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Excess mortality due to Depression and Anxiety in the United States: Results from a Nationally Representative Survey

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Abstract

Objectives—We compared the mortality of persons with and without anxiety and depression in a nationally representative survey and examined the role of socioeconomic factors, chronic diseases, and health behaviors in explaining excess mortality.

Methods—The 1999 National Health Interview Survey was linked with mortality data through 2011. We calculated the hazard ratio (HR) for mortality by presence or absence of anxiety/depression and evaluated potential mediators. We calculated the population attributable risk of mortality for anxiety/depression.

Results—Persons with anxiety/depression died 7.9 years earlier than other persons. At a population level, 3.5% of deaths were attributable to anxiety/depression. Adjusting for demographic factors, anxiety/depression was associated with an elevated risk of mortality (HR=1.61, 95% confidence interval [CI]=1.40, 1.84). Chronic diseases and health behaviors explained much of the elevated risk. Adjusting for demographic factors, people with past-year contact with a mental health professional did not demonstrate excess mortality associated with anxiety/depression while those without contact did.

Conclusions—Anxiety/depression presents a mortality burden at both an individual and population level. Our findings are consistent with targeting health behaviors and physical illnesses as strategies for reducing this excess mortality among people with anxiety/depression.

Keywords

NHIS; mental health; depression; anxiety; mortality

1. Introduction

Studies have long shown that persons with mental illness have higher mortality than persons without mental illness. Many studies followed persons in inpatient psychiatric treatment [1–3] or outpatient treatment [4,5] and compared their mortality experience with persons in the general population. Focusing on samples in treatment, however, excludes the majority of people with mental disorders who have not received treatment [6].

Among early studies based on the general population were follow-ups of some of the five Epidemiologic Catchment Area (ECA) communities [7]. A one-year follow-up of four sites found an adjusted OR for mortality associated with major depressive disorder of 2.6 (1.1, 6.0) [8]. In the Piedmont site, a 2-year follow-up of older participants found no relationship between depression and mortality [9]. Recent depression was associated with a two times higher mortality in a 9-year follow-up of the New Haven, Connecticut site, but recent anxiety disorders were not [10]. However, in the 27-year follow up of four ECA sites, neither depression nor anxiety disorders were associated with an increased risk of death [11].

Among the first nationally representative samples to be followed was the 1989 National Health Interview Survey (NHIS) [12,13]. In one study that followed white respondents 25 years and older for two and a half years, men with self-reported major depressive disorder had a 3.1 times higher mortality rate than men with no depression; however, there was no association in women [13]. In another study, Druss and colleagues examined the mortality experience of persons with self-reported mental illness over a 17 year follow-up and the factors associated with excess mortality. The authors found an HR of 2.1 for mortality associated with mental illness before adjustment for mediating factors. The mediating factors that contributed to the excess mortality included socioeconomic factors, health system factors and baseline medical status [12]. A notable omission was the lack of information on behavioral risk factors such as smoking and exercise, and their role in explaining excess mortality. Finally, a recent study examined the relationship of depression to mortality among persons 50 years and older by following the 1999 NHIS through 2006 and found an HR of 2.6 adjusting for demographic variables. [14].

A meta-analysis, focusing specifically on depression, found an overall relative risk of mortality of 1.8 associated with depression [15]. This meta-analysis demonstrates the varying approaches to measuring depression in these studies, including self-report and symptom-count measures..

In this paper, our goal is to compare the mortality of persons with and without measured anxiety and depression in a nationally representative survey and examine the role of various factors, including behavioral risk factors, in explaining excess mortality. We will compare age at death for all causes and certain specific causes of death and hazard ratios associated with depression/anxiety for particular causes of death. Then, using the population attributable risk, we will estimate the number of deaths attributable to anxiety and depression in one year. Finally, using a crude measure of treatment we will do stratified

analyses to determine whether treatment affects the mortality associated with depression/anxiety.

