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The Association of Psychiatric Illness and All-Cause Mortality in the National Department of Veterans Affairs Health Care System

Lydia A. Chwastiak, M.D., M.P.H.^{1,2}, Robert A. Rosenheck, M.D.^{1,2}, Rani Desai, Ph.D. M.P.H.^{1,2}, and Lewis E. Kazis, Sc.D.³

¹Department of Psychiatry, Yale University School of Medicine. New Haven, CT

²VA New England Mental Illness Research and Education Center; VA Connecticut Health Care System, West Haven, CT

³Center for the Assessment of Pharmaceutical Practices (CAPP), Department of Health Policy and Management, Boston University School of Public Health and the Center for Health Quality, Outcomes and Economic Research (CHQOER), Veterans Administration Medical Center, Bedford MA

Abstract

Objective—This study aims to assess the independent association of seven psychiatric illnesses with all-cause mortality in a representative national sample of veterans, after adjustment for demographic factors, psychiatric and medical co-morbidity, obesity, tobacco use and exercise frequency.

Methods—Analyses were conducted using data from the 1999 Large Health Survey of Veteran Enrollees (n = 559,985). Cox proportional hazards models were used to examine the relationship of seven psychiatric diagnoses with mortality. Date of all-cause mortality was determined from the Department of Veterans Affairs' Beneficiary Identification and Records Locator System. All-cause mortality rates were calculated as the total number of deaths in each group divided by the person-years of follow-up time in each group.

Results—27% of the subjects (n=131,396) died during the 9-year study period. Each of the psychiatric diagnoses was associated with significantly increased hazard ratio for all-cause mortality after adjusting for age, race and gender. Hazard ratios (95% CI) ranged from 1.02 (1.01, 1.04) for PTSD to 1.97 (1.89, 2.04) for alcohol use disorders. After adjustment for psychiatric and medical co-morbidity, obesity, current smoking and exercise frequency, alcohol and drug abuse and dependence and schizophrenia were statistically significantly associated with an increased risk of mortality.

Conclusions—In this study of a large representative national sample of veterans, schizophrenia and alcohol and drug use disorders were independently associated with an increased risk of all-cause mortality over a 9-year period.

Keywords

Mortality; Psychiatric Illness; Medical Co-morbidity; Veterans

Corresponding author: Lydia Chwastiak MD, MPH, Connecticut Mental Health Center; 34 Park Street, W205; New Haven CT 06519, phone: (203) 974-7771; fax: (203) 974-7322, lydia.chwastiak@yale.edu.

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Background

An increased risk of mortality has been reported among persons with several psychiatric disorders. A recent systematic review of 37 articles from 25 countries demonstrated a standardized all-cause mortality ratio (95% CI) among individuals with schizophrenia of 2.50 (2.18–2.83), compared to the general population. (1). A population-based study of 11-year mortality among persons with schizophrenia in Finland also demonstrated this excess mortality, with the greatest mortality gap among young persons (2). Several studies have suggested that as many as 60% of premature deaths in persons with schizophrenia are due to medical conditions such as cardiovascular, pulmonary and infectious diseases (3). Studies of patients with bipolar disorder have also reported mortality rates approximately twice that of the general population (4–7). There has been consistent evidence in the literature of high mortality rates among individuals with alcohol and substance use disorders (8–10), and of an even greater increase in mortality rates when these disorders co-occur with other psychiatric disorders (11).

Major depressive disorder has also been associated with increased mortality rates (6,12–15). Among patients with type 2 diabetes, for example, major depression has been associated with a greater than twofold increase in mortality. (16) The literature on the association between Posttraumatic Stress Disorder (PTSD) and premature mortality, however, has been less consistent. Some studies have suggested that Vietnam veterans with PTSD are at increased risk of death from multiple causes (17). In one study of 8,000 Vietnam Theater veterans, PTSD was significantly associated with twice the risk of postwar all-cause mortality. Other studies, however, have found that primary care patients with a history of PTSD were not at increased risk of death compared with patients with neither depression nor PTSD. (18)

