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A POSITIVE PHQ-2 DEPRESSION SCREEN AMONG HOSPITALIZED HEART FAILURE PATIENTS IS ASSOCIATED WITH ELEVATED 12-MONTH MORTALITY

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Abstract

Background—Given the association of depression with poorer cardiac outcomes, an American Heart Association Science Advisory has advocated routinely screening cardiac patients for depression using the two-item Patient Health Questionnaire (PHQ-2) “at a minimum.” Yet, the prognostic value of the PHQ-2 among HF patients is unknown.

Methods and Results—We screened hospitalized HF patients (ejection fraction (EF) <40%) that staff suspected may be depressed with the PHQ-2, and then determined vital status at up to 12-months follow-up. At baseline, PHQ-2 depression-screen positive patients (PHQ-2 (+); N=371) compared to PHQ-2 screen-negative patients (PHQ-2 (−); N=100) were younger (65 vs. 70), and more likely to report NYHA class III/IV than class II symptoms (67% vs. 39%) and lower levels of physical and mental health-related quality of life (all $p \leq 0.002$), but were similar on other characteristics (65% male, 26% mean EF). At 12-months, 20% of PHQ-2 (+) vs. 8% of PHQ-2 (−) patients had died ($p=0.007$) and PHQ-2 status remained associated with both all-cause (hazard ratio (HR): 3.1 (95% CI: 1.4–6.7); $p=0.003$) and cardiovascular mortality (HR: 2.7 (1.1–6.6); $p=0.03$) even after adjustment for age, gender, EF, NYHA class, and a variety of other covariates.

Conclusions—Among hospitalized HF patients, a positive PHQ-2 depression screen is associated with an elevated 12-month mortality risk.

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DISCLOSURES

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Keywords

Depression; heart failure; Patient Health Questionnaire; mortality

INTRODUCTION

Heart failure (HF) is a common and growing health problem that affects over 5.7 million Americans with over 660,000 newly diagnosed cases, 277,000 deaths, and \$39 billion in direct and indirect costs yearly.¹ HF is also the leading cause for hospitalization among Medicare patients, and its five-year mortality rate following first hospitalization exceeds that of all cancers except lung.² Moreover, heart failure remains the only major cardiovascular disease whose mortality rate has been essentially unchanged over the past decade despite recent advances in its therapeutic management.¹

One potential contributor to these persistently poor outcomes is the presence of unrecognized and inadequately treated depression. Depression is highly prevalent among HF patients^{3, 4} and strong evidence has linked it to increased morbidity and mortality,^{5–11} higher levels of health services utilization,¹² and reduced health-related quality of life (HRQoL) independent of disease severity^{9, 13, 14} and even at subsyndromal elevations of mood symptoms.^{8, 9}

Several depression screening instruments have been validated for use in cardiac populations and found to have similar psychometric characteristics.¹⁵ Given these similarities, a recent American Heart Association (AHA) Science Advisory has advocated a strategy of increased awareness and screening of coronary heart disease (CHD) patients for depression with the two-item Patient Health Questionnaire (PHQ-2)¹⁶ “at a minimum”, followed by the nine-item PHQ (PHQ-9)¹⁷ to investigate positive screens and provide a severity score that can be used to guide treatment selection and monitoring.¹⁸ Unlike other instruments, the PHQ-2 requires nominal training and time to administer and, thus, is feasible for routine use in clinical practice. Still, its prognostic value among patients with HF is unknown. We addressed this question as part of a study to inform later development of a trial to examine the impact of screening and treating depression among patients with HF.

METHODS

Study Setting

We screened HF patients for depression prior to hospital discharge at 4 university-affiliated Pittsburgh-area hospitals, implementing a protocol approved by the Institutional Review Board of the University of Pittsburgh before the start of patient enrollment.

Patient Population

We targeted enrollment of 372 PHQ-2 (+) subjects based on sample size calculations designed to identify the predictive PHQ-9¹⁷ cut-point score for determining mortality using receiver operating characteristic (ROC) analyses by NYHA class and gender (6 separate analyses), with 80% power, 70–85% sensitivity, 50% minimum specificity, and 90% confidence.¹⁹ For comparison purposes, we also planned to enroll a convenience sample of 100 PHQ-2 (–) hospitalized HF patients who met all protocol-eligibility criteria.