2. METHODS

2.1 Survey/Population

The NHIS is a complex sample survey conducted continuously by the National Center for Health Statistics (NCHS). Information is gathered through face-to-face household interviews. The linkage of NHIS participants to NDI data was approved by the NCHS Ethics Review Board (ERB). All respondents gave explicit oral consent to participate in the survey. Data from the NHIS are weighted to account for different probabilities of selection and for non-response and are poststratified to census control totals in order to provide estimates for the U.S. civilian, noninstitutionalized population. More details of the NHIS design, methodology and weighting have been published elsewhere [16]. This report is based on information from the 1999 sample adult questionnaire which is administered to one randomly selected adult in each family. There were 30,801 sample adults in 1999. The final sample adult response rate of 69.6% is calculated by multiplying the household level response rate (87.6%), the conditional family level response rate (98.3%) and the conditional sample adult response rate (80.8%).

There were 1682 people (5.5%) ineligible for matching with the National Death Index (NDI) because of lack of sufficient identifying information. Special weights were used in the analyses to adjust for those people ineligible for matching. There were 680 people without information on anxiety/depression. This report is based on sample adults who had information on anxiety/depression and on mortality, a total of 28,439 respondents.

2.2 Measurement of anxiety and depression

The 1999 sample adult questionnaire included a mental health supplement made up of three modules from the Composite International Diagnostic Interview – Short Form (CIDI-SF) [17] which follows DSM-IV criteria to evaluate the presence or absence of mental disorders. The CIDI-SF is based on the full CIDI, a structured diagnostic interview designed for use by lay interviewers which asks about the presence of symptoms of various disorders [18]. The CIDI-SF modules included were the major depressive episode, generalized anxiety disorder (GAD) and panic attack modules. The exposure anxiety/depression is defined as persons who had any one or more of the three disorders compared with persons with none of the disorders.

2.3 Outcome

The 1999 NHIS has been linked to mortality data through December 31, 2011. Mortality status is ascertained primarily through probabilistic record matching with the National Death Index (NDI). The NDI is a NCHS centralized database of all U.S. deaths beginning in 1979. Matches are based on identifying information such as social security number, name and birthdate. Vital status is assigned to inexact matches using probability-based scores. Manual review is used to adjudicate in certain cases. Details on the matching methodology have

been published elsewhere [19]. The restricted-use mortality files were used in this study and provided vital status, cause of death and complete date of death.

The outcome variable is time to death. Follow-up time is defined as time from interview to death for decedents and interview to Dec. 31, 2011 for survivors. The mean length of follow-up was 6.5 years for decedents and 12.5 years for survivors.

2.4 Covariates

Covariates were selected a priori as potential confounders or mediators of the relationship between anxiety and depression and mortality. Potential confounders included age, sex and race/ethnicity (Hispanic, non-Hispanic white, non-Hispanic black and other). We defined mediators as a factor in the causal pathway between mental illness and mortality that is also a factor amenable to change. Potential mediators of the relationship included education, household income, self-reported smoking, exercise and BMI, and comorbid chronic diseases. We classified education and income as mediators rather than confounders because research has shown that mental illness leads to lower educational attainment [20,21] and unemployment, as well as lower income among those who are employed [22]. Chronic diseases were self-reported, doctor-diagnosed diseases including heart disease, diabetes, hypertension, cancer, stroke and lung disease. Heart disease was defined as a yes answer to ever being told that one had angina, coronary heart disease, other heart trouble, myocardial infarction or congestive heart failure. Lung disease was defined as having current asthma or ever having emphysema or chronic bronchitis. As a measure of comorbidity or disease burden, a variable was created from a count of the six chronic diseases.

As our crude measure of treatment we used the answer to the following question: “During the PAST 12 MONTHS, have you seen or talked to any of the following health care providers about your own health?...a mental health professional such as a psychiatrist, psychologist, psychiatric nurse, or clinical social worker?”

2.5 Analysis

First we examine the baseline characteristics of persons with each of the three individual disorders and persons with none of the three disorders. The significance of differences between major depression and no major depression, panic disorder and no panic disorder, GAD and no GAD, and no depression/anxiety and any depression/anxiety was tested using the chi-square statistic. Because of the multiple comparisons, a p-value of 0.01 was used to indicate significance in Table 1.

To test our conception of the variables education, income, chronic diseases, exercise, smoking and BMI as mediators, we fit three regression models, adjusting for age, for each variable as suggested by Baron and Kenny [23].

