POPULATIONS AT RISK

Effects of Drug Abuse and Mental Disorders on Use and Type of Antiretroviral Therapy in HIV-infected Persons

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OBJECTIVE: **To distinguish the effects of drug abuse, mental disorders, and problem drinking on antiretroviral therapy (ART) and highly active ART (HAART) use.**

DESIGN: **Prospective population-based probability sample of 2,267 (representing 213,308) HIV-infected persons in care in the United States in early 1996.**

MEASUREMENTS: **Self-reported ART from first (January 1997–July 1997) to second (August 1997–January 1998) follow-up interviews. Drug abuse/dependence, severity of abuse, alcohol use, and probable mental disorders assessed in the first follow-up interview. Adjusted odds ratios (AORs) and 95% confidence intervals (CIs) estimated from weighted models for 1) receipt of any ART, and 2) receipt of HAART among those on ART.**

RESULTS: **Of our study population, ART was reported by 90% and HAART by 61%. Over one third had a probable mental disorder and nearly half had abused any drugs, but drug dependence (9%) or severe abuse (10%) was infrequent. Any ART was less likely for persons with dysthymia (AOR, 0.74; CI, 0.58 to 0.95) but only before adjustment for drug abuse. After full adjustment with mental health and drug abuse variables, any ART was less likely for drug dependence (AOR, 0.58; CI, 0.34 to 0.97), severe drug abuse (AOR, 0.52; CI, 0.32 to 0.87), and HIV risk from injection drug use (AOR, 0.55; CI, 0.39 to 0.79). Among drug users on ART, only mental health treatment was associated with HAART (AOR, 1.57; CI, 1.11 to 2.08).**

CONCLUSIONS: **Drug abuse-related factors were greater barriers to ART use in this national sample than mental disorders but once on ART, these factors were unrelated to type of therapy.**

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Welcome recent advances in treatment have significantly reduced the morbidity and mortality associated with human immunodeficiency virus (HIV) type 1 infection.[1,2] Yet access to these improved treatments has been inequitable,[3] with serious deficiencies reported in the antiretroviral treatment of drug users.[4–6] After first detection of an elevated viral load, delay before starting protease inhibitors has been reported to be longer for drug users and persons with depressive symptoms.[7] Mental disorders are highly prevalent in HIV-infected persons[8] as well as in substance abusers,[9] and many persons with HIV are current or former drug users. Thus the relative contributions of drug abuse, mental disorders, and alcohol use to deficient ART prescribing patterns for HIV-infected persons merit examination. Health care and social support programs should be especially attentive to addressing such potentially key barriers to antiretroviral treatment.

We used data from a nationally representative sample of persons in care for HIV in 1996 to examine the effects of previous substance abuse and probable mental disorders on 2 outcomes: 1) any antiretroviral treatment and 2) highly active antiretroviral therapy (HAART) with 3 or more drugs including at least 1 protease inhibitor or non-nucleoside reverse transcriptase inhibitor among persons on combination therapy. By 1996, monotherapy was considered a less effective form of treatment[10] and by 1997, treatment with only 2 reverse transcriptase inhibitors was also viewed as less acceptable.[11] We predicted that persons with mental health disorders or substance abuse histories would be less likely to receive any treatment and, when treated, would be more likely to receive the "less acceptable" forms of treatment.

METHODS

Sampling Design

The data come from the HIV Cost and Services Utilization Study (HCSUS), a nationally representative

probability sample of HIV-infected adults receiving care in the contiguous United States in 1996. Full details of the sampling design and the sample have been previously reported.[12,13] Briefly, the sample was drawn from persons aged 18 years or older with known HIV infection and at least 1 visit for regular or ongoing care to a medical provider during a "population definition period" from January 5 to February 29, 1996. The sample excluded persons with care solely from military or prison medical care sites or emergency departments.

The HCSUS employed a multistage design in which geographical areas, medical providers, and patients were sampled. First, we sampled 28 Metropolitan Statistical Areas (MSAs) and 24 clusters of rural counties. Second, we sampled 58 urban and 28 rural "known providers" from lists of all providers noted by local informants as providing HIV care. Moreover, we randomly selected approximately 4,000 physicians in selected specialties from the American Medical Association's Physician Masterfile. From these "other providers," we sampled 87 urban and 23 rural providers caring for HIV-infected patients. Third, we sampled HIV-infected patients treated by participating providers in the population definition period. The RAND and local institutional review boards reviewed all consent forms and informational materials.

