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Depression Symptoms and Treatment Among HIV Infected and Uninfected Veterans

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Abstract

Depression is one of the most common comorbid conditions affecting persons with HIV. We compared depressive symptoms and depression treatment using data from the Veterans Aging Cohort Study (VACS), a prospective cohort of HIV-infected and uninfected subjects. We identified subjects with a Patient Health Questionnaire score of 10 or greater. Treatment was defined as prescription of a selective serotonin reuptake inhibitor (SSRI) or mental health counseling. Overall, 16% of 4,480 subjects had depressive symptoms, and HIV-infected patients were more likely to have had depressive symptoms (OR = 1.38, 95% CI = 1.18, 1.62). Geographic

site of care and having a mental health provider at the clinic was associated with treatment. In multivariable models restricted to 732 patients with depressive symptoms, receipt of depression treatment did not differ by HIV status (Adjusted OR = 1.11, 95% CI = 0.80, 1.54). Non-Hispanic whites were more likely to receive treatment (Adjusted OR = 2.09, 95% CI 1.04, 4.24). Primary care and HIV providers were equally unlikely to treat active depressive symptoms. Treatment variation by race, site, and availability of a mental health provider, suggests targets for intervention.

Keywords

HIV-infection; Depression; Psychiatric status rating scales; Anti-depressive agents

Introduction

As people with HIV live longer due to improved antiretroviral treatment (Palella et al. 2006; Braithwaite et al. 2005), healthcare providers must increasingly address complex medical and psychiatric comorbid conditions (Goulet et al. 2007). Depression is one of the most frequently encountered comorbid conditions affecting persons with HIV (Basu et al. 2005). Untreated depression is highly prevalent (Ciesla and Roberts 2001; Colibazzi et al. 2006; Kilbourne et al. 2002), and is associated with decreased medication adherence, reduced quality of life, and shortened survival (Mayne et al. 1996; Uldall et al. 1998).

Despite the association of active depressive symptoms with adverse outcomes, HIV care providers report significantly less comfort in prescribing antidepressants, compared to general internists (Fultz et al. 2005). The current study assesses whether there are differences in depression treatment by HIV-infection status among subjects who screened positive for active depressive symptoms.

Method

Participants and Procedures

The Veterans Aging Cohort Study (VACS) is a multi-site, prospectively enrolled cohort study of HIV-infected patients attending Infectious Disease (ID) clinics and an age-, race-, and site-frequency matched comparison group of HIV-uninfected patients in General Medicine (GM) clinics. VACS has been described in detail elsewhere (Justice et al. 2006). Briefly, VACS is being conducted at eight Veterans Administration (VA) healthcare facilities in the United States, including sites in: Atlanta, GA; Baltimore, MD; Bronx, NY; Houston, TX; Los Angeles, CA; Manhattan, NY; Pittsburgh, PA; and Washington, D.C. The data in the present study consists of the VACS cross-sectional baseline wave, and was collected between June 2002 and September 2004. As of September 2004, 5,998 subjects had enrolled (2,979 HIV-infected, 3,019 uninfected). In all, 58% of HIV-infected patients seen during this interval in infectious disease (ID) clinics at participating sites were enrolled. The VACS has been IRB-approved at the coordinating center at the VA Connecticut Healthcare System, at Yale University, and each of the local sites. All subjects gave written informed consent.

Subjects were included in the present study if their Patient Health Questionnaire (PHQ-9) score was 10 or greater. We excluded women ($n = 316$), those with schizophrenia ($n = 511$), and patients with post-traumatic stress disorder ($n = 689$). We also excluded those receiving a monoamine oxidase inhibitor or a tricyclic antidepressant (TCA; $n = 2$), because of the small number of patients on those specific medications, and the potential use of those medications for other indications (e.g. TCA for pain management). Of the eligible subjects

($N = 4,480$), 16% ($n = 732$) had a PHQ-9 score of 10 or greater. HIV infected veterans were significantly more likely to have a score of 10 or greater (18% vs. 14%, chi-square = 15.37, $df = 1$). The analytic sample thus consisted of 732 subjects.

