and death in the women taking antidepressants who had been referred for coronary angiography (13).

Several review articles have also been conducted on this topic. In a narrative review redundant. Rozanski et al. explained paths from psychosocial factors to CAD (25). Hemingway and Marmot also conducted a systematic review and showed that all the 11 eligible studies reported that psychological distress significantly increased the adjusted relative risk of development of coronary disease (9). Prospective studies have consistently suggested that negative affect predicts CAD (25, 27, 28). Depression is associated with CAD morbidity and mortality, even after controlling for the traditional CAD risk factors, such as serum cholesterol, blood pressure, and

smoking (9, 26, 29). Although multiple behavioral pathways have been proposed to explain how depression is linked to development and progression of CAD (13, 30), our study suggested that the link between depression and CAD may be independent of smoking, exercise, and BMI.

The findings of the current study may have important clinical or public health implications for primary prevention of heart disease in the community. Depression is the most common psychiatric disorder in the general population (31). About 20% of older adults in the US (aged ≥ 65 years) have CAD (32, 33). Future studies should determine whether promotion of mental health in depressed individuals reduces morbidity and mortality associated with coronary heart disease in the populations. We argue that individuals with high depressive

symptoms or depression who have not already developed heart disease should receive screening and evaluation for development of heart disease more closely compared to their non-depressed counterparts. Patients with depression (or high symptoms of depression) may benefit from targeted interventions with educational components on the risk of heart disease. To conclude, high level of depressive symptoms at baseline predicted new onset of heart disease over 20 years among the individuals older than 50 years in the United States.

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Authors' Contribution

Maryam Moghani Lankarani and Shervin Assari designed the study and analyzed, drafted, and revised the manuscript.

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