Of 4,042 eligible subjects sampled, we interviewed 76%, with 71% (N = 2,864) completing long-form interviews. We obtained abbreviated or proxy interviews for an additional 5% deemed too ill to complete the long-form interview and basic data from providers for a further 16%. These data were used to develop nonresponse weights. The overall coverage rate for long-form interviews is 68%.

Baseline interviews using computer-assisted personal interviewing (CAPI) instruments began in January 1996 and ended 15 months later. Most baseline interviews (91%) were in person and the remainder by telephone. The first and second follow-up interviews using CAPI were held from January through July 1997 and August 1997 through January 1998 and completed by 2,466 and 2,267 patients, respectively. A median of 199 days (interquartile range: 165–233 days) elapsed between follow-up interviews. Of 597 patients who did not complete all interviews, 236 (40%) were deceased by the second follow-up. Univariate analyses are based on 2,267 patients who provided all three waves of data (79% of the initial baseline cohort) and multivariate analyses are based on 2,245 patients with complete data on study variables.

Study Variables

Antiretroviral Therapy. We studied self-reported antiretroviral treatment from the second follow-up interview, at which time HAART was the recommended initial form of treatment. Subjects were shown names and pictures of: nucleoside analogues (i.e., zidovudine [ZDV], didanosine [ddI], zalcitabine [ddC], stavudine [D4T], and lamivudine [3TC]), non-nucleoside reverse transcriptase inhibitors (i.e., nevirapine and delavirdine), and protease inhibitors (i.e., saquinavir, ritonavir, indinavir, and nelfinavir). Respondents indicated whether they had taken each drug since the first follow-up interview and the number of days taking multiple drugs. We analyzed antiretroviral use for the preceding 6 months. For 48 respondents missing some 6-month treatment data, we imputed treatment from responses regarding antiretroviral use on the day of the interview.

We classified self-reported antiretroviral treatment since the last interview as: (a) none; (b) non-HAART, including monotherapy or 2 or more drug combination therapy but not HAART; or (c) HAART. HAART was defined as one protease inhibitor or a non-nucleoside reverse transcriptase inhibitor with any of the following drug pairs: ZDV+ddI, ZDV+ddC, ZDV+3TC, D4T+ddI, or D4T+3TC as recommended by the International AIDS Society-USA Panel.[11]

Drug Abuse and Dependence, Alcohol Use, and Probable Mental Disorders. Information on drug abuse, alcohol use, and mental disorders was obtained only in the first follow-up interview. We asked about use in the past 12 months of: heroin, cocaine, amphetamines, marijuana, inhalants, sedatives, analgesics, and hallucinogens. To identify potential drug abuse, we inquired if each class of drugs had been used "without a doctor's prescription, in larger amounts than prescribed, or for longer periods than prescribed." For a summary measure of drug abuse severity, we adapted a measure by Phin et al.[14] based on a sum of weights for each type of drug in specific classes of drugs abused (i.e., weight = 1 for marijuana or analgesics; weight = 2 for sedatives, inhalants, hallucinogens or amphetamines; and weight = 3 for cocaine or heroin). A weight of $\geq$5 signifies "high" severity of drug abuse. To assess drug dependence in the past year, we used a screener developed by Rost et al.[15] The screener asks about using increasing amounts of drugs in the past 12 months to get the same effect or having any emotional or psychological problem resulting from drug abuse, such as feeling depressed or suspicious of people or having strange ideas. These questions pertained to all drugs abused and not to each drug separately. A final drug abuse measure was based on a history of injection drug use as the respondent's self-reported HIV transmission risk category.

Similar to measures of problem drinking used in other research,[16] alcohol use in the 4 weeks before the first follow-up interview was classified as: none; non-heavy (i.e., always <5 drinks/day); heavy (i.e., $\geq$5 drinks on 1 to 4 occasions); or frequent heavy (i.e., $\geq$5 drinks on $\geq$5 occasions).

Probable mental disorders were measured by the Short-Form of the World Health Organization Composite International Diagnostic Interview (CIDI-SF).[17] We used CIDI modules to assess 4 common disorders in the 12 months before the first follow-up interview: major depression, dysthymia, generalized anxiety disorder, and panic disorder. A positive score reflects a substantial likelihood

of a DSM-IIIR diagnosis due to sufficiently intense and/or prolonged symptoms. However, we use the term "probable" mental disorder because we did not confirm the DSM-IIIR diagnosis. Severe mental diseases such as manic depression or schizophrenia were deemed too rare to study in this sample using HIV care. We derived indicators for the presence of any of these mental disorders, for each disorder separately, and for the total number of disorders.

