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Depressive symptoms are associated with incident coronary heart disease or revascularization among Blacks but not among Whites in the Reasons for Geographical and Racial Differences in Stroke (REGARDS) Study

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Abstract

Purpose—To examine the association of depressive symptoms with coronary heart disease (CHD) endpoints by race and income.

Methods—Study participants were Blacks and Whites (n=24,443) without CHD at baseline from the national REasons for Geographical and Racial Differences in Stroke (REGARDS) cohort. Outcomes included acute CHD and CHD or revascularization. We estimated race-stratified multivariable Cox proportional hazards models of incident CHD and incident CHD or revascularization with the 4-item Center for Epidemiological Studies-Depression scale, adjusting for risk factors.

Results—Mean follow-up was 4.2±1.5 years, CHD incidence was 8.3 events per 1000 person years (n=366) among Blacks and 8.8 events per 1000 person years (n=613) among Whites. After adjustment for age, sex, marital status, region, and socioeconomic status, depressive symptoms were significantly associated with incident CHD among Blacks [HR 1.39 (95%CI 1.00-1.91)], but not among Whites [HR 1.10 (95%CI 0.74-1.64)]. In the fully-adjusted model, compared to Blacks who reported no depressive symptoms, those reporting depressive symptoms had greater risk for the composite endpoint of CHD or revascularization [HR 1.36 (95%CI 1.01-1.81)]. Depressive symptoms were not associated with incident CHD endpoints among Whites.

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Conclusions—High depressive symptoms were associated with higher risk of CHD or revascularization for Blacks but not Whites.

Keywords

coronary disease; epidemiology; depressive symptoms; myocardial infarction

Coronary heart disease (CHD) affects about 14 million men and women in the US.^{1,2} Although mortality from CHD has declined over the last few decades due to improved quality of care and primary prevention efforts,³ Blacks continue to have markedly higher risk for CHD mortality than Whites.^{2,4} This disparity is in part due to differences in risk factors such as hypertension, diabetes, chronic kidney disease and smoking, which are a greater burden among Blacks than Whites.^{5,6,7} Less clear is the role of non-traditional risk factors such as depressive symptoms, which also influence CHD incidence and mortality.^{8,9}

Depressive symptoms is considered a non-traditional risk factor, in that it is usually not considered a primary predictor of CHD risk as are more traditional, clinical risk factors. Clinicians rarely screen their patients for depressive symptoms, which is often viewed as a modifiable risk factors for heart disease, and thus a non-traditional risk factor.¹⁰ Research has reported that the prevalence of self-report depressive symptoms is higher among non-Hispanic Blacks than non-Hispanic Whites in the general adult population,¹¹⁻¹³ and that depressive symptoms is more severe among Blacks than Whites, though the lifetime prevalence of major depressive disorder is higher among Whites.¹⁴ In older adults there is no clear understanding of the existence of racial disparities in depressive symptoms. While some researchers have reported that older Whites have higher symptom levels than do Blacks,¹⁵ others have found little evidence that there is a disparity in depressive symptoms among older Blacks and Whites.¹⁶ Clearly, Black-White disparities in depressive symptoms is not as conclusive as evidence for disparities among young-to-middle-age Blacks and Whites.¹²

The majority of published reports have examined the associations of depressive symptoms and cardiovascular disease (CVD) endpoints (e.g., total mortality, incident ischemic heart disease and stroke) among Whites.^{4,9,17,18} Little is known about the association of depressive symptoms with incident CHD among Blacks,⁸ and results are mixed. One report concluded that depressive symptoms were more strongly associated with CVD risk among Blacks than Whites.⁹ Another study found that there are no racial differences in the association of depressive symptoms and CVD risk factors such as hypertension risk.¹⁹ Studies have reported a stronger association of depressive symptoms with CVD risk factors (hypertension, diabetes and subclinical disease) among Blacks than among Whites.²⁰⁻²⁴ Clearly, much of the work on Blacks has centered around the association between depressive symptoms and CVD risk factors. This demonstrates why the role of depressive symptoms in the etiology of CHD risk among Blacks and Whites is important.

High depressive symptoms among Blacks may stem from multiple sources, including earning low income, psychological stress, and living in residentially segregated neighborhoods that may limit access to quality mental health care, which also leads to less treatment of mental illness.^{14,25-27} These factors are more prevalent among Blacks than

Whites and are critical to explaining the role depressive symptoms play in the race-CHD pathway. While findings have shown associations of depressive symptoms with CHD among both Blacks and Whites, the burden of depressive symptoms may be more severe among Blacks and low-income families since their depressive symptoms are not treated as often as those among Whites and high-income families.^{14,28}

