Mortality After Diagnosis of Psychiatric Disorders and Co-Occurring Substance Use Disorders Among HIV-Infected Patients

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Abstract

We examined the associations between psychiatric diagnoses, substance use disorders, health services, and mortality among 9751 HIV-infected patients (≥ 14 years old) in a large, private medical care program, in a retrospective cohort design over a 12-year period. All study data were extracted from computerized clinical and administrative databases. Results showed that 25.4% ($n = 2472$) of the 9751 study subjects had received a psychiatric diagnosis (81.1% had major depression, 17.1% had panic disorder, 14.2% had bipolar disorder, and 8.1% had anorexia/bulimia); and 25.5% ($n = 2489$) had been diagnosed with substance use disorder; 1180 (12.1%) patients had received both psychiatric and substance diagnoses. In comparison to patients with neither a psychiatric diagnosis nor a SU diagnosis, the highest risk of death was found among patients with dual psychiatric and substance use diagnoses who had no psychiatric treatment visits and no substance treatment (relative hazards [RH] = 4.17, 95% confidence interval [CI] = 2.35 to 7.40). Among dually diagnosed patients, receiving psychiatric and/or substance use disorder treatment somewhat reduced the risk of death compared to patients with neither diagnosis. The lowest risks of death were observed among patients with a single diagnosis who had received corresponding treatment. Our study findings suggest that screening for psychiatric and substance problems at the initiation and during the course of HIV/AIDS treatment and providing psychiatric and substance use disorder treatment may extend life for these vulnerable patients.

Introduction

WITH THE INTRODUCTION OF combination antiretroviral therapy^{1–3} mortality among HIV-infected patients diminished significantly. However, some patient subgroups have different survival patterns,^{4–7} and have shown less decline in death rates.⁸ These include patients with psychiatric or substance use disorders, which are highly prevalent among patients treated for HIV/AIDS.^{9–11} There is also a high co-occurrence between psychiatric and substance use disorders among the HIV-infected,¹² as in other populations; and severity is greater in each type of disorder when there is co-occurrence.^{13,14} Together they place individuals at elevated risk for poor health outcomes.

Because psychiatric and substance use (SU) disorders frequently co-occur, it is important to examine the combined impact of these disorders among people with HIV infection. Research among HIV-infected patients has shown an associ-

ation between depression symptoms, HIV disease progression and mortality^{15–19}; and mental illness and substance abuse are barriers to optimal adherence to combination antiretroviral regimens.^{20,21} One study of U.S. veterans found that survival was associated with greater number of mental health visits.²² Yet few studies^{8,23} have examined survival patterns for HIV-infected individuals who use alcohol or illicit drugs, but are generally not injection drug users, and have been diagnosed with psychiatric or SU disorders from a private health plan; nor have studies examined both psychiatric and SU disorders in relation to mortality.

Previous research has shown that access to psychiatric and SU disorder care among HIV-infected patients varies based on sociodemographic factors and HIV illness severity.^{24,25} The current study compares mortality in HIV-infected patients diagnosed with psychiatric disorders and/or SU disorders to patients without either diagnosis receiving medical care from a private, fully integrated health plan where access to care and

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ability to pay for care are not significant factors. We also examine the effects of accessing psychiatric or SU treatment services. Improvement in depression has been associated with better adherence to combination antiretroviral therapy and increased CD4 cell counts.²⁶ Social support for HIV-infected patients has been associated with improved immune system functioning.²⁷ Therefore, we hypothesize that accessing services is associated with decreased mortality among patients with HIV infection.

Methods

Study population

We conducted a retrospective observational cohort study for years 1996 to 2007 among HIV-infected patients who were members of the Kaiser Permanente Northern California (KPNC) health plan. The KPNC is an integrated health care system with a membership of 3.5 million individuals, representing 34% of the insured population in Northern California. The membership is representative of the northern California population with respect to race/ethnicity, gender, and socioeconomic status, except for some underrepresentation of both extremes of the economic spectrum.²⁸ HIV-infected patients are seen at medical centers throughout the KPNC 17-county catchment region.

