Impact of Psychiatric Comorbidity on Mortality in Veterans with Type 2 Diabetes

James J. Prisciandaro, Ph.D.,¹ Mulugeta Gebregziabher, Ph.D.,^{2,3} Anouk L. Grubaugh, Ph.D.,^{1,2}
Gregory E. Gilbert, MSPH,² Carrae Echols, M.S.,² and Leonard E. Egede, M.D., M.S.^{2,4,5}

Abstract

Background: Particular psychiatric disorders, such as depression, have a significant and negative effect on diabetes outcomes. However, we know very little about the impact of other psychiatric disorders, and of the effect of multiple psychiatric comorbidities, on the clinical course of diabetes. As such, the present study examined the impact of a wide range of psychiatric comorbidities on all-cause mortality in individuals with type 2 diabetes.

Methods: Retrospective follow-up was conducted of 15,065 veterans with type 2 diabetes enrolled in hospital care between 1997 and 2006. Clinical diagnoses from patient records were used to construct four psychiatric disorder scales: internalizing (i.e., depression and anxiety); externalizing (i.e., alcohol and drug abuse); psychotic; and bipolar. Longitudinal relationships were examined between these scales and mortality using Cox regression.

Results: Only externalizing disorders were significantly associated with mortality: hazard ratio = 1.22 (95% confidence interval = 1.02–1.47). In other words, each additional diagnosed externalizing disorder increased an individual's chance of dying over the follow-up period by 22%. This association remained significant when demographics and medical comorbidities were statistically controlled, but was rendered nonsignificant when medication adherence was introduced to the regression model.

Conclusions: The results provide evidence that among individuals with diabetes, alcohol and drug abuse/dependence have a significant impact on mortality. This increased risk of mortality may have been due to the association between psychiatric disorders and adherence to antidiabetes medications observed in the present study. Individuals with co-occurring diabetes and alcohol or drug abuse should be targeted for intensive interventions given their acute increased risk of mortality.

Introduction

EXTANT RESEARCH SUGGESTS that psychiatric illness is overrepresented among individuals with diabetes^{1,2} and that it has a negative effect on diabetes outcomes. A study of approximately 500,000 veterans with diabetes found that 31% were diagnosed with a psychiatric disorder and that those with psychiatric disorders had higher rates of macrovascular complications and metabolic decompensation.³ Other studies examining the effect of specific psychiatric disorders have also demonstrated relatively poor outcomes among individuals with diabetes. For example, depression has been associated with decreased adherence to medical recommendations, poor glycemic control, increased healthcare costs, and increased

mortality.^{4–7} Furthermore, schizophrenia has been associated with increased incidence of diabetic ketoacidosis, poor glycemic control, and mortality.^{8,11}

Of particular concern, there is growing evidence that psychiatric illness is associated with increased mortality in individuals with diabetes.^{6,9–11} These data mirror findings from the general population, which demonstrate a link between the presence of a wide range of psychiatric disorders and increased mortality.¹² Unfortunately, however, no studies have examined the relationship between a broad range of psychiatric disorders, or the additive effects of multiple psychiatric disorders, on mortality among individuals with diabetes. Instead, extant research has typically focused on the association between a single psychiatric disorder and mortality—most of

¹Department of Psychiatry and Behavioral Sciences, ³Division of Biostatistics, Bioinformatics, and Epidemiology, ⁴Division of General Internal Medicine and Geriatrics, and ⁵Center for Health Disparities Research, Medical University of South Carolina, Charleston, South Carolina.