Depressive symptoms may also impact CHD through a number of possible pathways. Depressed persons more likely engage in unhealthy behaviors such as eating high fat diets, drink alcohol, become physically inactive and smoke, thereby increasing their risk for CHD.^{29,30} Other research suggest that depressive symptoms impact CHD through poor treatment adherence and more underlying disease severity.³¹ Depressive symptoms may also affect CHD incidence through neuroendocrine changes that trigger physiological responses involving the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic-parasympathetic systems, which play a central role in the pathophysiology of CHD.^{32,33} Other pathophysiological effects of negative emotional states that may contribute to atherogenesis include autonomic imbalance, serotonergic dysfunction, secretion of proinflammatory cytokines, and platelet activation.^{8,34-36} Another line of work proposes that the mechanism by which depressive symptoms contributes to CHD is due to treatment where anti-depressant medications may contribute to cardiotoxicity.³⁷

Few studies have examined the association of depressive symptoms with incident CHD and revascularization (or coronary artery bypass surgery), and the extent to which that association is impacted by income in a large sample of Blacks and Whites. The objective of this study was to examine the association of depressive symptoms with incident acute CHD or coronary revascularization in the national REasons for Geographical and Racial Differences in Stroke (REGARDS) study. We hypothesized that depressive symptoms at baseline would be associated with incident CHD or revascularization for Blacks more so than for Whites, and that associations would vary by income.

Methods

Design and Procedures

REGARDS is a national population-based, cohort study of US community-dwelling adults aged >45 years recruited from January 2003 to October 2007 to determine the causes of racial and geographical differences in stroke mortality. REGARDS recruited 30,239 participants (42% Black and 55% women). Race was self-reported. Data for this study were collected by REGARDS-MI, an ancillary study of REGARDS that adjudicates all heart-related events and merges these data with the existing REGARDS data. Participants were recruited from a commercial list of US residents using mail and telephone contacts. Baseline data were collected on participants' demographic characteristics, medical history, stroke symptom history, health behaviors, functional status and psychological measures using computer-assisted telephone interviews (CATI). In-home examinations were conducted by trained health care professionals utilizing standardized protocols to collect clinical measures (i.e., blood pressure, height and weight, waist circumference), blood and urine samples, electrocardiograms (ECGs), and medication use by pill bottle review. Blood and urine

samples were centrally analyzed at the University of Vermont, and ECGs were read centrally at the Wake Forest University ECG reading center.

Participants or their proxies were followed up every 6 months by telephone interview with retrieval of medical records for reported hospitalizations. Deaths were detected by report of next of kin or through online sources (e.g., Social Security Death Index) and the National Death Index. Proxies or next of kin were interviewed about the circumstances surrounding death, including the presence of chest pain. Death certificates and autopsy reports also were obtained to adjudicate cause of death and cardiovascular outcomes were adjudicated using methods previously described.⁶ Myocardial infarctions (MIs) were classified as definite, probable or possible. Definite MIs were those with diagnostic cardiac enzymes or ECG. Probable MIs were those with elevated but not diagnostic (i.e., equivocal) enzymes with a positive but no diagnostic ECG; or, if enzymes were missing, with a positive ECG in the presence of ischemic signs or symptoms. Only definite or probable MIs were incorporated as events in this study. Cases were assigned to 2 adjudicators and disagreements were adjudicated by committee. The test for agreement between adjudicators produced a level greater than 0.80 for the presence of definite or probable MI or definite or probable acute CHD death.⁶ Further discussion of the methodological details and procedures are available elsewhere.³⁸ This study excluded REGARDS participants with baseline CHD defined as a self-reported history of myocardial infarction, coronary artery bypass surgery, percutaneous coronary intervention, or evidence of myocardial infarction by ECG. REGARDS was approved by the Institutional Review Boards of all participating institutions and study participants provided informed consent.

Outcome Measures

The dependent variables included incident acute CHD and a composite endpoint consisting of incident acute CHD or coronary revascularization. Incident acute CHD was defined as a definite or probable MI or acute CHD death. Acute CHD death is a death that is judged to be due to myocardial infarction within the past 28 days, or sudden cardiac death, based on review of medical records, death certificates, interviews with proxies and autopsy reports, where available. Our definition was derived from following an American Heart Association position statement that provided guidance for the definition of acute CHD in epidemiologic and clinical studies.³⁹ Coronary revascularization, the process of restoring the flow of blood to the heart, included percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG). The follow-up time for each participant was calculated from the date of the in-home visit to the date of first acute CHD event, for the first endpoint, or the date of first revascularization/acute CHD event, for the second endpoint, or date of death or last follow-up date. Events through December 31, 2009 were included in this analysis. At that time, 9.5% of the original sample was lost to follow-up.