From 12/2007 to 4/2009, study nurse-recruiters approached hospital personnel to inquire if they were caring for any patients with heart failure who had a cardiac ejection fraction (EF) of under 40% and suspect might be depressed, and if so to ask for the patient’s verbal agreement permitting the recruiter to approach. If the patient agreed, our nurse-recruiter

explained our study to the patient, reviewed our enrollment criteria, and then obtained the patient's signed informed consent to undergo our screening procedure. We required all patients: (a) have a documented EF <40% as determined by echocardiogram, cardiac catheterization, or multiple gated acquisition scan; (b) New York Heart Association (NYHA) class II–IV cardiac symptoms; (c) no current alcohol dependence or other substance abuse disorder; (d) score ≥ 24 on the Folstein Mini-Mental State Examination²⁰ to ensure mental capacity to provide informed consent and reliable responses to our assessment instruments; (e) be medically stable and not have another medical condition known to be fatal within 6 months; (f) be discharged home or to short-term rehabilitation; and (g) be English speaking, have no communication barrier, and have a household telephone. While patients prescribed antidepressant pharmacotherapy at baseline were included in our PHQ-2 depression screen-positive (+) cohort provided they screened positive on the PHQ-2 and met all other eligibility criteria, they were excluded from our PHQ-2 screen-negative (–) cohort.

Baseline Assessment

The PHQ-2 assesses for the presence of the two cardinal symptoms of depression over the past two weeks: “Little interest or pleasure in doing things” and “feeling down, depressed, or hopeless”.¹⁶ We defined a positive PHQ-2 depression screen (PHQ-2 (+)) as patient endorsement of one or both of its items, and a negative screen (PHQ-2 (–)) when the patient responded negatively to both of these items. This classification has 90% sensitivity and 69% specificity for the diagnosis of major depression among CHD patients when measured against the “gold-standard” Diagnostic Interview Schedule.²¹

Prior to a study subject's hospital discharge, our nurse-recruiters administered the 9-item Patient Health Questionnaire (PHQ-9)¹⁷ to ascertain the severity of mood symptoms; the SF-36 to assess mental (SF-36 MCS) and physical (SF-36 PCS) HRQoL²²; the PRIME-MD Anxiety Module to determine the presence of an anxiety disorder²³ and conducted a chart review to collect baseline sociodemographic and clinical data. Following the baseline assessment, the recruiters distributed an NIMH brochure entitled “Depression and Heart Disease”²⁴ to all screened patients to heighten their awareness of the impact of mood disorders on heart disease. We also encouraged PHQ-2 screen positive patients via telephone and by mailed letter that they contact their primary care physician (PCP) to discuss this clinical finding, and we sent a similar letter to their PCP also encouraging follow-up.

Vital Status

We ascertained vital status via telephone contact with patients and/or their designated secondary contacts (e.g., spouse, adult child). A study physician classified cause of death (cardiovascular or other) through a review of medical records, obituary notices, and/or written summaries of interviews with secondary contacts and discussions with subjects' physicians as necessary.

Statistical Analyses

We compared baseline sociodemographic, diagnostic, symptom severity, functional status, and current treatment for depression by PHQ-2 status using t-tests for continuous data and chi-squared analyses for categorical data. We used Kaplan-Meier analyses to calculate incidence of all-cause and cardiovascular deaths by PHQ-2 status with log-rank tests to evaluate these differences for statistical significance and Cox models to adjust for differences in baseline covariates. To control for possible confounders of the relationship between mood symptoms and mortality, we adjusted for several recognized predictors of HF mortality.^{25, 26} They included the presence of anemia (hemoglobin <10 g/dl), diabetes, hyponatremia (sodium <136 mEq/L), renal insufficiency (creatinine >1.7 mg/dL), systolic and diastolic blood pressure, and use of an angiotensin-converting enzyme inhibitor (ACE-I)

or an angiotensin receptor blocker (ARB) medication, and use of coumadin. As antidepressant medication use could affect mortality risk,^{27, 28} we repeated our multivariate analyses excluding those PHQ-2 (+) patients using an antidepressant at baseline. All analyses were performed with SAS statistical software (SAS Institute Inc., Cary NC).

Role of the Funding Source

The funding source had no involvement in the study design, data collection, data analysis, data interpretation, or writing of this report.