Measures

All subjects completed a self-administered questionnaire at study entry which included information on: demographic characteristics; the Patient Health Questionnaire (PHQ-9) for assessing depressive symptoms (Martin et al. 2006; Kroenke et al. 2001); alcohol (Saunders et al. 1993) and substance use; medication adherence; and other variables. We collected data on medical and psychiatric diagnoses from VA administrative data using International Classification of Diseases, Ninth Revision (ICD-9) codes. Information on prescription medications were retrieved from VA pharmacy records, and laboratory data (e.g. HIV viral load, and CD4+ cell counts) from the VA electronic medical record system (questionnaires and ICD-9 coding are available at <http://www.vacohort.org>).

We used the PHQ-9 to assess active depressive symptoms (Spitzer et al. 1999). The PHQ-9 is a modified version of the PRIME-MD that specifically addresses major depressive disorder. The presence of each of nine DSM-IV criteria is rated by the patient as “0” (not at all) to “3” (nearly every day). The PHQ-9 is valid for both criteria-based diagnosis and symptom severity evaluation. A cutoff score of 10 or more has a sensitivity of 88% and a specificity of 88% for a clinicians’ diagnosis of depression. The PHQ-9 has good operating characteristics in a variety of settings including primary care (Martin et al. 2006; Chen et al. 2006; Huang et al. 2006; Lowe et al. 2004a, b; Kroenke et al. 2001).

Outcomes Examined

We measured depression treatment as a dichotomous variable based on receipt of one or more prescription for a selective serotonin reuptake inhibitor (SSRI) or one or more visit to mental health clinic in the 6 months prior to or following administration of the PHQ-9. We choose this time frame to allow providers an opportunity to respond to depressive symptoms. The following SSRI were available within the VA formulary during the time of the study: fluoxetine, sertraline, paroxetine, fluvoxamine, citalopram, or escitalopram.

One of us (KS) surveyed the VACS sites to determine if a mental health care provider was on-site in each General Medicine and Infectious Disease clinic. We defined a mental health provider as any individual trained and designated via job description to screen and/or treat patients identified as having a mental health disorder. These providers could be social workers, registered nurses, nurse practitioners, physician assistants, psychologists or psychiatrists.

Data Analyses

Descriptive statistics comparing participants with and without HIV were calculated using chi-square analysis for categorical variables, and Student’s *t*-test (assessed for equal variances) for continuous variables. Multivariable logistic regression was used to assess whether HIV status was associated with receipt of treatment, adjusting for potential confounding variables. Full models were constructed using all variables in the descriptive statistics. We controlled for the following demographic and clinical factors: age (in years), race (black, white non-Hispanic, Hispanic, and other, using other as the referent group), the presence of medical comorbidity (alcohol disorder, drug disorders, coronary artery disease, diabetes mellitus, hypertension and pulmonary disorders), and site of care (i.e. each of the eight VACS sites). Study sites were assigned a letter in the results in order to protect anonymity. The outcomes of interest, receipt of an SSRI, or receipt of an SSRI and/or

mental health counseling, were examined in separate models. Statistical analyses were performed using SAS version 9.1.3 (SAS, Inc., Cary, North Carolina).

Results

Subject Characteristics

The majority of the 732 subjects in the analytic sample were non-white: 53% were black and 12% were Hispanic. Subjects had a mean age of 48 years. Fifty-nine percent of subjects ($n = 434$) were HIV-infected. HIV-uninfected subjects were significantly more likely to have been diagnosed with coronary artery disease, diabetes mellitus, and hypertension (Table 1).

Depressive Symptoms

Each PHQ-9 survey item was analyzed by HIV status in order to examine differences in the distribution of psychiatric and neurovegetative symptoms (Table 2). HIV-uninfected subjects were significantly more likely to report higher levels of low self-esteem, and to report psychomotor changes. HIV-uninfected subjects were more likely to report low self-esteem, concentration difficulties, and psychomotor changes occurring “nearly every day” (Table 2 and Fig. 1).