Main exposure variable

The primary independent variable was derived from the Center for Epidemiological Studies-Depression (CES-D)-4-item scale (version 17) to evaluate depressive symptoms. This measure was derived from the 20-item CES-D scale. Scores range from 0 to 12; a score ≥ 4 indicates an elevated level of psychologic distress.⁴⁰ Scores were categorized as normal (<4)

or depressed (≥ 4). The internal consistency of the 4-item scale was high in this sample ($\alpha=0.80$) when compared to that of the 20-item scale measured across studies which ranges from 0.85 to 0.90.⁴¹

Other Covariates

Other covariates included demographic, socioeconomic status (SES), health behaviors, and physiological variables. Demographic characteristics included age (continuous variable), sex [male=1; female=0 (referent)], race [black=1; white=0 (referent)], marital status [single=0 (referent); divorced=1; widowed=2; other=3; married=4], and region of residence [stroke belt=1; stroke buckle=2; other=0 (referent)]. The “stroke belt” is a region of states in the southeast with stroke mortality rates 1.3-1.5 times greater than the rest of the US; the “stroke buckle” is a region of counties in North and South Carolina and Georgia with stroke mortality rates higher than the rest of the nation;⁴² and the “other” category includes states where stroke rates are lower than those found in the stroke belt or buckle. SES included educational attainment [<HS diploma=0 (referent); HS diploma=1], annual family income [<\$35,000/year=0 (referent); \$35,000 or more/year=1], and residence in a census tract with poverty level of 30% or more [poverty level <30%=0 (referent); poverty level 30% or more=1].⁴³ Health behaviors included physical activity [no exercise=0 (referent); any weekly exercise=1], smoking [none=0 (referent); current smoker=1] and alcohol consumption [past or never=0 (referent); current use=1]. Physiological variables included systolic blood pressure [SBP<120=0 (referent); 120-139=1; >140 mmHg=2], total cholesterol [<200=0 (referent); 200-239=1; >240 mg/dL=2], high density lipoprotein (HDL) cholesterol [men: <40=1; >40 mg/dL=0 (referent); women: <50=1; >50 mg/dL=0 (referent)], albuminuria [<30=0 (referent); 30-300=1; >300 mg/g=2], triglycerides [<150=0 (referent); >150 mg/dL=1], natural log-transformed high sensitivity C-reactive protein (hs-CRP) [<3=0 (referent); >3 mg/dL=1], diabetes status [defined as fasting blood sugar >126 mg/dL, a non-fasting blood sugar >200 mg/dL, a self-reported history of diabetes, or treatment with a diabetes medication (referent is not diabetic)], body mass index [BMI: < 25=0 (referent), 25-29.9=1, $\geq 30 \text{ kg/m}^2=2$], use of statins or hydroxymethylglutaryl-coenzyme A (HMG CoA) reductase inhibitors [no=0 (referent); yes=1], use of anti-hypertensive medications [no=0 (referent); yes=1] and use of antidepressant medications [no=0 (referent); yes=1].

Statistical analysis

Longitudinal associations of depressive symptoms with incident acute CHD (acute CHD death, nonfatal MI, or coronary revascularization) by race were examined among participants free of CHD at baseline. Baseline characteristics of REGARDS participants were calculated for those who did not report elevated depressive symptoms (CES-D < 4) and those who did (CES-D ≥ 4). Associations of depressive symptoms with CHD endpoints were examined by estimating hazard ratios (HR, 95% Confidence Interval–CI) for the two endpoints (incident CHD and incident CHD or revascularization) in sequential Cox proportional hazards models. Model 1 adjusted for age, sex, marital status and geographic region of residence. Model 2 adjusted for variables in model 1 plus family income, educational attainment, US census tract level of poverty. Model 3 adjusted for model 2 covariates plus physical activity, smoking, and alcohol consumption. Model 4 adjusted for

model 3 variables plus diabetes status, BMI, natural log-transformed hs-CRP, systolic blood pressure, total and HDL cholesterol, urinary albumin, triglycerides, use of statins, use of anti-hypertensive medications, and use of anti-depressants.

Because of our interest in racial differences in depressive symptoms and CHD endpoints,⁹ race-stratified multivariable analyses were conducted *a priori*. A test for interaction between race and depressive symptoms was calculated in fully-adjusted models to examine effect modification by race. The results of the significant p-values for interaction are presented in race-stratified models below. The Kaplan-Meier method was used to calculate the cumulative incidence of each endpoint by depressive symptoms (CES-D < 4 vs. CES-D ≥ 4) among Blacks and Whites. A test for interaction between income status (<\$35,000 vs. ≥\$35,000) and depressive symptoms status was also calculated to assess effect modification by income. This interaction was a significant threshold for psychosocial influences in a prior analysis.⁴⁴ The results of the significant p-values for interaction are presented in income-stratified models below.

A total of 5,914 study participants were missing one or more covariates, with the highest number of missing data for income (n=3,016), hs-CRP (n=1,519) and urinary albumin (n=1,117). Therefore, multiple imputation of missing data by chained equations was conducted using 5 datasets. All statistical analyses were performed using SAS version 9.2 (SAS Institute, Inc. Cary, NC) and STATA version 12 (STATA Corp, College Station, TX).

