Depressive Symptoms and Risk of Cardiovascular Events in Blacks

Findings From the Jackson Heart Study

Emily C. O'Brien, PhD; Melissa A. Greiner, MS; Mario Sims, PhD; Natalie Chantelle Hardy, MPH; Wei Wang, PhD; Eyal Shahar, MD, MPH; Adrian F. Hernandez, MD, MHS; Lesley H. Curtis, PhD

Background—Most studies of depression and cardiovascular risk have been conducted in white populations. We investigated this association in a community-based cohort of blacks.

Methods and Results—We used data from the Jackson Heart Study to investigate associations of baseline depressive symptoms between 2000 and 2004 with incident stroke and coronary heart disease (CHD) during 10 years. We used Kaplan–Meier estimates and Cox proportional hazards models to assess cardiovascular event risk using 3 exposure variables: any depressive symptoms (Center for Epidemiological Studies Depression score ≥16); none (score <16), minor (score 16 to <21), and major depression (score≥21); and Center for Epidemiological Studies Depression score per 1-SD increase. Models were adjusted for a stroke or CHD risk score and behavioral risk factors. Of 3309 participants with no stroke history, 738 (22.3%) had baseline depressive symptoms. A similar proportion with no previous CHD had baseline depressive symptoms (21.8%). The unadjusted 10-year risk of stroke was similar among participants with any compared with no depressive symptoms (3.7% versus 2.6%; *P*=0.12). Unadjusted CHD rates were higher among participants with depressive symptoms (5.6% versus 3.6%; *P*=0.03), and differences persisted after adjustment for clinical and behavioral risk factors but not after adjustment for coping strategies. In adjusted models comparing major versus no depressive symptoms, patients with major depressive symptoms had a 2-fold greater hazard of stroke (hazard ratio, 1.95; 95% confidence interval, 1.02–3.71; *P*=0.04). In continuous models, a 1-SD increase in Center for Epidemiological Studies Depression score was associated with a 30% increase in adjusted incident stroke risk (*P*=0.04). Similar associations were observed for incident CHD in models adjusted for clinical and behavioral risk factors, but associations were not significant after adjustment for coping strategies.

Conclusions—In a community-based cohort of blacks, major depressive symptoms were associated with greater risks of incident stroke and CHD after adjustment for clinical and behavioral risk factors. (***Circ Cardiovasc Qual Outcomes*. 2015;8:552-559. DOI: 10.1161/CIRCOUTCOMES.115.001800.)**

Key Words: cardiovascular diseases ■ depression ■ proportional hazards models ■ risk factors ■ stroke

Although depression has long been recognized as a common consequence of acute cardiovascular outcomes, it may also be an important risk factor for first-ever stroke and coronary heart disease (CHD). Prospective studies[1–5] and meta-analyses[6–8] have found positive associations between depressive symptoms and incident cardiovascular disease after adjustment for other psychosocial and physiological risk factors. Yet, most studies of depression and cardiovascular outcomes have been conducted in white populations. Knowledge about depression and cardiovascular outcomes in blacks is limited, despite higher rates of severe and disabling clinical depression and a greater degree of undertreatment than in white populations.[9] A recent analysis of the Chicago Health and Aging project found associations between a composite measure of psychological distress and stroke mortality and incidence among black adults.[10] However, this study was limited to adults aged >65 years. The link between depression and incident cardiovascular disease may be especially important in younger populations.[1,11]

The objectives of this study were to examine associations between depressive symptoms and incident stroke and CHD in a community-based cohort of blacks. We hypothesized that baseline depressive symptoms are positively associated with adverse cardiovascular outcomes after adjustment for sociodemographic and clinical characteristics. A secondary hypothesis was that this association is attenuated after adjustment

Received February 20, 2015; accepted October 8, 2015.

From the Department of Medicine, Duke Clinical Research Institute (E.C.O., M.A.G., N.C.H., A.F.H., L.H.C.) Duke University School of Medicine, Durham, NC; Department of Medicine, University of Mississippi Medical Center, Jackson (W.W.) and Department of Epidemiology and Biostatistics, Mel and Enid Zuckerman College of Public Health, University of Arizona, Tucson (E.S.).

The content of this article is solely the responsibility of the authors and does not necessarily represent the official views of the National Heart, Lung, and Blood Institute, the National Institute on Minority Health and Health Disparities, or the National Institutes of Health.

The Data Supplement is available at http://circoutcomes.ahajournals.org/lookup/suppl/doi:10.1161/CIRCOUTCOMES.115.001800/-/DC1.

Correspondence to Emily C. O'Brien, PhD, Duke Clinical Research Institute, PO Box 17969, Durham, NC 27715. E-mail emily.obrien@duke.edu.

WHAT IS KNOWN

- Previous studies have found that depression is predictive of adverse cardiovascular events.
- Compared with white populations, blacks have higher rates of severe depression, but there is limited data on the prognostic significance of depression in black cohorts.

WHAT THE STUDY ADDS

- Depression was common in this black population, affecting nearly one quarter of cohort participants.
- Participants with depressive symptoms had more comorbidities, lower physical activity, and lower socioeconomic status.
- Even after adjusting for clinical and behavioral risk factors, major depressive symptoms were associated with a nearly 2-fold increase in incidence of stroke and coronary heart disease.

for behavioral risk factors, antidepressant medication use, and self-reported coping strategies.

Methods

Data Sources

We used data from the Jackson Heart Study, a community-based cohort study of blacks in Jackson, Mississippi, designed to investigate risk factors for cardiovascular disease.[12] The study enrolled 5301 participants aged 21 to 94 years from 4 populations: community volunteers from the Jackson metropolitan area (30%), randomly selected residents of Jackson (17%), participants in the Jackson site of the Atherosclerosis Risk in Communities (ARIC) cohort study[13] (22%), and family members of Jackson Heart Study participants (31%). All participants underwent a baseline examination between 2000 and 2004 to collect data on demographic characteristics, socioeconomic characteristics, medical history, physical examination, laboratory values, cardiac test results, behavioral factors, and medications. Deaths and nonfatal events were ascertained via annual telephone calls, review of death certificates, and abstraction of medical records for relevant *International Classification of Diseases, Ninth Revision, Clinical Modification* codes through 2010. The Jackson Heart Study was approved by the institutional review boards of Jackson State University, Tougaloo College, the University of Mississippi Medical Center, and the Duke University Health System. All study participants gave written informed consent.

Study Population

We included all Jackson Heart Study participants who completed at least 16 of the 20 Center for Epidemiological Studies Depression (CES-D) scale screening questions at baseline. We excluded participants who had a history of stroke at baseline (n=234) from analyses of incident stroke and participants with a history of CHD (n=425) from analyses of incident CHD. For models including self-reported coping strategies, we excluded 383 participants for stroke analysis and 367 in the CHD analysis.

Exposure Definition

We defined the presence of any depressive symptoms as a binary variable based on a score of ≥16 on the CES-D at baseline.[14] The score is the sum of the 20 questions with a possible range of 0 to 60. We further classified participants into major and minor depressive symptomatology for secondary analyses using the following CES-D cut points: minor (score of 16 to <21) and major (score of ≥21). We also examined CES-D score as a continuous variable in SD units, translated as CES-D score per 1-SD increase.

Outcome Ascertainment

Strokes and CHD (ie, myocardial infarction, fatal CHD, or cardiac procedure) were ascertained via directed patient queries during annual telephone follow-up and ongoing surveillance of hospitalizations, with subsequent transmission of hospital records and death certificates to a medical record abstraction unit for review. A computer-generated diagnosis with physician adjudication was used to classify hospitalized and fatal stroke and CHD events. We included all events that occurred within 10 years of the baseline examination date based on a median of 8 years of follow-up time and a 75th percentile of 10 years.

