

Bipolar Medication Use and Adherence to Antiretroviral Therapy Among Patients With HIV-AIDS and Bipolar Disorder

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Objective: The study examined relationships between adherence to bipolar medication and to antiretroviral therapy, measured by medication fills, among patients with diagnoses of bipolar disorder and HIV infection. **Methods:** A retrospective study was conducted of Medicaid claims data (2001–2004) from eight states, focusing on antiretroviral adherence. The unit of analysis was person-month (N=53,971). The average observation period for the 1,687 patients was 32 months. Analyses controlled for several patient characteristics. **Results:** Patients possessed antiretroviral

drugs in 72% of the person-months. When a bipolar medication prescription was filled in the prior month, the rate of antiretroviral possession in the subsequent month was 78%, compared with 65% when bipolar medication was not filled in the prior month ($p<.001$). Odds of antiretroviral possession were 66% higher in months when patients had a prior-month supply of bipolar medication. **Conclusions:** Bipolar medication adherence may improve antiretroviral adherence among patients with bipolar disorder and HIV infection. (*Psychiatric Services* 62: 313–316, 2011)

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Rates of HIV infection are elevated among people with severe mental illness compared with the general population (1). This increase likely reflects a range of factors, including risky behaviors secondary to psychiatric symptoms (2) and co-occurring substance use disorders (3).

Individuals with bipolar disorder generally require long-term pharmacotherapy and attention to psychosocial stressors to promote stability. Manic symptoms, such as poor impulse control and impaired judgment, as well as a high rate of comorbid substance abuse may increase risk of HIV infection (4), which is el-

evated among persons with bipolar disorder (5).

Antiretroviral therapy is the principal treatment for HIV-AIDS, and because suboptimal adherence can result in resistant viral strains and disease progression, medication adherence is vital for public health and for individual outcomes (6). Severe psychiatric disorders and substance abuse both influence adherence to antiretroviral therapy (7). An observational study suggested that the impact may differ by disorder; the effects of schizophrenia on adherence to antiretroviral therapy may be less than those of major depression and bipolar disorder (8). Clinical characteristics of bipolar disorder that increase risk of HIV infection, including manic symptoms and co-occurring substance use disorders, may also put optimal adherence in jeopardy.

If mania and other psychiatric symptoms decrease adherence to antiretroviral therapy, then treating these symptoms may increase adherence. Yet support for this hypothesis is surprisingly limited; we are not aware of published studies that examine this issue among persons with bipolar disorder. Among patients with HIV-AIDS and depression, some evidence points to an association between antidepressant adherence and antiretroviral adherence (9,10), but difficulties estab-

lishing the nature of the association with observational data have been noted.

In this study we examined adherence to antiretroviral therapy among persons living with HIV-AIDS who had a diagnosis of bipolar disorder. We report associations with demographic and clinical characteristics. We hypothesized that bipolar medication adherence in the preceding month would be associated with adherence to antiretroviral therapy in the following month and that a comorbid diagnosis of a substance use disorder would be associated with lower rates of adherence to antiretroviral therapy.

Methods

This study utilized Medicaid Analytic Extract data sets from 2001 to 2004 from eight states, which contained data for 4,568,010 individuals who were enrolled in Medicaid for at least one month. The eight states were California, New York, New Jersey, Georgia, Ohio, Illinois, Texas, and Florida. Person- and claims-level information was used, including *ICD-9-CM* diagnosis codes, National Drug Codes, and pharmacy dispense dates for every medication for which a prescription was filled. *ICD-9-CM* codes used to identify bipolar disorder were 296.0, 296.1, and 296.4–296.8; for HIV they were 042–044; for substance use disorders they were 291, 292, and 303–305; and for schizophrenia the code was 295.

Using a person-month as the unit of analysis, we classified each person-month as covered or not covered by antiretroviral therapy and by medication for bipolar disorder. Medications for bipolar disorder included lithium, antipsychotics, and the anticonvulsants carbamazepine, oxcarbazepine, valproate, and lamotrigine. We excluded gabapentin and topiramate, which do not demonstrate efficacy in randomized clinical trials. Because most Medicaid prescriptions for antiretroviral therapy and bipolar medications were for 30 days, with only 2% of antiretroviral therapy and 3% of bipolar medication prescriptions exceeding 31 days, we classified each calendar month as

covered if a prescription for the medication was filled in that month.

Participants were aged 18 to 65 years and during 2001–2004 had at least one inpatient or two outpatient claims for bipolar disorder, one inpatient or outpatient claim for HIV, plus at least one pharmacy claim for antiretroviral therapy and one for bipolar medications. We analyzed treatment episodes, defined as starting with the first month during which prescriptions for both bipolar and antiretroviral medications were filled. Only patients who remained enrolled in Medicaid for at least one year after this start date were included. Patients who also had a diagnosis of schizophrenia were excluded. Finally, we included only fee-for-service beneficiaries who were continuously enrolled in Medicaid and who did not receive long-term care or have nursing home days. Covariates included the state and the beneficiary's gender, age, race-ethnicity, and diagnosed substance use disorders.