The study population consisted of 11,132 HIV-infected patients who received health care at KPNC at some time between January 1, 1996 and December 31, 2006. The study sample included all HIV-infected patients who were 14 years of age or older ($n = 10,794$) on or after January 1, 1996 and had at least 6 months membership during the first year of study observation ($n = 9834$). This minimum age was chosen because the KPNC membership has very few HIV patients under age 14, children are likely to receive different psychiatric diagnoses than adolescents and adults (e.g., developmental disorders, conduct disorder), diagnosis of SU problems generally occurs later than age 13, and children are likely to receive services for these disorders in pediatrics departments rather than in the health plan's specialty psychiatry and SU treatment programs. Patients could enter the study until December 31, 2006. In the data analyses, we also excluded 83 patients whose SU disorder diagnosis status was unclear (e.g., patient is seen once at a SU treatment clinic but has no prior or subsequent SU disorder diagnosis). This resulted in a study analysis sample of 9751 patients.

Data sources

Since 1988, the KPNC Division of Research (DOR) has maintained a surveillance system of patients who are HIV-1-seropositive, ascertained through monitoring electronic inpatient, outpatient, laboratory testing, and pharmacy dispensing databases for sentinel indicators of probable HIV-infection. HIV-1 seropositivity is then confirmed through review of patient medical records. Ascertainment of HIV-infected patients by this registry has been shown to be at least 95% complete. The HIV registry contains information on patient demographics (e.g., gender, birth date, race/ethnicity), HIV transmission risk group (men who have sex with men, injection drug use, heterosexual sex, other, unknown), dates of known HIV infection, and AIDS diagnoses. KPNC also maintains complete and historical electronic databases on

hospital admission/discharge/transfer data, prescription dispensing, outpatient visits, and laboratory tests results, including CD4 T-cell counts and HIV-1 RNA levels. Mortality information including date and cause of death are obtained from hospitalization records, membership files, California death certificates, and Social Security Administration databases. Mortality data were complete through December 31, 2007.

Antiretroviral (ARV) medication prescription data were obtained from KPNC pharmacy databases. Approximately 97% of members fill their prescriptions at KPNC pharmacies, including patients whose prescriptions are obtained through the Ryan White AIDS Drug Assistance Program. ARV medication data included date of first fill, dosage, and days supply, as well as data on all refills. Patients were classified as: currently receiving combination-ARV (protease inhibitor [PI]-based, non-nucleoside reverse transcriptase inhibitor [NNRTI]-based, or nucleoside reverse transcriptase inhibitor [NRTI]-based regimens of 3 or more drugs), current dual NNRTI/NRTI ARV use, past (not current) ARV use, or never users (reference category).

Psychiatric disorder diagnosis and treatment

Psychiatric diagnoses were assigned by providers. One or more diagnoses can be coded by ICD-9 in the KPNC administrative databases.^{29,30} Psychiatric diagnoses selected for this study were the most common and serious psychiatric disorders diagnosed among health plan members including schizophrenic disorders (including schizo-affective type), major depressive disorder, bipolar affective disorder, neurotic disorders (including panic disorder), hysteria, phobic disorders, obsessive-compulsive disorder, anorexia nervosa, and bulimia. We examined the impact of having one or more of these psychiatric disorders in aggregate, as in prior HIV studies.³¹ Within the health plan, psychiatry can be accessed directly by patients. Mild cases of depression and anxiety may be addressed in primary care with medication but moderate to severe cases are referred to psychiatry. Treatment in psychiatry includes assessment, psychotherapy and medication management. Patients diagnosed with a psychiatric disorder generally return to psychiatry for individual and/or group psychotherapy and/or medication evaluations. Our measure of psychiatric treatment was whether or not a patient had visits to a psychiatric clinic after a psychiatric diagnosis,^{32,33} obtained from automated databases.

Substance use dependence or abuse diagnosis and treatment

A diagnosis of ICD-9 substance dependence or abuse can be made by the patient's clinician in primary care, SU disorder treatment, or psychiatry as a primary or secondary diagnosis.^{34,35} Diagnostic categories include all alcoholic psychoses, drug psychoses, alcohol dependence syndrome, drug dependence (including opioid, barbiturate, sedative/tranquilizer, cocaine, cannabis, amphetamine, and hallucinogen dependence but excluding tobacco dependence), alcohol abuse, cannabis abuse, hallucinogen abuse, barbiturate abuse, sedative/tranquilizer abuse, opioid abuse, cocaine abuse, and amphetamine abuse; as well as multiple substance abuse and unspecified substance abuse. In our analyses we classified patients as having one or more (any) diagnoses of substance abuse and/or dependence versus no diagnosis.