Covariates

Because of the low number of events relative to the number of potential confounding variables, we created a single composite risk score separately for stroke and CHD covariate adjustment to avoid biased regression estimates.[15,16] We calculated a 10-year stroke risk score for each participant by fitting a separate incident stroke model on the entire Jackson Heart Study cohort with no previous stroke at baseline (5067 participants and 153 stroke events), using Cox proportional hazards regression. Regression variables included age, sex, body mass index, systolic blood pressure, dialysis, previous myocardial infarction, diabetes mellitus, hypertension, atrial fibrillation, left ventricular hypertrophy, history of cardiovascular disease, smoking history, antihypertensive medication use, and antithrombotic medication use. To ascertain left ventricular hypertrophy, we used a quantitative left ventricular mass measurement from echocardiography when available (missing for 35% of participants); otherwise, we ascertained left ventricular hypertrophy based on a qualitative assessment of mild, moderate, or severe. We then used the X-β ($\sum \beta_j X_j$) from this model as a continuous stroke risk score variable. A similar process was used to create a 10-year CHD risk score among participants with no previous CHD at baseline (n=4876 participants, 192 CHD events). For the incident CHD model, we included all variables in the stroke model except for previous myocardial infarction and history of cardiovascular disease, and added variables for total cholesterol, lipid-lowering medications, and previous stroke.

Mediating Variables

Hypothesized mediators of the association between depressive symptoms and cardiovascular outcomes included socioeconomic status (education level and annual family income), alcohol use (mean number of drinks per day), physical activity (mean number of activity hours per week), antidepressant use (α-2 receptor antagonists [tetracyclics], monoamine oxidase inhibitors, modified cyclics, selective serotonin reuptake inhibitors, tricyclic agents, and miscellaneous antidepressants), and self-reported coping strategies (engagement and disengagement subscale scores on the Coping Strategies Inventory-Short Form).[17]

Statistical Analysis

A copy of the a priori statistical analysis plan is provided in the Appendix I in the Data Supplement. We tested for differences in the distribution of baseline characteristics by the presence of depressive symptoms at baseline using χ^2 tests for categorical variables and Kruskal–Wallis tests for continuous variables. We used Kaplan–Meier methods to calculate the cumulative incidence of first stroke or incident CHD by the presence of depressive symptoms at baseline and tested for differences between the groups using log-rank tests. We estimated covariate-adjusted associations between depressive symptoms and cardiovascular outcomes using Cox proportional hazards models with censoring at the time of death, participant

Table 1. Baseline Characteristics of the Study Population

Characteristic	Depressive Symptoms		*P* Value
	No (n=2571)	Yes (n=738)	
Age, median (IQR), y	54.3 (44.9–63.7)	52.2 (42.9–63.0)	0.003
Women, No. (%)	1627 (63.3)	536 (72.6)	<0.001
Medical history, No. (%)			
Atrial fibrillation	4 (0.2)	2 (0.3)	0.52
Cardiovascular disease	127 (4.9)	68 (9.2)	<0.001
Diabetes mellitus	497 (19.3)	170 (23.0)	0.03
Dialysis	8 (0.3)	5 (0.7)	0.16
Heart failure	151 (5.9)	78 (10.6)	<0.001
Hypertension	1491 (58.0)	451 (61.1)	0.13
Left ventricular hypertrophy	178 (6.9)	57 (7.7)	0.46
Myocardial infarction	85 (3.3)	51 (6.9)	<0.001
Physical examination, median (IQR)			
Body mass index, kg/m^2	30.5 (27.0–35.1)	31.1 (27.1–36.5)	0.02
Systolic blood pressure, mm Hg	124.0 (114.0–135.0)	125.0 (114.0–136.0)	0.30
Waist circumference, cm	98.0 (89.0–108.0)	101.0 (89.0–111.0)	0.01
Socioeconomic characteristics, No. (%)			
Education			
Less than high school	284 (11.0)	145 (19.6)	<0.001
High school graduate	1014 (39.4)	385 (52.2)	
College degree	699 (27.2)	139 (18.8)	
Graduate or professional degree	574 (22.3)	69 (9.3)	
Annual family income			
<$20 000	474 (18.4)	258 (35.0)	<0.001
$20 000–$50 000	807 (31.4)	233 (31.6)	
$50 000–$75 000	482 (18.7)	88 (11.9)	
>$75 000	467 (18.2)	48 (6.5)	
Missing	341 (13.3)	111 (15.0)	
Medications, No. (%)			
Anticoagulant agent	15 (0.6)	8 (1.1)	0.15
Antidepressant agent	106 (4.1)	84 (11.4)	<0.001
Antihyperlipidemic agent	295 (11.5)	76 (10.3)	0.37
Antihypertensive agent	733 (28.5)	243 (32.9)	0.02
Antiplatelet agent	22 (0.9)	5 (0.7)	0.64
Antithrombotic agent (anticoagulant, antiplatelet, or cyclooxygenase-2 inhibitor)	182 (7.1)	85 (11.5)	<0.001
Cyclooxygenase-2 inhibitor	147 (5.7)	73 (9.9)	<0.001
Missing	181 (7.0)	64 (8.7)	0.14
Behavioral factors			
Drinks per day in the previous year, median (IQR)	0.2 (0.7)	0.2 (0.9)	0.96
Hours of physical activity per week, No. (%)			
None	1088 (42.3)	383 (51.9)	<0.001
<1 h	268 (10.4)	83 (11.2)	
1 to <2 h	480 (18.7)	115 (15.6)	
2 to <3 h	214 (8.3)	64 (8.7)	
3 to <4 h	182 (7.1)	33 (4.5)	
≥4 h	339 (13.2)	60 (8.1)	

(*Continued*)

Table 1. Continued

Characteristic	Depressive Symptoms		*P* Value
	No (n=2571)	Yes (n=738)	
Smoking history, No. (%)			
Never smoked	1837 (71.5)	471 (63.8)	<0.001
Former smoker	486 (18.9)	128 (17.3)	
Current smoker	248 (9.6)	139 (18.8)	
CSI-SF scores, median (IQR)			
Disengagement score	22.0 (20.0–25.0)	25.0 (22.0–28.0)	<0.001
Engagement score	29.0 (26.0–32.0)	26.0 (23.0–29.0)	<0.001
Stroke risk scores, median (IQR)			
Framingham stroke risk score	5.0 (2.0–9.0)	6.0 (3.0–10.0)	0.007
Internally derived stroke risk score	4.9 (4.0–5.7)	4.9 (3.9–5.9)	0.30

CSI-SF indicates coping skills inventory-short form; and IQR, interquartile range.

loss to follow-up, or the end of study event surveillance follow-up (December 31, 2011).

We examined associations for stroke and CHD separately using 3 depressive symptom variables: any depression (yes or no), depressive symptom category (none, minor, or major), and CES-D score per 1-SD increase. For each depression variable, we ran 5 sequential models: (1) an unadjusted model in which depression was the only variable, (2) a model that included adjustment for stroke or CHD risk score and socioeconomic status, (3) a model that included adjustment for stroke or CHD risk score, socioeconomic status, and behavioral risk factors, (4) a model that included adjustment for stroke or CHD risk score, socioeconomic status, behavioral risk factors, and antidepressant medication use, and (5) a model that included the adjustment for stroke or CHD risk score, socioeconomic status, behavioral risk factors, antidepressant use, and coping strategies. In model 5, we excluded participants who had missing data for any part of the Coping Strategies Inventory-Short Form. In all models, we tested the proportionality assumption for the depression variable by including an interaction variable for the interaction between the depression variable and log of survival time.

Because of the high proportion of participants who did not complete the CES-D, we examined the baseline characteristics of the study population by CES-D completion. For variables with low rates of missingness (<5% of records), we imputed continuous variables to the overall median value, dichotomous variables to no, and multichotomous variables to the most frequent categorical value.[18] For variables with >5% missingness (ie, medications and income), we treated missing values as a separate category.[19,20] We used a 2-tailed α=0.05 to establish statistical significance and calculated 95% confidence intervals (CIs). We used SAS version 9.3 for all analyses (SAS Institute, Cary, NC).

Results

Of 5301 participants in the Jackson Heart Study who completed the baseline examination, we excluded participants with previous stroke (n=234) and additionally those with incomplete CES-D information (n=1758) for the stroke analysis. Among 3309 participants in the final study cohort, 738 (22.3%) had depressive symptoms at baseline. Table 1 shows the distribution of baseline characteristics among participants with depressive symptoms at baseline and those without (Table I in the Data Supplement shows the baseline characteristics by major, minor, and no depressive symptoms). Participants who reported depressive symptoms were younger on average and were more likely to be women than those who did not. Participants with depressive symptoms were significantly more likely to have a history of cardiovascular disease, diabetes mellitus, heart failure, previous myocardial infarction, and zero hours of weekly physical activity and to be current smokers. Median body mass index and waist circumference were higher among participants with depressive symptoms. Antidepressant use was low among participants with depressive symptoms at baseline (11.4%). Participants who did not complete the CES-D were younger on average, were more likely to be men, and had lower levels of education than those who completed the CES-D (Table II in the Data Supplement).