Depression Treatment

Overall, 36% of all subjects were prescribed an SSRI. There was no significant difference in receipt of SSRI by HIV status (Table 3). Without regard to receipt of SSRI, 28% of subjects received mental health counseling; HIV-uninfected subjects were significantly more likely to have had counseling. There was no difference in the combined outcome of prescription of an SSRI and/or mental health counseling by HIV-status (49% vs. 48%, $P = 0.80$).

There was no significant difference in age by receipt of SSRI (48.4 years in both cases). There was a significant difference in receipt of an SSRI by race; non-Hispanic white subjects were more likely to be prescribed an SSRI than black, Hispanic, and other subjects (51%, 30%, 28%, and 36%, respectively, $P < 0.0001$). There were no significant differences in receipt of SSRI by presence of comorbid conditions.

Site Variation

Sites varied with respect to prescription of SSRI and/or provision of mental health counseling (Table 4). Over all sites, 36% of subjects received an SSRI, and there was significant variation by site, with the proportion ranging from 20% at Site F to 50% at Site G. HIV-uninfected subjects were most likely to have received an SSRI at site G. Overall, 48% of subjects received either an SSRI and/or mental health counseling, with significant variation by site. There was significant variation in the proportion of HIV-uninfected and HIV-infected patients receiving SSRI and/or mental health counseling by site.

Overall, subjects at sites with onsite mental health providers were not more likely to be prescribed an SSRI (39% vs. 34%, chi-square = 1.93, $df = 1$, $n = 732$). However, subjects at facilities with mental health providers were significantly more likely to receive an SSRI and/or mental health counseling (58% vs. 42%, chi-square = 16.72, $df = 1$, $n = 732$).

Multivariable Models

There was no significant difference in receipt of SSRI by HIV status, after controlling for patient age, race and number of comorbid conditions, and site of care (Table 5). Patients at site ‘G’ were significantly less likely to receive an SSRI compared to those at site ‘D’, the referent group. There was no significant difference in receipt of SSRI and/or mental health

counseling by HIV-status (Table 6). White, non-Hispanic subjects were more than twice as likely to receive treatment. Subjects at site 'E' were significantly more likely to receive either SSRI and/or mental health counseling, while subjects at site 'G' were significantly less likely to receive such treatment.

Discussion

Less than 50% of subjects with depressive symptoms consistent with a diagnosis of major depressive disorder receive treatment. Contrary to our hypothesis, this low proportion of treatment does not vary by HIV status. Of note, more HIV-infected veterans have sufficient symptom burden to qualify as depressed, but among those considered depressed, uninfected veterans have more severe depressive symptoms.

We found no difference in depression treatment by HIV status, despite ID providers reporting less comfort with such treatment. Depressed HIV-uninfected subjects have an equally low chance of treatment compared to depressed HIV-infected subjects.

Barriers to providing depression treatment may be acting uniformly across ID and GM clinics. These barriers may include competing demands for provider attention and treatment due to other comorbid conditions, the provider's belief that the patient's symptoms are due to medical disease rather than to mental illness, and patient reticence to accept depression treatment. Therefore, the most medically sick patients may be least likely to be treated due to competing demands on the clinicians' time, concerns regarding polypharmacy, compromised organ function and higher degree of frailty (Colibazzi et al. 2006). However, our analysis did not demonstrate differences in treatment status by medical comorbidities.

While depressive symptoms are more common among HIV-infected subjects than among uninfected subjects, HIV-infected subjects also experience depression differently and some of the depressive symptoms experienced by HIV-infected subjects may have a medical origin. Of note, uninfected subjects reported more frequent cognitive-affective and neurovegetative symptoms: low self-esteem, difficulty with concentration and psychomotor changes, and also score higher in symptom severity. The only symptom more frequent among HIV-infected veterans was appetite change which can reflect a side effect of antiretroviral medications.