Results

Sample Characteristics

Five hundred sixty nine participants were missing any follow up data and 182 participants were missing the CES-D scale; after excluding 5,227 participants with CHD at baseline, the study sample included 24,261 participants (Blacks = 10,265; Whites = 13,996). Depressive symptoms were more prevalent among Blacks (13.1%) than Whites (8.5%), $p < 0.001$. Baseline characteristics by depressive symptoms among participants without CHD at baseline are presented in Table 1. Participants who reported CES-D ≥ 4 were more likely to be younger (mean age 62.5 years), female, Black, reside in the stroke belt, have less than a high school education, and earn income less than \$35,000 than those who reported CES-D < 4. A greater percentage of participants who reported higher depressive symptoms scores had BMI ≥ 30, SBP ≥ 140 mmHg, hsCRP ≥ 3 mg/dL (49.5%), and diabetes (26.7%) than those who reported normal scores. A greater percentage of those with elevated depressive symptoms reported smoking and fewer reported getting any exercise.

Incidence Rates

Overall mean follow-up was 4.2±1.5 years, CHD incidence was 8.3 events per 1000 person-years (n=366 events) among Blacks and 8.8 events per 1000 person-years (n=613 events) among Whites ($p=0.0015$). Table 2 present the associations of baseline depressive symptoms with incident acute CHD alone and the composite measure of incident acute CHD or revascularization stratified by race. Among Whites, depressive symptoms were not associated with incident acute CHD in any of the models. Among Blacks, the HR for

incident acute CHD was 1.54 (95% CI 1.12-2.12) for participants who reported CES-D scores ≥ 4 compared to those who reported CES-D scores < 4 adjusting for age, sex, marital status and region (Model 1). After adjustment for SES, the HR for incident CHD attenuated but remained significant (HR, 1.39; 95% CI 1.00-1.91) (Model 2). After adjustment for the remaining covariates, the HR was attenuated further and no longer significant. Depressive symptoms were not associated with the composite measure acute CHD or revascularization in any of models for Whites. Among Blacks, however, after full adjustment, the HR for the composite outcome acute CHD or revascularization was 1.36 (95% CI 1.01-1.81) for participants who reported CES-D scores ≥ 4 compared to those who reported CES-D scores < 4 . From Model 1 to Model 4, there was modest attenuation but the HR remained statistically significant.

The cumulative incidence of acute CHD and, separately, acute CHD or revascularization, with depressive symptom levels by race are presented in Figure 1. Figure 1a shows Blacks who reported CES-D scores ≥ 4 had a greater cumulative incidence of CHD than Blacks who reported CES-D scores < 4 ($p=0.03$). Whites had similar cumulative incidence of CHD regardless of CES-D status (Figure 1b). Blacks who reported CES-D scores ≥ 4 had a significantly greater cumulative incidence of CHD or revascularization than Blacks who reported CES-D scores < 4 ($p=0.007$) (Figure 1c). Whites had similar cumulative incidence of CHD or revascularization regardless of CESD status (Figure 1d).

In models stratified on income (Table 3), we found that among participants with an annual income $< \$35,000$, the HR for incident CHD was 1.38 (95% CI 1.03-1.83) for those who reported CES-D scores ≥ 4 compared to those reported CES-D scores < 4 adjusting for demographics, SES and behaviors (Model 3). After adjustment for the physiological factors, the HR attenuated and was of marginal statistical significance. Among participants with an annual income $\geq \$35,000$, depressive symptoms were not associated with incident CHD in any of the models. Depressive symptoms were associated with acute CHD or revascularization in fully-adjusted models for participants who earned $< \$35,000$ (HR, 1.34; 95% CI 1.04-1.72). From Model 1 to Model 4, there was some modest attenuation, but the HR remained statistically significant. Among participants who earned $\geq \$35,000$, depressive symptoms were not associated with incident CHD or revascularization in any of the models.

Discussion

In this contemporary national study, depressive symptoms were associated with incident acute CHD among Blacks but not Whites. Depressive symptoms were also associated with incident acute CHD or revascularization among Blacks but not Whites. Depressive symptoms were also associated with the CHD/revascularization endpoint for low-income but not high-income individuals. Our findings highlight that many Blacks, who are at greater risk for low-income status, may incur risk for CHD because of depressive symptoms, contributing to long-standing disparities in CHD in the US.

Previous studies have examined the associations of depressive symptoms and CVD.^{4,9,17,18,45} One study examined depressive symptoms (CES-D 10-item scale) and overall CVD mortality (ischemic heart disease-IHD and stroke) in Blacks and Whites aged

65 and older in a Chicago area study, and found that elevated depressive symptoms were associated with CVD mortality among Blacks but not Whites.⁹ Another study examined the association of depressive symptoms (CES-D 8-item scale) with CVD mortality (IHD and stroke) in Blacks and Whites age 50 years and older using the Health and Retirement Study, and found that depressive symptoms were associated with overall CVD mortality in Blacks but not Whites.⁴ Similarly, we found in fully-adjusted models that depressive symptoms were predictive of incident acute CHD among Blacks, but not Whites. Our study is distinct from previous studies in that it is a national study with a large sample of Blacks (n=10,265), and younger age range (adults aged >45).

