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Depressive symptoms and incident heart failure risk in the Southern Community Cohort Study

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Abstract

OBJECTIVES: To examine whether greater frequency of depressive symptoms associates with increased risk of incident HF.

BACKGROUND: Depressive symptoms associate with adverse prognosis in patients with prevalent heart failure (HF). Their association with incident HF is less studied, particularly in low-income and minority individuals.

METHODS: We studied 23,937 Black or White Southern Community Cohort Study (SCCS) participants (median age 53 years, 70% Black, 64% women) enrolled between 2002 and 2009, without prevalent HF, receiving Centers for Medicare and Medicaid Services (CMS). Cox models adjusted for traditional HF risk factors, socioeconomic and behavioral factors, social support, and anti-depressant medication were used to quantify the association between depressive symptoms assessed at enrollment via the Center for Epidemiologic Studies Depression Scale (CESD-10) and incident HF ascertained from CMS ICD-9 (428.x) and −10 (I50, I110) codes through December 31, 2016.

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RESULTS: The median CESD-10 score was 9 (IQR: 5, 13). Over a median 11-year follow-up, 6081 (25%) participants developed HF. The strongest correlates of CESD-10 score were anti-depressant medication use, age, and socioeconomic factors, rather than traditional HF risk factors. Greater frequency of depressive symptoms associated with increased incident HF risk (per 8-unit higher CESD-10 HR 1.04, 95% CI: 1.00, 1.09; p = 0.038) without variation by race or sex. The association between depressive symptoms and incident HF varied by anti-depressant use (interaction-p = 0.03) with increased risk among individuals not taking anti-depressants.

CONCLUSION: In this high-risk, low-income, predominantly Black cohort, greater frequency of depressive symptoms significantly associates with higher risk of incident HF.

Tweet:

In a high-risk low-income cohort, depressive symptoms associate with greater risk of incident heart failure independent of traditional risk factors.

Keywords

Heart failure; depression; Center for Epidemiologic Studies Depression Scale

INTRODUCTION

Heart failure (HF) affects between 6–7 million adults in the United States and is particularly common in the southeast.(1) While traditional cardiovascular risk factors, such as hypertension (HTN), diabetes (DM), and obesity account for a substantial portion of HF risk, the contribution of social determinants of health is garnering increased attention.(2–5) Psychosocial factors, such as depression, can modulate relationships between social determinants and disease.(4) Among patients with prevalent coronary artery disease (CAD) and HF, depressive symptoms associate with adverse prognosis.(6–11) Whether depressive symptoms associate with increased risk for incident HF, independent of traditional risk factors and social factors is less characterized.

The lifetime prevalence of depression in the general population is estimated at 16%, corresponding to 35 million U.S. adults.(12) Despite this high prevalence, the relationship of depression with new-onset HF has received relatively little attention.(13–16) The few studies were limited by low rates of incident HF or included predominantly white or male individuals. Low-income and minority populations often face challenges with respect to social determinants of health, which may increase risk for adverse outcomes. Investigating the role of depressive symptoms in HF development among high-risk individuals could provide novel insights for prevention. Therefore, in the Southern Community Cohort Study (SCCS), a predominantly low-income Black population, we tested the hypothesis that depressive symptoms associate with increased risk of HF, independent of traditional risk factors and social factors.

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METHODS

Study population

The SCCS is a prospective cohort composed of low-income predominantly Black adults living in 12 southeastern states. A detailed description of the study methods has been previously published.(17) Briefly, the SCCS was designed to investigate incidence of cancer and other chronic diseases in a population often underrepresented in other cohort studies. Between 2002 and 2009, adults aged 40 to 79 years (n = 84,797) were enrolled, primarily (86%) from community health centers (CHC). All participants provided written informed consent. Protocols were approved by the Institutional Review Boards of Vanderbilt University Medical Center and Meharry Medical College.

This analysis included 23,937 participants meeting the following criteria at enrollment: 1) either aged ≥65 years or aged <65 years who either reported coverage by Centers for Medicare and Medicaid Services (CMS) at enrollment or had a CMS claim within 90 days of SCCS enrollment, as previously described (18,19); 2) free from prevalent HF; 3) completed the Center for Epidemiologic Studies Depression questionnaire (CESD-10); and 4) without a history of myocardial infarction (MI) or coronary artery bypass, given that depression associates with HF risk in the setting of prevalent CAD.(20) The analysis was restricted to self-reported Black and non-Hispanic White participants, as low numbers in other racial groups precluded stable statistical analysis.