Of 5301 participants in the Jackson Heart Study who completed the baseline examination, we excluded participants with previous CHD (n=425) and additionally those with incomplete CES-D information (n=1698) from the incident CHD analysis. Among 3178 participants in the final study cohort, 692 (21.8%) had depressive symptoms at baseline. The distribution of baseline characteristics by depressive symptoms in the incident CHD cohort was similar to that of the incident stroke cohort (Table III in the Data Supplement shows the baseline characteristics of the incident CHD cohort by depressive symptoms, and Table IV in the Data Supplement shows the baseline characteristics of the incident CHD cohort by major, minor, and no depressive symptoms).

As shown in Figure 1, participants with depressive symptoms had higher cumulative incidence of stroke than those without. The unadjusted 10-year cumulative incidence of stroke was 3.7% (n=23 stroke events; 95% CI, 2.4%–5.8%; censoring rates: death [63 (8.5%)], loss to Jackson Heart Study [JHS] surveillance [83 (11.2%)], <10-year follow-up [437 (59.2%)]) for participants with depressive symptoms and 2.6% (n=56 stroke events; 95% CI, 2.0%–3.4%; censoring rates: death [170 (6.6%)], loss to JHS surveillance [255 (9.9%)], and <10-year follow-up [1619 (63.0%)]) for those with no depressive symptoms (*P*=0.12; Figure 1A). When we stratified participants by minor and major depressive symptoms (Figure 1B), the highest 10-year cumulative incidence rates of stroke were observed for participants with major depressive symptoms (5.4%; 95% CI, 3.1%–9.4%), followed by those with no depressive symptoms (2.6%; 95% CI, 2.0%–3.4%) and those with minor depressive symptoms (2.0%; 95% CI, 1.0%–4.3%; *P*=0.04).

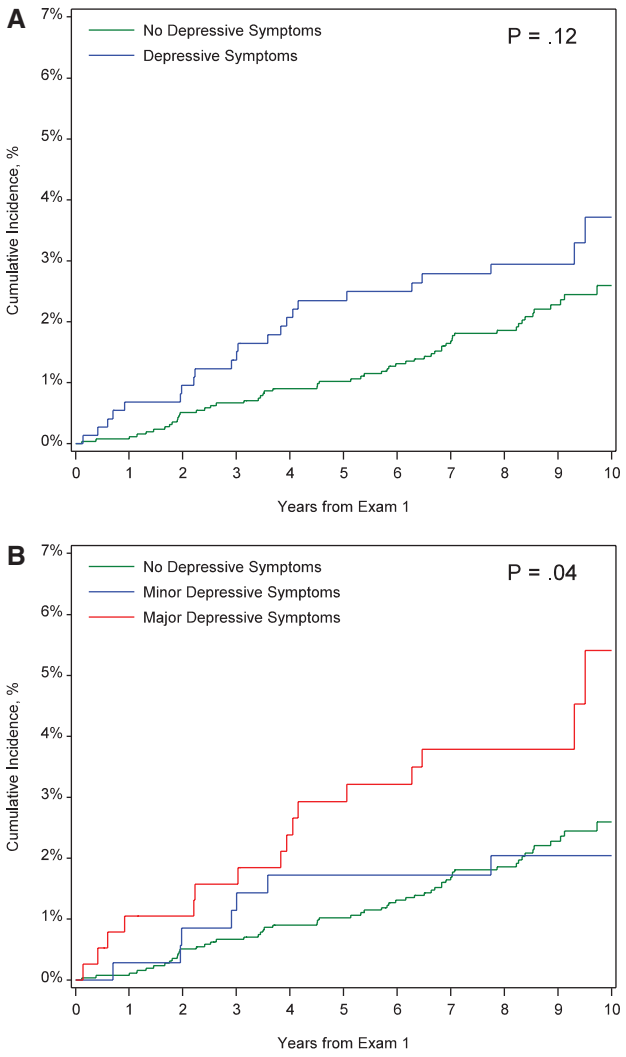

Figure 1. Kaplan–Meier curves for incident stroke among patients with and without depressive symptoms at baseline (**A**) and with no, minor, or major depressive symptoms at baseline (**B**).

The unadjusted 10-year cumulative incidence of CHD was 5.6% (n=34 CHD events; 95% CI, 4.0%–7.8%; censoring rates: death [52 (7.5%)], loss to JHS surveillance [79 (11.4%)], and <10-year follow-up [400 (57.8%)]) for participants with depressive symptoms and 3.6% (n=79 stroke events; 95% CI, 2.9%–4.6%; censoring rates: death [143 (5.8%)], loss to JHS surveillance [244 (9.8%)] and <10-year follow-up [1576 (63.4%)]) for those with no depressive symptoms (*P*=0.03; Figure 2A). When we stratified participants by minor and major depressive symptoms, the highest 10-year cumulative incidence rates of CHD were observed for participants with major depressive symptoms (5.8%; 95% CI, 3.7%–9.0%), followed by those with minor depressive symptoms (5.3%; 95% CI, 3.2%–8.8%) and those with no depressive symptoms (3.6%; 95% CI, 2.9%–4.6%; *P*=0.06; Figure 2B).

Table 2 shows hazard ratios for the unadjusted and adjusted associations between the presence of depressive symptoms and incident stroke and CHD. The presence of any depressive symptoms was not significantly associated with stroke in unadjusted or adjusted models, but was associated with a 58% increase in the hazard of incident CHD in unadjusted models. In models classifying depressive symptoms as major, minor, or none, major depressive symptoms were associated with a 2-fold increase in the hazard of stroke compared with no depressive symptoms (Table 3). This association persisted after adjustment for stroke risk, socioeconomic status, behavioral risk factors, antidepressant use, and coping strategies. Similar associations were observed in incident CHD models, with a 76% increase in incident CHD among patients with major versus no depressive symptoms. This increase in risk persisted after adjustment for the incident CHD risk score, socioeconomic status, behavioral risk factors, and antidepressant use, but was no longer significant after adjustment for coping strategies.

We further examined the association between continuous CES-D score per 1-SD increase and stroke risk. The unadjusted risk of incident stroke increased by 26% per 1-SD increase in CES-D (Table 4). After adjustment, each SD increase in CES-D score was associated with a statistically significant 30% increase in the risk of incident stroke (hazard ratio per 1-SD increase, 1.30; 95% CI, 1.02–1.66; *P*=0.04). We also observed positive associations for continuous CES-D

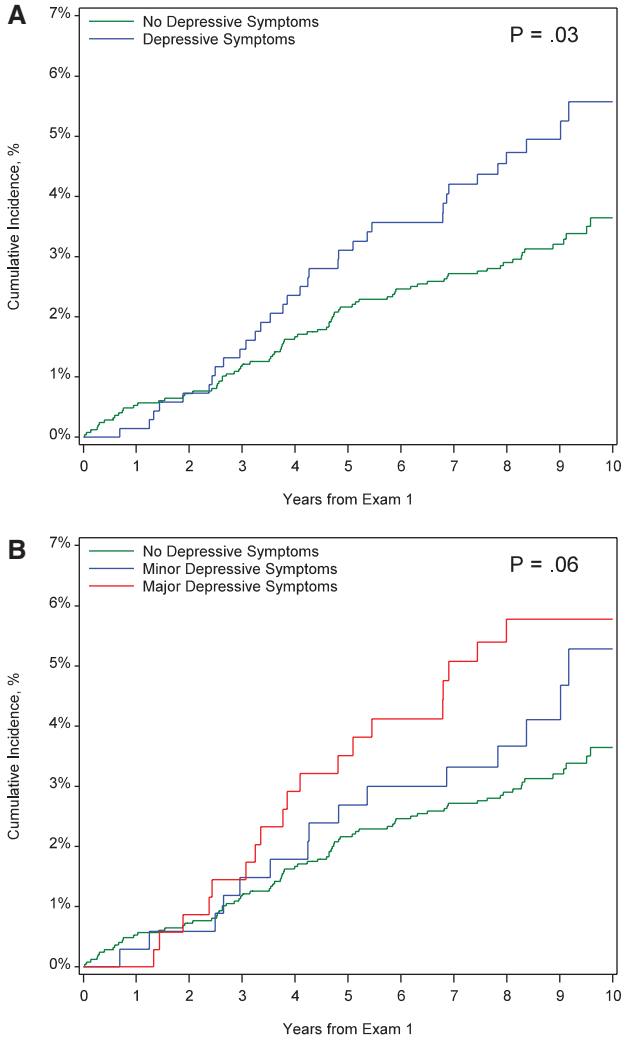

Figure 2. Kaplan–Meier curves for incident coronary heart disease among patients with and without depressive symptoms at baseline (**A**) and with no, minor, or major depressive symptoms at baseline (**B**).