These previous studies of the increased mortality rates associated with psychiatric illness have had significant limitations. In most studies, the study samples have not been representative of the population. The comparison groups have differed from the samples with psychiatric illness in important ways, some of which may have been more important contributors to the observed increase in mortality than the psychiatric illness per se. Very few previous studies have accounted for the effect of medical co-morbidity on the observed increase in mortality associated with psychiatric illness, and even fewer have accounted for the impact of health behaviors as potential mediators (18). Moreover, previous studies have not accounted for the complex psychiatric co-morbidity that is typical of patients in psychiatric care (19). A recent study of more than 35, 000 veterans in primary care reported a much more modest increase in the risk of mortality associated with depression (hazard ratio = 1.17), after adjusting for medical co-morbidity and tobacco, alcohol and drug use. In this study, PTSD was not associated with an increased risk of death, and neither was the co-occurrence of depression and PTSD after adjustment for medical co-morbidity and tobacco and drug use (18). Accurate estimates of the increased mortality risk that is independently associated with a psychiatric illness has critical importance both for the development of specific interventions to improve medical outcomes among these vulnerable populations, and for public health policy and the targeting of resources.

The current study utilizes data from the 1999 Large Health Survey of Veteran Enrollees (LHS) the largest and most detailed survey of users of national VA health services ever conducted (20). We seek to assess the independent association of seven psychiatric illnesses with all-cause mortality in this representative national sample of VA patients, after adjustment for sociodemographic factors, psychiatric co-morbidity, medical co-morbidity, obesity, and health behaviors (tobacco use and exercise frequency).

Methods

Sample

Analyses were conducted using data from the 1999 Large Health Survey of Veteran Enrollees (LHS) (20). The LHS was a structured questionnaire that documented sociodemographic characteristics, health status, health behaviors and health care needs. The LHS included a medical co-morbidity index which was based on patient self-report of diagnoses (21), and the Veterans RAND 36 item Health Survey (VR-36), which was modified from the Medical Outcomes Study Short Form 36 survey (SF-36) version 1.0 (22) and specifically validated among veterans (23). Patients were sampled from the March 1999 – September 1999 VA enrollment files. A total of 1,406,049 enrollees were sent surveys and 887,775 returned the questionnaire, for a response rate of 63.1% (20). Veterans who returned the LHS survey did not differ from non-responders with respect to sociodemographic characteristics (20). A total of 559,985 respondents had complete data on survey variables used in this study.

Definitions and Measures

Psychiatric diagnoses—Veterans with psychiatric illness were identified from diagnostic information available in VA administrative records linked to the survey by social security number and included all veterans with at least one inpatient or two outpatient visits with an ICD-9-CM code (24) for any of seven psychiatric diagnoses (as a primary or secondary diagnosis): schizophrenia or schizoaffective disorder (295.xx), bipolar disorder (296.0x, 296.1x, 296.40–296.89), major depressive disorder (296.2–296.39), other depression (300.4x, 296.9x, 311.xx, 301.1x), PTSD (309.81), alcohol abuse or dependence (303.xx or 305.00), or drug abuse or dependence (292.01–292.99 or 304.xx or 305.20–305.99).

Mortality—The primary outcome of the study was the date of all-cause mortality. Mortality status was assessed for the 9 years from the completion of the LHS survey in 1999. Mortality was determined from the Department of Veterans Affairs' Beneficiary Identification and Records Locator System (BIRLS). In several studies, the sensitivity (i.e., the proportion of the true number of deaths) of mortality information from BIRLS ranged between 80.0% and 94.5%, compared to the sensitivity of mortality information purchased from the National Death Index (NDI) which ranged from 87.0% to 97.9% (25–27). BIRLS does not include information about cause of death.

Medical co-morbidity—Medical co-morbidity was evaluated based on patient self-report of medical diagnoses in the LHS survey. Veterans were specifically asked about the presence of twelve common chronic medical conditions in the survey, and the count of these diagnoses was used in the analyses.

Physical health status—Physical health status was evaluated by the physical component scale (PCS) of the Short Form-36 for Veterans, an adapted form of the Medical Outcomes Study Short Form 36 (22) designed specifically for use with veterans (23). It consists of the same 36 items and 8 domains as the MOS SF-36: physical functioning, role limitations due to physical problems, bodily pain, general health perception, energy/vitality, social functioning, role limitations due to emotional problems, and mental health. Responses in the two role functioning scales are a 5-point ordinal scale (ranging from 'no, none of the time' to 'yes, all of the time'), which differs from the dichotomous responses in the MOS SF-36 (28). The PCS is standardized to the national U.S. population with a mean of 50 and a standard deviation of 10, where higher scores denote better health status.