To our knowledge, no study has examined the association of depressive symptoms with a composite endpoint of CHD or revascularization among Blacks and Whites. Though there was some attenuation from Model 1 to 4, we found that elevated depressive symptoms were significantly associated with incident CHD or revascularization among Blacks. Depressive symptoms are associated with behaviors (physical inactivity, smoking) that may contribute to artery blockage and the need for CABG to restore the flow of blood to the heart. However, even after adjustment for exercise and smoking, associations were significant for Blacks. Research has also shown that a bi-directional association exists between CABG and depression and depressive symptoms, in that knowledge of bypass surgery predicts depression.⁴⁶ Studies have also reported that patients with elevated depressive symptoms are at risk for CHD mortality and cardiac events after CABG.⁴⁷⁻⁵⁰ These and other factors may explain the robust associations of depressive symptoms with incident CHD or revascularization among Blacks. To our knowledge, no study has examined depressive symptoms as the primary predictor of revascularization among a large sample of Blacks. This gap in the literature demonstrates the need for further understanding this association among Blacks and Black-White differences and how they contribute to racial disparities.

In our examination of the effect modification of income, we found that depressive symptoms had differing effects for those with high and low income, suggesting that depressive symptoms are more important for low-income (than high-income) persons in predicting CHD. Unfortunately, the study had insufficient numbers of events to further explore race differences among low- and high-income participants with high and low depressive symptoms separately. Even in the income-stratified analyses, there were few events among those with depressive symptoms, and we urge caution in interpreting results therein. This level of detail must be examined in future work in order to better understand the social, economic and psychological contributors to racial disparities in CHD.⁵¹

Limitations of this study include the inability to draw causal inferences, although REGARDS-MI is a prospective study that allowed for the measurement of depressive symptoms and other covariates as antecedents to CHD endpoints. Second, using self-report measures such as depressive symptoms, SES, and behaviors may misclassify the domain of interest and potentially bias results. The CES-D scale we used is a screening measure to identify depressive symptomatology and not to diagnose clinical depressive symptoms.⁴¹ Third, we used the 4-item CES-D scale, whereas the 20-item CES-D scale is more widely used, and depressive symptoms either in the past or during follow-up were not available. Fourth, possible selection bias may have occurred due to the imputation of missing income

data. Persons with missing income data may have had a pre-clinical disease or depressive symptoms prior to baseline (not captured in our study). Finally, the relatively small number of events may have contributed to the lack of a dose-response effect of depressive symptoms on CHD risk.

This study makes contributions to understanding CHD disparities by race. First, REGARDS-MI is a large, national cohort of Blacks and Whites that examines the role depressive symptoms play in explaining CHD disparities. Previous studies have used older, smaller samples to examine associations of depressive symptoms and CVD endpoints. Second, this study adds revascularization as a clinical endpoint. Previous studies mainly examine the manner in which CABG contributes to depressive symptoms and not the reverse association. Third, to our knowledge, this is first study that found significant associations of depressive symptoms (using the 4-item CES-D scale) with CHD risk in a large sample of Blacks. Therefore, this shorter scale may be appropriate for testing depressive symptomatology in Black populations. Finally, this study explored in depth how race, income and depressive symptoms contribute to CHD disparities.

Conclusion

Understanding the extent to which depressive symptoms are associated with incident acute CHD and incident CHD or revascularization and how it varies by race and income may provide a better understanding of racial disparities in CHD. Much research has been devoted to understanding this disparity by examining traditional biological and behavioral factors; however, more research is needed that link this disparity to non-traditional psychosocial factors such as depressive symptoms and income, in a large sample of Blacks and Whites.

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Abbreviations

REGARDS	Reasons for Geographic And Racial Differences in Stroke Study
CHD	coronary heart disease
CVD	cardiovascular disease
CATI	computer-assisted telephone interview

ECG	electrocardiogram
MI	myocardial infarction
PCI	percutaneous coronary intervention
CABG	coronary artery bypass grafting
CES-D	Center for Epidemiological Studies-Depression
SES	socioeconomic status
HS	high school
SBP	systolic blood pressure
DBP	diastolic blood pressure
HDL	high density lipoprotein
hs-CRP	high sensitivity C-reactive protein
BMI	body mass index
HMG CoA	hydroxymethylglutaryl-coenzyme A
HR	hazard ratio
CI	confidence interval
SAS	Statistical Analysis System
IHD	ischemic heart disease