Table 2. Association Between Any Depressive Symptoms and Incident Stroke and CHD

Model	Hazard Ratio (95% CI)	*P* Value
Incident stroke		
Model 1. Unadjusted	1.47 (0.90–2.38)	0.12
Model 2. Adjusted for stroke risk score and socioeconomic status	1.30 (0.79–2.14)	0.30
Model 3. Model 2 plus behavioral risk factors	1.30 (0.79–2.14)	0.30
Model 4. Model 3 plus antidepressant use	1.33 (0.81–2.20)	0.26
Model 5. Model 4 plus coping strategies	1.28 (0.74–2.23)	0.37
Incident CHD		
Model 1. Unadjusted	1.58 (1.05–2.36)	0.03
Model 2. Adjusted for CHD risk score and SES	1.54 (1.02–2.34)	0.04
Model 3. Model 2+behavioral risk factors	1.54 (1.01–2.33)	0.04
Model 4. Model 3+antidepressant use	1.55 (1.02–2.35)	0.04
Model 5. Model 4+coping strategies	1.41 (0.90–2.21)	0.14

CHD indicates coronary heart disease; CI, confidence interval; and SES, socioeconomic status.

and incident CHD, with a 19% increase in CHD risk for each 1-SD increase in CES-D score. This association also persisted after adjustment for incident CHD risk score, socioeconomic status, behavioral risk factors, and antidepressant use, but was attenuated and no longer significant after adjustment for coping strategies.

Discussion

We investigated associations between depressive symptoms and incident cardiovascular outcomes in a community-based cohort of blacks. Depressive symptoms were present in nearly one quarter of cohort participants. Participants who reported depressive symptoms had greater comorbidity burden and more cardiovascular risk factors, were more likely to be current smokers, reported less physical activity, and had lower socioeconomic status. Unadjusted rates of incident stroke and CHD were higher among participants with depressive symptoms than those without. After adjustment for baseline risk, relevant confounders, and hypothesized mediators, major depressive symptoms were associated with a 2-fold increase in incident stroke risk. In adjusted analyses of continuous CES-D, each 1-SD increase in the score was associated with a 30% increase in the hazard of incident stroke. We observed similar patterns for incident CHD, but these associations were attenuated after adjustment for coping strategies.

Depression is increasingly recognized as an important risk factor for adverse cardiovascular events. Investigators from the Framingham Heart Study reported a 4-fold increase in risk of stroke or transient ischemic attack among cohort participants aged ≤65 years with depressive symptoms (CES-D≥16).[1] However, results from other studies have been less conclusive,[21,22] and the majority of work to date has been conducted in white populations. Evidence from the Chicago Health and Aging Project suggests that unadjusted stroke incidence rates were higher among older blacks (mean age, 77 years; n=2649) reporting psychological distress (a composite measure of depressive symptoms, perceived stress, neuroticism, and life dissatisfaction) than those who reported no distress.[10] Similar to our findings, this association was attenuated after adjustment for stroke risk factors. Positive associations were found among 2557 blacks who reported depressive symptoms in the Health and Retirement Study.[23] However, neither study included younger adults, a population that may be especially vulnerable to adverse cardiovascular effects of clinical depression.[1] In addition, these studies relied on administrative claims and self-report for event ascertainment. Although the association between depressive symptoms and incident CHD has been more fully explored, few studies have examined these associations in black patients, and

Table 3. Association Between Minor and Major Symptoms and Incident Stroke and CHD

	Depressive Symptoms			
Model	Minor vs None, HR (95% CI)	*P* Value	Major vs None, HR (95% CI)	*P* Value
Incident stroke				
Model 1. Unadjusted	0.91 (0.42–2.00)	0.82	2.00 (1.15–3.48)	0.01
Model 2. Adjusted for stroke risk score and socioeconomic status	0.80 (0.36–1.75)	0.57	1.82 (1.02–3.22)	0.04
Model 3. Model 2 plus behavioral risk factors	0.78 (0.35–1.72)	0.54	1.86 (1.05–3.30)	0.03
Model 4. Model 3 plus antidepressant use	0.79 (0.36–1.74)	0.56	1.93 (1.09–3.42)	0.03
Model 5. Model 4 plus coping strategies	0.75 (0.32–1.78)	0.52	1.95 (1.02–3.71)	0.04
Incident CHD				
Model 1. Unadjusted	1.39 (0.80–2.42)	0.24	1.76 (1.07–2.90)	0.03
Model 2. Adjusted for CHD risk score and SES	1.27 (0.72–2.22)	0.41	1.87 (1.12–3.13)	0.02
Model 3. Model 2+behavioral risk factors	1.26 (0.72–2.20)	0.42	1.87 (1.12–3.13)	0.02
Model 4. Model 3+antidepressant use	1.26 (0.72–2.20)	0.43	1.90 (1.13–3.20)	0.01
Model 5. Model 4+coping strategies	1.19 (0.66–2.15)	0.55	1.67 (0.95–2.93)	0.07

CHD indicates coronary heart disease; CI, confidence interval; HR, hazard ratio; and SES, socioeconomic status.

Table 4. Association Between CES-D Score and Incident Stroke and CHD*

Model	Hazard Ratio (95% CI)	*P* Value
Incident stroke		
Model 1. Unadjusted	1.26 (1.04–1.53)	0.02
Model 2. Adjusted for stroke risk score and socioeconomic status	1.239 (0.998–1.538)	0.052
Model 3. Model 2 plus behavioral risk factors	1.241 (1.001–1.537)	0.048
Model 4. Model 3 plus antidepressant use	1.27 (1.02–1.57)	0.03
Model 5. Model 4 plus coping strategies	1.30 (1.02–1.66)	0.04
Incident CHD		
Model 1. Unadjusted	1.187 (1.002–1.407)	0.047
Model 2. Adjusted for CHD risk score and SES	1.22 (1.02–1.48)	0.03
Model 3. Model 2+behavioral risk factors	1.22 (1.02–1.47)	0.03
Model 4. Model 3+antidepressant use	1.23 (1.02–1.49)	0.03
Model 5. Model 4+coping strategies	1.17 (0.95–1.45)	0.13

CES-D indicates Center for Epidemiological Studies Depression; CHD, coronary heart disease; CI, confidence interval; and SES, socioeconomic status.

*Events occurring within 10 years of the baseline examination (median follow-up time=8 years; 75th percentile=10 years).

existing studies have produced mixed results.[4,24,25] Our study builds on previous work in a well-characterized cohort with a large sample of blacks and detailed information on cardiovascular risk factors and physician-adjudicated events.

Our finding of increased event risk in patients with major but not minor depressive symptoms is consistent with previous work on psychological correlates of adverse health outcomes.[26–28] In a cohort study of the association between CES-D score and cardiac mortality, Penninx et al[29] reported a nearly 2-fold increase in excess mortality associated with major depressive symptoms compared with minor depressive symptoms. It is possible that minor depressive symptoms represents a more sensitive but less specific classification of the exposure of interest. It may also be that reports of minor depression are more reflective of daily mood fluctuations rather than long-term dysthymia, and therefore are less predictive of long-term cardiovascular risk. Future analyses are needed to further elucidate the excess cardiovascular risk associated with minor depressive symptoms in blacks. In addition, in contrast to results from incident stroke models, we found that the association between depressive symptoms and CHD risk was no longer significant after adjustment for coping strategies. It is possible that coping strategies are particularly important for mitigating the increased CHD risk associated with depressive symptoms, but not for the increased risk of stroke. Although outside the scope of this analysis, this hypothesis warrants additional study.