RESULTS

Medical staff at the four study hospitals identified 857 HF patients of whom our nurse recruiters were able to approach and consent 589 (69%) for our screening procedure that was conducted on the median of hospital admission day 4 (mean 5.2 days; range 0–38 days). Of the 520 who completed the PHQ-2, 401 (77%) were PHQ-2 (+) and 371 (93%) then met all protocol-eligibility criteria. However, there was no difference in the rate of PHQ-2 (+) status by quartile of screening day (e.g., 80% PHQ-2 (+) in quartile 1 screened on admission days 0–2 vs. 77% PHQ-2 (+) in quartile 4 screened on admission day 8 or later; $p=0.48$). Of the 119 PHQ-2 (–) patients, 100 (84%) met all protocol-eligibility criteria making for a total of 471 study subjects (Figure 1). Later, we confirmed vital status at up to 12-months follow-up on all 471 study patients (100%) as of 12/31/09.

Baseline Patient Characteristics

As portrayed in Table 1, PHQ-2 (+) patients compared to PHQ-2 (–) patients were younger (65 vs. 70), and more likely to report NYHA III/IV symptoms (67% vs. 39%), higher levels of mood symptoms (PHQ-9 mean score: 11.3 vs. 3.5), and lower levels of physical (SF-12 PCS: 30.7 vs. 34.3) and mental HRQoL (SF-12 MCS: 44.4 vs. 58.5) (all $p \leq 0.002$). While the two groups were similar on other objective sociodemographic and clinical characteristics (e.g., 65% male, 85% White, 41% diabetic, 26% mean EF, 82% beta-blocker use), PHQ-2 (+) patients tended to use coumadin anticoagulation therapy at a lower rate than PHQ-2 (–) patients (37% vs. 48%; $p=0.06$). Moreover, of the 26% (97) of PHQ-2 (+) patients using an antidepressant, 94% were taking either a selective serotonin reuptake inhibitor (SSRI) or serotonin-norepinephrine reuptake inhibitor (SNRI) (91/97), and just 2% (2/97) were using a tricyclic antidepressant at a guideline-recommended dosage for treating depression.²⁹

Clinical Outcomes

As of 12/31/09, we identified 83 deaths: 75 among PHQ-2 (+) and 8 among PHQ-2 (–) patients, including 55 (66%) for cardiovascular causes.

At 12-month follow-up, 20% of PHQ-2 (+) and 8% of PHQ-2 (–) patients had died ($p=0.007$) (Figure 2a), and an affirmative response to either or both PHQ-2 items conferred a similar risk of mortality (20% for a “yes” answer to “little interest or pleasure doing things”; 19% for “feeling down, depressed or hopeless”; and 20% for “yes” answers to both items). Additionally, a positive PHQ-2 screen was associated with an increased risk of mortality for cardiovascular causes (14% vs. 6%; $p=0.05$) (Figure 2b) that was also similar by item response (e.g., 13% for a “yes” to “little interest or pleasure doing things”; and 12% for “feeling down, depressed or hopeless”).

After adjusting for gender, age, EF, NYHA class, presence of an anxiety disorder, diabetes, renal insufficiency, blood pressure, and a variety of other possible confounders of HF mortality,^{25, 26} 12-month all-cause mortality remained significantly associated with PHQ-2 (+) status (PHQ-2 (+) vs. PHQ-2 (–) hazard ratio (HR): 3.1 (95% CI: 1.4–6.7); $p=0.003$),

age (≥ 65 vs. < 65 ; HR: 2.1 (1.3–3.4); $p=0.004$), presence of renal insufficiency (HR: 1.8 (1.1–2.9); $p=0.01$), use of an ACE-I or ARB (HR: 0.6 (0.4–1.0); $p=0.04$), and use of a beta-blocker (HR: 0.6 (0.3–0.9); $p=0.03$) (Table 2). Moreover, PHQ-2 (+) status remained associated with an increased risk of mortality for cardiovascular causes (HR: 2.7 (1.1–6.6); $p=0.03$). Given the possibly beneficial effects of SSRI antidepressants on cardiovascular outcomes,³⁰ we excluded the 97 patients using an any antidepressant at baseline and found an essentially similar impact of PHQ-2 (+) status on 12-month risk of both all-cause (HR: 3.0 (1.4–6.4); $p=0.006$) and cardiovascular mortality (HR: 2.5 (1.0–6.2); $p=0.05$).