Depressive symptoms and medications

Depressive symptoms were ascertained using the 10-item version of the CESD Scale; a widely used, reliable, and validated tool for determining the frequency of depressive symptoms over a one-week period.(21–24) A score ≥10 (max 30) indicates clinically relevant depressive symptoms.(23,24) At enrollment, participants reported current prescriptions for anti-depressant/anxiolytic medications and history of physician diagnosed depression.

Additional details regarding the study population, depressive symptoms and medications, cardiovascular and behavioral risk factors, and social determinants of health are provided in the Supplemental Appendix.

Outcome

Incident HF was determined via linkage with CMS Research Identifiable Files and was defined as the first occurrence of a medical claim with an *International Classification of Diseases*, 9th revision (ICD-9), discharge code of 428.x (428.0–428.9) or 10th revision (ICD-10) code of I50 or I110 within the Medicare institutional, Part B carrier, outpatient-based claims files, or Medicaid Analytic Extract Inpatient and Other Services claims files, as previously described.(19) Vital status was determined via National Death Index linkage. Censoring occurred at date of HF event, death, or December 31, 2016, whichever occurred first.(19)

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Statistical Analysis

For descriptive statistics, participants were categorized according to CESD-10 score <10, 10–19, or ≥20. Continuous data was summarized as median (25^{th}, 75^{th} percentiles) and categorical data as percentage, unless otherwise specified. Comparisons were made using Kruskal-Wallis or Pearson chi-squared tests.

Multivariable ordinal logistic regression was performed to identify correlates of CESD-10 score. Multivariable Cox models were used to test whether depressive symptoms associate with increased risk of incident HF and a composite of death or HF. A test for a non-linear association between CESD-10 and HF was not significant; therefore, CESD-10 was modeled as a linear variable. A sensitivity analysis was performed in which CESD-10 score was replaced with a binary variable for whether a clinical diagnosis of depression was present at enrollment or not, defined as self-report of a physician diagnosis of depression or use of anti-depressant/anxiolytic medication. Models were adjusted for demographics (age, sex, and race), comorbidities (HTN, HLD, DM, BMI, stroke or TIA, and smoking), socioeconomic (income, education, employment, and enrollment source [CHC vs. general population]), behavioral (alcohol intake, sedentary activity, and physical activity), social support factors (marital status, the number of people providing emotional support or help in an emergency), and anti-depressant/anxiolytic use. Continuous variables were modeled using restricted cubic spline terms with 4 knots.

To address reverse causation; namely, the possibility undiagnosed HF contributed to depressive symptoms at enrollment, we performed a sensitivity analysis excluding individuals who developed HF within 3 months of enrollment. Additional exploratory analyses included examining the interaction of CESD-10 with race, sex, race-sex groups, and anti-depressant medications. Analyses were performed using R (The R project, Vienna, Austria).

RESULTS

Baseline characteristics

In the 23,937 participants, CESD-10 scores <10, 10–19, and ≥ 20 were present in 55%, 37%, and 8%, respectively. The median (25^{th}, 75^{th} percentile) CESD-10 score was 9 (5, 13). Table 1 displays baseline characteristics by CESD-10 score. Individuals with higher CESD-10 scores were younger and more often female and white. CESD-10 score inversely associated with education, income, and employment. HTN and DM were common and present with similar prevalence across CESD-10 score. BMI was greater among participants with higher CESD-10 scores.

Behavioral differences were apparent across CESD-10 scores. Participants reporting more frequent depressive symptoms were more often current smokers and more sedentary. Alcohol intake positively correlated with CESD-10 score. Additionally, lack of social support associated with increased frequency of depressive symptoms. Participants with higher CESD-10 scores had fewer social connections as demonstrated by marital status and fewer emotionally or financially supportive relationships. Anti-depressant/anxiolytic use and

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prior diagnosis of depression was more common among participants with higher CESD-10 scores.

Correlates of CESD-10 score were examined in a multivariable ordinal logistic regression with results shown in Supplemental Figures 1 A and B and Supplemental Table 1. Anti-depressant use and socioeconomic factors most strongly associated with CESD-10 score. In contrast, traditional cardiovascular risk factors, such as DM, HLD, BMI, history of stroke or TIA, and HTN contributed little to the overall variance in CESD-10 score despite significant associations.