We use Cox proportional hazards models to calculate HRs for mortality by presence or absence of anxiety/depression. To evaluate mediators to the relationship we entered blocks of potential mediators one at a time to the base model of anxiety/depression, age, sex and race/ethnicity. The blocks of mediators included socio-demographic mediators of education and household income, behavioral risk factors including smoking, exercise and BMI, and

then chronic disease. Because the summary variable of the count of chronic diseases explained the same amount of model variance as entering each disease separately, we used the count variable for chronic disease. Finally we entered all the potential confounders and mediators in one model. For each model we examined the effect of the various mediators on the HR associated with anxiety/depression. In a sub-analysis, we calculated the HRs associated with anxiety/depression at different lengths of follow-up, adjusting for age, sex and race/ethnicity.

The Division of Vital Statistics at NCHS codes causes of death according to ICD-10 and also provides lists categorizing causes into summary groups for tabulation and presentation purposes. We used the list of 113 categories of causes of death. We looked at the top five causes of death in all persons in 1999, heart disease, cancer, stroke, unintentional injuries and chronic lower respiratory diseases [24]. Instead of unintentional injuries, we looked at all external causes of death which include unintentional injuries, homicide and suicide. Infection as a cause of death was also examined as historically it has been an important cause of differences in mortality between persons with and without mental illness [3]. The crude, average age of death for all causes and for each of the six causes for persons with and without anxiety/depression was calculated, as was the difference in average age of death between persons with and without anxiety/depression. HIV-related death and suicide were also examined although results were based on very small numbers of deaths. The HRs associated with anxiety/depression, adjusted for age, sex and race/ethnicity, were calculated for each of the above-mentioned causes of death. The HRs were calculated without making any adjustments to account for competing risks. We calculated the percentage of deaths attributable to anxiety/depression using the population attributable risk formula $b((r-1)/r)$ where b is the prevalence of the risk factor in the cases and r is the relative risk for which we substituted the HR [25]. This formula is suggested when there is confounding and an adjusted relative risk will be used [25,26]. We used the relative risk adjusted by age, sex and race/ethnicity which are all confounders. The other covariates are mediators rather than confounders, so we did not adjust for them in determining the hazard ratio to use in the equation. By multiplying the percent of deaths attributable to anxiety/depression by the number of deaths among persons aged 18 and over (in the year 2011), we calculated the approximate number of deaths attributable to anxiety/depression in 2011. Analyses were done with SUDAAN software which incorporates the weights and calculates appropriate standard errors taking into account the complex design of the NHIS (RTI). The population attributable risk (PAR) was calculated by entering the SUDAAN-generated prevalence of anxiety/depression in the cases and HR into the PAR formula.

3. RESULTS

The prevalence of major depression was 6.4% while the prevalence of panic disorder and GAD were 2.8% each. The prevalence of any of the three, termed anxiety/depression, was 8.9% (data not shown). Over the 13-year follow-up, 408 (13.0%) people with anxiety/depression died while 4027 (13.3%) persons without anxiety/depression died. The number of deaths in persons with major depression, GAD and panic disorder were 314 (13.6%), 139 (14.2%) and 97 (9.7%) respectively.

Persons with major depression, panic disorder, GAD, and any of the three were significantly less likely to be older or male than persons with no major depression, no panic disorder, no GAD and no anxiety/depression respectively (Table 1). People without anxiety/depression were twice as likely to be age 75 and older as persons with anxiety/depression, 7.6% and 3.6% respectively. The four exposures were also significantly more likely than their counterparts to have lower education and household income, and to have more chronic diseases. Almost 67% of persons without anxiety/depression reported no chronic diseases, but only half of persons with anxiety/depression reported no chronic diseases. Persons with anxiety/depression were more likely to smoke and more likely to be obese than persons without anxiety/depression. While only 9.5% of persons without anxiety/depression smoked a pack of cigarettes a day or more, 21% of persons with anxiety/depression did. All differences between any anxiety/depression and no anxiety/depression were significant at the $p < .001$ level except for race/ethnicity.

Education, income, smoking, BMI, physical activity, and chronic disease all fulfilled the criteria for mediators described by Baron and Kenny [23].

The HR for mortality associated with anxiety/depression in the model controlling for age, sex and race/ethnicity was 1.6 with a 95% CI of (1.4, 1.8) (Table 2). Model 2 controls for the above plus the potential mediators household income and education each of which are significantly associated with mortality. The HR for mortality associated with anxiety/depression is 1.5 (1.3, 1.7). The third model demonstrates a strong dose-response relationship between number of chronic diseases and mortality. The HR for mortality associated with anxiety/depression is slightly reduced to 1.3 (1.1, 1.5). Including the behavioral risk factors, smoking, exercise and BMI, in the model with age, sex and race/ethnicity also reduces the HR for mortality associated with anxiety/depression to 1.3 (1.2, 1.5). Finally the model containing all the potential mediators at once results in a HR for mortality associated with anxiety/depression of 1.1 (0.9, 1.2) indicating that the association is no longer significant.

