

Factors Associated With Antiretroviral Therapy Adherence and Medication Errors Among HIV-Infected Injection Drug Users

Julia H. Arnsten, MD, MPH,* Xuan Li, MS,* Yuko Mizuno, PhD,† Amy R. Knowlton, MPH, ScD,‡
 Marc N. Gourevitch, MD, MPH,§ Kathleen Handley,|| Kelly R. Knight, MEd,¶
 and Lisa R. Metsch, PhD# for the INSPIRE Study Team

Background: Active drug use is often associated with poor adherence, but few studies have determined psychosocial correlates of adherence in injection drug users (IDUs).

Methods: Of 1161 Intervention for Seropositive Injectors—Research and Evaluation study enrollees, 636 were taking antiretrovirals. We assessed self-reported adherence to self-reported antiretroviral regimens and medication errors, which we defined as daily doses that were inconsistent with standard or alternative antiretroviral prescriptions.

Results: Most subjects (75%, n = 477) self-reported good ($\geq 90\%$) adherence, which was strongly associated with an undetectable viral load. Good adherence was independently associated with being a high school graduate, not sharing injection equipment, fewer depressive symptoms, positive attitudes toward antiretrovirals, higher self-efficacy for taking antiretrovirals as prescribed, and greater sense of responsibility to protect others from HIV. Medication errors were made by 54% (n = 346) and were strongly associated with a detectable viral load and fewer CD4 cells. Errors were independently associated with nonwhite race and with depressive symptoms, poorer self-efficacy for safer drug use, and worse attitudes toward HIV medications.

Conclusions: Modifiable factors associated with poor adherence, including depressive symptoms and poor self-efficacy, should be targeted for intervention. Because medication errors are prevalent and associated with a detectable viral load and fewer CD4 cells, interventions should include particular efforts to identify medication taking inconsistent with antiretroviral prescriptions.

Key Words: adherence, antiretrovirals, HIV, injection drug use, medication errors

(*J Acquir Immune Defic Syndr* 2007;46:S64–S71)

During the past decade, largely as a result of potent antiretroviral regimens, HIV has transformed from rapidly progressive and universally fatal to a chronic and often stable disease. Although early antiretroviral regimens involved large pill burdens and complex dosing schedules, improvements in these regimens have made HIV medication adherence similar to adherence in other asymptomatic diseases that require lifelong therapy, such as diabetes and hypertension.¹ Because of the unique nature of HIV's pathogenesis, however, realizing the full clinical benefit of antiretroviral therapy still requires strict adherence. Poor antiretroviral adherence may result not only in reduced treatment efficacy from increased viral replication but in the selection of drug-resistant HIV strains. The development of viral mutations that confer medication resistance is especially concerning because it can leave HIV providers and patients with few or no effective medication options and lead to the spread of drug-resistant HIV.^{2,3} Because it is unknown exactly how much adherence is necessary to prevent the emergence of drug-resistant virus⁴ or to delay disease progression,^{5,6} near-perfect adherence remains a goal for HIV-infected patients and their health care providers.

Active drug use, particularly active cocaine use, has been associated with poor antiretroviral adherence,^{7–12} but many studies have lacked sufficient numbers of active drug users to determine correlates of adherence in active injection drug users (IDUs).^{13–15} General antiretroviral adherence behaviors among drug users have been widely studied, but detailed data about the influence of different substances of abuse (eg, cocaine vs. heroin) or patterns of use (eg, daily vs. binge use) on adherence have only recently begun to be reported.^{8,10,11,16–19} In addition, although lack of social support and depressive symptoms have been correlated with poor

Received for publication July 20, 2006; accepted August 3, 2007.

From the *Division of General Internal Medicine, Albert Einstein College of Medicine and Montefiore Medical Center, Bronx, NY; †Division of HIV/AIDS Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention, Atlanta, GA; ‡Department of Health, Behavior and Society, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD; §Division of General Internal Medicine, Department of Medicine, New York University School of Medicine, New York, NY; ||Health Resources and Services Administration Global AIDS Program, Rockville, MD; ¶Department of Medicine, University of California at San Francisco, San Francisco, CA; and the #Department of Epidemiology and Public Health, Leonard M. Miller School of Medicine, University of Miami, Miami, FL.

Supported by the Centers for Disease Control and Prevention and the Health Resources and Services Administration.

The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.

The authors report no conflicts of interest in connection with this article.

Correspondence to: Julia H. Arnsten, MD, MPH, Division of General Internal Medicine, Albert Einstein College of Medicine and Montefiore Medical Center, 111 East 210th Street, Bronx, NY 10467 (e-mail: jarnsten@montefiore.org).

Copyright © 2007 by Lippincott Williams & Wilkins

antiretroviral therapy adherence, including among drug users,^{11,20–23} little is currently known about the association of other psychosocial factors with adherence in IDUs. Such factors include self-efficacy (for disclosing drug use and for taking medications as prescribed), health-related factors (communication with medical providers, feeling in control of one's health, attitudes toward HIV medications, and self-perceived health status), sense of responsibility for protecting drug or sex partners from becoming infected with HIV, and personal empowerment.