Incident HF and Survival

Over a median 11 years (25^{th}, 75^{th} percentile: 8.6, 12.8) of follow-up, 6081 participants (25%) developed HF. Higher CESD-10 consistently associated with increased risk for incident HF (Table 2). In an age-, sex-, and race-adjusted model, each 8 point higher CESD-10, corresponding to the difference between the 25^{th} to 75^{th} percentiles of CESD-10 scores (5, 13), significantly associated with increased risk for incident HF (HR 1.17, 95% CI: 1.13–1.21; p <0.001). The association between CESD-10 and HF risk was attenuated but still significant after adjustment for traditional clinical HF risk factors (HR 1.11, 95% CI: 1.07–1.15; p <0.001). With further adjustment for socioeconomic and behavioral factors, social support and anti-depressant/anxiolytic use, higher CESD-10 score remained significantly associated with increased risk for incident HF (HR 1.04, 95% CI: 1.00–1.09; p = 0.038); Table 2, Supplemental Table 2, and Supplemental Figure 2. Central Illustration illustrates the predicted probability of incident HF at 5 years according to CESD-10 score. Results for the composite outcome of time to incident HF or death were similar (HR 1.04, 95% CI: 1.00–1.07; p = 0.032).

To address the potential for reverse causation, we repeated the analysis after excluding 189 participants who developed HF within 3 months of enrollment. Our results did not substantially differ (HR 1.04, 95% CI: 1.00–1.09, p = 0.045). In another sensitivity analysis, we examined whether a diagnosis of depression, defined as a composite of self-reported history of depression or anti-depressant/anxiolytic medication use, associates with incident HF, with similar findings (HR 1.06, 95% CI:1.00–1.13, p = 0.045). Additionally, enrollment characteristics of participants who did and did not develop HF over the follow-up period are shown in Supplemental Table 3.

For the primary outcome of incident HF, we tested whether the association between depressive symptoms and HF risk varied by anti-depressant/anxiolytic medication use or by race, sex, or race-sex groups. The CESD-10 by anti-depressant/anxiolytic medication interaction term was significant (p = 0.03). Figure 1 demonstrates CESD-10 score associated with increased HF risk among participants without anti-depressant/anxiolytic use (HR 1.07, 95% CI: 1.02–1.12; p = 0.006), but not among participants using these medications (HR 1.00, 95% CI: 0.94–1.07; p = 0.91). We did not find evidence for significant variation in the risk of incident HF according to CESD-10 score by race, sex, or race-sex groups (interaction-p > 0.25 for all).

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DISCUSSION

In a large, low-income, predominantly Black cohort of individuals residing in the southeastern United States at high risk for HF, individuals reporting a greater frequency of depressive symptoms at enrollment had significantly higher risk of incident HF independent of traditional cardiovascular risk factors, or socioeconomic and behavioral characteristics. Although the effect size was relatively small, the clinical significance of the increased risk of HF associated with higher CESD-10 scores may be substantial. CESD-10 score ≥10, an accepted threshold indicative of clinically relevant depressive symptoms, was common in our cohort, present in 45% of individuals; a prevalence exceeding DM (25%) and HLD (37%). Collectively, our findings suggest attention to depressive symptoms assessed using the clinically available CESD-10 score may help identify individuals at greater risk for the development of incident HF.

Distinct from other U.S. based community cohort studies (Cardiovascular Health Study [CHS], Multi-Ethnic Study of Atherosclerosis [MESA], and Yale Health and Aging Project [YHAP]), we demonstrate a significant association between greater depressive symptoms and incident HF (Table 3). Although a significant positive association between depressive symptoms or clinical diagnosis of depression has been demonstrated in a clinical cohort, an ancillary study of a hypertension clinical trial, and 2 European cohorts, compared with those studies, our SCCS cohort included the greatest proportion of Black individuals, was of substantially lower SES, had 2–15 times greater prevalence of depression, and had the highest incidence of HF (Table 3). Moreover, our analysis included adjustment for a greater number of social determinants of health compared with other studies. Insofar as the SCCS includes individuals not represented in most other cohorts, our findings are not only novel, but of potential clinical relevance as nearly one in two individuals in this population reported substantial depressive symptoms.