The need for greater understanding of associations between depressive symptoms and cardiovascular outcomes in blacks is particularly salient in light of reported racial disparities in disease severity, timely diagnosis, and the use of pharmacotherapy. Although evidence suggests that blacks are more likely to visit a primary care physician for mental health–related concerns,[30] they may also be less likely to have depression detected in primary care settings.[31] Blacks report higher rates of disabling depression compared with white persons, and blacks are also less likely to be prescribed evidence-based pharmacotherapy.[9] In 1 study of antidepressant use among Medicaid recipients, black patients were significantly less likely than white patients to receive selective serotonin reuptake inhibitors at the time of the initial depression diagnosis than were white patients.[32] However, these treatment differences may be at least partly a result of patient preferences. Previous research suggests that black patients are less likely than white patients to find antidepressant medication acceptable[33] and less likely to think that depression is biologically based.[34] Consistent with previous findings, we found that only 11.4% of participants with depressive symptoms were treated with antidepressants at baseline. In addition, the relatively high rate of Jackson Heart Study participants who did not complete the CES-D scale may represent reluctance to disclose mental health information because of cultural stigma associated with depression.[35]

There are several limitations to our study. First, we did not have information on changes in depressive symptomatology over time. Second, we used the CES-D, a validated screening tool, to identify depressive symptomatology, consistent with what has been used in previous studies of depression and cardiovascular disease. However, because we did not have information on clinically diagnosed depression, some misclassification of depression status is possible. Third, we did not have information on traumatic brain injury or disability; however, we did include a detailed set of clinical comorbid conditions in adjustment models and an indicator for weekly physical activity level. We also did not have baseline CES-D information on 1889 participants in the Jackson Heart Study. The full distribution of baseline characteristics by CES-D completion is provided in Table II in the Data Supplement. Finally, the Jackson Heart Study cohort represents a population with relatively high socioeconomic status, with nearly half of cohort members reporting a college education or higher. Therefore, the results may not be generalizable to populations of lower socioeconomic status.

Our study has several unique strengths. First, the Jackson Heart Study is the largest US-based cohort with contemporary data on cardiovascular risk factors among blacks, a population with a greater burden of severe depression than white populations. Second, we were able to examine multiple measures of depressive symptoms using a validated scale. Third, we had detailed information on a wide range of clinical confounders and socioeconomic indicators not typically available in administrative or retrospective registry data sets. Finally, all cardiovascular events in the Jackson Heart Study were adjudicated by clinical reviewers, reducing the potential for event misclassification.

In conclusion, we found a positive association between major depressive symptoms and risk of incident stroke and incident CHD, which persisted after multivariable adjustment for clinical and behavioral risk factors. Future work characterizing the burden of depression over time and risk of adverse cardiovascular events in blacks is warranted.

Acknowledgments

We thank the staff and participants of the Jackson Heart Study for their important contributions to this work. Damon M. Seils, MA, Duke University, assisted with article preparation.

Sources of Funding

The Jackson Heart Study is supported by contracts HHSN268201300046C, HHSN268201300047C, HHSN268201300048C, HHSN268201300049C, and HHSN268201300050C from the National Heart, Lung, and Blood Institute and the National Institute on Minority Health and Health Disparities. Research reported in this article was supported by grant R01HL117305 from the National Heart, Lung, and Blood Institute.

Disclosures

None.