KPNC provides comprehensive outpatient SU treatment available to all members of the health plan. Services include both day hospital and traditional outpatient programs,³⁶ both of which include eight weeks of individual and group therapy, education, relapse prevention, family therapy, with aftercare visits once a week for ten months. In addition to these primary services, ambulatory (and inpatient) detoxification and residential services are available, as needed. A small proportion of patients engage in residential SU treatment, conducted by contractual agreement with outside institutions. These data are available in the KPNC referrals and claims databases. As with psychiatric treatment, in the current study SU treatment initiation was measured as having one or more visits to an outpatient program or a stay in a residential SU treatment unit following diagnosis.

Study outcome

The primary outcome examined in this study was all-cause mortality, with cohort follow-up through December 31, 2007.

Statistical methods

Analyses focused on diagnoses of psychiatric disorders with and without co-occurring SU diagnoses as the primary predictors of interest. The distribution of demographic, clinical and behavioral characteristics was compared between patients with and without a major psychiatric diagnosis; statistical significance was assessed using the χ^2 test. The distribution of cause of death was examined by psychiatric diagnostic status (any major diagnosis versus none); statistical significance was assessed using the χ^2 test or Fisher's exact test where table cells were sparsely (counts <5) populated. Cox proportional hazards regression was used to obtain point and interval estimates of mortality relative hazards associated with psychiatric diagnosis/treatment status and SU problems diagnosis/treatment status, with each of these two time-dependent covariates measured at three levels: no diagnosis, diagnosis with treatment, diagnosis without treatment. With the goal of examining the joint effects of these two covariates on mortality, results are expressed as hazard ratios for combinations of psychiatric diagnosis/treatment and SU diagnosis/treatment levels, with no diagnosis of either comorbidity as the referent. These estimates were adjusted for an *a priori* chosen set of available covariates, including age at entry into study, race/ethnicity, gender, HIV transmission risk group, CD4 T-cell counts and HIV RNA levels and ARV treatment modeled as time-dependent covariates, year of known HIV infection, AIDS diagnosis prior to entry into study, and evidence of hepatitis C viral infection. Initial modeling results demonstrated a significant interaction between psychiatric and SU diagnosis/treatment status in Cox regression models ($p = 0.0008$). Therefore, relative hazard estimates of interest were obtained via appropriate linear combinations of parameter estimates from a fully saturated model (main effects and interaction terms included in all models).

Although a significant minority of patients remained ARV-naïve throughout the study follow-up, we wanted to estimate adherence to combination highly active antiretroviral therapy (HAART) stratified by psychiatric diagnosis and SU diagnosis status for study participants who did receive HAART. Adherence was measured using electronic pharmacy dispensing

refill records; the "days supply of HAART medication (including carry-over of pills left over from the previous dispensing) was divided by the "total time (days) elapsed between first day of HAART initiation and last day of HAART medication supply"³⁷ over the first 12 and 24 months of study follow-up. Mean and standard deviation (SD) of adherence were then estimated by diagnostic status category. All data analyses were conducted using SAS software, version 9.1 (SAS, Inc., Cary, NC).

Results

Among the 9757 HIV-infected patients in our study sample, 25.4% ($n = 2472$) had received a psychiatric diagnosis, and 25.5% ($n = 2489$) had been diagnosed with SU disorder; 1180 (12.1%) patients had received both psychiatric and SU problem diagnoses. The most prevalent psychiatric disorders included major depression (81.1% of the 2472 patients diagnosed with psychiatric disorder), panic disorder (17.1%), bipolar disorder (14.2%), and anorexia/bulimia (8.1%). Multiple drug dependence/abuse (41.0%) and alcohol alone (32.7%) were the most prevalent SU diagnoses. Other single SU diagnoses included cannabis (8.5%), amphetamines (7.7%), cocaine (3.9%), opioids (1.9%), alcohol or drug psychoses (1.8%), and unspecified (18.8%); 47.6% had a single SU diagnosis. In contrast, a recent study of the KPNC general health plan membership found that 10.8% were diagnosed with depression and 2.1% were diagnosed with an SU disorder based on medical records.³⁸

The distributions of demographic and HIV-related clinical and behavioral characteristics by psychiatric diagnosis status are presented in Table 1. The results of χ^2 tests indicate significant differences in most characteristics between those patients with and without a psychiatric diagnosis. However it can be seen that the categories of these characteristics were still very similar in distribution in both groups. Finding significant results for very small differences in distributions is likely the consequence of having a very large sample size in this study. The majority of patients were white, male, 30–49 years of age at baseline, and belonged to the men who have sex with men (MSM) HIV transmission risk group. CD4 T-lymphocyte cell counts measured at or near time of study entry were comparable in both patients with and without a psychiatric diagnosis. Similar results were observed for HIV RNA levels. Of the 2472 patients with a psychiatric diagnosis, 83.9% had one or more psychiatry department visits.