We examined depressive symptoms assessed by CESD-10 on a continuous scale and found a linear increase in incident HF risk with greater frequency of depressive symptoms. This finding suggests the presence of risk for HF among individuals with even sub-clinical depressive symptoms. Our approach contrasts with prior studies examining the association between depression and incident HF using categorical scales. For example, in the Systolic Hypertension in the Elderly Program (n = 4,538), participants with depression defined as a CES-D score ≥ 16 had a 2-fold greater risk of incident HF compared with individuals with CES-D scores <16.(14) A similar risk estimate for the association between depression, defined at a threshold CES-D score ≥ 21, and incident HF was found in the YHAP (n = 2501) for women (HR 1.96, 95% CI: 1.11–3.46) but not men (HR 0.62, 95% CI: 0.23–1.71).(13) In contrast, among a predominantly male (93.4%) veteran population with no baseline cardiovascular disease (CVD) (n = 236,079) a clinical diagnosis of major depressive disorder was associated with incident HF (HR 1.21, 95% CI:1.13–1.28) after adjustment for demographic, behavioral, CVD risk factors and psychotropic medications. (15) In our study, a sensitivity analysis demonstrated a clinical diagnosis of depression significantly associated with incident HF, HR 1.06 (95% CI:1.00–1.13, p = 0.045). Prior studies demonstrated the incidence and prevalence of depression is higher in women and concordantly we found higher CESD-10 scores among women.(25) We did not, however,

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observe sex-based variation in the association between depressive symptoms and risk of incident HF. Moreover, we did not observe effect modification by race, addressing a gap rarely examined in prior studies which included predominantly white individuals.

In contrast to the aforementioned studies, in MESA, psychosocial factors, including depressive symptoms, were not associated with incident HF overall, although participants reporting poor health at baseline and high depressive symptoms had a trend toward 2-fold higher risk of incident HF.(16) The contrasting results between SCCS and the other U.S. based community cohort studies (MESA, CHS, YHAP) may be due to differences in cohort characteristics with fewer risk factors and a wider range of socioeconomic status compared with SCCS participants (Table 3). A recent study found a significant association between depressive symptoms and incident CVD, defined as coronary heart disease (CHD) or stroke.(26) Using the CES-D, the effect size was of a similar magnitude to our study with a hazard ratio per 1 standard deviation increase in depression score of 1.06 (95% CI 1.04–1.08) for the composite endpoint of CHD or stroke, while adjusting for age, sex, smoking status, and history of diabetes. The authors noted that the association persisted even at levels that would be considered sub-clinical depressive symptoms, consistent with our findings.

We found psychosocial and behavioral factors, rather than traditional clinical cardiovascular risk factors, most strongly correlated with frequency of depressive symptoms. Participants with higher CESD-10 scores were more likely to have lower socioeconomic status, poor lifestyle behaviors, and less social support, but had similar rates of HTN and DM compared with individuals with lower CESD-10 scores. These findings may help providers identify individuals with greater likelihood of having depressive symptoms for whom evaluation may be indicated. Moreover, these findings suggest the association between depressive symptoms and risk for HF is unlikely to be fully explained by either traditional cardiovascular risk factors leading to depressive symptoms or conversely depressive symptoms augmenting susceptibility to traditional cardiovascular risk factors.

The mechanisms by which depressive symptoms may associate with the risk of incident HF independent of traditional CV risk factors are not well understood. A comprehensive review of potential mechanisms has been summarized by others.(27–31) Briefly, the available evidence suggests individuals with depression have abnormalities in the hypothalamic-pituitary axis, neurohormonal and autonomic nervous system, immune and vascular systems, which have been implicated in the pathogenesis of HF. For example, individuals with depression display excess catecholamine and cortisol secretion, increased sympathetic tone and autonomic nervous system dysregulation, increased pro-inflammatory cytokines, dysregulation of platelet and endothelial function, and behavioral changes in diet, physical activity, and medical adherence. Additional studies are needed to further elucidate the pathophysiologic and behavioral mechanisms underlying the association between depressive symptoms and risk of HF.