References

1. Salaycik KJ, Kelly-Hayes M, Beiser A, Nguyen AH, Brady SM, Kase CS, Wolf PA. Depressive symptoms and risk of stroke: the Framingham Study. *Stroke*. 2007;38:16–21. doi: 10.1161/01.STR.0000251695.39877.ca.
2. O'Donnell MJ, Xavier D, Liu L, Zhang H, Chin SL, Rao-Melacini P, Rangarajan S, Islam S, Pais P, McQueen MJ, Mondo C, Damasceno A, Lopez-Jaramillo P, Hankey GJ, Dans AL, Yusoff K, Truelsen T, Diener HC, Sacco RL, Ryglewicz D, Czlonkowska A, Weimar C, Wang X, Yusuf S; INTERSTROKE investigators. Risk factors for ischaemic and intracerebral haemorrhagic stroke in 22 countries (the INTERSTROKE study): a case-control study. *Lancet*. 2010;376:112–123. doi: 10.1016/S0140-6736(10)60834-3.
3. Jonas BS, Mussolino ME. Symptoms of depression as a prospective risk factor for stroke. *Psychosom Med*. 2000;62:463–471.
4. Ford DE, Mead LA, Chang PP, Cooper-Patrick L, Wang NY, Klag MJ. Depression is a risk factor for coronary artery disease in men: the precursors study. *Arch Intern Med*. 1998;158:1422–1426.
5. Sims M, Redmond N, Khodneva Y, Durant RW, Halanych J, Safford MM. 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 study. *Ann Epidemiol*. 2015;25:426–432. doi: 10.1016/j.annepidem.2015.03.014.
6. Dong JY, Zhang YH, Tong J, Qin LQ. Depression and risk of stroke: a meta-analysis of prospective studies. *Stroke*. 2012;43:32–37. doi: 10.1161/STROKEAHA.111.630871.
7. Pan A, Sun Q, Okereke OI, Rexrode KM, Hu FB. Depression and risk of stroke morbidity and mortality: a meta-analysis and systematic review. *JAMA*. 2011;306:1241–1249. doi: 10.1001/jama.2011.1282.
8. Rugulies R. Depression as a predictor for coronary heart disease. A review and meta-analysis. *Am J Prev Med*. 2002;23:51–61.
9. Williams DR, González HM, Neighbors H, Nesse R, Abelson JM, Sweetman J, Jackson JS. Prevalence and distribution of major depressive disorder in African Americans, Caribbean blacks, and non-Hispanic whites: results from the National Survey of American Life. *Arch Gen Psychiatry*. 2007;64:305–315. doi: 10.1001/archpsyc.64.3.305.
10. Henderson KM, Clark CJ, Lewis TT, Aggarwal NT, Beck T, Guo H, Lunos S, Brearley A, Mendes de Leon CF, Evans DA, Everson-Rose SA. Psychosocial distress and stroke risk in older adults. *Stroke*. 2013;44:367–372. doi: 10.1161/STROKEAHA.112.679159.
11. Shah AJ, Ghasemzadeh N, Zaragoza-Macias E, Patel R, Eapen DJ, Neeland IJ, Pimple PM, Zafari AM, Quyyumi AA, Vaccarino V. Sex and age differences in the association of depression with obstructive coronary artery disease and adverse cardiovascular events. *J Am Heart Assoc*. 2014;3:e000741. doi: 10.1161/JAHA.113.000741.
12. Taylor HA Jr, Wilson JG, Jones DW, Sarpong DF, Srinivasan A, Garrison RJ, Nelson C, Wyatt SB. Toward resolution of cardiovascular health disparities in African Americans: design and methods of the Jackson Heart Study. *Ethn Dis*. 2005;15(4 suppl 6):S6–S4.
13. The Atherosclerosis Risk in Communities (ARIC) Study: design and objectives. The ARIC Investigators. *Am J Epidemiol*. 1989;129:687–702.
14. Radloff L. The CES-D scale: a self-report depression scale for research in the general population. *Appl Psychol Meas*. 1977;1:385–401.
15. Arbogast PG, Kaltenbach L, Ding H, Ray WA. Adjustment for multiple cardiovascular risk factors using a summary risk score. *Epidemiology*. 2008;19:30–37. doi: 10.1097/EDE.0b013e31815be000.
16. Arbogast PG, Ray WA. Performance of disease risk scores, propensity scores, and traditional multivariable outcome regression in the presence of multiple confounders. *Am J Epidemiol*. 2011;174:613–620. doi: 10.1093/aje/kwr143.
17. Addison CC, Campbell-Jenkins BW, Sarpong DF, Kibler J, Singh M, Dubbert P, Wilson G, Payne T, Taylor H. Psychometric evaluation of a Coping Strategies Inventory Short-Form (CSI-SF) in the Jackson Heart Study cohort. *Int J Environ Res Public Health*. 2007;4:289–295.
18. Harrell FE Jr. Multivariable modeling strategies. In: Harrell FE Jr, ed. *Regression Modeling Strategies: With Applications to Linear Models, Logistic Regression, and Survival Analysis*. New York: Springer-Verlag; 2001:53–85.
19. Keenan PS, Normand SL, Lin Z, Drye EE, Bhat KR, Ross JS, Schuur JD, Stauffer BD, Bernheim SM, Epstein AJ, Wang Y, Herrin J, Chen J, Federer JJ, Mattera JA, Wang Y, Krumholz HM. An administrative claims measure suitable for profiling hospital performance on the basis of 30-day all-cause readmission rates among patients with heart failure. *Circ Cardiovasc Qual Outcomes*. 2008;1:29–37. doi: 10.1161/CIRCOUTCOMES.108.802686.
20. Krumholz HM, Wang Y, Mattera JA, Wang Y, Han LF, Ingber MJ, Roman S, Normand SL. An administrative claims model suitable for profiling hospital performance based on 30-day mortality rates among patients with heart failure. *Circulation*. 2006;113:1693–1701. doi: 10.1161/CIRCULATIONAHA.105.611194.
21. Jackson CA, Mishra GD. Depression and risk of stroke in midaged women: a prospective longitudinal study. *Stroke*. 2013;44:1555–1560. doi: 10.1161/STROKEAHA.113.001147.
22. Wassertheil-Smoller S, Applegate WB, Berge K, Chang CJ, Davis BR, Grimm R Jr, Kostis J, Pressel S, Schron E. Change in depression as a precursor of cardiovascular events. SHEP Cooperative Research Group (Systoloc Hypertension in the elderly). *Arch Intern Med*. 1996;156:553–561.
23. Glymour MM, Yen JJ, Kosheleva A, Moon JR, Capistrant BD, Patton KK. Elevated depressive symptoms and incident stroke in Hispanic, African-American, and White older Americans. *J Behav Med*. 2012;35:211–220. doi: 10.1007/s10865-011-9356-2.
24. Lewis TT, Guo H, Lunos S, Mendes de Leon CF, Skarupski KA, Evans DA, Everson-Rose SA. Depressive symptoms and cardiovascular mortality in older black and white adults: evidence for a differential association by race. *Circ Cardiovasc Qual Outcomes*. 2011;4:293–299. doi: 10.1161/CIRCOUTCOMES.110.957548.
25. Capistrant BD, Gilsanz P, Moon JR, Kosheleva A, Patton KK, Glymour MM. Does the association between depressive symptoms and cardiovascular mortality risk vary by race? Evidence from the Health and Retirement Study. *Ethn Dis*. 2013;23:155–160.
26. Koenig HG, George LK. Depression and physical disability outcomes in depressed medically ill hospitalized older adults. *Am J Geriatr Psychiatry*. 1998;6:230–247.
27. Vogt T, Pope C, Mullooly J, Hollis J. Mental health status as a predictor of morbidity and mortality: a 15-year follow-up of members of a health maintenance organization. *Am J Public Health*. 1994;84:227–231.
28. Goldston K, Baillie AJ. Depression and coronary heart disease: a review of the epidemiological evidence, explanatory mechanisms and management approaches. *Clin Psychol Rev*. 2008;28:288–306. doi: 10.1016/j.cpr.2007.05.005.
29. Penninx BW, Guralnik JM, Mendes de Leon CF, Pahor M, Visser M, Corti MC, Wallace RB. Cardiovascular events and mortality in newly and chronically depressed persons >70 years of age. *Am J Cardiol*. 1998;81:988–994.
30. Snowden LR, Pingitore D. Frequency and scope of mental health service delivery to African Americans in primary care. *Ment Health Serv Res*. 2002;4:123–130.
31. Borowsky SJ, Rubenstein LV, Meredith LS, Camp P, Jackson-Triche M, Wells KB. Who is at risk of nondetection of mental health problems in primary care? *J Gen Intern Med*. 2000;15:381–388.
32. Melfi CA, Croghan TW, Hanna MP, Robinson RL. Racial variation in antidepressant treatment in a Medicaid population. *J Clin Psychiatry*. 2000;61:16–21.
33. Cooper LA, Gonzales JJ, Gallo JJ, Rost KM, Meredith LS, Rubenstein LV, Wang NY, Ford DE. The acceptability of treatment for depression among African-American, Hispanic, and white primary care patients. *Med Care*. 2003;41:479–489. doi: 10.1097/01.MLR.0000053228.58042.E4.
34. Givens JL, Houston TK, Van Voorhees BW, Ford DE, Cooper LA. Ethnicity and preferences for depression treatment. *Gen Hosp Psychiatry*. 2007;29:182–191. doi: 10.1016/j.genhosppsych.2006.11.002.
35. Menke R, Flynn H. Relationships between stigma, depression, and treatment in white and African American primary care patients. *J Nerv Ment Dis*. 2009;197:407–411. doi: 10.1097/NMD.0b013e3181a6162e.

Depressive Symptoms and Risk of Cardiovascular Events in Blacks: Findings From the Jackson Heart Study

Emily C. O'Brien, Melissa A. Greiner, Mario Sims, Natalie Chantelle Hardy, Wei Wang, Eyal Shahar, Adrian F. Hernandez and Lesley H. Curtis

Circ Cardiovasc Qual Outcomes. 2015;8:552-559
doi: 10.1161/CIRCOUTCOMES.115.001800
Circulation: Cardiovascular Quality and Outcomes is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 1941-7705. Online ISSN: 1941-7713

Supplemental Material

Supplemental Table 1. Baseline Characteristics of the Incident Stroke Cohort by Depression Category

Supplemental Table 2. Baseline Characteristics of Overall JHS population by completion of CES-D questionnaire

Supplemental Table 3. Baseline Characteristics of the Incident CHD Cohort by Depressive Symptoms

Supplemental Table 4. Baseline Characteristics of the Incident CHD Cohort by Depression Category

Supplemental Table 1. Baseline Characteristics of the Incident Stroke Cohort by Depression Category[a]

Characteristic	Depressive Symptoms			*P* Value
	None (n = 2571)	Minor (n = 354)	Major (n = 384)	
Age, median (IQR), y	54.3 (44.9-63.7)	54.3 (43.5-64.5)	50.5 (41.8-60.6)	< .001
Women, No. (%)	1627 (63.3)	253 (71.5)	283 (73.7)	< .001
Medical history, No. (%)				
Atrial fibrillation	4 (0.2)	1 (0.3)	1 (0.3)	.81
Cardiovascular disease	127 (4.9)	25 (7.1)	43 (11.2)	< .001
Diabetes mellitus	497 (19.3)	80 (22.6)	90 (23.4)	.08
Dialysis	8 (0.3)	3 (0.8)	2 (0.5)	.29
Heart failure	151 (5.9)	32 (9.0)	46 (12.0)	< .001
Hypertension	1491 (58.0)	227 (64.1)	224 (58.3)	.09
Left ventricular hypertrophy	178 (6.9)	24 (6.8)	33 (8.6)	.48
Myocardial infarction	85 (3.3)	19 (5.4)	32 (8.3)	< .001
Physical examination, median (IQR)				
Body mass index, kg/m2	30.5 (27.0-35.1)	31.1 (27.4-36.3)	31.1 (26.9-36.6)	.07
Systolic blood pressure, mm Hg	124.0 (114.0-135.0)	125.5 (115.0-136.0)	123.5 (112.0-135.0)	.10
Waist circumference, cm	98.0 (89.0-108.0)	100.5 (89.0-111.0)	101.0 (89.0-111.0)	.03
Socioeconomic, No. (%)				
Education				< .001
Less than high school	284 (11.0)	66 (18.6)	79 (20.6)	
High school graduate	1014 (39.4)	180 (50.8)	205 (53.4)	
College degree	699 (27.2)	70 (19.8)	69 (18.0)	
Graduate or professional degree	574 (22.3)	38 (10.7)	31 (8.1)	
Family income				< .001
< $20,000	474 (18.4)	105 (29.7)	153 (39.8)	
$20,000-$50,000	807 (31.4)	120 (33.9)	113 (29.4)	
$50,000-$75,000	482 (18.7)	46 (13.0)	42 (10.9)	
> $75,000	467 (18.2)	34 (9.6)	14 (3.6)	
Missing	341 (13.3)	49 (13.8)	62 (16.1)	
Medications, No. (%)				
Anticoagulant agent	15 (0.6)	4 (1.1)	4 (1.0)	.35
Antidepressant agent	106 (4.1)	25 (7.1)	59 (15.4)	< .001
Antihyperlipdemic agent	295 (11.5)	37 (10.5)	39 (10.2)	.67
Antihypertensive agent	733 (28.5)	124 (35.0)	119 (31.0)	.03
Antiplatelet agent	22 (0.9)	3 (0.8)	2 (0.5)	.79