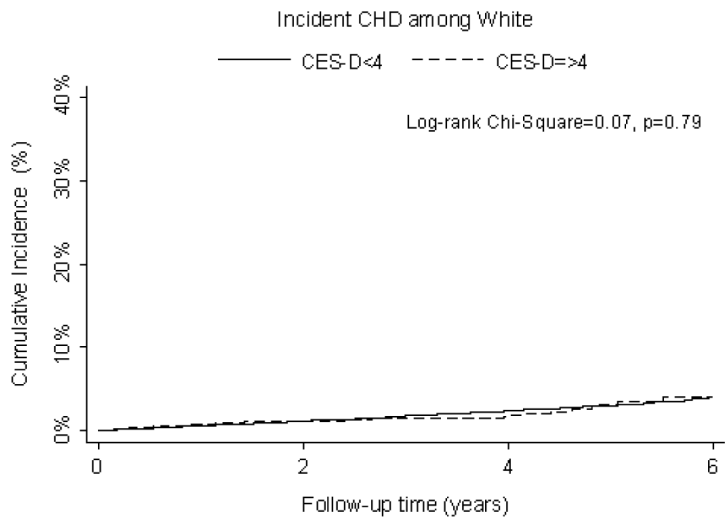
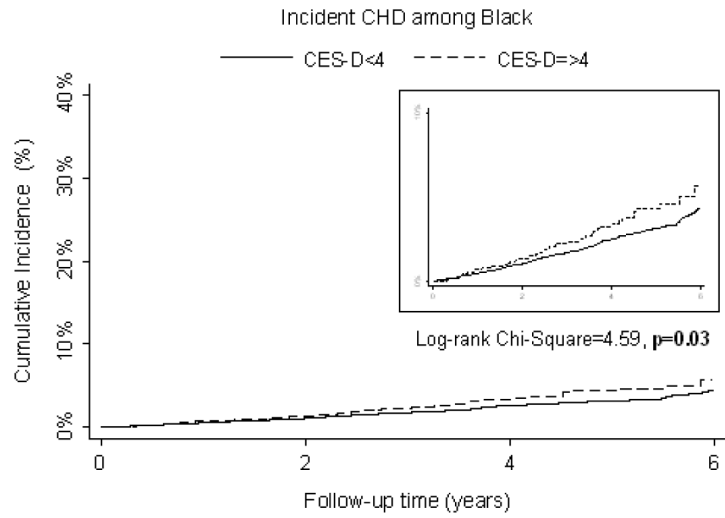
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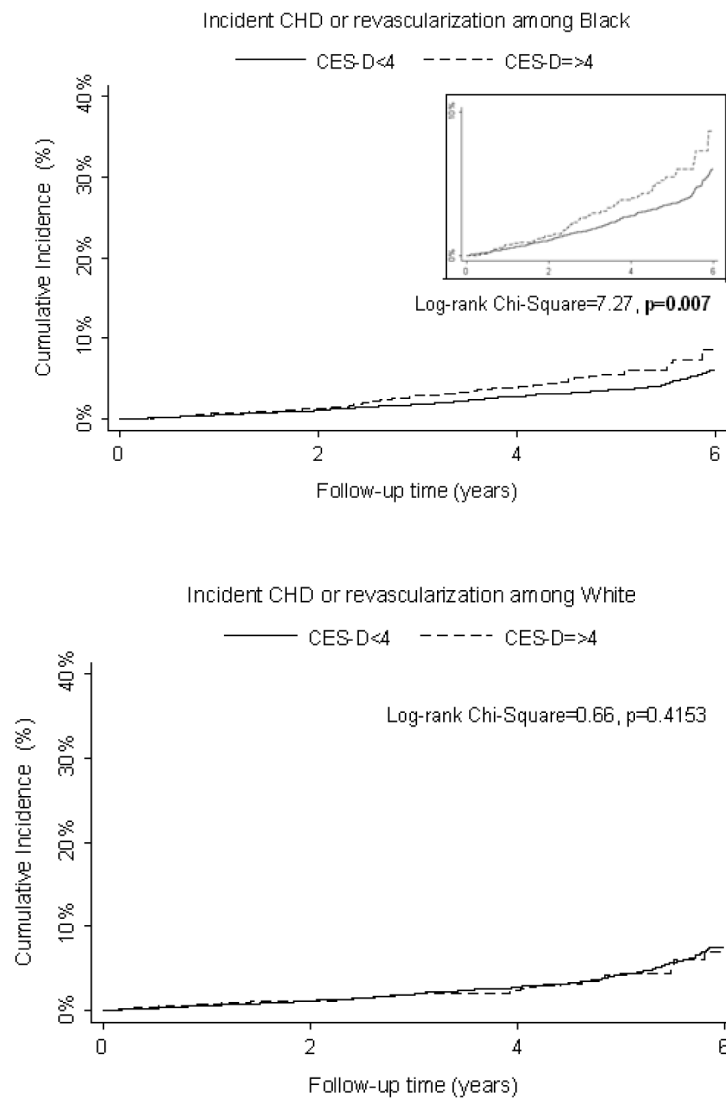


Figure 1. Cumulative incidence Kaplan-Meier graphs for (A) incident acute CHD among Blacks, (B) incident acute CHD among Whites, (C) incident acute CHD or revascularization among Blacks, and (D) incident acute CHD or revascularization among Whites comparing participants that reported elevated depressive symptoms (CES-D \geq 4) to participants that reported no depressive symptoms (CES-D < 4). A log-rank test was performed and the p-value is reported. CHD indicates coronary heart disease; CES-D, Center for Epidemiological Studies-Depression.