Whether treatment of depression improves HF outcomes may warrant further investigation. Among patients with prevalent HF, depression is associated with worse outcomes and increased mortality rate.(8–10) To date, two trials have reported the effect of drug-based treatment of depression on cardiovascular outcomes among patients with prevalent HF. The

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primary result in both trials was neutral, however, a post-hoc analysis of the Sertraline Against Depression and Heart Disease in Chronic Heart Failure (SADHART-CHF) trial found improved outcomes in the subset of patients who achieved remission of depression.(32–34) Other clinical trials have investigated the effects of interventions targeting depression on outcomes in patients with prevalent HF (Supplemental Table 4). Although not a randomized trial, in the previously mentioned study of veterans without prevalent HF, all anti-depressant classes, except tricyclics, significantly associated with lower risk of incident HF.(15) Similarly, we found the risk of incident HF in relation to depressive symptoms varied according to anti-depressant use. Higher CESD-10 scores only associated with higher HF risk in individuals who were not receiving anti-depressant medications. A prior study in the SCCS demonstrated racial disparities in the treatment of depression with less anti-depressant use in Black participants at all levels of depressive symptoms.(35) Although fewer Black participants reported anti-depressant use in our analysis (White 40%, Black 21%), we did not find evidence for a differential association between CESD-10 score and risk of incident HF according to race or sex, even when accounting for anti-depressant use. While we recognize our study was not a clinical trial specifically designed to test whether treatment of depressive symptoms reduces the risk of incident HF, our findings in the context of the existing literature suggest HF risk associated with depressive symptoms may be modifiable. The role for and mechanisms by which anti-depressant therapy may reduce the risk of incident HF could not be elucidated from this study design but are questions for future investigation.

Though our study is the largest U.S. community-based cohort to examine incident HF risk associated with depressive symptoms and included a relatively younger population with a greater proportion of Black and female individuals of low socioeconomic status compared with prior studies, limitations should be noted.(13–15) First, our results may not be generalizable to other populations as we specifically investigated the impact of depressive symptoms in a low-income and minority population. Second, we used CESD-10 to determine presence and severity of depressive symptoms. Although CESD-10 is not designed to diagnose depression, CESD-10 is a validated tool for assessing depressive symptoms, with a score ≥10 correlated with clinically relevant depressive symptoms.(24,36) Third, depressive symptoms and covariates were assessed at a single point at study enrollment. This approach, however, not only aligns with prior studies of depression and cardiovascular risk, but also clinical practice in which prognostication is based on data available at the time of assessment, rather than accounting for future occurrence of comorbidities or lifestyle changes.(6,14) We appreciate, however, that CESD-10 scores, comorbidities, and other health determinants may vary over time, such that their consideration over the life course should be an aim of future analyses.(37) While we excluded individuals with a history of myocardial infarction or coronary artery bypass grafting at enrollment, we were unable to account for interim CAD events after enrollment. Prior data from MESA, however, indicates interim myocardial infarction was less likely to contribute to incident HF, particularly in Blacks.(38) Fourth, we could not account for unmeasured clinical factors, such as left ventricular ejection fraction and/or circulating markers of myocardial injury or stress, which may be on the causal pathway associating depressive symptoms and HF risk. Understanding these relationships is a future direction.

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Fifth, medical history and health behaviors were ascertained via self-report, which could introduce misclassification bias; although prior studies in SCCS demonstrate the validity of this approach.(17)

CONCLUSION

In a large, high risk, low-income, and predominantly Black cohort from the southeastern United States, depressive symptoms significantly associate with greater risk of incident HF. In this cohort, depression is very common and a potentially modifiable mechanism contributing to the increased risk of HF, particularly in populations with less favorable social determinants of health.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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LIST OF ABBREVIATIONS

HF	heart failure
SCCS	Southern Community Cohort Study
CES-D	Center for Epidemiologic Studies Depression Scale
MI	myocardial infarction
CAD	coronary heart disease
CVD	cardiovascular disease
HTN	hypertension
DM	diabetes mellitus
HLD	hyperlipidemia
BMI	body mass index

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Clinical Perspectives:

Competency in Medical Knowledge:

Depressive symptoms are common in low-income populations and represent a potentially modifiable risk factor for incident heart failure.

Translational Outlook:

Future research should examine the role of anti-depressant therapies in reducing risk for incident heart failure.