²Center for Disease Prevention and Health Interventions for Diverse Populations, Ralph H. Johnson VA Medical Center, Charleston, South Carolina.

which has focused exclusively on the role of depression,^{6,9,10} with a few recent studies examining the relationship between mortality and severe forms of mental illness among individuals with diabetes.¹¹

The simultaneous consideration of the impact of various psychiatric illnesses on diabetes outcomes is important for two reasons: (1) Being diagnosed with multiple versus single psychiatric diagnoses is the norm rather than the exception in most settings, and greater illness burden is typically associated with increased negative outcomes.¹³ (2) Separately investigating the relationship between individual psychiatric disorders and diabetes outcomes can be misleading because it does not allow for the separation of unique and shared effects among psychiatric disorders and outcomes. For example, separate investigations of the impact of posttraumatic stress disorder (PTSD) and depression on glycemic control found that both disorders were associated with significantly elevated glycosylated hemoglobin (HbA1c). However, a simultaneous investigation of PTSD, depression, and glycemic control found that PTSD was not significantly related to glycemic control after controlling for depression.¹⁴

A common model of psychiatric comorbidity uses latent factors to organize psychopathology^{15,16} and is ideal for examining the simultaneous impact of various psychiatric disorders on mortality because this model adequately accounts for the overlap between disorders and because it allows for a direct investigation of the impact of psychiatric comorbidity on outcomes. This model originally posited that commonly co-occurring psychiatric disorders can be validly represented by two latent factors of psychiatric illness: internalizing (e.g., depression and anxiety) and externalizing (e.g., drug and alcohol abuse). Recently, others have expanded the model to include psychotic disorders.¹⁷ Thus, three latent dimensions of psychiatric disorders—internalizing, externalizing, and psychotic disorders—can represent most psychiatric disorders with good reliability and validity.^{15,17} Bipolar disorders have traditionally been excluded from these investigations and thus must be considered separately.

In light of the extant literature, the present study investigated the relationship between a wide range of psychiatric disorders and all-cause mortality in a large ($n = 15,065$) sample of veterans with type 2 diabetes. The available evidence suggested that we would find a positive relationship between our psychiatric disorder predictors and mortality and that we would see poorer outcomes among those with multiple, rather than one or two, psychiatric disorders. As mentioned previously, these data are novel and significant in that they account for the simultaneous impact of a range of psychiatric disorders on mortality, which has not previously been explored.

Subjects and Methods

Design of study, definition of variables, and data

Creation of study data set. We created a data set of 15,065 adults with type 2 diabetes who were enrolled in hospital care at a Veterans Administration (VA) facility in the Southeastern United States between 1997 and 2006 using multiple patient and administrative files from the Veterans Health Administration (VHA) Decision Support System (DSS). The VHA DSS is a national automated management information system that integrates data from clinical and financial systems for both

inpatient and outpatient care. Individuals with type 2 diabetes were identified on the basis of having at least two International Classification of Diseases, Ninth Revision (ICD-9) codes for diabetes in either outpatient or inpatient files and having two or more visits each year since diagnosis based on a previously validated algorithm.¹⁸

Demographic variables and medical comorbidities. Covariates for predictive models were identified a priori and were selected from participants' first medical records during the study period. Age was treated as a continuous variable. Race/ethnicity was classified as non-Hispanic white, non-Hispanic black, Hispanic, and other/missing. Given the large amount of missing race information in VHA databases, we re-analyzed the data using three different methods: (1) we analyzed the data by removing those with missing race data, (2) we added "other/missing race" as a separate group in the analysis, and (3) we imputed the missing race information via multiple imputation. The results were consistent and similar across methods, so we chose to represent missing race information as a separate group in the analysis. Marital status was classified as never married, married, or separated/widowed/divorced. Employment was classified as employed, unemployed, or retired. Relevant medical comorbidity variables (stroke, coronary heart disease, congestive heart failure, hypertension, and cancer) were defined based on enhanced ICD-9 codes using validated algorithms.¹⁹ Poor glycemic control at baseline was defined as HbA1c >8%. Compliance to insulin or oral hypoglycemic medications was represented by the medication possession ratio, which reflects the percentage of time patients had access to antidiabetes medications; non-compliance was defined as medication possession ratio <80%.