Respondents reported if they "visited a mental health provider on an individual or family basis for emotional or personal problems" from the baseline until the first follow-up interview. Similarly, respondents indicated if they had "attended any 12-step or self-help groups (such as Alcoholics Anonymous, Narcotics Anonymous, or Cocaine Anonymous), received any professional or residential care, or had any overnight stays for drug or alcohol-related problems" since the baseline. We derived separate variables for any mental health care and for drug/alcohol treatment.

Clinical and Medical Care Characteristics. Patient clinical data included self-reported lowest CD4 cell count before the first follow-up interview (i.e., >500, 200–500, 50–199, <50 $\times$ 10^9/L), and clinically defined AIDS before the first follow-up interview. The self-reported lowest CD4 count was found to have very good agreement ($\kappa = 0.74$) with that determined from a chart review validation study (personal communication Sandra Berry, RAND). Self-reported outpatient visits between baseline and the first follow-up interview served as a measure of engagement in health care. A dichotomous variable indicated if respondents had participated in a clinical trial during which they received medication.

Analyses

To minimize possible confounding, drug abuse and mental health disorders were assessed at the first follow-up interview while antiretroviral treatment was evaluated for the period between the first and second follow-up interviews. We used the χ^2 test to examine unadjusted associations of key study variables with antiretroviral therapy pattern, i.e., none, non-HAART, or HAART. To incorporate the ordinal nature of this 3-category dependent variable in multivariate analyses, treatment status was partitioned into 2 dichotomous variables. First, we compared persons receiving none versus any antiretroviral therapy. Second, among treated persons, we compared HAART to non-HAART use. The 2 outcome variables correspond to a "continuation-ratio" logit analysis,[18] chosen because ordinal logistic regression analyses did not satisfy the proportional odds assumption and the two continuation-ratio analyses were independent.

In multivariate logistic regression analyses controlling for demographic, clinical, and socioeconomic characteristics, each drug abuse and mental disorder variable was entered separately into the models to avoid potential collinearity. In the next models, summary indicators of drug abuse and mental disorders were examined. Finally, we compared HAART users to all others in the full study sample and examined interactions to evaluate whether any negative effect of drug abuse-related factors was greater in patients with a mental disorder.

Analyses incorporate an analytic weight for each respondent adjusting for 1) differential selection probabilities across subgroups; 2) differential cooperation rates using supplemental data (i.e., short-form and proxy interviews, and nonresponse data) on nonresponding patients and providers; 3) seeing multiple sampled providers resulting in multiple opportunities to be sampled; and 4) dropout between the baseline and second follow-up interview. Using the analytic weight is necessary to generalize from the sample to the target population. Decedents between first and second interviews were considered ineligible and are not part of the target population. All analyses adjusted standard errors for the complex survey design, using linearization methods implemented in Stata statistical software (Stata Corp., College Station, Tex).

RESULTS

Our sample of 2,267 persons represents 213,308 HIV-infected individuals in care. Approximately one fourth were women and one half from minority racial-ethnic groups. Most were 26 to 49 years old, with only 4% aged 18 to 25, and 11% aged 50 or more. About half had a high school degree or less education. Only 17% were uninsured, while 32% had private coverage, 29% had only Medicaid, and 22% had Medicare with or without Medicaid coinsurance. At the first follow-up interview, 22% had a lowest CD4 count below 50 $\times$ 10^9/L and 8% had a lowest reported CD4 cell count above 500 $\times$ 10^9/L. Injection drug use was the HIV transmission risk for 24%. Ninety percent of the study population reported any antiretroviral therapy between the first and second follow-up interviews, corresponding to the second half of 1997 (Table 1). Monotherapy was rare (3%), but about one quarter of the sample reported taking a non-HAART combination and 61% took HAART.

Nearly half reported substance abuse, but only 9% reported drug dependence in the 12 months preceding the first follow-up interview. One third reported abusing only marijuana while at least 10% abused analgesics, sedatives, or cocaine, respectively. Heroin or hallucinogen abuse was rare. Not shown, the total number of drugs abused was: 1 (23%), 2 (13%), 3 (4%), or 4 or more (6%). Approximately one quarter had a "low" drug abuse severity score of 1 or 2, indicating neither cocaine nor heroin abuse, while 10% received a "high" score of at least 5 (i.e., multiple substance abuse). Problem drinking (i.e., $\geq$5 glasses on at least one day[28]) was reported by about 15%. Only 13% reported any treatment for drug or alcohol abuse between baseline and first follow-up interviews.