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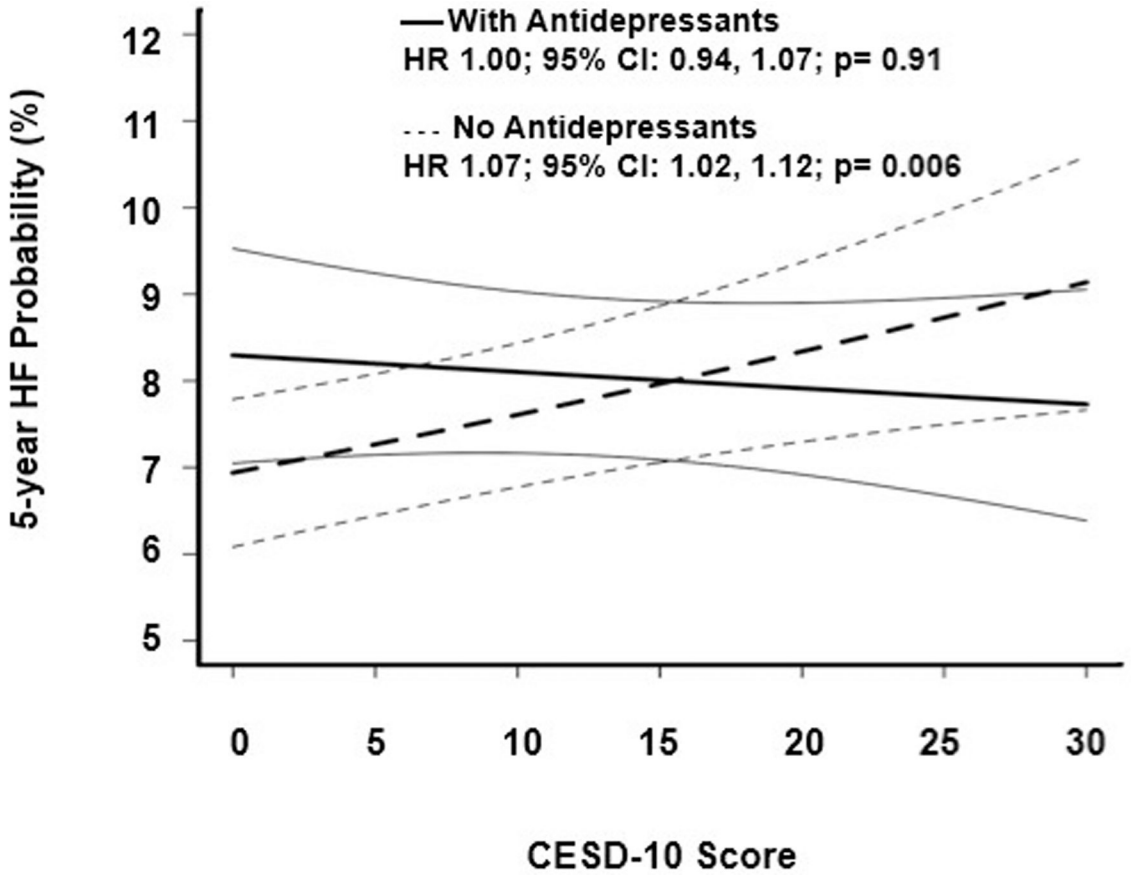

Figure 1. Differential association between CESD-10 score and HF risk according to anti-depressant/anxiolytic use in the Southern Community Cohort Study.

Risk of incident HF varies by anti-depressant/anxiolytic use. In participants taking anti-depressants/anxiolytics, greater frequency of depressive symptoms did not associate with increased HF risk in a multivariable adjusted analysis.