Obesity—The impact of obesity on mortality was assessed by the inclusion of body mass index (BMI) in the regression analyses. Obesity has been associated with increased mortality

in the general population (29–30) and with increased medical costs among persons with serious mental illness (31). BMI (kg/m^2) was calculated from self-reported items in the questionnaire for height and weight data collected in the survey. The items used to calculate BMI had been previously validated (32). Using the BMI categories adopted by the NHLBI and WHO (33–34), BMI levels were categorized as normal weight (BMI 18.5–24.9); overweight (BMI 25.0–29.9); mild obesity (BMI 30.0–35.0), and moderate to severe obesity (BMI >35.0).

Health behaviors—The LHS survey included questions about tobacco use and exercise frequency. Two questions assessed tobacco use: 1) Have you smoked at least 100 cigarettes in your life; and 2) Do you now smoke cigarettes every day, some days or not at all. For the purpose of analyses, a dichotomous variable of "current daily smoker" was defined as a subject who had smoked at least 100 cigarettes in his/her lifetime and was currently smoking every day or some days.

The exercise frequency question asked respondents how often do you engage in regular activities (e.g., brisk walking, jogging, bicycling, etc) long enough to work up a sweat? Categorical responses ranged from never to more than five times per week. For the purposes of analyses, responses were dichotomized into less than 3 times per week or 3 or more times per week, according to the physical activity guidelines of the American College of Sports Medicine and the American Heart Association (all healthy adults ages 18 to 65 years should have vigorous intensity aerobic physical activity for at least 20 minutes on three days per week) (35).

Statistical methods

First, we examined the association between each of the seven psychiatric diagnoses and mortality using Cox proportional hazards models and adjusting for the potentially confounding covariates of age, race, and gender. All-cause mortality rates were calculated as the total number of deaths in each group divided by the person-years of follow-up time in each group. Follow-up time for each individual was calculated as the time between completion of the LHS survey in 1999 and either the date of death or the end of the study period in 2008.

Next, a Cox proportional hazards model was conducted in order to evaluate the independent effect of each of the psychiatric diagnoses on mortality risk—i.e., to adjust for the potentially confounding effect of psychiatric co-morbidity. This model evaluated the impact of psychiatric co-morbidity, controlling for sociodemographic characteristics (age, race, gender, education, and service connection). Service connection reflects compensation for a disability connected to military service, and may affect priority for healthcare services. Each of the psychiatric diagnoses was simultaneously entered as an independent variable, and the reference group was patients with none of these diagnoses. A final model included potential mediators of the relationship between psychiatric illness and increased mortality: medical co-morbidity, physical health status (V-SF36 PCS), and obesity, current tobacco use and exercise frequency. Analyses were conducted in Proc Phreg of SAS® software, version 9.1 (SAS Institute Inc., Cary NC). The study was approved by the VA Connecticut IRB.

Results

The demographics and clinical characteristics of the sample are shown in Table 1. The mean age of study subjects was 64.1 years, and the sample was 95.9% male and 84.9% Caucasian. Rates of the seven psychiatric diagnoses ranged from 1.9% for bipolar disorder and substance use disorders to 6.2% for PTSD. These rates are representative of those of the general VA population, as we have previously shown (36). Subjects had a mean of 4.4 chronic medical conditions, and 31.5% of subjects were obese (BMI > 30 kg/m^2). 26.2% of subjects met criteria

for current smoker (smoked at least 100 cigarettes in lifetime and were currently smoking every day or some days). 39.9% of the sample reported no regular exercise.

Twenty-seven percent of the subjects (n=131,396) died during the 9-year study period. The results of the Cox proportional hazard models conducted for each of the seven psychiatric diagnoses demonstrated significantly increased hazard ratios for mortality (after adjusting for age, race and gender) for patients with each of the psychiatric diagnoses (Table 2). Hazard ratios (95% CI) for all-cause mortality ranged from 1.02 (1.01, 1.04) for PTSD to 1.97 (1.89, 2.04) for alcohol abuse and dependence, reflecting the increased mortality risk of veterans with these disorders compared to veterans with none of the psychiatric disorders.

Cox proportional hazards models were then conducted to evaluate the independent effect of each of the seven psychiatric diagnoses (net the effect of other psychiatric diagnoses) on increased mortality risk. Inclusion of all seven psychiatric diagnoses in a model demonstrated an independent effect on increasing all-cause mortality for each of the psychiatric diagnoses except PTSD, but these hazard ratios were much smaller in magnitude compared to the individual models, and ranged from 1.06 (1.01, 1.10) for bipolar disorder to 1.63 (1.59, 1.68) for alcohol abuse and dependence. In this model, an increased risk of mortality was also associated with increasing age, service-connected disability, and among veterans who were male or African American. Higher education and Hispanic ethnicity were associated with decreased risk of mortality during the study period (Table 3).