Severity of drug abuse was positively associated with drug dependence; 41% of persons with high severity abuse (i.e., a score of $\geq$5) were dependent versus 6% for low severity or no abuse ($P < .001$). A history of injection

Table 1. Bivariate Associations Between Self-reported Illicit Drug Use-related Factors from Baseline to First Follow-up Interview and Antiretroval Treatment from First to Second Follow-up Interview

Factor*	Unweighted, *n*	Weighted, %	ART Treatment, %†		
			No ART Use	ART Therapy (not HAART)	HAART Use
Total population (*N* = 2,267)		100	10.1	29.0	60.9
Any drug abuse‡					
No	1,228	54	9.2	31.8	59.1
Yes	1,039	46	11.2	25.6	63.2
Any drug dependence‖					
No	2,050	91	9.0	29.3	61.7
Yes	214	9	20.5	25.7	53.8
Abused cocaine§					
No	1,988	89	9.3	29.1	61.7
Yes	279	11	16.1	28.6	55.3
Abused heroin§					
No	2,207	98	9.8	29.1	61.2
Yes	60	2	24.4	23.7	51.8
Abused analgesics					
No	1,982	90	9.5	29.8	60.7
Yes	285	10	14.3	23.2	62.5
Abused sedatives					
No	2,010	88	9.7	29.8	60.6
Yes	257	12	13.9	22.0	64.1
Abused amphetamines‖					
No	2,095	93	9.6	29.9	60.6
Yes	172	7	17.0	17.4	65.6
Abused marijuana					
No	1,530	68	9.8	30.0	60.2
Yes	737	32	10.8	26.8	62.4
Abused inhalants					
No	2,098	92	10.2	29.3	60.5
Yes	169	8	9.1	25.1	65.8
Abused hallucinogens					
No	2,222	98	10.0	29.3	60.7
Yes	45	2	14.8	11.7	73.5
Drug abuse severity score‡					
0	1,329	54	9.1	31.8	59.1
1	399	17	9.8	27.2	63.0
2	151	7	8.2	22.1	69.7
3	207	9	9.0	26.1	64.9
4	114	4	8.7	29.9	61.5
5+	265	10	18.6	23.3	58.1
HIV exposure from injection drug use§					
No	1,736	76	8.8	28.7	62.5
Yes	531	24	14.4	29.7	55.9
Alcohol use (past 4 weeks)					
Did not drink alcohol	1,085	48	10.4	29.1	60.6
<5 glasses	804	36	8.5	30.7	60.8
5 or more glasses on 1–4 days	245	11	13.2	23.2	63.6
5 or more glasses on ≥5 days	129	6	12.0	28.5	59.5
Drug/alcohol abuse treatment					
No	1,972	87	10.0	28.1	61.9
Yes	294	13	10.9	34.1	55.0

* *Drug abuse and drug dependence assessed in the past 12 months and alcohol use assessed in the past 4 weeks.*
† *Entries in columns 3–6 are row percentages. Analyses conducted on weighted data.*
‡ $P < .05$.
§ $P < .01$.
‖ $P < .001$.

drug use was more common in persons with recent drug dependence (48 vs 22% of nondrug dependent persons, $P < .001$), and among those with high severity abuse (42 vs 22% of low severity users, $P < .001$). The overall pattern of antiretroviral use (i.e., none, non-HAART, or HAART) was significantly associated with recent drug abuse, severity of drug abuse, drug dependence, and HIV transmission from injection drug use (Table 1). In all

these groups, no treatment was more likely than in persons without these behaviors. Drug dependent persons, cocaine or heroin abusers, and persons with an injection drug use history were less likely to receive HAART, as were persons attending a 12-step or self-help program. HAART use was substantially higher for persons abusing amphetamines.

A probable mental disorder in the past year, most commonly depression or dysthymia, was identified for 38%; one fifth had more than one mental disorder (Table 2). One fourth received some mental health treatment. Probable mental disorders were more common among drug dependent than nondependent persons (64% vs 35%, $P < .001$) or those with high severity drug abuse (52% vs 36%, $P < .001$) (data not shown). Antiretroviral treatment status was significantly associated with any mental disorder and (nonlinearly) with the number of disorders. For specific disorders, any antiretroviral therapy was less likely for persons with dysthymia and generalized anxiety disorder (GAD). HAART use was more likely for persons with GAD or all four mental disorders.