The proportion of patients with any ARV therapy experience at baseline was similar across psychiatric disorder status, with on average 35% of all patients having no ARV experience. Throughout study follow-up, approximately 25% of all patients remained ARV naïve. Among those who were receiving HAART during study follow-up, mean adherence was estimated as 82.4% (standard deviation [SD] = 21.9%) among patients with a psychiatric diagnosis at 12 months after initiation of HAART and 83.7% (SD = 22.0%) among patients with no psychiatric diagnoses; similar mean adherence was observed at 24 months. Patients diagnosed with SU problems showed mean adherence of 81.1% (SD = 23.4%) at 12 months after initiating HAART in comparison to 83.5% (SD = 22.0%) among patient without a SU problem diagnosis. Because adherence rates were similar across diagnostic status, we did not conduct a subanalysis of ARV-experienced

TABLE 1. DISTRIBUTION OF STUDY CHARACTERISTICS BY PSYCHIATRIC DIAGNOSIS STATUS AMONG 9751 KPNC HIV-INFECTED PATIENTS, 1996–2006

Characteristic	Psychiatric diagnosis status		χ^2	p Value
	No (n = 7279) N (%)	Yes (n = 2472) N (%)		
Age			26.2	<0.001
< 30 years	876 (12)	250 (10)		
30–39	2932 (40)	1091 (44)		
40–49	2339 (32)	824 (33)		
50–59	907 (12)	252 (10)		
60+	225 (3)	55 (2)		
Race/ethnicity			81.7	<0.001
White	4164 (57)	1612 (65)		
Black	1316 (18)	381 (15)		
Hispanic	965 (13)	309 (13)		
Other	378 (5)	110 (4)		
Unknown	456 (6)	60 (2)		
Gender			10.8	0.001
Male	6608 (91)	2188 (89)		
Female	671 (9)	284 (11)		
Risk group			32.1	<0.001
Heterosexual contact	1003 (14)	308 (12)		
Men who have sex with men (MSM)	4716 (65)	1650 (67)		
Injection drug use (IDU)	277 (4)	107 (4)		
MSM and IDU	260 (4)	133 (5)		
Coagulation disorder/transfusion	109 (1)	31 (1)		
Unknown	914 (13)	243 (10)		
CD4 cell count at baseline			10.0	0.075
≥ 500	1438 (20)	516 (21)		
350–499	1336 (18)	467 (19)		
201–349	1342 (18)	473 (19)		
100–200	915 (13)	317 (13)		
< 100	993 (14)	339 (14)		
Unknown	1255 (17)	360 (15)		
HIV RNA level at baseline			21.8	<0.001
< 10 ^{2.7}	1651 (23)	574 (23)		
10 ^{2.7} –<10 ^{3.3}	460 (6)	182 (7)		
10 ^{3.3} –<10 ^{4.7}	2078 (29)	779 (32)		
≥ 10 ^{4.7}	1531 (21)	499 (20)		
Unknown	1559 (21)	438 (18)		
Antiretroviral therapy experience at baseline			9.4	0.002
Never	2646 (36)	814 (33)		
Ever	4633 (64)	1658 (67)		
AIDS diagnosis at baseline			0.002	0.967
No	5321 (73)	1806 (73)		
Yes	1958 (27)	666 (27)		
Hepatitis C viral infection			19.9	<0.001
No	6577 (90)	2155 (87)		
Yes	702 (10)	317 (13)		
Time from known HIV-infected to baseline			7.2	0.028
< 1 year	2924 (40)	952 (39)		
1–5 years	2093 (29)	680 (28)		
6+ years	2262 (31)	840 (34)		
Visits to psychiatric clinic			2922.9	<0.001
No	5624 (77)	398 (16)		
Yes	1655 (23)	2074 (84)		
Substance abuse/dependence diagnosis			859.2	<0.001
No	5970 (82)	1292 (52)		
Yes	1309 (18)	1180 (48)		
Visits to substance use treatment clinic			497.4	<0.001
No	6896 (95)	1974 (80)		
Yes	383 (5)	498 (20)		
Total	7279 (100)	2472 (100)		