The threshold score for depression with the PHQ-9 was established in an otherwise healthy population. Some of the symptoms included in the PHQ-9 can be caused by medical disease. For example, in HIV-infected subjects, concentration difficulties could stem from HIV-associated cognitive deficits (Colibazzi et al. 2006). Clinical distinction between depressive symptoms and somatic symptoms may become even less clear in advanced stages of medical disease (Kilbourne et al. 2002). Some experts have suggested that cognitive-affective symptoms (anhedonia, depressed mood, low self esteem, and suicidality) should be weighted more heavily than neurovegetative symptoms (sleep change, fatigue, appetite change, concentration difficulty, and psychomotor change) among those with complex chronic diseases such as HIV or cancer [personal communication, Dr. Kroenke]. Our findings support this suggestion, but to date, no new thresholds have been established for the PHQ-9.

We found a lower prevalence of depression treatment for minority subjects. These results are concerning since all patients presumably have equal access to care within the VA system. Other studies have also found a racial disparity in depression treatment (Charbonneau et al. 2003; Simpson et al. 2007). It is unclear whether this is due to an under diagnosis of depression, an under treatment of recognized depression, a lack of presorting symptoms, or an under utilization of depression care among minority patients. However,

both blacks and Hispanic patients have been reported to mount greater resistance to depression treatment (Van Voorhees et al. 2003), and may be more likely to endorse fear of the addictive qualities of medications, and a greater belief in non-medical treatments such as prayer, for their hesitation to start antidepressant therapy (Cooper et al. 2003).

The demonstrated site variation suggests that higher rates of treatment are achievable. Subjects receiving care in a clinic with a mental health provider on site are more likely to receive treatment when considering SSRI or mental health counseling. This finding has important implications for service delivery and the desirability of providing onsite resources for mental health and substance abuse.

This study has limitations. First, we used a cross-sectional design and cannot ascribe causation to the observed associations. Our sample consists of VACS subjects with depressive symptoms, not a diagnosis of major depression, and the provision of SSRI in subjects with dysthymia is not standard practice. However, the PHQ-9 has demonstrated good association with a diagnosis of depression in several clinical settings.

Nevertheless, the potential overlap of neurovegetative symptoms and chronic disease symptoms discussed above complicates depression screening. The DSM-IV specifies that to achieve a formal diagnosis, an individual must report active depressive symptoms that are not due to physiological effects of a substance or a general medical condition (American Psychiatric Association 2000). It would be valuable to formally diagnose screen-positive subjects via clinician evaluation. As a result, our definition of depression may result in estimates biased toward lower treatment rates. Successfully treated patients, those who were not currently depressed and hence did not score above the PHQ-9 threshold for depression, were omitted, and depressed veterans receiving mental health counseling outside the VA could not be counted in our assessment of mental health treatment. Finally, we were unable to assess the adequacy of the treatment received.

The study also has strengths. First, we do not depend on usual care depression diagnosis. By using a uniformly-applied screening tool conducted at time of enrollment, we include all patients with active depressive symptoms, some of which may have escaped clinical detection. Another strength is that the VA is largely a closed system of care, we have demonstrated that 98–100% of veterans in care receive all prescription medications from the VA outpatient pharmacies because of financial incentives (Liu et al. 2006). Of the VACS sample, 96% of enrolled HIV-infected subjects report getting all of their HAART medication from VA pharmacies (Justice et al. 2006). Therefore it is unlikely that we underreport prescription of SSRI.

In closing, we find that depressive symptoms are commonly left untreated in both primary care and infectious disease clinics within the Veterans Healthcare System. This is true despite electronic clinical reminders and national depression treatment performance measures. Considerable site variation suggests that higher rates of treatment are achievable—particularly with the integration of mental health into routine care. While comorbid disease complexity or HIV infection did not explain differences in treatment rates, race/ethnicity did play a role. Further, HIV infected individuals experienced a different profile of depressive symptoms than their uninfected counterparts. These findings support continued universal screening for depressive symptoms within the VHA followed by an individualized care plan, and follow-up. Individualization should be based on input from the patient and provider alike to ensure that patients are fully informed of the potential benefits of depression treatment as well as counseled on methods to integrate depression care into their larger healthcare plan.

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Fig. 1.