In our models using different lengths of follow-up, we found that the HRs for mortality associated with anxiety/depression decreased in magnitude as the length of follow-up increased although the HRs were not significantly different. In a three-year follow-up ending December 31, 2002, the HR for mortality, adjusted for age, sex and race/ethnicity was 2.2 (1.7, 2.8). In a five-year follow-up, the HR was 2.0 (1.6, 2.4), and after an eight-year follow-up, the HR was 1.8 (1.5, 2.1).

Persons with anxiety/depression died an average of 7.9 years earlier than persons without anxiety/depression. Among persons who died of infection, cancer, heart disease, lung disease and external causes, persons with anxiety/depression died significantly earlier than persons without anxiety/depression. Differences in age at death ranged from 5.3 years for lung disease to 15.2 years for infections. The difference in the mean age of death for stroke was not significant. The HR for mortality associated with anxiety/depression was significant for all causes except external causes (Table 3). The HR for HIV-related death associated with anxiety/depression was 14.4 (4.7, 44.0) although this estimate is based on a small number of deaths, reflected, in part, by the wide confidence interval. The HR for suicide associated

with anxiety/depression, again based on a small number of deaths, was not significant (data not shown).

The prevalence of anxiety/depression among the decedents was 9.2%. The HR for mortality associated with anxiety/depression was 1.6 in the model adjusting for age, sex and race/ethnicity. Thus using the population attributable risk formula, we determined that 3.5% of mortality in the population was attributable to anxiety/depression. The number of deaths per year among persons 18 and over in 2011 was 2,513,171. This leads to the estimate of 87,961 deaths being attributable to anxiety/depression each year.

We stratified the population by whether or not they had seen a mental health professional in the past year. Among persons who saw a mental health professional in the past year, anxiety/depression was not associated with higher mortality (Table 4). Among persons who had not seen a mental health professional in the past year, anxiety/depression was associated with increased mortality with a HR of 1.6 (1.4, 1.9) after adjusting for age, sex and race/ethnicity. After adjusting for education and income, the HR was 1.5 (1.3, 1.8). After adding health behaviors to the model, the HR was 1.3 (1.1, 1.5). The further addition of chronic disease decreased the HR to 1.1 (0.9, 1.3).

4. DISCUSSION

Persons with anxiety/depression in a nationally representative sample had a 60% higher mortality and died an average of 8 years earlier than persons without these illnesses. We calculated that 3.5% of deaths, or approximately 88,000 deaths, were attributable to anxiety/depression each year. This is similar to the population attributable risk for diabetes [27]. Compared to severe mental illness, the risk ratios of mortality for anxiety/depression are lower (1.6 in the current study compared to over 3 for schizophrenia) [28]. However, due to the higher prevalence of anxiety/depression, the number of deaths attributable to anxiety/depression is higher (3.5%) than the less common, but more severe mental illnesses (1.3% for schizophrenia) [29]. From a public health perspective, it is imperative to understand and address the factors that contribute to excess mortality among people with depression/anxiety.

We examined the HRs for mortality while varying the length of follow-up, hypothesizing that misclassification of anxiety/depression would increase as time from baseline increased and would result in lower HRs for longer follow-up. The HR for mortality, adjusted for age, sex and race/ethnicity, was 2.2 (1.7, 2.8) for three years of follow-up and declined as the follow-up time lengthened. This phenomenon may partially explain why 1-year [8] and 9-year [10] ECA follow-ups had significant results while the 27-year follow-up [11] did not. However, one analysis of depression and mortality among women 65 years of age and over found that the HR for mortality was weaker at a 2-year follow-up than it was at a 6-year follow-up [30].