Primary independent variables. Selection of ICD-9 codes to represent psychiatric disorders was guided by the demarcation of ICD-9 codes in the DSM-IV; subjects were classified as having a given psychiatric disorder if they had an ICD-9/DSM-IV code for that disorder in their inpatient or outpatient records. Psychiatric disorders were classified using the dimensional models of Krueger¹⁵ and Sbrana et al.¹⁷ and were represented by three manifest dimensional variables (internalizing, externalizing, psychotic), and one dichotomous variable (Bipolar I Disorder; ICD-9/DSM-IV codes 296.0, 296.4–296.7). According to recommended guidelines, the internalizing dimension included (each disorder is followed by its ICD-9/DSM-IV codes): Generalized Anxiety Disorder (300.02), Major Depressive Disorder (296.2 or 296.3), Dysthymic Disorder (300.4), PTSD (309.81), Panic Disorder (300.01 or 300.21), and Agoraphobia (300.22 or 300.21). The externalizing dimension included Alcohol Abuse (305.00), Alcohol Dependence (303.9), Drug Abuse (305.1–305.9), and Drug Dependence (304.0–304.9). The psychotic dimension included Schizophrenia (295.1–295.3, 295.6), Schizophreniform Disorder (295.4), and Schizoaffective Disorder (295.4). These dimensions were constructed as manifest additive scales with each additional diagnosis within a given dimension adding 1 point to a veteran's total score for that dimension.

Outcome measures. The primary outcome was all-cause mortality measured as time to death. The reliability of VA mortality data is well supported.²⁰

Statistical analysis

First, we described the demographic and clinical characteristics of the study population; group differences between participants with and without psychiatric illnesses were tested using appropriate between-subjects statistical methods. Second, Cox regression was used to model the association between psychiatric disorders and time to death. Four regression models were estimated, with each subsequent model introducing additional covariates of interest: model 1 = psychiatric disorders, model 2 = model 1 + demographics, model 3 = model 2 + medical comorbidities (including baseline HbA1c), and model 4 = model 3 + compliance to antidiabetes medications. All-cause mortality or time to death was defined as the number of years from age at time of entry into the cohort to age at time of death or censoring. Mortality was coded "1" for death and "0" if censored. Appropriateness of the assumption of proportionality was determined by examining $\log[-\log(\text{time})]$ plots and by testing the coefficients of the interactions of time with the respective covariate in multivariate analyses. Model selection was conducted using information criteria (e.g., Akaike Information Criterion, Bayesian Information Criterion). The final Cox model was adjusted for all covariate psychiatric disorders, demographic variables, and medical comorbidities. Inference on parameters was based on the sandwich variance estimator, which accounts for the possible bias in the variance of the estimated parameters due to unaccounted random effects.²¹ The Kaplan-Meier method was used to plot the survival function. Residual analysis was used to assess goodness of fit of the models from each stage. All data analyses were conducted using SAS version 9.1.3 (SAS Institute, Cary, NC).

Results

Descriptive analyses

Tables 1 and 2 contain descriptive information on the demographics of the sample, medical comorbidities, and psychiatric disorders. Participants had a mean age of 66 years, and 97.1% were male. At least one internalizing or externalizing disorder was present in 11.9% and 14.9% of participants, respectively. Of the participants, 2.3% were diagnosed with at least one psychotic disorder, and 1.9% were diagnosed with Bipolar I Disorder. The internalizing disorders scale was significantly (i.e., all $P < 0.001$) correlated with the externalizing ($r = 0.38$) and psychotic ($r = 0.26$) disorders scales and with Bipolar I Disorder ($r = 0.28$). The externalizing disorders scale was also significantly correlated with the psychotic disorders scale ($r = 0.21$) and with Bipolar I Disorder ($r = 0.21$). Finally, Bipolar I Disorder was significantly correlated with the psychotic disorders scale ($r = 0.38$). Average HbA1c was 6.81%, first HbA1c was 6.58%, and last HbA1c was 7.04%. Approximately 16% (15.7%; $n = 2,359$) of the sample died during the study time frame. Notably, among other differences (see Table 1), individuals with psychiatric disorders had significantly higher noncompliance to antidiabetes medications than did individuals without psychiatric disorders.