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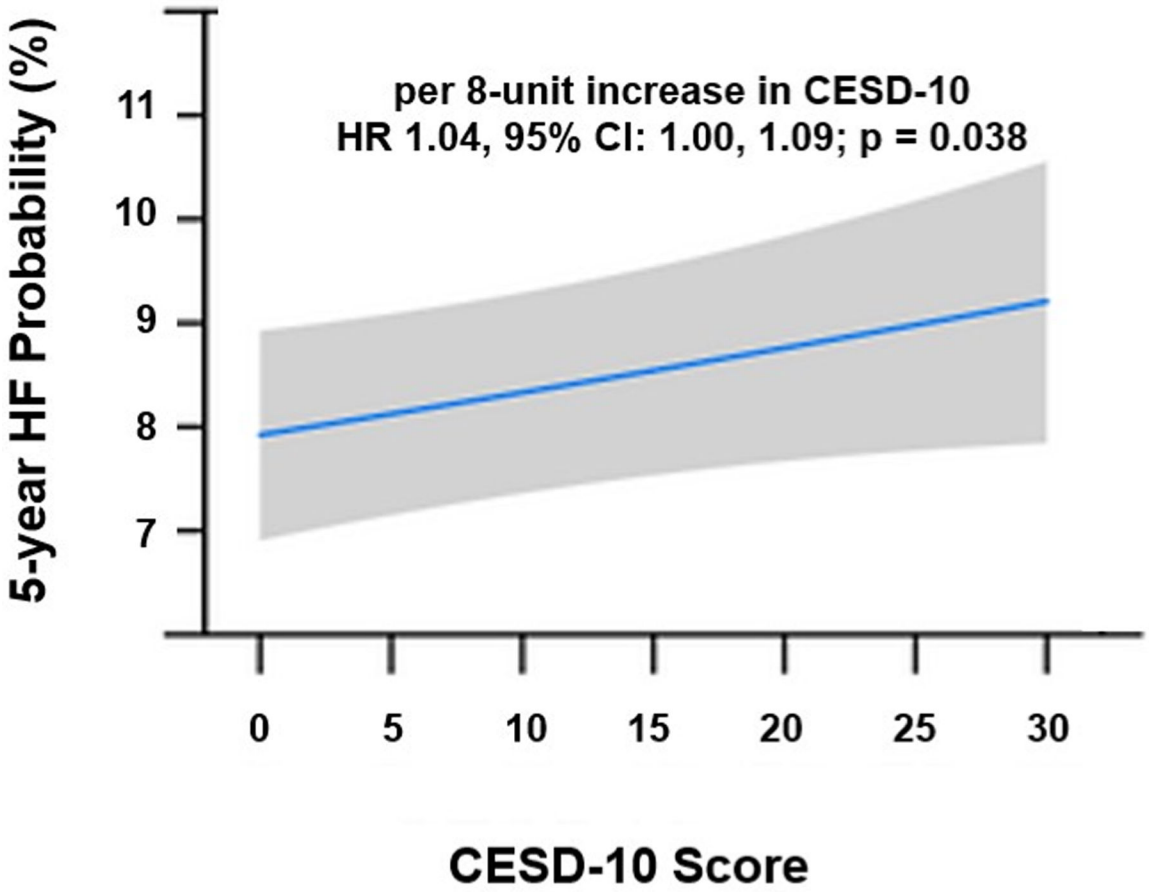

Central Illustration. Five-year risk of incident HF according to CESD-10 score in the Southern Community Cohort Study.

Greater frequency of depressive symptoms associated with increased risk of incident HF, including at levels considered to represent sub-clinical depression. Results shown are from the multivariable-adjusted Cox model including all variables shown in Table 2, Model 3.

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Table 1.

Baseline Characteristics of 23,937 Southern Community Cohort Study Participants by CESD-10 Score

Characteristic	CESD-10 Score <10 (N=13176)	10–19 (N=8837)	≥ 20 (N=1924)	*p*
Age, years	57 (48, 67)	51 (45, 58)	49 (45, 54)	<0.001
Female, %	60	66	78	<0.001
Black, %	71	72	59	<0.001
Education, %				<0.001
<High school	34	43	43	
HS/vocational/junior college	55	52	53	
≥ College degree	11	5	4	
Annual income < $15,000, %	63	78	83	<0.001
Employed, %	19	12	8	<0.001
Comorbidities, %				
Hypertension	61	61	60	0.79
Diabetes	25	26	25	0.23
Hyperlipidemia	38	35	38	<0.001
Cerebrovascular disease	8	9	10	<0.001
BMI	28.9 (24.8, 34.0)	29.3 (24.7, 35.3)	29.9 (25.0, 36.3)	<0.001
Smoking, %				<0.001
Current	34	48	55	
Former	28	20	16	
Never	38	33	29	
Physical activity				
Sitting, hrs/day	8.0 (5.4,11.0)	8.2 (5.5,12.0)	9.0 (6.0, 13.0)	<0.001
Total activity, met-hrs/day	13.9 (7.4, 23.6)	12.6 (6.3, 22.9)	11.5(4.8, 22.2)	<0.001
Alcohol per day[a]	0.96±3.3	1.4±4.2	1.3±4.2	<0.001
Marital Status, %				<0.001
Married	33	24	21	
Divorced or separated	31	36	46	
Widowed	16	12	10	
Never married	20	27	22	
Close friends/relatives, n	4 (2, 8)	3 (1, 5)	2 (1, 3)	<0.001
Help in emergency, n	3 (2, 5)	2 (1, 4)	2 (1, 3)	<0.001
Anti-depressants/anxiolytics, %	16	36	59	<0.001
History of Depression, %	18	44	71	<0.001

[a]All continuous variables are displayed as median (25^{th}, 75^{th} percentile) except where indicated by ([a]) for which mean ± SD is displayed. BMI = body mass index, hrs= hours, HS= high school

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Table 2.