Potential factors in the causal pathway between mental illness and mortality included income and education, higher rates of comorbid physical illness and unhealthy behaviors such as smoking, and lower rates of exercise. Persons with anxiety/depression in the 1999 NHIS had higher rates of every chronic physical illness examined, and were more likely to

have multiple chronic physical illnesses, than persons without anxiety/depression. Many studies have demonstrated this relationship [31,32], which could result from mental disorders increasing the risk for physical illness, physical illness leading to mental disorders, and common risk factors contributing to both [33,34]. Persons with anxiety/depression also had higher rates of smoking and lower rates of exercise. These two factors, physical illness and behaviors, contributed greatly to the excess mortality seen in people with anxiety/depression. Targeting modifiable behaviors is one route for potentially reducing physical illness and excess mortality among people with anxiety/depression.

Persons with anxiety/depression were younger at death than persons without anxiety/depression in almost every cause of death examined. HRs for cause-specific death associated with anxiety/depression were significant for every cause examined except external causes. The significant HR for heart disease and lung disease has been shown in other studies [35–38]. Studies on the relationship between anxiety/depression and cancer, however, have had mixed results [35,36,39]. At least one study has found that incidence of cancer between persons with mental illness and those without is similar, but the case-mortality rate is higher for those with mental illness [40]. In our results, the higher cancer mortality rate among people with anxiety/depression was not explained solely by smoking-related cancers (data not shown), which indicates that targeting only the higher rate of smoking among persons with anxiety/depression will not close the mortality gap. Among the specific causes of death, infections had the highest HR, which was largely driven by HIV deaths. While the age at death from HIV was similar for those with and without anxiety/depression, the rate of HIV death was much higher among those with anxiety/depression. A similar result was seen in a study of mortality of persons with severe mental illness. The SMR for HIV death in that study was 13.3, higher than that for any other cause of death [41].

Recognizing challenges in inferring causality from observational data, the results suggest that mental health treatment may ameliorate the effect of anxiety/depression on mortality. The results are particularly striking given that treated individuals are more likely to have severe illness, and depression severity is associated with mortality [41–43]. Other studies have also found that mortality is lower in the group who received treatment. One study, comparing 12 weeks of antidepressant treatment to fewer than 11 weeks of treatment, found that all-cause mortality was decreased among persons who took the full 12 weeks of antidepressant treatment [45]. An older study, following inpatients, found that those who received ECT had lower mortality than those who received no treatment or inadequate treatment [46]. As observed in the full model, adverse health behaviors and comorbid physical illnesses explained much of the excess mortality risk seen in persons without contact with a mental health professional.

4.1 Limitations

This study has some limitations. Although one of the major aims of the weighting procedures is to adjust for non-response, they cannot compensate for all non-response. We do not know, for example, if persons who declined to participate in the sample adult interview were more likely to have anxiety/depression.

The 680 persons who were excluded because of the lack of information on mental illness were different from the 28,439 people in the study. They were more likely to be older, more likely to be poor, less likely to be never smokers, less likely to exercise and had more chronic illnesses (data not shown). Except for older age, all of these characteristics are associated with an increased risk of anxiety/depression. The weighted overall mortality rate for those with missing data on anxiety/depression was 20% while it was 13.3% among those with data on anxiety/depression. It is difficult to assess the impact the missing data would have on our conclusions, but it is possible that the differentials in mortality by anxiety/depression would be underestimated.

Our independent variable and all covariates were assessed at one point in time, 1999, so we cannot be sure that anxiety/depression preceded the hypothesized mediators. Furthermore, lifetime prevalence of anxiety and depression and corresponding burden of mortality is likely greater than the one year prevalence captured in this study.

There may have been some misclassification in our study. As the follow-up period got longer, respondents may have newly developed anxiety/depression or those who had it at baseline may have recovered. This type of misclassification would likely bias our mortality estimates toward the null, and thus strengthens our conclusions. There may also have been some misclassification of the exposure group at baseline.

Although we were able to examine the contribution of a wide range of variables to mortality, there are likely other confounders and/or mediators that we did not include in our models. An example might be comorbidity with other mental and substance use disorders.

In addition, we were hampered in our evaluation of deaths due to suicide because of the small number of deaths. Our measure of treatment does not distinguish between people who had a single contact with a mental health professional and those who had multiple contacts. The measure provides no information on persons who have been prescribed antidepressant medication by their primary care physician. Future research could further examine the effect of duration and different types of depression treatment, including psychotropic medication, on mortality.