Among the 371 PHQ-2 (+) HF patients, the 12-month incidence of all-cause mortality was similar by level of PHQ-9 score ($p=0.58$; Figure 3). Furthermore, ROC analyses were unable to identify any PHQ-9 cut-point score that significantly predicted an elevated risk of mortality by gender and NYHA class.

DISCUSSION

Hospitalized HF patients who were suspected by staff of being depressed and then screened positive for depressive symptoms on the PHQ-2 prior to discharge experienced a significantly elevated 12-month risk of all-cause and cardiovascular mortality compared to HF patients who screened negative for depressive symptoms. This elevated risk persisted even after adjustment for the severity of heart disease, a variety of other baseline covariates associated with HF mortality, and the presence of a co-morbid anxiety disorder. Furthermore, no follow-up PHQ-9 score level identified any PHQ-2 (+) patients at particularly greater risk of mortality. Our findings are enhanced by our administration of a validated and clinically-efficient depression screening and assessment tool, confirmation of the systolic heart failure using objectively measured criteria, longitudinal study design, complete ascertainment of vital status, and statistical adjustments for a variety of potential confounders.

Despite advances in treatment methods, heart failure remains the only major cardiovascular condition whose mortality has not declined in recent years.¹ Given the 40% prevalence of depression among hospitalized HF patients reported by a recent meta-analysis³ and multiple reports that associate depression with a doubled mortality risk,^{3, 5, 8, 31} our findings have important implications for new approaches to reduce HF mortality. Indeed, the minimal burden placed on providers and patients through administration of the PHQ-2, versus more lengthy depression screening instruments and those that require highly trained personnel to administer, could enable depression screening to become part of routine cardiac care.

Given the elevated prevalence of depression among patients with CHD, its consistent association with adverse clinical outcomes, and underrecognition in this population by clinicians,^{32–34} the recent AHA Science Advisory has advocated a strategy of increased awareness and screening of CHD patients for depression to identify those who may require further assessment and treatment.¹⁸ Yet these recommendations have been controversial as depression screening alone has not been demonstrated to improve clinical outcomes.¹⁵ Data from randomized trials has recently emerged to support the Science Advisory when screening is coupled with a treatment program^{35–37}; still, none of those studies focused on HF patients.

Also pertinent to clinicians, our findings suggest depressive symptoms may influence patients' perception of the severity of their HF to a greater extent than its objective severity as measured by their cardiac ejection fraction. Gottlieb et al. reported similar findings after they adjusted for a wide variety of objective measures of exercise capacity and physiology among 2,322 HF patients with NYHA class II–IV symptoms enrolled in the HF-ACTION

trial,¹⁴ as have other investigators.^{31, 38} Unrecognized and inadequately treated depression may therefore lead to over-use of health services and increased potential for iatrogenic harm as clinicians attempt to allieviate heart failure “symptoms” through additional tests, “therapeutic” trials and adjustments of pharmacotherapy, and referrals to specialists. Increased awareness of the impact of depression on cardiac symptoms by patients and clinicians and follow-up evaluations for patients who screen positive for depression as recommended by the AHA could potentially improve patients’ perceptions of their cardiac disease, physical functioning, and HRQoL.^{35–37} However, evidence from well-designed clinical trials is presently lacking to confirm the effectiveness of this strategy among HF patients.³⁹

The generalizability and validity of our study findings is possibly limited as depressed patients are less likely to participate in clinical research than non-depressed patients⁴⁰ and we did not systematically screen all hospitalized HF patients for mood symptoms. Given the emphasis of our study on enrolling PHQ-2 positive patients, our study nurses requested that hospital staff obtain Health Insurance Portability and Accountability Act (HIPAA) approval allowing them to approach patients most likely to meet eligibility criteria for study enrollment. Indeed, the 79% of study patients who screened PHQ-2 positive for depressive symptoms is approximately double the prevalence of depression reported by a meta-analysis involving 2,667 hospitalized HF patients (38% prevalence using “liberal cutoffs”)³ and thus may not be representative of other populations of HF patients. Yet we identified similar rates of medical co-morbidity, gender, and employment status at baseline by PHQ-2 status, and adjusted our findings for a variety of characteristics demonstrated to affect HF mortality and PHQ-2 status remained an independent prognostic marker. Furthermore, focusing our screening efforts on patients who had a higher suspicion for depression likely increased the positive predictive value of our PHQ-2 screen. Thus the 0.14 negative likelihood ratio and 4% posterior probability for major depression among PHQ-2 negative patients indicates that a negative PHQ-2 screen can effectively rule-out the presence of major depression.²¹