Controlling only for sociodemographic and clinical factors, persons with drug dependence had 60% lower adjusted odds of any antiretroviral therapy (Table 3). In separate adjusted models, previous cocaine, heroin, sedative, or amphetamine abuse also showed significant negative associations with antiretroviral treatment. The adjusted odds of antiretroviral therapy dropped by 12% for each unit increase in the drug severity score. HIV transmission from injection drug use reduced the odds of antiretroviral therapy by 50%. No factor was negatively associated with HAART use among persons receiving antiretroviral therapy, but amphetamine and hallucinogen abuse showed positive effects. Problem drinking was not associated with antiretroviral therapy use or type of treatment among users.

Mental health factors showed weaker adjusted associations than observed for drug abuse-related factors (Table 4) but dysthymia was associated with nearly a 26% reduction in the adjusted odds of antiretroviral treatment and mental health treatment associated with nearly a 30% reduction. On the other hand, the adjusted odds of HAART among persons on antiretroviral therapy were 31% higher for those with any mental disorder and 51% and 61% higher for those in mental health care or with GAD, respectively.

To assess associations adjusting for both types of factors, we estimated logistic regression models including the summary variables in Table 5. The drug abuse-related variables continued to show strong negative effects on use

Table 2. Bivariate Associations Between Mental Disorders from Baseline to First Follow-up Interview and Antiretroviral Treatment Between First and Second Follow-up Interviews

			ART Treatment, %†		
Factor*	Unweighted, *n*	Weighted, %	No ART use	ART Therapy (not HAART)	HAART use
Any mental disorder‡					
No	1,388	62	9.6	31.0	59.4
Yes	879	38	11.0	25.6	63.4
Depression					
No	1,618	72	9.6	30.0	60.4
Yes	649	28	11.3	26.3	62.4
Dysthymia‡					
No	1,810	80	9.2	29.4	61.5
Yes	457	20	13.8	27.4	58.8
Panic disorder					
No	2,055	91	10.2	28.8	61.0
Yes	212	9	8.8	30.8	60.4
Generalized anxiety disorder‡					
No	2,015	89	10.0	29.9	60.1
Yes	252	11	11.4	20.9	67.7
Number of mental disorders§					
0	1,388	62	9.6	31.0	59.4
1	430	18	9.0	23.6	67.4
2	258	12	12.5	30.1	57.4
3	140	6	14.9	18.3	66.9
4	51	2	8.4	41.0	50.5
Visited mental health provider‡					
No	1,654	74	9.6	31.1	59.3
Yes	613	26	11.7	22.8	65.5

* *Mental health treatment in the 12 months prior to first follow-up interview.*

† *Entries in columns 3–6 are row percentages. Analyses conducted on weighted data.*

‡ $P < .05$.

§ $P < .01$.

Table 3. Adjusted Odds for Each Drug and Alcohol Abuse Factor Entered Separately in Multivariate Models Predicting 2 Outcomes Including Antiretroviral Therapy (ART) and HAART Among ART Users

	Adjusted Odds Ratio (95% CI)†	
Factor*	ART vs None	HAART vs Non-HAART
Any drug dependence	0.40‖ (0.27 to 0.59)	1.01 (0.72 to 1.40)
Any drug abuse	0.71 (0.49 to 1.03)	1.21 (0.92 to 1.59)
Abused cocaine	0.52‖ (0.37 to 0.73)	0.94 (0.70 to 1.27)
Abused heroin	0.40§ (0.22 to 0.72)	1.11 (0.52 to 2.37)
Abused analgesics	0.66 (0.37 to 1.17)	1.27 (0.89 to 1.80)
Abused sedatives	0.54§ (0.36 to 0.83)	1.25 (0.71 to 2.19)
Abused amphetamines	0.42‖ (0.27 to 0.65)	1.52‡ (1.03 to 2.24)
Abused marijuana	0.75 (0.53 to 1.05)	1.02 (0.84 to 1.22)
Abused Inhalants	1.11 (0.59 to 2.08)	1.09 (0.72 to 1.67)
Abused hallucinogens	0.53 (0.12 to 2.27)	2.65‡ (1.13 to 6.25)
Drug/alcohol abuse treatment	0.94 (0.64 to 1.37)	0.78 (0.55 to 1.10)
Drug abuse severity score (linear)	0.88‖ (0.83 to 0.93)	1.03 (0.97 to 1.10)
Severe drug abuse (score = 5+)	0.38‖ (0.24 to 0.58)	1.09 (0.72 to 1.66)
Injection drug use HIV exposure	0.50‖ (0.38 to 0.66)	0.94 (0.69 to 1.27)
Alcohol use		
<5 glasses	1.20 (0.59 to 1.52)	0.83 (0.66 to 1.06)
>5 glasses on 1–4 days	0.83 (0.49 to 1.38)	1.18 (0.91 to 1.52)
>5 glasses on 5 or more days	0.94 (0.59 to 1.52)	0.95 (0.62 to 1.45)