Characteristic	Depressive Symptoms			*P* Value
	None (n = 2571)	Minor (n = 354)	Major (n = 384)	
Antithrombotics (anticoagulant, antiplatelet, or COX-2 inhibitor)	182 (7.1)	45 (12.7)	40 (10.4)	< .001
COX-2 inhibitor	147 (5.7)	38 (10.7)	35 (9.1)	< .001
Missing	181 (7.0)	28 (7.9)	36 (9.4)	.25
Behavioral factors				
Drinks per day in the prior year, mean (IQR)	0.2 (0.7)	0.2 (0.5)	0.3 (1.1)	.19
Hours of physical activity per week, No. (%)				< .001
None	1088 (42.3)	178 (50.3)	205 (53.4)	
< 1 hour	268 (10.4)	46 (13.0)	37 (9.6)	
1 to < 2 hours	480 (18.7)	62 (17.5)	53 (13.8)	
2 to < 3 hours	214 (8.3)	30 (8.5)	34 (8.9)	
3 to < 4 hours	182 (7.1)	12 (3.4)	21 (5.5)	
≥ 4 hours	339 (13.2)	26 (7.3)	34 (8.9)	
Smoking history, No. (%)				< .001
Never smoked	1837 (71.5)	235 (66.4)	236 (61.5)	
Former smoker	486 (18.9)	64 (18.1)	64 (16.7)	
Current smoker	248 (9.6)	55 (15.5)	84 (21.9)	
CSI-SF, median (IQR)				
Disengagement score	22.0 (20.0-25.0)	24.0 (21.0-27.0)	26.0 (23.0-29.0)	< .001
Engagement score	29.0 (26.0-32.0)	26.0 (24.0-30.0)	25.0 (22.0-28.0)	< .001
Stroke risk scores, median (IQR)				
Framingham stroke risk score	5.0 (2.0-9.0)	7.0 (3.0-10.0)	6.0 (2.0-10.0)	.009
Internally derived stroke risk score	4.9 (4.0, 5.7)	5.0 (3.9, 6.0)	4.8 (3.8, 5.7)	.13

Abbreviations: COX-2, cyclooxygenase-2; CSI-SF, Coping Strategies Inventory-Short Form; IQR, interquartile range.

[a] Categorical variables are presented as frequencies, and continuous variables are presented as medians with interquartile ranges (IQR) or means with (SD)

Supplemental Table 2. Baseline Characteristics of Overall JHS population by completion of CES-D questionnaire

	Completed CES-D	Did Not Complete CES-D	p-value
N	3,412	1,889	
Demographics			
Age, median (IQR), y	54.2 (44.5, 63.8)	58.9 (47.6, 67.1)	< .001
Female sex, No. (%)	2,228 (65.3)	1,139 (60.3)	< .001
Medical History, No. (%)			
Atrial fibrillation	7 (0.2)	11 (0.6)	.02
Cardiovascular disease	298 (8.7)	274 (14.5)	< .001
Diabetes	707 (20.7)	445 (23.6)	.02
Dialysis	13 (0.4)	14 (0.7)	.08
Heart failure	248 (7.3)	150 (7.9)	.37
Hypertension	2,029 (59.5)	1,223 (64.7)	< .001
Left ventricular hypertrophy	249 (7.3)	156 (8.3)	.21
Myocardial infarction	155 (4.5)	135 (7.1)	< .001
Physical examination, median (IQR)			
BMI, kg/m2	30.6 (27.0, 35.5)	30.5 (26.5, 35.4)	.18
Systolic blood pressure, mmHg	124.0 (114.0, 135.0)	127.0 (116.0, 140.0)	< .001
Waist circumference, cm	98.0 (89.0, 109.0)	100.0 (90.0, 110.0)	.002
Socioeconomic, No. (%)			
Education			< .001
Less than high school	461 (13.5)	532 (28.2)	
High school graduate	1,442 (42.3)	785 (41.6)	
College degree	852 (25.0)	362 (19.2)	
Graduate or professional degree	657 (19.3)	210 (11.1)	
Family income			< .001
<$20,000	776 (22.7)	548 (29.0)	
$20,000-$50,000	1,067 (31.3)	580 (30.7)	
$50,000-$75,000	581 (17.0)	228 (12.1)	

	Completed CES-D	Did Not Complete CES-D	p-value
>$75,000	522 (15.3)	201 (10.6)	
Missing	466 (13.7)	332 (17.6)	
Medications, No. (%)			
Anti-coagulant	29 (0.8)	50 (2.6)	< .001
Anti-depressant	205 (6.0)	106 (5.6)	.56
Anti-hyperlipdemic	400 (11.7)	247 (13.1)	.15
Anti-hypertensive	1,033 (30.3)	662 (35.0)	< .001
Anti-platelet	42 (1.2)	40 (2.1)	.01
Anti-thrombotics (Anti-coagulant or Anti-platelet or COX-2 inhibitor)	298 (8.7)	209 (11.1)	.006
Cyclooxygenase [COX-2] inhibitor	231 (6.8)	125 (6.6)	.83
Missing medications	255 (7.5)	153 (8.1)	.41
Behavioral factors			
Drinks per day in the prior year, mean (IQR)	0.2 (0.7)	0.3 (0.9)	.09
Hours of physical activity per week, No. (%)			< .001
None	1,532 (44.9)	1,008 (53.4)	
<1 hour	362 (10.6)	189 (10.0)	
1- <2 hours	610 (17.9)	257 (13.6)	
2- <3 hours	283 (8.3)	144 (7.6)	
3- <4 hours	222 (6.5)	106 (5.6)	
4+ hours	403 (11.8)	185 (9.8)	
Smoking history, No. (%)			.001
Never smoked	2,361 (69.2)	1,224 (64.8)	
Former smoker	643 (18.8)	380 (20.1)	
Current smoker	408 (12.0)	285 (15.1)	
Coping strategies: CSI-SF, median (IQR)			
Disengagement score	23.0 (20.0, 25.0)	23.0 (20.0, 26.0)	.10
Engagement score	28.0 (25.0, 31.0)	28.0 (25.0, 31.0)	.09

Supplemental Table 3. Baseline Characteristics of the Incident CHD Cohort by Depressive Symptoms

	No Depressive Symptoms	Depressive Symptoms	p-value
N	2,486	692	
Demographics			
Age, median (IQR), y	53.8 (44.6, 63.5)	51.4 (42.5, 62.3)	< .001
Female sex, No. (%)	1,583 (63.7)	506 (73.1)	< .001
Medical History, No. (%)			
Atrial fibrillation	5 (0.2)	1 (0.1)	.76
Stroke	52 (2.1)	27 (3.9)	.007
Diabetes	458 (18.4)	151 (21.8)	.04
Dialysis	6 (0.2)	3 (0.4)	.40
Heart failure	127 (5.1)	70 (10.1)	< .001
Hypertension	1,377 (55.4)	403 (58.2)	.18
Left ventricular hypertrophy	158 (6.4)	43 (6.2)	.89
Physical examination, median (IQR)			
BMI, kg/m2	30.4 (26.9, 35.1)	31.2 (27.1, 36.5)	.01
Systolic blood pressure, mmHg	123.0 (113.0, 135.0)	124.0 (113.0, 135.0)	.44
Waist circumference, cm	98.0 (89.0, 108.0)	100.0 (89.0, 111.5)	.01
Total cholesterol, mg/dL	196.0 (174.0, 222.0)	194.0 (169.0, 218.0)	.006
Socioeconomic, No. (%)			
Education			< .001
Less than high school	276 (11.1)	127 (18.4)	< .001
High school graduate	973 (39.1)	364 (52.6)	< .001
College degree	686 (27.6)	135 (19.5)	< .001
Graduate or professional degree	551 (22.2)	66 (9.5)	< .001
Family income			< .001
<$20,000	461 (18.5)	240 (34.7)	< .001
$20,000-$50,000	779 (31.3)	219 (31.6)	.88
$50,000-$75,000	474 (19.1)	81 (11.7)	< .001
>$75,000	454 (18.3)	48 (6.9)	< .001