Cox regression of psychiatric disorders and mortality

Table 3 contains the results from Cox regression models with psychiatric spectra predicting mortality. Results from the unadjusted regression model suggested that only externaliz-

ing disorders were significantly associated with mortality (hazard ratio [HR] = 1.22; 95% confidence interval [CI] = 1.02–1.47). In other words, each additional diagnosed externalizing disorder increased an individual's chances of dying over the follow-up period by 22%. The association between externalizing disorders and mortality remained significant when demographics (HR for externalizing disorders = 1.31; 95% CI = 1.09–1.59) and medical comorbidities (including baseline HbA1c) (HR for externalizing disorders = 1.21; 95% CI = 1.01–1.46) were statistically controlled. However, once noncompliance to antidiabetes medications was added to the adjusted model, externalizing disorders and mortality were no longer significantly associated (HR = 1.12; 95% CI = 0.91–1.37).

Conclusions

The present study examined the longitudinal relationship between a wide range of psychiatric disorders and all-cause mortality in 15,065 veterans with type 2 diabetes. Psychiatric disorders were associated with a wide-range of risk factors for mortality, including poor glycemic control and medication noncompliance. Only externalizing disorders (i.e., substance use disorders) were significantly associated with mortality in the present sample. In unadjusted statistical models, each additional externalizing disorder increased individuals' likelihood of dying over the follow-up period by 22%. Interestingly, the relationship between externalizing disorders and mortality remained significant when demographics and medical comorbidities (including baseline glycemic control) were statistically controlled, but was rendered nonsignificant once medication compliance was introduced to the model. This pattern of findings suggests that individuals with externalizing disorders may have been at increased risk for mortality because of their poor compliance to antidiabetes medications. However, given the small difference in glycemic control between individuals with and without psychiatric disorders in the present study, it is possible that participants' poor compliance to antidiabetes medications merely reflected their noncompliance to medical recommendations in general. Noncompliance to medical recommendations has been shown to predict mortality in past research.²² In contrast to externalizing disorders, internalizing, psychotic, and bipolar disorders were not associated with mortality.

To the authors' knowledge, this is the first study to examine the effects of a wide range of psychiatric disorders and comorbidities on mortality in individuals with type 2 diabetes. Prior studies have been limited in scope to a single psychiatric disorder.^{6,9–11} Given that individuals suffering from psychiatric illness typically have two or more co-occurring psychiatric disorders, the results from the present study are highly relevant and can be used to better understand the interplay among diabetes, psychiatric illness burden, and critical outcomes such as mortality. The results from the present study also suggest that the deleterious effects of psychiatric disorders on diabetes outcomes are fairly specific. Whereas externalizing disorders were uniquely associated with mortality, internalizing, psychotic, and bipolar disorders were not. Although previous research has found associations among mortality and internalizing, psychotic, and bipolar disorders in individuals with diabetes,^{6,9–11} this research has not controlled for externalizing psychopathology. As such, observed

TABLE 1. SAMPLE CHARACTERISTICS (N = 15,065)