** Drug abuse, drug dependence, and drug and mental health treatment assessed in the past 12 months while alcohol use assessed in the past 4 weeks before the first follow-up interview.*
† Weighted analyses of any ART based on entire sample (unweighted N = 2,245, dropping 22 cases with missing data); analyses of HAART versus other ART based only on those receiving some ART (unweighted N = 2,013). Entries are adjusted odds ratios for each variable entered separately in a logistic regression model, controlling for gender, race/ethnicity, age, education, insurance, lowest CD4 cell count, AIDS diagnosis, clinical trial participation, and receipt of any outpatient visits.
‡ P < .05.
§ P < .01.
‖ P < .001.

of antiretroviral therapy, but mental disorders had no significant effects. Drug and/or alcohol treatment was positively, but not significantly, related to receipt of antiretroviral therapy. Conversely, mental health care was negatively, but nonsignificantly, associated with receipt of any antiretroviral therapy.

Among persons reporting antiretroviral therapy, adjusted odds of HAART were 52% greater for those with mental health care. Any probable mental disorder was associated with higher adjusted odds of receiving HAART, but the confidence limits cross one. Additional analyses (not shown) examining specific mental disorders indicated that GAD was positively associated with HAART (AOR 1.47; 95% CI, 1.03 to 2.11). Drug and alcohol abuse treatment is unrelated to HAART among persons on any form of antiretroviral therapy.

To check that we did not miss important associations in our "continuation-ratio" logit analysis approach, we re-estimated the HAART model for the entire study sample, comparing HAART to no or non-HAART treatment. Results were similar, except that mental health care had a slightly weaker effect (AOR, 1.33; 95% CI, 1.01 to 1.75). Our conclusions also did not change in analyses repeating the models in Table 5 excluding persons who might not have been candidates for treatment because they never had a CD4 cell count under 500 (8%). Finally, no significant

Table 4. Adjusted Odds for Each Mental Health Factor Entered Separately in Multivariate Models Predicting 2 Outcomes Including Antiretroviral Therapy (ART) and HAART Among ART Users

	Adjusted Odds Ratio (95% CI)†	
Factor*	ART vs None	HAART vs Non-HAART
Any mental disorder	0.88 (0.70 to 1.11)	1.31‡ (1.05 to 1.63)
Depression	0.86 (0.66 to 1.11)	1.12 (0.86 to 1.47)
Dysthymia	0.74‡ (0.58 to 0.95)	1.12 (0.84 to 1.48)
Generalized anxiety disorder	0.97 (0.62 to 1.50)	1.61‡ (1.12 to 2.33)
Panic disorder	1.15 (0.67 to 1.98)	0.93 (0.68 to 1.29)
Number of psychiatric disorders (linear)	0.93 (0.83 to 1.05)	1.08 (0.96 to 1.21)
Mental health provider care	0.71‡ (0.52 to 0.98)	1.51§ (1.13 to 2.01)

** Mental health treatment assessed in the past 12 months.*
† Weighted analyses of any ART use based on entire sample (unweighted N = 2,245, dropping 22 cases with missing data); analyses of HAART versus other ART based only on those receiving some ART (unweighted N = 2,013). Entries are adjusted odds ratios for each variable entered separately in a logistic regression model, controlling for gender, race/ethnicity, age, education, insurance, lowest CD4 cell count, AIDS diagnosis, clinical trial participation, and receipt of any outpatient visits.
‡ P < .05.
§ P < .01.
‖ P < .001.