Table 1
 Baseline Characteristics by Depressive Symptoms among REGARDS Participants Without Coronary Heart Disease at Baseline (N=24,261)^a

	CES-D < 4 (n =21,731)	CES-D 4 (n =2,530)	P-value
Demographics:	n (%)	n (%)	
Age, years, M \pm SD	64.3 \pm 9.3	62.5 \pm 9.7	<.001
Female	12,330(56.7)	1,848(73.0)	<.001
Black	8,923(41.0)	1,342(53.0)	<.001
Marital status			<.001
Married	13,185(60.7)	988(39.1)	
Single	1,151(5.3)	204(8.1)	
Divorced	3,189(14.7)	524(20.7)	
Widowed	3,754(17.3)	705(27.9)	
Other	452(2.1)	109(4.3)	
Region of residence			<.001
Non-belt	9,789(45.1)	984(38.9)	
Belt	7,439(34.2)	958(37.9)	
Buckle	4,503(20.7)	588(23.2)	
Socioeconomic status:			
Education < HS	2,245(10.3)	570(22.6)	<.001
Income < \$35 ,000/yr	8,415(44.1)	1,507(69.7)	<.001
Residence in a census tract with poverty level of 30% or more,	2,793(14.2)	484(21.4)	<.001
Physiological Variables:			
BMI (kg/m ²):			<.001
< 25	5,516(25.6)	550(21.9)	
25-29	8,020(37.2)	815(32.5)	
30	8,048(37.3)	1,143(45.6)	
SBP (categories):			0.003
<120 mmHg	6,869(31.7)	779(30.9)	
120-139 mmHg	10,553(48.7)	1,178(46.7)	

	CES-D < 4 (n =21,731)	CES-D 4 (n =2,530)	P-value
140 mmHg	4,251(19.6)	567(22.5)	
Total cholesterol (categories):			0.03
<200 mg/dL	12,013(57.6)	1,318(54.9)	
200-239 mg/dL	6,322(30.3)	767(32.0)	
240 mg/dL	2,510(12.0)	316(13.2)	
Physiological Variables:	n (%)	n (%)	
HDL-cholesterol (<40 mg/dL in men or <50 mg/dL in women)	7,114(34.3)	899(37.7)	0.001
Urine Albumin to Creatinine Ratio, median [25 th , 75 th percentile], log-transformed	1.95[1.50-2.66]	2.03[1.57-2.84]	<.001
Triglycerides (150 mg/dL)	5,565(26.7)	721(30.1)	0.0005
Highly sensitive C-reactive protein (3 mg/dL)	8,003(39.3)	1,165(49.5)	<.001
Diabetes	3,908(18.7)	650(26.7)	<.001
Current Medication use			
Statins	6,043(28.1)	760(30.4)	0.02
Anti-hypertensives	10,330(48.0)	1,372(54.9)	<.001
Health Behaviors:			
Current smoker	2,832(13.1)	602(23.9)	<.001
Exercise (any)	14,525(67.9)	1,369(54.9)	<.001
Current Alcohol Use	11,600(53.4)	1,168(46.2)	<.001

Abbreviations: REGARDS - Reasons for Geographic And Racial Differences in Stroke Study, CES-D - Center for Epidemiological Studies-Depression, CHD - coronary heart disease, HS - high school, BMI - body mass index, SBP - systolic blood pressure, DBP - diastolic blood pressure HDL - high-density lipoprotein.

^a Baseline CHD is defined as history of self-reported myocardial infarction (MI), coronary artery bypass graft, angioplasty, stenting, or evidence of MI via electrocardiograph. Participants missing follow-up (n=513) or baseline CES-D (n=182) are excluded.