In the final model, an increased number of co-morbid chronic medical conditions was associated with increased risk of mortality (HR [95% CI] of 1.08 [1.06, 1.10]), and better physical health status was associated with decreased risk of mortality 0.97 (0.97, 0.97). Current smoking was associated with increased mortality risk, and exercise frequency of more than three times per week was associated with decreased mortality risk. Underweight, overweight and obesity were also associated with significantly increased mortality risk in this model. After adjustment for these covariates, the increased risk of mortality persisted among veterans with schizophrenia, drug use disorders, or alcohol use disorders, but not among veterans with bipolar disorder, major depressive disorder, or other depressive disorders. The greatest all-cause mortality risk was associated with alcohol abuse or dependence (HR [95% CI] of 1.33 [1.29, 1.37]).

Discussion

This study examined mortality risk over a 9-year period among a representative national sample of veterans treated in the VA health care system, and provides evidence that alcohol and drug abuse and dependence and schizophrenia are independently associated with an increased risk of mortality. These diagnoses were statistically significantly associated with an increased risk of mortality, even after adjustment for psychiatric and medical co-morbidity, obesity, current smoking and exercise frequency. Previous studies have evaluated the impact of individual psychiatric disorders on mortality, but patients who present to care typically have complex psychiatric co-morbidity (19), so analyses of the impact of a single disorder may be misleading. In our study, after adjustment for the presence of co-occurring psychiatric illnesses, six of the seven psychiatric diagnoses were associated with an increased risk of all-cause mortality during the study period.

The study findings suggest that much of the observed association between various psychiatric disorders and mortality is mediated by smoking and sedentary lifestyle. Indeed, the increased mortality risk among veterans with bipolar disorder, major depressive disorder, or other depressive disorders did not persist after adjustment for the potentially mediating factors of medical co-morbidity, smoking, obesity, and exercise frequency. This suggests that medical

co-morbidity may in large part explain the increased mortality risk among patients with these diagnoses reported in previous studies. These findings are consistent with a recent study of a large sample of outpatients with coronary heart disease, in which the association between depressive symptoms and adverse cardiovascular events was largely explained by behavioral factors, particularly physical inactivity. (37) Our results differ from those of a recent report of a large national VA sample, in which a diagnosis of depression or dysthymia (but not PTSD) was associated with increased risk of mortality over a 2-year period, after adjustment for demographics, medical co-morbidity, drug and alcohol use and a history of smoking. (18) The hazard ratio for the increased risk of mortality for veterans with depression in that study was 1.17 (95% CI 1.06–1.28), which is similar in magnitude to the hazard ratio in the current study before adjustment for medical co-morbidity. The differences between the hazard ratios in the adjusted models in the two studies may reflect methodological differences between the two studies, including the definition of depression, the evaluation of medical co-morbidity, the adjustment for alcohol use, and the length of the study period.

Our study failed to demonstrate an independent effect of PTSD on mortality, and it appears that the impact of co-morbidity on this group was particularly pronounced. This may have been due to the demographics of the sample, and in particular that the mean age of subjects was 64. In previous studies which have reported increased mortality among veterans with PTSD, the majority of deaths have been due to "external causes" (accidents and suicides) which may be particularly relevant in the first few years after combat exposure. Subjects in this study were evaluated in 1999, decades after active duty in some cases. Moreover, cause of death was not available in BIRLS. These limitations significantly limit the generalizability of the PTSD findings to those veterans currently returning from combat in Iraq and Afghanistan, a group who are much younger and have higher rates of drug and alcohol use.

The increased mortality risk associated with schizophrenia in our adjusted analyses was considerably smaller in magnitude than has been reported in previous studies (1.2 compared to 2.5). This difference may in large part be explained by the adjustment for health behaviors which may mediate the relationship between psychiatric illness and mortality. But there are two other possible explanations for the decreased risk observed in this study compared to previous studies. In this study, veterans with schizophrenia were compared to a "control" population who are also veterans seeking care at VA medical centers, and who are therefore similar with respect to unmeasured but potentially confounding covariates that may be associated with increased mortality. This strength of the LHS dataset addresses a major limitation of most of the previous studies. Second, it is also possible that the hazard ratio for mortality is in reality lower among persons with schizophrenia who are treated within the VA system, when compared to that of patients treated outside of the VA (as in many of the previous studies). The VA is the largest integrated healthcare system in the nation, and may provide higher quality of medical care to individuals with serious mental illness, who often experience fragmented care in community settings. Indeed, in a large study comparing mortality rates between VA enrollees and participants in the Medicare Advantage Program, after controlling case-mix differences, mortality rates were lower among patients receiving care through the VA. (38)