Variable	All subjects	No disorders	1 + disorders	P value ^a
Sample size	15,065	11,832	3,233	
Age (years) [mean (SD)] ^b	66 (11.8)	67 (11.8)	63 (11)	< 0.0001 ^c
Male ^b	14,628 (97.1)	11,500 (97.2)	3,128 (96.8)	0.1847
Female	437 (2.9)	332 (2.8)	105 (3.2)	
Non-Hispanic white ^d	7,097 (47.1)	5,449 (46.1)	1,648 (51)	< 0.0001 ^c
Non-Hispanic black	3,916 (26)	2,709 (22.9)	1,207 (37.3)	
Hispanic	68 (0.5)	59 (0.5)	9 (0.3)	
Other/missing race	3,984 (26.4)	3,615 (30.6)	369 (11.4)	
Married ^d	9,818 (65.2)	7,987 (67.5)	1,831 (56.6)	< 0.0001 ^c
Never married	968 (6.4)	670 (5.7)	298 (9.2)	
Divorced	4,274 (28.4)	3,170 (26.8)	1,104 (34.1)	
Employed ^d	3,171 (21)	2,580 (21.8)	591 (18.3)	< 0.0001 ^c
Retired	4,644 (30.8)	3,942 (33.3)	702 (21.7)	
Unemployed	7,219 (47.9)	5,285 (44.7)	1,934 (59.8)	
Service connected disability (dichotomized) ^b	5,791 (38.4)	4,079 (34.5)	1,712 (53)	< 0.0001 ^c
Service connected disability <50% ^b	3,103 (20.6)	2,385 (20.2)	718 (22.2)	< 0.0001 ^c
Service connected disability ≥50%	2,691 (17.9)	1,695 (14.3)	996 (30.8)	
Average HbA1c (%) [mean (SD)] ^b	6.81 (0.96)	6.81 (0.95)	6.80 (1.00)	0.2232
First HbA1c (%) [mean (SD)] ^b	6.58 (0.92)	6.59 (0.92)	6.53 (0.95)	< 0.0001 ^c
Last HbA1c (%) [mean (SD)] ^b	7.04 (1.19)	7.03 (1.16)	7.06 (1.29)	0.0515
HbA1c >8% ^d	1,407 (12.4)	1,060 (12.0)	347 (13.7)	0.0269
MPR (%) [mean (SD)] ^b	83.6 (25.69)	84.9 (25.07)	78.7 (27.36)	< 0.0001 ^c
Noncompliant (MPR <80%) ^d	3,622 (32.1)	2,624 (29.5)	998 (41.8)	< 0.0001 ^c
Cancer ^b	790 (5.2)	538 (4.5)	252 (7.8)	< 0.0001 ^c
CHD ^b	2,017 (13.4)	1,369 (11.6)	648 (20)	< 0.0001 ^c
CHF ^b	1,128 (7.5)	771 (6.5)	357 (11)	< 0.0001 ^c
Hypertension ^b	3,686 (24.5)	2,391 (20.2)	1,295 (40.1)	< 0.0001 ^c
Psychiatric disorders, total [mean (SD)]	0.50 (1.26)	0.00 (0.00)	2.34 (1.77)	NA
Stroke ^b	440 (2.9)	293 (2.5)	147 (4.5)	< 0.0001 ^c
Dead ^b	2,359 (15.7)	1,815 (15.3)	544 (16.8)	0.0393
Time to death (quarters) [mean (SD)] ^b	16.12 (13.96)	18.61 (13.67)	15.36 (14.59)	0.0010 ^c
Time to death (quarters) (median)	15.00	17.00	14.00	
Follow-up (quarters) [mean (SD)] ^b	19.44 (14.11)	18.87 (14.06)	21.41 (14.12)	< 0.0001 ^c
Follow-up (quarters) (median)	19.00	18.00	21.00	< 0.0001 ^c

Data are count (percentage).

^aComparisonwise alpha levels were calculated using the Bonferroni method to control the experimentwise alpha level at 0.05. Comparisonwise alpha levels were 0.05/21 = 0.00238.

^bWilcoxon two-sample test.

^cSignificant; $P \leq 0.00238$.

^dPearson χ^2 test.

CHD, coronary heart disease; CHF, congestive heart failure; HbA1c, glycosylated hemoglobin; MPR, medication possession ratio; NA, not applicable.

relationships between psychiatric disorders and mortality in past research may have been due to the unmodeled association between psychiatric disorders and substance misuse (i.e., externalizing disorders). Alternatively, given the scarcity of existing research on the relationship between psychiatric disorders and mortality in individuals with diabetes, between-study discrepancies may be attributable to methodological differences. For example, Katon et al.¹⁰ used a questionnaire to identify cases of depression, whereas the present study used clinical diagnoses of major depressive disorder.