TABLE 2. CAUSE OF DEATH BY PSYCHIATRIC DIAGNOSIS STATUS

Cause of death	Psychiatric diagnosis status		
	None	Had ≥ 1 dx	p Value
HIV/AIDS	431 (61)	156 (58)	0.493
Cancer	87 (12)	33 (12)	0.974
Cardiovascular	53 (7)	18 (7)	0.691
Liver disease	12 (2)	4 (1)	0.222 ^a
Bacterial, viral, parasitic infection	19 (3)	10 (4)	0.384
Blood (anemia, hemophilia) disease	4 (1)	3 (1)	0.200 ^a
Digestive disease	7 (1)	5 (2)	0.130 ^a
Metabolic disorder	7 (1)	2 (1)	0.288 ^a
Respiratory disease	15 (2)	1 (0)	0.035 ^a
Accident, violence	11 (2)	7 (3)	0.109 ^a
Suicide	12 (2)	11 (4)	0.026
Other	7 (1)	4 (1)	0.198 ^a
Unknown	46 (6)	14 (5)	0.469
All Causes	711 (100)	268 (100)	

^aFisher's exact test.

patients only, where adherence would have been included as a covariate in the regression model.

The distribution of cause of death cross-tabulated by psychiatric diagnosis is presented in Table 2. The majority of deaths among patients with or without a psychiatric diagnosis were attributed to HIV/AIDS. The remaining causes of death had proportionately the same distribution across categories of psychiatric diagnosis status, with the possible exception of suicide which was twice as common among patients with a psychiatric diagnosis in comparison to patients with no diagnosis. Examining all-cause mortality for the entire study follow-up, we found an age-adjusted mortality rate of 28.6 (95% confidence interval [CI] = 23.5–33.7) deaths per 1000 person-years for patients with a psychiatric diagnosis versus 17.5 (95% CI = 15.7–19.3) deaths for those without a psychiatric diagnosis.

To examine the joint effects of psychiatric diagnosis, psychiatric treatment visits, SU diagnosis, and SU treatment on mortality, relative hazards (RH) were estimated using Cox proportional hazards regression. As mentioned in Statistical methods, the effects of psychiatric diagnosis/treatment and SU diagnosis/treatment were not additive, with statistically significant interactions between these covariates. RHs and 95% Confidence Intervals estimated from unadjusted (crude hazard ratios) and adjusted (for potential confounders) models are presented in Table 3. Categories of diagnosis and treatment are ordered from lowest to highest RH in the unadjusted model 1. In comparison to patients with neither a psychiatric diagnosis nor a SU diagnosis (reference category), the highest risk of dying was found among patients with dual (psychiatric and SU) diagnoses but who had no psychiatric treatment visits and no SU treatment (RH = 4.17, 95% CI = 2.35–7.40). This effect was somewhat attenuated after adjustment for potential confounders (model 2) but remained statistically significant (RH = 2.71, 95% CI = 1.51–4.85). Similar results were observed for patients who had a psychiatric diagnosis but no psychiatric services and no SU diagnosis (crude RH = 3.91, 95% CI = 2.83–5.40; adjusted RH = 3.00,

95% CI = 2.17–4.17. Other effect estimates revealed that among the dual diagnosed patients having psychiatric treatment visits and/or SU treatment the risk of death was somewhat reduced but still significantly higher compared to patients with neither diagnosis. Elevations in the risk of death were lowest among patients who had a single diagnosis with corresponding treatment visits. As shown in Table 1, some patients had visits to psychiatry department clinics but did not receive a psychiatric diagnosis. We conducted a sensitivity analysis where the fully adjusted model 2 was estimated excluding those patients who had visited psychiatry clinics but did not receive a psychiatric diagnosis. The results of this reduced sample analysis showed RHs (95% CIs) that were very similar to those parameter estimates in model 2.