Proportion of patients reporting depression symptoms “Nearly Every Day” *Note:* See Table 2 for complete description of PMD items, responses, and tests of significance between HIV – and HIV+ responders

Table 1

Demographic and clinical description of patients with depressive symptoms

Characteristics	Total <i>n</i> = 732	HIV– <i>n</i> = 298	HIV+ <i>N</i> = 434	χ^2 (df, <i>N</i>) ^a
Age (mean)	48.5 (±8.1)	48.6 (±8.3)	48.4 (±8.0)	0.37 (730, 732)
Race, %				3.91 (3, 732)*
Black	54	52	54	
White, non-Hispanic	29	33	27	
Hispanic	12	11	13	
Other	5	4	6	
Alcohol abuse, %	40	37	42	1.78 (1, 732)
Drug abuse, %	47	45	49	0.89 (1, 732)
Coronary artery disease, %	14	20	9	17.86 (1, 732)**
Diabetes mellitus, %	22	29	17	14.93 (1, 732)**
Hypertension, %	49	64	38	48.46 (1, 732)**
Pulmonary disorder, %	21	20	22	0.37 (1, 732)

^aStudent's *t*-test for age*
 $P \leq 0.05$,**
 $P \leq 0.001$, comparing HIV-uninfected to HIV-infected subjects

Table 2

PHQ-9 symptom frequency by HIV status

	Total% (n = 732)	HIV- (n = 298)	HIV+ (n = 434)	χ^2_a	χ^2_b
1. [Anhedonia] Little interest or pleasure in doing things					
Not at all	9	10	9	0.99	0.51
Several days	27	26	27		
> ½ the days	31	29	32		
Nearly every day	33	35	32		
2. [Depressed mood] Feeling down, depressed, or hopeless					
Not at all	6	4	7	6.86	3.17
Several days	25	21	27		
> ½ the days	32	34	32		
Nearly every day	37	41	35		
3. [Sleep change] Trouble falling/staying asleep, sleeping too much					
Not at all	7	8	6	4.58	0.13
Several days	15	17	14		
> ½ the days	28	24	30		
Nearly every day	50	51	49		
4. [Fatigue] Feeling tired or having little energy					
Not at all	4	4	4	0.84	0.7
Several days	15	16	15		
> ½ the days	32	32	31		
Nearly every day	49	47	50		
5. [Appetite change] Poor appetite or overeating					
Not at all	20	24	17	5.89	0.01
Several days	22	21	23		
> ½ the days	28	26	30		
Nearly every day	29	29	29		
6. [Low self-esteem] Feeling bad about yourself—or that you are a failure or have let yourself or your family down					
Not at all	14	11	16	30.03**	29.36**
Several days	20	15	23		

	Total% (n = 732)	HIV- (n = 298)	HIV+ (n = 434)	χ^2a	χ^2b
> 1/2 the days	27	23	30		
Nearly every day	39	51	31		
7. [Concentration difficulty] Trouble concentrating on things, such as reading the newspaper or watching television					
Not at all	22	21	23	5.19	4.33*
Several days	24	21	26		
> 1/2 the days	26	26	26		
Nearly every day	29	33	26		
8. [Psychomotor change] Moving or speaking so slowly that other people could have noticed. Or...being so fidgeting or restless that you have been moving around a lot...					
Not at all	44	43	45	10.26**	8.96*
Several days	23	19	25		
> 1/2 the days	18	17	18		
Nearly every day	15	20	12		
9. [Suicidality] Thoughts that you would be better off dead or of hurting yourself in some way					
Not at all	50	45	53	5.25	2.49
Several days	27	29	25		
> 1/2 the days	12	12	12		
Nearly every day	11	13	10		

* $P \leq 0.05$,

** $P \leq 0.001$

^a Comparing distribution of all responses by HIV status; df = 3 and $N = 723$ for all comparisons

^b Comparing proportion responding 'nearly every day' by HIV status, df = 1 and $N = 723$ for all comparisons