Association of incident cardiac events with depressive symptoms at baseline by race among REGARDS participants free of CHD at baseline (N=24,261)^a

Table 2

	N ^b	Events ^c	Model 1 ^d HR (95% CI)	Model 2 ^e HR (95% CI)	Model 3 ^f HR (95% CI)	Model 4 ^g HR (95% CI)
Incident Acute Coronary Heart Disease - Whites						
CES-D < 4(ref)	12808	340	1.0	1.0	1.0	1.0
CES-D 4	1188	27	1.21 (0.81-1.81)	1.10 (0.74-1.64)	1.03 (0.69-1.54)	0.99 (0.66-1.48)
Incident Acute Coronary Heart Disease - Blacks						
CES-D < 4(ref)	8923	242	1.0	1.0	1.0	1.0
CES-D 4	1342	46	1.54 (1.12-2.12)	1.39 (1.00-1.91)	1.32 (0.95-1.83)	1.29 (0.93-1.79)
Incident Acute Coronary Heart Disease or Coronary Revascularization - Whites						
CES-D < 4(ref)	12808	575	1.0	1.0	1.0	1.0
CES-D 4	1188	38	1.11 (0.80-1.56)	1.02 (0.73-1.42)	0.96 (0.69-1.35)	0.92 (0.66-1.29)
Incident Acute Coronary Heart Disease or Coronary Revascularization - Blacks						
CES-D < 4(ref)	8923	307	1.0	1.0	1.0	1.0
CES-D 4	1342	59	1.57 (1.18-2.09)	1.43 (1.07-1.90)	1.37 (1.03-1.83)	1.36 (1.01-1.81)

Abbreviations: REGARDS - Reasons for Geographic And Racial Differences in Stroke Study, CHD - coronary heart disease, HR - hazard ratio, CI - confidence interval, CES-D - Center for Epidemiological Studies-Depression, ref - referent.

^a Persons with baseline CHD excluded. 182 participants, missing baseline CES-D assessment are excluded. Multiple imputation for missing data in covariates, including 'refused' category in income and based on 5 models.

^b Average number across 5 imputation models

^c Average number of events across 5 imputation models

^d Model1 adjusts for age, gender, marital status, region.

^e Model2 adjusts for Model1 + education, income, residence in census tract with poverty level of 30% or more

^f Model3 adjusts for Model2 + physical activity, smoking, alcohol consumption

^g Model4 adjusts for Model3 + diabetes, Body Mass Index, log transformed hsCRP, systolic blood pressure, total cholesterol, HDL, log transformed urinary albumin to creatinine ratio, triglycerides, use of anti-hypertensive medication, use of statins

Bolded p-values < 0.05.

Table 3

Association of incident cardiac events with depressive symptoms at baseline by income among REGARDS participants free of CHD at baseline (N=24,261)^a

	N ^b	Events ^c	Model 1 ^d HR (95% CI)	Model 2 ^e HR (95% CI)	Model 3 ^f HR (95% CI)	Model 4 ^g HR (95% CI)
Incident Acute Coronary Heart Disease – Annual Income < \$35,000						
CES-D < 4(ref)	9,796	325	1.0	1.0	1.0	1.0
CES-D 4	1,754	63	1.41 (1.07-1.86)	1.43 (1.07-1.90)	1.38 (1.03-1.83)	1.33 (1.00-1.77)
Incident Acute Coronary Heart Disease – Annual income \$35,000						
CES-D < 4(ref)	11,935	257	1.0	1.0	1.0	1.0
CES-D 4	776	10	0.86 (0.45-1.67)	0.70 (0.33-1.47)	0.63 (0.30-1.33)	0.58 (0.27-1.23)
Incident Acute Coronary Heart Disease or Coronary Revascularization - Annual Income < \$35,000						
CES-D < 4(ref)	9,806	445	1.0	1.0	1.0	1.0
CES-D 4	1,752	84	1.42 (1.12-1.80)	1.42 (1.11-1.83)	1.38 (1.08-1.77)	1.34 (1.04-1.72)
Incident Acute Coronary Heart Disease or Coronary Revascularization - Annual Income \$35,000						
CES-D < 4(ref)	11,925	437	1.0	1.0	1.0	1.0
CES-D 4	778	13	0.73 (0.41-1.29)	0.56 (0.29-1.09)	0.53 (0.28-1.03)	0.54 (0.28-1.02)

Abbreviations: REGARDS - Reasons for Geographic And Racial Differences in Stroke Study, CHD - coronary heart disease, HR - hazard ratio, CI - confidence interval, CES-D - Center for Epidemiological Studies-Depression, ref - referent.

^a Persons with baseline CHD excluded. 182 participants, missing baseline CES-D assessment are excluded. Multiple imputation for missing data in covariates, including "refused" category in income and based on 5 models.

^b Average number across 5 imputation models

^c Average number of events across 5 imputation models

^d Model1 adjusts for age, gender, marital status, region, race

^e Model2 adjusts for Model1+ education, residence in census tract with poverty level of 30% or more

^f Model3 adjusts for Model 2 + physical activity, smoking, alcohol consumption

^g Model4 adjusts for Model3 + diabetes, Body Mass Index, log transformed hsCRP, systolic blood pressure, total cholesterol, HDL, log transformed urinary albumin to creatinine ratio, triglycerides, use of anti-hypertensive medication, use of statins **Bolded p-values < 0.05.**