Using multivariate logistic regression, we treated a refill for antiretroviral therapy in a given month as a dependent variable and treated a refill for bipolar medication in the prior month as a predictor variable. We chose this “lagged” strategy because same-month correlations between bipolar medication refills and antiretroviral refills would have included, for example, simultaneous refills occurring in a single pharmacy visit and would therefore have been less reflective of a causal direction running from bipolar treatment to antiretroviral adherence. Independent variables included patient characteristics, as well as the interaction of each covariate with the indicator of lagged bipolar medication possession, in order to delineate whether the effect of bipolar medication use varied by patient characteristics. Analyses took into account statistical dependence of repeated observations within individuals by using the cluster option within the logistic regression procedure in Stata, version 9.2. We utilized SAS, version 9.2, for data management. This research was approved by the Rutgers University Institutional Review Board.

Results

We identified 10,971 beneficiaries with both bipolar disorder and HIV infection. The criteria regarding age, long-term and managed care, and one year of continuous enrollment after the start of the treatment episode reduced the sample to 2,631. Eliminating beneficiaries with schizophrenia reduced the sample to 1,687. The mean±SD observation period for the 1,687 persons was 32±4.6 months (N=53,971 person-months). Antiretroviral therapy medications were refilled in 72% of the months, and bipolar medications were refilled in 55%.

Confirming our primary hypothesis, we found that adherence to bipolar medication was associated with higher rates of adherence to antiretroviral therapy in the following month. As shown in Table 1, when bipolar medication was not filled in the prior month, the rate of antiretroviral fill in the subsequent month was 65%, compared with an antiretroviral fill rate of 78% when bipolar medication was filled in the previous month. The association remained significant after the analysis controlled for demographic characteristics and diagnoses of comorbid substance use disorders and their interactions. Adherence to antiretroviral therapy was higher for men than women. Fill rates for antiretroviral medications were highest for beneficiaries aged ≥50 and lowest for the youngest beneficiaries. As hypothesized, diagnosis of a comorbid substance use disorder was associated with a significantly lower antiretroviral adherence rate (adjusted odds ratio=.62).

Discussion

We found a temporal association between receipt of bipolar medication and subsequent receipt of antiretroviral therapy in an analysis that controlled for several potentially confounding background demographic and clinical variables. Limitations should be noted. By requiring one year of observation, we may have missed less stable patients. Clinical status was observed by diagnoses, which lack valuable details (for example, a diagnosis of a substance

Table 1

Characteristics associated with filled antiretroviral prescriptions among adult Medicaid patients with diagnoses of bipolar disorder and HIV infection^a

Characteristic	Total N of person months	Antiretroviral prescription filled during month				
		N of person-months	Rate (%)	AOR	z	p
All person-months	53,971	38,813	71.9			
Gender						
Female	19,797	13,234	66.9	.78	-3.01	.003
Male	34,174	25,579	74.9	1.00		
Race-ethnicity						
Caucasian	26,453	19,330	73.1	1.00		
Black	13,125	8,982	68.4	.86	-1.47	.143
Hispanic	7,346	5,388	73.4	.95	-.43	.664
Other	7,047	5,113	72.6	.84	-1.51	.132
Age						
18–35	11,543	7,564	65.5	1.00		
36–49	35,728	26,041	72.9	1.36	3.38	.001
≥50	6,700	5,208	77.8	1.59	3.16	.002
Substance use disorder diagnosis						
No	25,077	19,025	75.6	1.00		
Yes	28,894	19,788	68.5	.62	-5.79	<.001
Filled prescription for bipolar disorder medication in prior month						
No	24,445	15,827	64.8	1.00		
Yes	29,526	22,986	77.9	1.66	4.26	<.001
Interaction with indicator for filled prescription for bipolar disorder medication in prior month						
Female				.97	-.30	.767
Black				.92	-.71	.480
Hispanic				1.03	.25	.800
Other race-ethnicity				1.14	.91	.362
Age 36–49				.93	-.66	.508
Age ≥50				.95	-.28	.781
Substance use disorder diagnosis				1.15	1.50	.134

^a Adjusted odds ratios (AORs) are based on a logistic regression model.

use disorder does not necessarily indicate actual use during the observation period). It cannot be determined from prescription claims whether a patient ingests a medication. Experimental designs—particularly randomized controlled trials—are required to isolate a specific medication effect, although practical and ethical difficulties in this research area make randomized controlled trials challenging. Nevertheless, future investigations that include longitudinal collection of data on symptoms would allow researchers to assess the role of symptom control, mood stabilization, active substance use, and phase of disorder in supporting adherence to antiretroviral therapy for patients with bipolar illness and HIV-AIDS. The study was also limited to adult

Medicaid beneficiaries in various phases of bipolar disorder who had already initiated bipolar medications and antiretroviral therapy. It is not clear whether similar results would have been obtained for other patient populations.

Conclusions

Our findings converge with those of previous research in suggesting that among persons with HIV and serious mental illness, adherence to a psychoactive medication regimen can improve adherence to antiretroviral therapy (8). Because of the central clinical importance of antiretroviral adherence, it seems appropriate that patients with bipolar disorder and HIV have individualized and ongoing assessments of their capacity to adhere to antiretro-

viral therapy. Adherence may fluctuate with clinical status. The findings underline the importance of psychopharmacological treatment in this population, both to benefit bipolar symptoms and to promote antiretroviral adherence.

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