4.2 Strengths

The strengths of the study include the large, nationally representative sample and the use of a structured diagnostic interview to determine depression and anxiety status rather than relying on self-report. The breadth of the NHIS also allowed us to investigate the contributions of many different domains to the mortality associated with anxiety/depression, especially the behavioral domain, smoking and exercise.

5. Conclusions

People with depression and anxiety experience significant excess mortality compared to people without these disorders. The number of deaths due to depression and anxiety is equivalent to some of the leading causes of death in the United States. Supporting mental health treatment and targeting adverse health behaviors and physical illnesses may be

important mechanisms for reducing excess mortality among people with depression and anxiety.

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Baseline characteristics of persons with major depression, generalized anxiety disorder, panic disorder (the three diagnoses are not mutually exclusive) and none of these three disorders: NHIS 1999

Table 1

	Major depressive episode ^a n=2033	Generalized anxiety disorder ^a n=864	Panic Attack ^a n=816	Any anxiety/depression ^b n=2737	No anxiety/depression n=25,702
	% (SE)	% (SE)	% (SE)	% (SE)	% (SE)
Age	**	**	**	**	
18–34	33.1 (1.3)	32.3 (2.0)	34.3 (2.0)	33.7 (1.2)	32.1 (0.4)
35–49	36.8 (1.2)	38.8 (1.9)	42.9 (2.1)	37.1 (1.1)	31.5 (0.3)
50–64	20.7 (1.2)	20.1 (1.6)	17.4 (1.5)	20.2 (1.0)	19.7 (0.3)
65–74	5.8 (0.6)	4.6 (0.8)	4.5 (0.8)	5.4 (0.5)	9.2 (0.2)
75+	3.6 (0.4)	4.2 (0.8)	1.0 (0.3)	3.6 (0.4)	7.6 (0.2)
Sex	**	**	**	**	
Men	34.0 (1.2)	32.1 (1.8)	30.1 (2.0)	33.4 (1.0)	49.3 (0.4)
Race/ethnicity	**				
Hispanic	7.8 (0.6)	10.9 (1.1)	7.7 (1.0)	8.7 (0.6)	10.4 (0.3)
Non-Hispanic black	11.3 (0.8)	10.6 (1.2)	12.2 (1.3)	11.1 (0.8)	11.3 (0.3)
Other	3.5 (0.5)	3.5 (0.8)	2.9 (0.8)	3.2 (0.4)	3.9 (0.2)
Non-Hispanic white	77.4 (1.2)	75.0 (1.8)	77.3 (1.8)	77.0 (1.0)	74.4 (0.4)
Education	*	**	*	**	
< high school	20.0 (1.0)	24.5 (1.7)	19.3 (1.7)	20.2 (0.9)	17.7 (0.3)
High school diploma or GED	32.7 (1.3)	36.5 (2.0)	35.7 (1.9)	33.4 (1.1)	29.9 (0.4)
> high school	47.4 (1.4)	39.0 (1.9)	45.0 (2.0)	46.4 (1.2)	52.4 (0.5)
Household income	**	**	**	**	
<\$20,000 per year	31.2 (1.2)	38.6 (1.9)	29.7 (1.8)	30.4 (1.1)	19.9 (0.4)
Smoking	**	**	**	**	
Current ≥ 1 pack/day	22.7 (1.1)	23.9 (1.6)	24.1 (1.7)	21.0 (1.0)	9.5 (0.2)
Current < 1 pack/day	17.4 (0.9)	18.3 (1.5)	15.8 (1.5)	17.0 (0.8)	12.7 (0.2)
Former	20.8 (1.0)	18.0 (1.6)	18.6 (1.6)	20.5 (0.9)	23.3 (0.3)
Never	39.1 (1.2)	39.8 (1.9)	41.5 (2.1)	41.6 (1.1)	54.6 (0.4)