Table 5. Adjusted Odds Associated with Illicit Drug Use and Mental Health Factors in Multivariate Models Predicting 2 Outcomes Including Antiretroviral Therapy (ART) and HAART Among ART Users

	Adjusted Odds Ratio (95% CI)†	
Factor*	ART vs None	HAART vs Non-HAART
Drug dependence (past 12 months)	0.58‡ (0.34 to 0.97)	0.96 (0.64 to 1.43)
Severe drug abuse	0.52‡ (0.32 to 0.87)	1.10 (0.71 to 1.70)
HIV transmission: injection drug use	0.55§ (0.39 to 0.79)	0.97 (0.68 to 1.38)
Drug/alcohol abuse treatment	1.41 (0.83 to 2.41)	0.72 (0.50 to 1.05)
Any mental disorder	1.10 (0.85 to 1.42)	1.19 (0.95 to 1.50)
Mental health provider care	0.76 (0.55 to 1.05)	1.52§ (1.11 to 2.08)

* *Drug abuse severity, drug dependence, mental disorders, drug/alcohol abuse treatment and mental health treatment assessed in the past 12 months before the first follow-up interview. Entries are adjusted odds ratios, controlling for gender, race/ethnicity, age, education, insurance, lowest CD4 cell count, AIDS diagnosis, participation in clinical trials, and prior receipt of any outpatient visits.*

† *Weighted analyses of any ART based on entire sample (unweighted* N *= 2,245, dropping 22 cases with missing data); analyses of HAART receipt based only on those receiving some combination therapy (unweighted* N *= 2,013). Reference groups: no drug dependence, low (<5) drug use severity, HIV transmission category—other than injection drug use, no drug treatment, no mental disorder, and no mental health provider visit.*

‡ $P < .05$.

§ $P < .01$.

‖ $P < .001$.

interactions appeared between any probable mental disorder and severe drug abuse or drug dependence that would have an increased likelihood of no antiretroviral treatment for persons with dual mental and drug abuse disorders. Moreover, depressed persons without any recent drug abuse did not differ significantly from drug abusers (with or without depression) in receipt of any treatment or use of HAART (data not shown).

DISCUSSION

About one third of our national sample of HIV-infected persons in care, representing approximately 70,000 persons, reported recent severe drug abuse, drug dependence, or HIV exposure from injection drug use. Each of these drug abuse-related characteristics was independently associated with more than a 40% reduction in the adjusted odds of self-reported antiretroviral therapy. The negative effect of these factors remained after excluding persons with a high CD4 cell count ($>500 \times 10^9$/L) who might not have warranted treatment according to expert guidelines.[11] Similarly, nearly half of a Baltimore cohort of HIV-infected drug users and 40% of drug users in Vancouver reported no recent antiretroviral therapy in interviews conducted in 1996–1997.[5,19]

Substance abuse treatment programs with supplemental services may enhance access to HIV care.[20] Drug users in Vancouver who were not currently in drug or alcohol treatment had lower adjusted odds of antiretroviral therapy than those in treatment.[19] The adjusted odds of antiretroviral therapy were over 2-fold higher among HIV-infected pregnant women in methadone treatment than in nondrug users.[21] HAART was significantly less likely for out-of-treatment drug users in a study where physicians admitted that concern about adherence is a key barrier to prescribing HAART.[22] Physician concerns about drug users' adherence may be reduced when these individuals are in substance abuse treatment. In our final model, drug and/or alcohol treatment was associated with approximately a 40% increase in the adjusted odds of any antiretroviral therapy, but this association did not achieve statistical significance. Because the HCSUS sample is drawn from HIV-infected persons receiving ongoing care for HIV, the effect of receiving substance abuse treatment may be muted compared to samples of drug users not in longitudinal HIV care.

Persons who reported injection drug use as their HIV transmission risk had lower adjusted odds of antiretroviral therapy, even though 54% denied recent drug abuse in the interview. A national sample of specialists in infectious diseases denied considering former injection drug use negatively in their decision to prescribe HAART, although current heroin abuse or heavy alcohol use weighed "very much" against prescribing HAART.[23] One explanation for our results is that providers are inaccurate in distinguishing former from current users. Another possibility is that some respondents misrepresented their current drug abuse and were in fact still using. However, concerns about adherence for former drug users not in treatment may be unwarranted. In a cohort of post-partum HIV-infected women, prior drug users not in current methadone treatment were more likely to adhere to antiretroviral therapy than nondrug users.[24]

In our sample, drug abuse-related variables were not associated with HAART among patients taking antiretroviral therapy, suggesting that factors weighing against prescribing HAART may actually prevent the provider from prescribing any antiretroviral therapy at all. Alternately, patients might have refused treatment. A strong provider-patient relationship is associated with a lower refusal rate for antiretroviral therapy.[25] More studies are needed to distinguish provider- from patient-related reasons for the failure of 10% of patients in our population-based sample to receive antiretroviral therapy.