Risk of incident HF associated with CESD-10 score in the Southern Community Cohort Study

Model	Covariates	Hazard Ratio per 8 unit increase in CESD-10 score	95% CI	*p*
1	Age, sex, race	1.17	1.13, 1.21	<0.0001
2	Model 1 + HTN, HLD, DM, BMI, Stroke/TIA, smoking	1.11	1.07, 1.15	<0.0001
3	Model 2 + income, education, employment, alcohol, physical activity, marital status, close friends, help in emergency, anti-depressants	1.04	1.00, 1.09	0.038

BMI= body mass index, DM= diabetes, HLD= hyperlipidemia, HTN= hypertension, TIA= transient ischemic attack

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Table 3.

Novel characteristics of the SCCS compared with prior cohort studies investigating the association of depression with incident heart failure

Cohort	N	Age	Race (%)	Female (%)	SES Descriptors[a]	Depression Tool	Prevalence of Depression, % (n)	Incidence of HF, % (n)	Association with HF	Follow-up (years)
Community-based Cohort										
SCCS	23,937	40–79	Black: 70	64	**Income < 15k: 70%** **< High school: 38%** **Employed: 16%**	CESD-10	45% (10,761)	25% (6,081)	HR 1.04 (1.00–1.09) p = 0.038	Median 11
CHS (39)	4,114	≥ 65	Black: 14.2	59.2	*Income < 25k: 61%* (40) *Education (y): 13.9* (41) Employed: NR/NC	CESD-10	20.4% (840)	24% (970)	HR 1.08 (0.92–1.26) p = NS	Median 10.7
MESA (16)	6,782	45–84	Black: 27.9	52.9	*Income < 25k: 31%* (42) < High school: 18% *Employed: 49%* (43)	CES-D	12.9% (872)	3.6% (242)	HR 1.19 (0.76–1.85) p = NS	Mean 9.3
YHAP (13)	2,501	>65	Non-white: 19.1	58.1	Income: NR Education (y): ~9 Employment: NR	CES-D	7.5% (188)	12.5 % (313)	HR 1.52 (0.94–2.43) p = 0.09	Up to 14
Clinical Cohort										
VA (15)	236,079	50–80	Non-white: 17.4	6.6	Income: NR Education: NR Employed: NR	ICD-9	22.9% (54,062)	4.7% (10,994)	HR 1.21 (1.13–1.28)	Up to 6
Clinical-trial ancillary cohort										
SHEP (14)	4,538	>60	Non-white: 13.9	56.7	Income: NR *Education (y): 11.7* (44) Employment: NR	CES-D	4.9% (221)	3.4% (156)	HR 2.59 (1.57–4.27) p < 0.001	Median 4.5
International Studies										
HUNT (45)	62,567	≥ 20	No race reported (Norway)	52.1	Income: NR/NC **Education: Up to 12 years: 77%** Employed: NR	Hospital Anxiety and Depression Scale	3.2% (2,002)	2.4% (1,499)	HR 1.41 (1.07–1.87)[b]	Mean 11.3
UK (46)	~1.3[c] million	>30	Black: 1.6	46.4	**Lowest SES: 18.6%**	Diagnosis or medication	2.9% (39,747)	0.7% (9,397)	HR 1.17 (1.03–1.32)	Median 6.9

CES-D = Center for Epidemiologic Studies Depression Scale, CHS = Cardiovascular Health Study, HF = heart failure, HUNT = Nord-Trøndelag Health Study, ICD-9 = International Classification of Diseases -9th revision, MESA = Multi-Ethnic Study of Atherosclerosis, NR/NC = not reported, not calculable, SCCS = Southern Community Cohort Study, SES = socioeconomic status, SHEP = Systolic Hypertension in the Elderly, UK = United Kingdom, VA= Veterans Affairs, YHAP = Yale Health and Aging Project.

[a] SES descriptors: **bolded if adjusted for in analysis**, *italicized if based on whole cohort statistics*.

[b] HR reported for severe symptoms.

[c] Cohort 2.

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