Discussion

During 12 years of follow-up (1996–2007), we observed a higher mortality risk for HIV-infected patients diagnosed with both psychiatric and SU disorders in comparison to patients with neither diagnosis. However, we observed that psychiatric and SU treatment, in general, reduced mortality risk in single and dual diagnosed patients, and remained statistically significant even after adjustment for age, race, immune status, HIV viral load, antiretroviral therapy use, and other potential confounders. Accessing psychiatric treatment reduced mortality risk among dual diagnosed patients who were treated or not treated for SU disorder.

Previous studies of individuals with HIV infection have found that those with psychiatric disorders are at elevated risk for poor medication adherence and clinical outcomes.^{20, 38} There is substantial evidence that depression, stressful life events and trauma affect HIV disease progression and mortality.^{15, 39} This effect has been found even controlling for medication adherence, in a study that showed that HAART adherent patients with depressive symptoms were 5.90 times (CI = 2.55–13.68) more likely to die than adherent patients with no depressive symptoms.⁴¹ Depressive symptoms independently predicted mortality among women with HIV,¹⁸ and also in a separate study of men.¹⁷ Similarly, in multivariate analyses controlling for clinical characteristics and treatment, women with chronic depressive symptoms were 2 times more likely to die than women with limited or no depressive symptoms (relative risk [RR], 2.0; 95% CI 1.0–3.8).¹⁶ Among women with CD4 cell counts of less than 200 × 10⁶/L, HIV-related mortality rates were 54% for those with chronic depressive symptoms (RR, 4.3; 95% CI, 1.6–11.6) and 48% for those with intermittent depressive symptoms (RR, 3.5; 95% CI, 1.1–10.5) compared with 21% for those with limited or no depressive symptoms. Chronic depressive symptoms were also associated with significantly greater decline in CD4 cell counts after controlling for other variables.¹⁶ These mechanisms could help to explain the greater risk of mortality observed in our sample.

Our findings strongly highlight the importance of access to psychiatric and SU disorder treatment for this population. It was estimated that during a 6-month period, 61.4% of 231,400 adults in the United States receiving treatment for HIV/AIDS used psychiatric or SU disorder treatment services.⁴² A significant number of HIV-infected patients report accessing psychiatric services.²⁵ Such visits are associated with decreased risk of discontinuing HAART.²⁵ Burnam et al.⁴² found

TABLE 3. THE JOINT EFFECTS OF PSYCHIATRIC DIAGNOSIS, PSYCHIATRIC TREATMENT VISITS, SUBSTANCE USE DIAGNOSIS AND SUBSTANCE USE TREATMENT IN RELATION TO MORTALITY AMONG KPNC HIV-INFECTED PATIENTS: UNADJUSTED RELATIVE HAZARDS AND ADJUSTED FOR POTENTIAL CONFOUNDERS FROM COX REGRESSION MODELS