The current study findings suggest that externalizing disorders should be aggressively targeted given their negative effects on diabetes outcomes and also suggest that individuals with externalizing disorders may need relatively more acute and intensive care to reduce their unique short-term risk of mortality—likely due in part to the negative effects of substance abuse on medication compliance. Future research

should further examine the direct and indirect relationships between psychiatric disorders and mortality using structural equation modeling and should include relevant mediators such as medication adherence²³ and biological variables.²⁴ Furthermore, research similar to the present study should be conducted to explore the relationship between a wide variety of psychiatric disorders and other medical problems, such as cardiovascular disease.

The preceding discussion should be tempered by the limitations of the present study. First, the use of ICD-9 codes is potentially problematic because clinical diagnoses are less reliable than diagnoses from standardized interviews and because ICD-9 codes do not allow for the separation of current and lifetime psychiatric conditions. However, research has supported the reliability and validity of ICD-9 codes in administrative VA databases.^{25,26} One recent study found that using a conceptual approach to grouping diagnoses, similar to the one taken by the present study, provided positive/

TABLE 2. PREVALENCE (AND 95% CONFIDENCE INTERVAL) OF PSYCHIATRIC DISORDERS IN THE STUDY COHORT (N = 15,065)

<i>Spectrum disorder</i>	<i>% (95% confidence interval)</i>
Bipolar disorder	1.9 (0.3–3.5)
Externalizing disorders	14.9 (13.4–16.3)
Alcohol abuse	4.4 (2.9–6.0)
Alcohol dependence	4.1 (2.6–5.7)
Drug abuse	12.6 (11.1–14.1)
Drug dependence	1.9 (0.3–3.5)
Internalizing disorders	11.9 (10.4–13.4)
Generalized anxiety disorder	2.4 (0.8–4.0)
Major depressive disorder	7.8 (6.2–9.3)
Dysthymic disorder	4.6 (3.0–6.2)
Posttraumatic stress disorder	5.0 (3.5–6.6)
Agoraphobia	0.5 (0.0–2.1)
Panic disorder	1.1 (0.0–2.7)
Psychotic disorders	2.3 (0.7–3.9)
Schizophrenia	2.0 (0.5–3.6)
Schizophreniform disorder	0.6 (0.0–2.2)
Schizoaffective disorder	1.3 (0.0–2.8)

negative predictive values of 0.84/0.72, 0.82/0.88, and 0.58/0.97 for depression, anxiety, and psychosis, respectively.²⁵ Our use of a spectrum conceptualization of psychopathology may have further mitigated reliability concerns because distinguishing between depression/anxiety and substance use disorders is far easier than making a differential diagnosis between more nuanced classifications (e.g., social phobia vs. panic disorder). Second, veterans represent a specialized patient population that may not be representative of the broader U.S. population. Nonetheless, the high burden of psychiatric comorbidity in veterans makes them an ideal population to examine the relationship between psychiatric comorbidity and diabetes outcomes. Future replication and extension of the present work should use structured diagnostic interviews and nationally representative samples.

The above limitations notwithstanding, the present study demonstrated a significant relationship among externalizing disorders and mortality in a large sample of veterans with type 2 diabetes. These findings indicate that patients with externalizing disorders should be targeted for biopsychosocial interventions aimed at reducing their risk of death and that such interventions may be most effective if they specifically target increasing medication adherence.