	No Depressive Symptoms	Depressive Symptoms	p-value
Missing	318 (12.8)	104 (15.0)	.13
Medications, No. (%)			
Anti-coagulant	16 (0.6)	9 (1.3)	.08
Anti-depressant	97 (3.9)	77 (11.1)	< .001
Anti-hyperlipdemic	263 (10.6)	62 (9.0)	.21
Anti-hypertensive	680 (27.4)	216 (31.2)	.046
Anti-platelet	20 (0.8)	6 (0.9)	.87
Anti-thrombotics (Anti-coagulant or Anti-platelet or COX-2 inhibitor)	174 (7.0)	82 (11.8)	< .001
Cyclooxygenase [COX-2] inhibitor	140 (5.6)	67 (9.7)	< .001
Missing medications	171 (6.9)	60 (8.7)	.11
Behavioral factors			
Drinks per day in the prior year, mean (IQR)	0.2 (0.7)	0.2 (0.9)	.79
Hours of physical activity per week, No. (%)			< .001
None	1,046 (42.1)	353 (51.0)	< .001
<1 hour	257 (10.3)	77 (11.1)	.55
1- <2 hours	463 (18.6)	110 (15.9)	.10
2- <3 hours	208 (8.4)	59 (8.5)	.89
3- <4 hours	181 (7.3)	34 (4.9)	.03
4+ hours	331 (13.3)	59 (8.5)	< .001
Smoking history, No. (%)			< .001
Never smoked	1,799 (72.4)	446 (64.5)	< .001
Former smoker	452 (18.2)	122 (17.6)	.74
Current smoker	235 (9.5)	124 (17.9)	< .001
Coping strategies: CSI-SF, median (IQR)			
Disengagement score	22.0 (20.0, 25.0)	25.0 (22.0, 28.0)	< .001
Engagement score	29.0 (26.0, 32.0)	26.0 (23.0, 29.0)	< .001
Internally derived CHD risk score	2.6 (1.8, 3.4)	2.5 (1.7, 3.4)	.51

Abbreviations: COX-2, cyclooxygenase-2; CSI-SF, Coping Strategies Inventory-Short Form; IQR, interquartile range.

Supplemental Table 4. Baseline Characteristics of the Incident CHD Cohort by Depression Category

	No Depressive Symptoms	Minor Depressive Symptoms	Major Depressive Symptoms	p-value
N	2,486	340	352	
Demographics				
Age, median (IQR), y	53.8 (44.6, 63.5)	54.2 (43.4, 64.2)	49.2 (41.1, 59.0)	< .001
Female sex, No. (%)	1,583 (63.7)	246 (72.4)	260 (73.9)	< .001
Medical History, No. (%)				
Atrial fibrillation	5 (0.2)	0 (0.0)	1 (0.3)	.66
Stroke	52 (2.1)	13 (3.8)	14 (4.0)	.03
Diabetes	458 (18.4)	75 (22.1)	76 (21.6)	.13
Dialysis	6 (0.2)	2 (0.6)	1 (0.3)	.53
Heart failure	127 (5.1)	28 (8.2)	42 (11.9)	< .001
Hypertension	1,377 (55.4)	203 (59.7)	200 (56.8)	.31
Left ventricular hypertrophy	158 (6.4)	19 (5.6)	24 (6.8)	.79
Physical examination, median (IQR)				
BMI, kg/m2	30.4 (26.9, 35.1)	31.2 (27.5, 36.4)	31.2 (26.9, 36.5)	.04
Systolic blood pressure, mmHg	123.0 (113.0, 135.0)	126.0 (115.0, 136.5)	123.0 (111.0, 134.0)	.04
Waist circumference, cm	98.0 (89.0, 108.0)	100.0 (89.0, 112.0)	99.0 (88.5, 111.0)	.03
Total cholesterol, mg/dL	196.0 (174.0, 222.0)	196.5 (171.0, 219.0)	190.0 (168.0, 215.5)	.005
Socioeconomic, No. (%)				
Education				< .001
Less than high school	276 (11.1)	62 (18.2)	65 (18.5)	< .001
High school graduate	973 (39.1)	174 (51.2)	190 (54.0)	< .001
College degree	686 (27.6)	68 (20.0)	67 (19.0)	< .001
Graduate or professional degree	551 (22.2)	36 (10.6)	30 (8.5)	< .001
Family income				< .001
<$20,000	461 (18.5)	105 (30.9)	135 (38.4)	< .001
$20,000-$50,000	779 (31.3)	115 (33.8)	104 (29.5)	.47
$50,000-$75,000	474 (19.1)	43 (12.6)	38 (10.8)	< .001

	No Depressive Symptoms	Minor Depressive Symptoms	Major Depressive Symptoms	p-value
>$75,000	454 (18.3)	32 (9.4)	16 (4.5)	< .001
Missing	318 (12.8)	45 (13.2)	59 (16.8)	.12
Medications, No. (%)				
Anti-coagulant	16 (0.6)	5 (1.5)	4 (1.1)	.20
Anti-depressant	97 (3.9)	23 (6.8)	54 (15.3)	< .001
Anti-hyperlipdemic	263 (10.6)	35 (10.3)	27 (7.7)	.24
Anti-hypertensive	680 (27.4)	109 (32.1)	107 (30.4)	.12
Anti-platelet	20 (0.8)	5 (1.5)	1 (0.3)	.22
Anti-thrombotics (Anti-coagulant or Anti-platelet or COX-2 inhibitor)	174 (7.0)	49 (14.4)	33 (9.4)	< .001
Cyclooxygenase [COX-2] inhibitor	140 (5.6)	39 (11.5)	28 (8.0)	< .001
Missing medications	171 (6.9)	26 (7.6)	34 (9.7)	.16
Behavioral factors				
Drinks per day in the prior year, mean (IQR)	0.2 (0.7)	0.2 (0.5)	0.3 (1.1)	.13
Hours of physical activity per week, No. (%)				< .001
None	1,046 (42.1)	170 (50.0)	183 (52.0)	< .001
<1 hour	257 (10.3)	43 (12.6)	34 (9.7)	.37
1- <2 hours	463 (18.6)	59 (17.4)	51 (14.5)	.16
2- <3 hours	208 (8.4)	29 (8.5)	30 (8.5)	.99
3- <4 hours	181 (7.3)	12 (3.5)	22 (6.3)	.03
4+ hours	331 (13.3)	27 (7.9)	32 (9.1)	.003
Smoking history, No. (%)				< .001
Never smoked	1,799 (72.4)	228 (67.1)	218 (61.9)	< .001
Former smoker	452 (18.2)	61 (17.9)	61 (17.3)	.93
Current smoker	235 (9.5)	51 (15.0)	73 (20.7)	< .001
Coping strategies: CSI-SF, median (IQR)				
Disengagement score	22.0 (20.0, 25.0)	24.0 (22.0, 27.0)	26.0 (23.0, 29.0)	< .001
Engagement score	29.0 (26.0, 32.0)	26.0 (23.0, 30.0)	25.0 (21.0, 28.0)	< .001

	No Depressive Symptoms	Minor Depressive Symptoms	Major Depressive Symptoms	p-value
Internally derived CHD risk score	2.6 (1.8, 3.4)	2.6 (1.7, 3.5)	2.4 (1.6, 3.4)	.10

Abbreviations: COX-2, cyclooxygenase-2; CSI-SF, Coping Strategies Inventory-Short Form; IQR, interquartile range.