Critically, our finding that depression confers a significantly greater mortality risk is consistent with other studies that utilized highly trained personnel to administer complex depression rating scales that are far less practical for use in typical clinical settings.^{3, 4, 8–11} Indeed, the 8% incidence of all-cause mortality among PHQ-2 (+) patients at 3-months follow-up (Figure 2a) is similar to the 7% mortality rate at 12-weeks experienced by the 469 outpatients with HF and clinical depression that were enrolled in the SADHART-CHF trial (mean Hamilton Rating Scale Score for Depression at baseline: 18.3).³⁹ Additionally, the 20% 12-month mortality rate we observed is similar to the 12-month mortality rate reported by Jiang et al. among 302 hospitalized HF patients who scored 10 or above on the Beck Depression Inventory (BDI) prior to discharge.⁸ Finally, the validity of our findings is confirmed by our identification of ACE-I or ARB and beta-blocker use as protective for both all-cause and cardiovascular mortality in keeping with prior reports,^{26, 41} and multivariate models that uphold the adverse prognostic risk of a positive PHQ-2 de[ression screen even after adjusting for functional status, cardiac ejection fraction, and a variety of other baseline covariates associated with 12-month mortality risk.

Unlike other studies that used depression rating scales other than the PHQ-9,^{8, 42–44} we were unable to identify a dose-response relationship between level of mood symptoms and mortality risk. However, we “pre-screened” study patients for depression with the PHQ-2 and this step alone may be sufficient to identify HF patients at highest mortality risk. Still, Jiang et al. were also unable to identify a single BDI cutoff value that best predicted mortality using ROC analyses.⁸ Nevertheless, given the sensitivity and specificity of a positive PHQ-2 screen for major depression,²¹ we agree with the AHA Science Advisory recommendation that a positive PHQ-2 screen be so confirmed with the PHQ-9 or a more

formal interview¹⁸ before active depression treatment be initiated according to evidence-based guidelines^{45, 46} as a diagnosis of depression cannot be assumed from a positive screen.²¹

Our findings also highlight the need to better identify the mechanism(s) by which depression may exert its adverse impact on patients with HF. For example, the AHA Science Advisory recommends that patients with cardiac disease be carefully monitored for their adherence with recommended medical care. Yet while we found usage of ACE-Is, beta-blockers, and other medications proven to reduce HF mortality were similar by PHQ-2 status at baseline, we lacked pharmacy claims data to accurately assess medication adherence over the course of follow-up. Additionally, we lacked follow-up data on other factors known to be adversely affected by depression that may also have influenced mortality such as adherence with recommended diet and exercise, tobacco usage, social support, vagal tone, catecholamine and cortisol levels, thrombogenesis, and proinflammatory cytokines.^{5, 7, 47, 48} Still, we adjusted for the presence of an anxiety disorder that could have amplified mood symptoms, affected patients' willingness and ability to engage in the self-care needed to manage their HF,⁴⁹ and confounded the relationship between mood and outcomes we observed.⁵ Based on reports suggesting antidepressants may affect cardiovascular morbidity,^{28, 50, 51} we also repeated our models excluding those HF patients on antidepressant pharmacotherapy and obtained essentially the same results. Finally, while we encouraged all patients who screened positive for mood symptoms on the PHQ-2 to discuss further treatment options with their physician, we lacked information on what, if any treatment for depression they may have received over the course of follow-up.