A strength of the LHS dataset was the availability of information about obesity, tobacco use and exercise frequency, which allowed us to adjust for these potential mediators of the relationship between psychiatric illness and mortality. As expected, tobacco use was associated with increased risk of mortality, and increased exercise frequency was associated with decreased risk of mortality. The impact of overweight and obesity on risk of mortality was smaller than previously reported (29). This may be explained in part by the mean age of the sample, as obesity-related excess mortality has been shown to decrease with age (29,39), and the mean age of the LHS subjects was 64. A more likely explanation is that these results may

be due to suppression effects related to the other covariates that were included in the final model.

Our study had several limitations. First, psychiatric diagnoses were based on administrative data, and previous literature has demonstrated significant under-diagnosis of psychiatric illness (40–41). We attempted to diminish the impact of this under-diagnosis by identifying patients with psychiatric illness as having at least one inpatient or two outpatient encounters with either a primary or secondary diagnosis of the disorder. Moreover, any potential to bias our results would likely be to falsely attenuate the differences between the groups, as patients with disorders would have mistakenly been categorized as having no psychiatric illness. Second, medical co-morbidity was based on self-report of diagnoses from the LHS survey, and it is possible that this method underestimates the true burden of medical co-morbidity. Self-report of medical diagnoses has been shown to be a valid method for assessing co-morbidity, even in the presence of cognitive impairment and a significant burden of co-morbidity (42). Moreover, the use of administrative data to define medical co-morbidity among individuals with psychiatric illness is problematic, as they appear to utilize fewer outpatient medical services (36,43) and may therefore be given fewer diagnoses. The instrument used to assess medical co-morbidity in this study has been shown to be reliable and valid (21). Third, our findings may have limited generalizability outside of the VA system. But since the VA is an integrated system, our findings likely under-estimate the mortality risk of patients with schizophrenia, and alcohol and drug use disorders receiving medical and psychiatric services in the community. Finally, the BIRLS database does not include cause of death. Future research should explore the impact of psychiatric illness on specific causes of death, in particular cardiovascular mortality. Future research should also explore the impact of co-occurring psychiatric diagnoses on increased mortality risk, as the effects of multiple disorders are likely to be more than additive.

In conclusion, this study suggests that veterans diagnosed with schizophrenia, or alcohol or drug abuse or dependence have an increased risk of mortality compared to veterans without these disorders, even after adjustment for psychiatric and medical co-morbidity, obesity, current smoking, and exercise frequency. This is particularly concerning, as the VA is an integrated healthcare system in which medical care may be more accessible to persons with serious mental illness and substance use disorders. Given the increased burden of chronic medical illness among these vulnerable veterans, interventions are needed to improve chronic illness management and engagement in medical care.

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Glossary

VA	Department of Veterans Affairs
BIRLS	Beneficiary Identification and Records Locator System
PTSD	Posttraumatic Stress Disorder
BMI	Body Mass Index

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Table 1

Demographics and Clinical Characteristics of the 1999 Large Health Survey of Veterans (LHS) (n=559,985)

Characteristic	Percentage or Mean (standard deviation)
Age	64.1 (12.9)
Race	
White	84.9%
African American	9.4%
Hispanic	4.8%
Other	0.9%
Gender, % male	95.9%
Schizophrenia diagnosis	3.1%
Bipolar disorder diagnosis	1.9%
Major depressive disorder diagnosis	5.1%
Other depression diagnosis	5.5%
PTSD diagnosis	6.2%
Alcohol abuse or dependence diagnosis	4.0%
Drug abuse or dependence diagnosis	1.9%
Medical co-morbidity index (number of diagnoses) (n=501,161)	4.4 (2.9)
BMI (kg/ m ²), mean (SD) (n=548,480)	28. 5 (5.0)
% underweight (BMI < 18.5)	1.0%
% normal weight (BMI 18.5–25.0)	23.2%
% overweight (BMI 25.0–30.0)	44.3%
% obese (BMI >30)	31.5%
% of subjects who have smoked more than 100 cigarettes in lifetime (n=554,662)	78.1%
Current smoking (n= 554,231)	
Every day	20.4%
Some days	5.8%
Not at all	73.8%
Frequency of exercise (intense and long enough to work up a sweat) (n=553, 084)	
None	39.9%
Less than once per week	16.7%
1–2 times per week	16.6%
3–4 times per week	14.9%

Characteristic	Percentage or Mean (standard deviation)
5 or more times per week	11.9%

Table 2

Hazard ratios for mortality, adjusted for age, race and gender (95% CI) Cox Proportional Hazard Regression Models (131,396 events).