The instruments that we used to identify substance abuse and mental health disorders were selected in part to minimize respondent burden during the long HCSUS

interviews. To evaluate drug abuse, we used questions adapted from Phin et al.[14] instead of a more lengthy but discriminating instrument such as the Addiction Severity Index.[26] This approach may have failed to identify some drug users, but still revealed strong associations for the subset meeting this measure of severe drug abuse or dependence.

Problem drinking (i.e., more than 5 drinks on one occasion in the past 4 weeks) was not associated with a lower probability of receiving antiretroviral therapy after adjustment for diverse patient demographic and clinical factors. When we focused on the subset (6%) acknowledging frequent heavy drinking (i.e., $\geq$5 drinks on $\geq$5 occasions), we still did not find an association with antiretroviral treatment, even though it has been associated with poor adherence.[27] To assess alcohol use, we asked quantity/frequency questions. Had we used an alternative screener for alcohol problems such as AUDIT or MAST,[28] we might have improved our ability to define a group of alcohol abusers whose access to antiretroviral therapy was more compromised. However, as noted above, HCSUS may exclude many alcohol dependent HIV-infected persons not in ongoing care.

Over one third of our population had a recent probable mental disorder based on the CIDI-SF, our screening instrument.[17] Of the mental disorders studied, only persons with probable dysthymia had significantly lower adjusted odds of any antiretroviral treatment. Given the prevalence of dysthymia in this sample (20%), our data suggest that clinicians need to recognize that it may pose potential barrier to treatment. We were surprised that depression was not associated with either any antiretroviral treatment or HAART, because it is often associated with poor adherence.[29–31] However, specialists in infectious diseases considered depression much less important than substance abuse when deciding not to treat patients with HAART.[23]

The psychometric properties of the CIDI-SF are less well studied than the full CIDI.[32] The CIDI-SF compared favorably with an 8-item Center for Epidemiological Studies Depression Scale in regard to its association with physician-diagnosed depression and psychiatric treatment in an elderly population.[33] But the CIDI-SF can only identify probable mental health disorders and might have detected a less severely impaired group. We did not assess severe mental disorders such as psychosis, despite their likely impact on antiretroviral therapy use, because of the rarity of these conditions in persons with established HIV care.

The lack of an independent association of most mental disorders with treatment may be due in part to high prevalence of these conditions in drug users.[9,34] Another study of HIV-infected drug users also found a similar prevalence of depression or dysthymia (33%) to that in our subjects.[35] Because these conditions are common in drug users, we might not have been able to distinguish the effects of substance abuse and measured mental health conditions in fully adjusted models. We did not detect any interactions suggesting that mental disorders represented an additional barrier to antiretroviral treatment of drug users. On a positive note, we found that patients who had recently received mental health care were over 50% more likely to report taking HAART even after adjusting for other possible confounders.

Several limitations should be noted. Our data come from self report, which may be subject to recall bias. Second, drug abuse/dependence and mental disorders were assessed in a 12-month period before the interval when we evaluated antiretroviral treatment. Although we believe this approach reduces confounding with the effects of concurrent HIV-related treatment, these behaviors and conditions might have increased or diminished as barriers by the time that we evaluated treatment. Third, we did not report the associations of patient sociodemographic characteristics with HAART because these appear in a related HCSUS paper.[36] After adjustment, only lack of insurance (AOR, 0.71; CI, 0.53 to 0.95) was negatively associated with receiving HAART in that analysis. Finally, we did not find large effects. For example, the adjusted odds ratio of 0.58 for drug dependence translates into a probability of any antiretroviral treatment of 0.86 for drug dependent persons versus 0.91 for those who were not.

This study should be viewed as a contribution to the complex challenge of sorting out the relative effects and potential interventions of substance abuse and mental health factors to effective treatment for HIV. The study results are strengthened by our analysis of a nationally representative, large sample using uniformly collected data. Our data indicate that, to increase receipt of these life-prolonging medications, the health care system must focus particularly on HIV-infected persons with recent severe drug abuse or dependence as well as on those with a more distant history of injection drug use. Fortunately, mental health treatment appears to facilitate access to HAART.

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