TABLE 3. COX REGRESSION MODELS WITH PSYCHIATRIC DISORDERS, DEMOGRAPHICS, MEDICAL COMORBIDITIES AND NONCOMPLIANCE PREDICTING MORTALITY

<i>Label</i>	<i>Psychiatric comorbidity</i>		<i>Addition of demographics</i>		<i>Addition of medical comorbidities</i>		<i>Addition of noncompliance</i>	
	<i>HR</i>	<i>95% CI</i>	<i>HR</i>	<i>95% CI</i>	<i>HR</i>	<i>95% CI</i>	<i>HR</i>	<i>95% CI</i>
Bipolar disorder ^a	1.28	(0.84, 1.96)	1.29	(0.85, 1.98)	1.33	(0.87, 2.05)	1.35	(0.84, 2.17)
Externalizing disorders ^b	1.22	(1.02, 1.47)	1.31	(1.09, 1.59)	1.21	(1.01, 1.46)	1.12	(0.91, 1.37)
Externalizing disorders squared ^b	0.90	(0.83, 0.97)	0.90	(0.83, 0.98)	0.92	(0.85, 1.00)	0.96	(0.88, 1.04)
Internalizing disorders ^b	0.88	(0.73, 1.05)	0.91	(0.76, 1.10)	0.91	(0.76, 1.09)	0.90	(0.73, 1.10)
Internalizing disorders squared ^b	1.03	(0.97, 1.09)	1.03	(0.97, 1.09)	1.02	(0.97, 1.09)	1.03	(0.96, 1.10)
Psychotic disorders ^b	0.83	(0.42, 1.64)	0.84	(0.42, 1.65)	0.90	(0.45, 1.77)	0.97	(0.47, 2.01)
Psychotic disorders squared ^b	1.02	(0.77, 1.34)	1.01	(0.77, 1.33)	0.99	(0.75, 1.30)	0.96	(0.71, 1.29)
Age			1.04	(1.04, 1.05)	1.04	(1.03, 1.05)	1.04	(1.03, 1.05)
Non-Hispanic black ^c			0.89	(0.77, 1.01)	0.82	(0.71, 0.94)	0.84	(0.72, 0.97)
Hispanic ^c			1.11	(0.46, 2.69)	1.16	(0.48, 2.80)	1.35	(0.56, 3.26)
Other/unknown ^c			0.85	(0.73, 0.99)	0.91	(0.78, 1.06)	0.93	(0.79, 1.11)
Male ^d			1.86	(1.07, 3.22)	1.76	(1.01, 3.05)	2.15	(1.11, 4.16)
Employed ^e			0.31	(0.24, 0.39)	0.34	(0.27, 0.43)	0.35	(0.27, 0.45)
Retired ^e			0.71	(0.63, 0.80)	0.74	(0.66, 0.84)	0.74	(0.64, 0.84)
Never married ^f			1.62	(1.27, 2.06)	1.51	(1.18, 1.92)	1.38	(1.06, 1.81)
Divorced ^f			1.23	(1.09, 1.39)	1.16	(1.02, 1.31)	1.16	(1.01, 1.33)
Cancer ^a					2.12	(1.78, 2.52)	1.96	(1.61, 2.39)
CHD ^a					0.91	(0.77, 1.08)	0.87	(0.72, 1.06)
CHF ^a					1.49	(1.24, 1.78)	1.59	(1.31, 1.93)
Hypertension ^a					1.13	(0.96, 1.32)	1.04	(0.88, 1.24)
Stroke ^a					0.98	(0.75, 1.27)	1.01	(0.76, 1.35)
HbA1c >8%					2.04	(1.72, 2.41)	2.20	(1.85, 2.62)
Medication noncompliance ^g							1.20	(1.05, 1.36)

^aReference: no disease.

^bReference: number of disorders.

^cReference: non-Hispanic whites.

^dReference: female.

^eReference: unemployed.

^fReference: married.

^gMPR less than 80%.

CI, confidence interval; HR, hazard ratio.

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Address correspondence to:

James J. Prisciandaro, Ph.D.

Department of Psychiatry and Behavioral Sciences

Clinical Neuroscience Division

Medical University of South Carolina

67 President Street

P.O. Box 250861

Charleston, SC 29425

E-mail: priscian@musc.edu