	Major depressive episode ^a n=2033	Generalized anxiety disorder ^a n=864	Panic Attack ^a n=816	Any anxiety/depression ^b n=2737	No anxiety/depression n=25,702
	% (SE)	% (SE)	% (SE)	% (SE)	% (SE)
Exercise	**	**	*	**	
Unable to exercise	3.8 (0.5)	4.8 (0.8)	3.4 (0.7)	3.3 (0.4)	1.0 (0.1)
Never exercises	39.6 (1.3)	43.4 (2.1)	33.2 (1.9)	37.2 (1.1)	37.6 (0.5)
Exercises <5 times/week	27.3 (1.2)	25.9 (1.8)	34.2 (1.9)	30.0 (1.0)	32.9 (0.4)
Exercises ≥5 times/week	29.2 (1.2)	25.9 (1.9)	29.2 (1.9)	29.5 (1.0)	28.6 (0.4)
BMI	**	**	**	**	
<20	8.1 (0.7)	11.1 (1.5)	9.3 (1.2)	8.5 (0.6)	6.7 (0.2)
20 – <25	33.1 (1.3)	30.0 (1.9)	32.1 (2.0)	33.6 (1.2)	36.8 (0.3)
25 – <30	31.4 (1.2)	28.2 (1.8)	27.4 (1.7)	30.5 (1.0)	35.7 (0.3)
30 – <35	16.7 (1.0)	17.6 (1.6)	17.8 (1.6)	16.5 (0.9)	14.3 (0.2)
35+	10.8 (0.8)	13.1 (1.3)	13.3 (1.4)	10.9 (0.7)	6.5 (0.2)
Heart disease	**	**	**	**	
	18.2 (1.0)	18.9 (1.5)	18.8 (1.7)	17.8 (0.8)	10.3 (0.2)
Diabetes	**	*		**	
	8.4 (0.7)	9.2 (1.2)	7.2 (1.1)	8.2 (0.6)	5.1 (0.2)
Hypertension	**	**	**	**	
	26.6 (1.2)	28.0 (1.6)	26.0 (1.8)	25.9 (0.9)	18.7 (0.3)
Cancer	**			**	
	10.1 (0.8)	9.3 (1.1)	7.2 (1.1)	9.4 (0.6)	6.3 (0.2)
Stroke	**	**	*	**	
	4.2 (0.5)	4.9 (0.8)	4.3 (0.9)	4.0 (0.4)	1.9 (0.1)
Lung disease	**	**	**	**	
	18.2 (1.0)	22.3 (1.7)	21.6 (1.6)	18.6 (0.9)	6.6 (0.2)
Number of above chronic diseases:	**	**	**	**	
0	48.3 (1.3)	45.2 (2.1)	47.2 (2.1)	49.1 (1.1)	66.9 (0.4)
1	29.8 (1.2)	30.3 (1.9)	30.9 (1.8)	29.6 (1.0)	21.7 (0.3)
2	13.8 (0.9)	15.0 (1.3)	14.2 (1.4)	13.2 (0.8)	8.0 (0.2)
3+	8.1 (0.6)	9.4 (1.2)	7.7 (1.2)	8.1 (0.6)	3.4 (0.1)

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p-values refer to comparisons between the column heading and its opposite: major depressive episode vs. no major depressive episode, GAD vs. no GAD, panic attack vs. no panic attack. The three disorders are not mutually exclusive.

The final two columns are a direct comparison between any of the three disorders and none of the three disorders.

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Table 2

Hazard ratios for overall mortality from Cox Proportional Hazards Models.

	Model 1: Confounders	Model 2: Confounders plus Socioeconomic	Model 3: Confounders plus Chronic Diseases	Model 4: Confounders plus Behaviors	Model 5: Confounders plus all Mediators
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Anxiety/depression					
Yes	1.61 (1.40, 1.84)	1.51 (1.32, 1.73)	1.32 (1.14, 1.52)	1.33 (1.16, 1.53)	1.08 (0.93, 1.24)
No	1.00	1.00	1.00	1.00	1.00
Age in years	1.09 (1.09, 1.10)	1.09 (1.09, 1.09)	1.08 (1.08, 1.09)	1.10 (1.09, 1.10)	1.08 (1.08, 1.09)
Sex					
Male	1.45 (1.36, 1.56)	1.56 (1.45, 1.68)	1.42 (1.33, 1.53)	1.48 (1.37, 1.60)	1.51 (1.39, 1.64)
Female	1.00	1.00	1.00	1.00	1.00
Race/ethnicity					
Hispanic	0.80 (0.71, 0.90)	0.70 (0.61, 0.80)	0.83 (0.73, 0.94)	0.78 (0.68, 0.89)	0.77 (0.67, 0.89)
Non-Hispanic white	1.00	1.00	1.00	1.00	1.00
Non-Hispanic black	1.41 (1.26, 1.56)	1.26 (1.13, 1.41)	1.33 (1.19, 1.48)	1.31 (1.17, 1.46)	1.18 (1.05, 1.34)
Non-Hispanic other	0.89 (0.70, 1.12)	0.83 (0.64, 1.07)	0.89 (0.70, 1.15)	0.91 (0.71, 1.16)	0.84 (0.64, 1.11)
Family income					
< \$20,000 per year		1.46 (1.33, 1.59)			1.27 (1.15, 1.40)
>= \$20,000 per year		1.00			1.00
Education					
Less than high school		1.35 (1.23, 1.48)			1.17 (1.07, 1.28)
High school diploma or GED		1.18 (1.07, 1.29)			1.10 (1.00, 1.20)
More than high school		1.00			1.00
Number of chronic diseases					
0			1.00		1.00
1			1.43 (1.31, 1.57)		1.49 (1.36, 1.64)
2			2.04 (1.86, 2.25)		2.08 (1.87, 2.32)
3 or more			2.93 (2.57, 3.33)		2.87 (2.50, 3.30)
Exercise					