Data from clinical trials still remain necessary to determine whether depression screening and treatment can reduce mortality in patients with cardiovascular disease.^{52, 53} Nevertheless, safe and effective pharmacologic and counseling modalities for treating depression in patients with cardiovascular disease are presently available^{15, 30, 36, 37, 46, 54} that may improve HRQoL, physical functioning, and reduce hospital readmissions.^{35, 37, 45} An increasing number of hospitals and other healthcare delivery organizations already provide care management for HF patients based on the Chronic Care Model,^{55, 56} and these programs could be adopted to include depression care for greater efficiency. However, just one trial has examined the effectiveness of the Chronic Care Model for treating depression among patients with cardiac disease³⁵ and therefore we know very little about the impact of depression treatment on HF patients.³⁹

In conclusion, our findings confirm the independent and adverse prognostic impact conferred by the presence of even low levels of mood symptoms among hospitalized patients with HF and support the AHA's Science Advisory's recommendation to increase awareness and routinely screen all HF patients for depression using the PHQ-2. Although we were unable to identify a follow-up PHQ-9 cut-off score that conferred a particularly elevated mortality risk, we agree with the Science Advisory's screening algorithm that a positive depression screen be confirmed with the PHQ-9 and more comprehensive clinical evaluation, and treatment provided in accordance with evidence-based guidelines for treating depression.⁴⁶ Finally, well-designed and well-conducted clinical trials remain critical to establish whether screening HF patients for depression and providing effective treatment can reduce mortality and improve a broad variety of other outcomes of interest to patients, providers, health plans, and purchasers.

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Figure 1.
Study recruitment.

Figure 2a.

Figure 2b.

Figure 2.

Figure 2a. All cause mortality by PHQ-2 status. At 12-months follow-up, 20% of PHQ-2 positive and 8% of PHQ-2 negative patients died ($p=0.007$).

Figure 2b. Cardiovascular mortality by PHQ-2 status. At 12-months follow-up, 14% of PHQ-2 positive and 6% of PHQ-2 negative patients died ($p=0.05$).

Figure 3. 12-Month all-cause mortality by PHQ-9 level among PHQ-2 positive patients (N=371). All-cause mortality by PHQ-9 level was similar by level of PHQ-9 score ($p=0.58$).

Table 1

Baseline sociodemographic and clinical characteristics.

	PHQ-2 (+) (N =371)	PHQ-2 (-) (N =100)	P
Age, mean (SD) range	65.0 (13.4) 23–91	69.6 (11.4) 37–93	0.002
Male, % (N)	64% (237)	67% (67)	0.56
Caucasian, % (N)	85% (315)	86% (86)	0.79
Working, part-time or full-time, % (N)	20% (74)	21% (21)	0.82
NYHA Class, % (N)			0.0001
II	33% (123)	61% (61)	
III	39% (146)	32% (32)	
IV	28% (103)	7% (7)	
Body Mass Index, kg/m ² , mean (SD)	29.5 (7.2)	29.2 (7.5)	0.72
Systolic blood pressure, mm Hg, mean (SD)	134.2 (68.9)	145.4 (124.7)	0.39
Diastolic blood pressure, mm Hg, mean (SD)	78.9 (70.3)	93.1 (131.2)	0.30
Ejection fraction (%) (N)	25.8 (7.8)	25.3 (7.1)	0.51
Myocardial Infarction (MI), % (N)	51% (189)	58% (58)	0.25
Post-CABG surgery, % (N)	42% (158)	41% (41)	0.78
Diabetic, % (N)	42% (156)	38% (38)	0.47
Hypertensive, % (N)	77% (288)	74% (74)	0.45
Hyperlipidemia, % (N)	74% (276)	71% (71)	0.49
Atrial fibrillation, % (N)	41% (152)	41% (41)	0.99
Chronic obstructive pulmonary disease, % (N)	27% (101)	25% (25)	0.66
Renal insufficiency, % (N)	25% (94)	24% (24)	0.78
Sodium, mmol/L, mean (SD)	138.6 (3.8)	139.0 (4.0)	0.38
Hemoglobin, g/dL	12.6 (2.1)	12.7 (1.9)	0.72
ACE-I or ARB use, % (N)	74% (275)	67% (67)	0.16
Beta-blocker use, % (N)	83% (307)	79% (79)	0.39
Statin use, % (N)	57% (213)	66% (66)	0.12
Spironolactone use, % (N)	15% (54)	14% (14)	0.89
Coumadin use, % (N)	37% (139)	48% (48)	0.06