Characteristic		Model 1: unadjusted	Model 2: adjusted
<i>Psychiatric diagnosis and visits to psychiatric clinic status</i>	<i>Substance abuse diagnosis and visits to chemical dependency clinic status</i>	<i>RH (95% CI)</i>	<i>RH ((95% CI)</i>
No dx	No dx	1.00 (ref)	1.00 (ref)
Psychiatric dx with clinic visit	No dx	1.44 (1.15, 1.79)	1.42 (1.14, 1.77)
No dx	SU dx with clinic visit	1.66 (1.18, 2.34)	1.75 (1.23, 2.48)
Psychiatric dx with clinic visit	SU dx, no clinic visit	2.11 (1.65, 2.71)	2.08 (1.61, 2.68)
Psychiatric dx with clinic visit	SU dx with clinic visit	2.15 (1.58, 2.92)	2.39 (1.75, 3.27)
Psychiatric dx, no clinic visit	SU dx with clinic visit	2.73 (1.02, 7.30)	3.02 (1.13, 8.12)
No dx	SU dx, no clinic visit	2.73 (2.28, 3.27)	1.88 (1.56, 2.27)
Psychiatric dx, no clinic visit	No dx	3.91 (2.83, 5.40)	3.00 (2.17, 4.17)
Psychiatric dx, no clinic visit	SU dx, no clinic visit	4.17 (2.35, 7.40)	2.71 (1.51, 4.85)
Age			
< 30 years			1.00 (ref)
30–39			1.39 (0.99, 1.95)
40–49			2.22 (1.58, 3.11)
50–59			3.35 (2.36, 4.78)
≥ 60			6.59 (4.44, 9.76)
Race/Ethnicity			
White			1.00 (ref)
Black			0.85 (0.71, 1.00)
Hispanic			0.74 (0.60, 0.93)
Other			1.17 (0.87, 1.59)
Unknown			0.49 (0.24, 0.99)
Gender			
Male			1.00 (ref)
Female			0.77 (0.58, 1.02)
HIV risk transmission			
Heterosexual contact			1.00 (ref)
MSM			0.96 (0.76, 1.21)
IDU			0.92 (0.66, 1.29)
MSM and IDU			1.08 (0.74, 1.57)
Coagulation disorder/transfusion			1.11 (0.73, 1.68)
Unknown			1.18 (0.89, 1.56)
CD4 cell count at baseline			
≥ 500 cells/ μ L			1.00 (ref)
350–499			1.42 (1.06, 1.90)
201–349			2.20 (1.68, 2.88)
100–200			5.41 (4.13, 7.08)
< 100			21.49 (16.6, 27.8)
Unknown			0.58 (0.25, 1.37)
HIV RNA level at baseline			
< $10^{2.7}$			1.00 (ref)
$10^{2.7}$ – $>10^{3.3}$			0.86 (0.63, 1.17)
$10^{3.3}$ – $<10^{4.7}$			0.83 (0.69, 1.00)
$\geq 10^{4.7}$			1.23 (1.02, 1.49)
Unknown			1.61 (1.24, 2.10)
Antiretroviral therapy during follow-up			
Never			1.00 (ref)
HAART			0.57 (0.43, 0.74)
Mono-dual therapy			1.52 (1.17, 1.97)
Past use			2.40 (1.88, 3.06)
AIDS diagnosis at baseline			
No			1.00 (ref)
Yes			1.24 (1.08, 1.43)

dx, diagnosis; MSM, men who have sex with men; mono, single NRTI or NNRTI therapy; dual, two-drug (NRTI and/or NNRTI) therapy; NRTI, nucleoside reverse transcriptase inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; RH, relative hazard; SU, substance use; HAART, highly active retroviral therapy.

that those with less severe HIV-related illness were less likely to access psychiatric or SU disorder treatment. One study found that engagement in SU disorder treatment was not associated with a decrease in hospital use by HIV-infected individuals with a history of alcohol problems.⁴³ Improvement in depression was associated with increase in HAART adherence among injection drug users.²⁶

Study strengths and limitations

A limitation of our study may have been the differences in timing of the psychiatric diagnosis and/or SU diagnosis. Some patients in our sample may have received their psychiatric diagnosis shortly after the onset of symptoms or in the initial phase of substance dependence or abuse, while other patients may have been diagnosed at a more advanced stage. Some patients may have met the criteria for a psychiatric or SU diagnosis without receiving one. In addition, some study subjects may have received psychiatric care or informal SU disorder services (e.g., Alcoholics Anonymous) or self-pay services outside of the KPNC health plan, and our study does not have information about those services. We also could not control for level of comorbidity (e.g., Charlson index) for other (not HIV-related) diseases and conditions at baseline, because many patients had insufficient health plan membership time prior to study entry.

This study examined mortality among HIV-infected patients with private health insurance who received medical care in an integrated health plan, who had full access to psychiatric and SU disorder services, and who had received diagnoses of psychiatric disorder and substance dependence or abuse by a clinician. Our study was conducted among one of the largest clinical cohorts of HIV-infected patients in the United States. Given the current movement towards health-care reform, it is important to investigate survival patterns of HIV-infected individuals within a health plan with characteristics similar to those plans that may result from health reform.

In summary, higher mortality occurred among HIV-infected patients diagnosed with psychiatric and SU disorders for whom access to medical services and ability to pay for care are not significant factors. In this analysis we did not observe significant differences in cause of death by psychiatric disorder status. The occurrence of higher mortality among these dual diagnosed patients receiving HIV/AIDS care may indicate that even when psychiatric treatment and SU treatment is available but not accessed, HIV-infected patients with psychiatric and co-occurring substance problems remain vulnerable to less than optimal health outcomes. Our study findings suggest that screening for psychiatric disorder and for SU problems at the initiation of HIV/AIDS treatment (and throughout the course of HIV/AIDS patient care) and providing psychiatric and SU disorder treatment may prove beneficial and extend life for these heavily burdened patients.

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Author Disclosure Statement

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