	Hazard ratio (95% CI)
Alcohol abuse or dependence	1.97 (1.89, 2.04)
Drug abuse or dependence	1.79 (1.62, 1.97)
Schizophrenia	1.55 (1.48, 1.62)
Major depressive disorder	1.41 (1.34, 1.49)
Other depressive disorder	1.40(1.36, 1.43)
Bipolar disorder	1.32 (1.22, 1.43)
Posttraumatic stress disorder	1.02 (1.01, 1.04)

Table 3

Mortality rates of respondents to 1999 Large Health Survey of Veterans (n= 483,091). Cox Proportional Hazard Regression Models (131,396 events).

	Hazard ratio (95% CI)	
	With adjustment for psychiatric co-morbidity (and age, race, gender, education, and service-connected disability)	With adjustment for medical co-morbidity, BMI, current smoking, exercise frequency (and age, race, gender, education, and service-connected disability)
Age 40–49 ^a	2.70 (2.50, 2.92)	2.13 (1.95, 2.32)
Age 50–64 ^a	5.01 (4.73, 5.49)	3.64 (3.35, 3.96)
Age 65–74 ^a	10.76 (9.99, 11.59)	7.30 (6.72, 7.93)
Age 75–84 ^a	19.32 (17.93, 20.81)	12.13 (11.17, 13.18)
Age > 84 ^a	35.67 (32.98, 38.57)	20.18 (18.49, 22.02)
Male gender ^b	1.80 (1.73, 1.87)	1.64 (1.57, 1.71)
Education ^c	0.89 (0.88, 0.89)	0.96 (0.95, 0.96)
African American ^d	1.06 (1.02, 1.10)	1.00 (0.98, 1.02)
Hispanic ^d	0.78 (0.75, 0.79)	0.81 (0.79, 0.83)
Other race ^d	1.01 (0.99, 1.04)	0.94 (0.91, 0.96)
Service connection less than 50% ^e	1.16 (1.15, 1.18)	1.17 (1.15, 1.18)
Service connection greater than 50% ^e	1.21 (1.19, 1.23)	1.23 (1.21, 1.24)
Schizophrenia ^f	1.30 (1.25, 1.34)	1.13 (1.09, 1.16)
Bipolar disorder ^f	1.06 (1.01, 1.10)	0.99 (0.95, 1.04)
Major depressive disorder ^f	1.10 (1.07, 1.13)	0.92 (0.89, 0.99)
Other depression ^f	1.23 (1.20, 1.25)	1.00 (0.98, 1.02)
PTSD ^f	0.95 (0.93, 1.00)	0.91 (0.86, 0.98)
Alcohol use disorder ^f	1.63 (1.59, 1.68)	1.33 (1.29, 1.37)
Drug use disorder ^f	1.16 (1.10, 1.22)	1.11 (1.05, 1.16)
Medical co-morbidity ^g (# of conditions)		1.08 (1.06, 1.10)

	Hazard ratio (95% CI)
Physical health status (V-SF36 PCS) ^h	0.97 (0.96, 0.98)
BMI (kg/ m2)	
Underweight (<18.5) ⁱ	1.70 (1.63, 1.77)
Overweight (25.0–30.0) ⁱ	1.28 (1.27, 1.31)
Obese (>30) ⁱ	1.47 (1.45, 1.50)
Current daily smoker ^j	1.20 (1.19, 1.21)
Exercise frequency of 3 or more times per week ^k	0.89 (0.88, 0.90)

Reference groups for covariates:

^a age < 40;

^b female gender;

^c High school;

^d Caucasian race;

^e no service connection;

^f patients without the specified psychiatric diagnosis;

^g patients with no co-morbid medical diagnoses;

^h population norm for the VSF-36 PCS subscale = 50;

ⁱ normal weight (BMI 18.5–24.5);

^j non-smoker;

^k exercise frequency < 3 times per week.