	Model 1: Confounders	Model 2: Confounders plus Socioeconomic	Model 3: Confounders plus Chronic Diseases	Model 4: Confounders plus Behaviors	Model 5: Confounders plus all Mediators
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Unable to exercise				2.39 (1.95, 2.94)	1.78 (1.44, 2.20)
Never exercises				1.41 (1.29, 1.54)	1.34 (1.22, 1.47)
Exercises < 5/wk				1.06 (0.95, 1.18)	1.08 (0.96, 1.21)
Exercises ≥ 5/wk				1.00	1.00
Smoking					
≥ 1 pack/ day				2.30 (2.02, 2.61)	2.24 (1.97, 2.54)
< 1 pack/day				2.05 (1.81, 2.32)	2.00 (1.75, 2.27)
Former				1.25 (1.16, 1.36)	1.22 (1.12, 1.32)
Never				1.00	1.00
Self-reported BMI					
<20				1.43 (1.26, 1.63)	1.50 (1.31, 1.73)
20 to <25				1.00	1.00
25 to <30				0.88 (0.80, 0.95)	0.83 (0.76, 0.90)
30 to <35				0.94 (0.84, 1.06)	0.82 (0.72, 0.92)
35+				1.38 (1.17, 1.61)	1.09 (0.92, 1.28)

Differences in mean age of death by depression and anxiety for all causes and selected causes of death and hazard ratios for selected causes of death associated with depression/anxiety

Table 3

Cause of death	All causes	Heart disease	Cancer	Lung disease	Stroke	Infection	External causes
Depression/ anxiety							
Yes	66.8	70.9	64.9	71.8	76.7	56.5	51.2
No	74.7	77.4	70.9	77.1	80.6	71.7	58.6
Difference in age of death in years	7.9***	6.5***	6.0**	5.3*	3.9	15.2***	7.4*
Hazard ratio (95% CI) associated with depression/anxiety for each cause of death ^a	1.61 (1.40, 1.84)	1.43 (1.08, 1.89)	1.83 (1.45, 2.31)	2.40 (1.57, 3.66)	2.02 (1.30, 3.16)	3.09 (1.83, 5.20)	1.27 (0.82, 1.97)

^a Adjusted for age, sex and race/ethnicity.

*

p<0.05

**

p<0.01

p<0.001

Table 4

Hazard ratios for mortality associated with anxiety/depression, stratified by contact with a mental health professional.

	Saw mental health professional in past year n=1635	Did not see mental health professional in past year n=26559
	HR (95% CI)	HR (95% CI)
Anxiety/depression ^a		
Yes	1.14 (0.81, 1.61)	1.62 (1.38, 1.89)
No	1.00	1.00
Anxiety/depression ^b		
Yes	0.97 (0.68, 1.39)	1.52 (1.30, 1.77)
No	1.00	1.00
Anxiety/depression ^c		
Yes	0.89 (0.63, 1.27)	1.32 (1.13, 1.54)
No	1.00	1.00
Anxiety/depression ^d		
Yes	0.79 (0.55, 1.14)	1.08 (0.92, 1.27)
No	1.00	1.00

^a Adjusted for age in years, sex and race/ethnicity

^b Adjusted for above plus education and income

^c Adjusted for the above plus smoking, exercise and BMI

^d Adjusted for the above plus number of chronic diseases