	PHQ-2 (+) (N =371)	PHQ-2 (–) (N =100)	P
Aspirin use, % (N)	76% (282)	79% (79)	0.53
Implantable cardiac defibrillator, % (N)	38% (141)	29% (29)	0.10
Biventricular pacemaker/Cardiac resynchronization therapy, % (N)	19% (72)	21% (21)	0.72
PHQ-9, mean (SD)	11.3 (4.5)	3.5 (2.4)	0.0001
PHQ-9, % (N)			0.0001
0–4	5% (20)	72% (72)	
5–9	32% (119)	27% (27)	
10–14	36% (135)	1% (1)	
15+	26% (97)	0% (0)	
Anxiety disorder, % (N)	30% (110)	1% (1)	0.0001
Antidepressant use, % (N) *	26% (97)	--	
SSRI	20% (75)		
SNRI	4% (16)		
Bupropion	2% (6)		
TCA	1% (2)		--
SF-12 MCS	44.4 (11.3)	58.5 (6.8)	0.0001
SF-12 PCS	30.7 (9.2)	34.3 (10.6)	0.001

* Antidepressant use at baseline was an exclusion criterion for inclusion in our PHQ-2 (–) study cohort.

Abbreviations: ACE-I, Angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker medication; CABG, coronary artery bypass graft; CI, confidence interval; NYHA, New York Heart Association; PHQ, Patient Health Questionnaire; SF-12 MCS, Medical Outcomes Study Short Form Mental Component Scale; SF-12 PCS, Medical Outcomes Study Short Form Physical Component Scale; SSRI, Selective serotonin reuptake inhibitor; SNRI, Serotonin norepinephrine reuptake inhibitor; TCA, tricyclic antidepressant.

Table 2

Multivariate models of 12-month all-cause and cardiovascular mortality.

All-Cause Mortality	HR (95% CI)	P
PHQ-2 Status, (+) vs. (−)	3.1 (1.4–6.7)	0.003
Gender, female vs. male	1.3 (0.8–2.0)	0.28
Age ≥ 65 vs. <65	2.1 (1.3–3.4)	0.004
Ejection Fraction ≤ 30% vs. >30%	1.1 (0.6–1.7)	0.84
NYHA Class, III–IV vs. II	1.5 (0.9–2.6)	0.12
Anxiety disorder	0.8 (0.4–1.3)	0.33
Chronic obstructive pulmonary disease	1.1 (0.7–1.8)	0.72
Renal insufficiency	1.8 (1.1–2.9)	0.01
ACE-I or ARB use	0.6 (0.4–1.0)	0.04
Beta-blocker use	0.60 (0.3–0.9)	0.03
Coumadin use	0.9 (0.6, 1.4)	0.65
Diabetes	1.1 (0.7–1.7)	0.75
Hemoglobin <10 vs. ≥ 10 g/dL	1.4 (0.8–2.6)	0.26
Sodium, <136 vs. ≥ 136 mmol/L	1.4 (0.8–2.4)	0.18
Diastolic blood pressure, per 10-unit increase	1.1 (1.0–1.2)	0.27
Systolic blood pressure, per 10-unit increase	0.9 (0.9–1.0)	0.27
Cardiovascular Mortality	HR (95% CI)	P
PHQ-2 Status, (+) vs. (−)	2.7 (1.1–6.6)	0.03
Gender, female vs. male	1.4 (0.8–2.5)	0.21
Age ≥ 65 vs. <65	1.6 (0.9–2.9)	0.13
Ejection Fraction ≤ 30% vs. >30%	1.4 (0.7–2.8)	0.30
NYHA Class, III–IV vs. II	1.4 (0.7–2.7)	0.29
Anxiety disorder	0.9 (0.4–1.7)	0.70
Chronic obstructive pulmonary disease	1.1 (0.6–2.0)	0.69
Renal insufficiency	1.5 (0.9–2.8)	0.15
ACE-I or ARB use	0.4 (0.2–0.7)	0.003
Coumadin use	1.0 (0.6–1.7)	0.97
Beta-blocker use	0.6 (0.3–1.0)	0.05
Diabetes	1.5 (0.9–2.6)	0.17
Hemoglobin <10 vs. ≥ 10 g/dL	1.1 (0.5–2.4)	0.87
Sodium, <136 vs. ≥ 136 mmol/L	1.4 (0.8–2.8)	0.27
Diastolic blood pressure, per 10-unit increase	1.1 (1.0–1.2)	0.08
Systolic blood pressure, per 10-unit increase	0.9 (0.8–1.0)	0.09