Table 3

Provision of depression treatment by HIV status

Treatment	Total% <i>n</i> = 732	HIV– <i>n</i> = 298	HIV+ <i>N</i> = 434	χ^2 ^{<i>a</i>}
Prescription of SSRI, % of total	36	34	38	0.85
Any mental health counseling, % of total	28	33	23	4.52 [*]
Prescription of SSRI or mental health counseling, % of total	48	49	48	0.07

^{*a*} df = 1 and *N* = 723 for all comparisons^{*} *P* ≤ 0.05,^{**} *P* ≤ 0.001

Table 4

Difference in treatment rates by site and by presence of mental health provider at site

Site	SSRI (%)		SSRI or mental health services (%)			
	Total	HIV–	HIV+	Total	HIV–	HIV+
N	723	434	298	723	434	298
A (n = 117)	40	30	39	42	35	46
B (n = 80)	43	47	40	53	56	50
C (n = 66)	29	28	29	40	44	34
D (n = 146)	42	38	44	52	52	52
E (n = 88)	38	28	34	52	48	54
F (n = 98)	20	21	20	28	31	25
G (n = 22)	50	50	50	64	67	60
H (n = 115)	44	38	49	64	62	65
Total	36	34	38	48	49	48
χ^2 (df, N)	20.68 (7,732)**	14.87 (7,343)*	8.77 (7,298)	36.32 (7,732)**	23.96 (7,343)**	15.16 (7,732)*

* $P \leq 0.05$,

** $P \leq 0.001$

Table 5

Multivariable logistic regression of the association of prescription of an SSRI with patient demographic and clinical factors^a

	Adjusted OR	95% CI	<i>P</i>	
HIV-infected	1.36	0.97	1.91	0.08
Age	0.99	0.97	1.02	0.57
Race				
Other	1.00 (ref)			
Black	0.69	0.32	1.48	0.34
White, non-Hispanic	1.84	0.88	3.87	0.11
Hispanic	0.64	0.34	1.19	0.15
Alcohol abuse	1.08	0.71	1.63	0.72
Drug abuse	1.47	0.96	2.24	0.08
Coronary artery disease	0.97	0.59	1.58	0.89
Diabetes mellitus	1.42	0.95	2.14	0.09
Hypertension	1.20	0.83	1.73	0.33
Pulmonary disorder	1.07	0.72	1.59	0.73
Site A	0.83	0.49	1.42	0.50
Site B	1.25	0.70	2.23	0.46
Site C	0.71	0.36	1.39	0.31
Site D	1.00 (ref)			
Site E	1.31	0.78	2.22	0.31
Site F	0.64	0.36	1.13	0.12
Site G	0.45	0.25	0.84	0.01
Site H	1.15	0.45	2.93	0.78

^a All sites compared to Site D (clinic with largest number of patients)

Table 6

Multivariable logistic regression of the association of prescription of SSRI or mental health services with patient demographic and clinical factors^a

	Adjusted OR	95% CI	P-value	
HIV-infected	1.11	0.80 1.54	0.55	
Age	0.99	0.97 1.01	0.49	
Race				
Other	1.00 (ref)			
Black	0.82	0.40 1.68	0.59	
White, non-Hispanic	2.09	1.04 4.24	0.04	
Hispanic	0.69	0.39 1.24	0.22	
Alcohol abuse	1.42	0.95 2.11	0.09	
Drug abuse	1.17	0.78 1.76	0.44	
Coronary artery disease	0.94	0.58 1.51	0.79	
Diabetes mellitus	1.33	0.89 1.98	0.17	
Hypertension	1.20	0.84 1.71	0.31	
Pulmonary disorder	1.07	0.73 1.58	0.72	
Site A	0.70	0.41 1.17	0.17	
Site B	1.21	0.68 2.14	0.52	
Site C	0.72	0.38 1.35	0.30	
Site D	1.00 (ref)			
Site E	1.86	1.10 3.16	0.02	
Site F	1.00	0.57 1.73	0.99	
Site G	0.43	0.24 0.77	0.00	
Site H	1.26	0.48 3.33	0.64	

^a All sites compared to Site D (clinic with largest number of patients)