Patient errors in antiretroviral dosing represent an understudied and potentially modifiable form of poor adherence. Little prior research on HIV medication errors has been published, and it has focused primarily on hospital-based prescribing, dispensing, or administering errors by providers, with wrong medication, wrong dose, or wrong form of the drug as the principal outcome.²⁴ Two prior studies examining medication errors by patients found significant error rates. In a study of 110 mostly college-educated and insured patients, more than half made at least 1 error in describing their antiretroviral regimen using a computer-based interview, with 14% failing to name at least 1 of their medications and 14% identifying a medication not currently prescribed.²⁵ In another study of 224 patients in France, 22% of patients and 14% of those reporting good adherence failed to identify 1 or more of their antiretroviral medications accurately in a visual recognition test.²⁶ Many prior adherence studies that have relied on self-reported adherence have calculated adherence to a self-reported regimen without assessing the accuracy of the regimen.^{27,28} In this analysis, we therefore assessed adherence to self-reported antiretroviral regimens and medication errors, which we defined as daily doses that were inconsistent with standard or any alternative antiretroviral prescriptions. Although correcting errors is a necessary step to improving adherence and medication errors may be contributing to active drug users' lower rates of successful highly active antiretroviral therapy (HAART) use,^{10,29} medication errors have not previously been studied in HIV-infected active IDUs.

The goals of this analysis were to report rates of antiretroviral adherence and medication errors and to examine their correlates among HIV-infected active IDUs. Demographic, drug use, clinical, and psychosocial factors potentially associated with adherence or medication errors were investigated. Our objective was to develop findings to inform the design of intervention strategies to address adherence among HIV-infected drug users.

METHODS

Setting and Subjects

We analyzed baseline data from the Intervention for Seropositive Injectors—Research and Evaluation (INSPIRE) study, a 4-city randomized trial of a behavioral intervention to reduce transmission risk and improve adherence and health care utilization among HIV-infected drug users.³⁰ Between 2001 and 2003, HIV-infected adults reporting recent drug injection (at least once in the previous 12 months) and sexual activity with an opposite-gender partner (at least once in the

past 3 months) were recruited for the INSPIRE study using active and passive strategies in a variety of HIV care and community venues. Participants provided blood specimens for CD4 cell count and HIV viral load testing and completed an approximately 90-minute baseline audio computer-assisted self-interview (A-CASI). All research activities were approved in advance by institutional review boards at the collaborating sites and the Centers for Disease Control and Prevention (CDC).

Adherence and Medication Errors

During the baseline A-CASI, participants were asked whether they had a current prescription for any of a regularly updated list of antiretroviral medications and whether they had taken the medication for at least 1 day during the prior month. If they were taking antiretrovirals according to this definition, adherence to each antiretroviral medication was assessed by asking first about the precise antiretroviral regimen prescribed (doses per day and pills per dose) and then about the number of pills skipped during the preceding day. Adherence during the previous day was assessed separately for each antiretroviral medication. For this analysis, a weighted 1-day self-reported antiretroviral adherence rate was calculated for each participant by averaging the individual adherence rates for each antiretroviral medication. This mean rate gave equal weight to each medication regardless of pill burden, such that 50% adherence with a medication taken in the form of 1 pill twice per day (a single skipped pill in the prior day) was weighted the same as 50% adherence with a medication taken in the form of 6 pills twice per day (6 skipped pills in the prior day). Good adherence was defined as mean overall adherence $\geq 90\%$.^{31,32}

In addition to adherence to self-reported regimens, we assessed whether the self-reported regimen (doses per day and pills per dose) the participant reported was correct or incorrect, using a broad definition of standard and alternative antiretroviral prescriptions as the reference for a correct prescription. For this analysis, reported regimens were not compared with prescriptions written by HIV providers. Instead, a participant was classified as making a medication error if he or she reported antiretroviral doses that were inconsistent with current guidelines for standard or any alternative antiretroviral regimens. For example, a participant taking lamivudine plus zidovudine and efavirenz who reported that his or her prescription for lamivudine plus zidovudine was only for administration once per day would be classified as making a medication error, because this medication is almost always prescribed to be taken twice per day. The validity of this measure of medication errors was then tested by assessing its associations with HIV viral load and CD4 cell counts.

Of 1161 INSPIRE enrollees, 636 self-reported taking antiretrovirals at baseline and are the subject of this analysis.

Independent Variables

To assess factors associated with adherence and medication errors, data were collected in 4 domains: demographic, drug use, clinical, and psychosocial. Demographic characteristics included gender, age, race/ethnicity, educational status, study city, annual income, homelessness, lifetime history of incarceration, and employment. Drug use behaviors included recent cocaine use (any form), sharing or lending needles or

equipment with HIV-negative or unknown status partners, and recent (past 6 months) inpatient treatment for substance abuse or detoxification. Clinical characteristics included time since HIV diagnosis, duration of antiretroviral treatment, baseline CD4 cell count and viral load, and whether the participant believed that antiretroviral medications increased methadone metabolism (“eat the methadone”).^{33,34} Psychosocial variables were measured using previously validated or novel scales and included communication with medical providers,³⁵ feeling in control of one’s health, self-efficacy for disclosing drug use to medical providers, attitudes toward HIV medications, self-efficacy for taking medicines as prescribed, sense of responsibility for protecting drug or sex partners from becoming infected with HIV,³⁶ depressive symptoms,³⁷ self-perceived health status,³⁸ self-efficacy for safer drug use, social support,³⁹ and empowerment.⁴⁰

To assess communication with medical providers, subjects were asked about communication using a previously validated scale.³⁵ Examples of items in this scale include “My healthcare provider or doctor...listens to me,” “...cares about me,” and “...respects me.” This scale is reverse-coded, such that higher scores signify worse communication (Cronbach $\alpha = 0.95$).

Feeling in control of one’s health was assessed using a 4-item scale developed for the INSPIRE study. Items include (1) “I keep a list of symptoms to tell my healthcare provider,” (2) “I ask my healthcare provider to explain a word that I don’t know,” (3) “I tell my healthcare provider my symptoms,” and (4) “I make and keep my appointments with my healthcare provider every 3 to 4 months.” Higher scores indicate greater feelings of control (Cronbach $\alpha = 0.63$).

Self-efficacy for disclosing drug use to providers was assessed using a 6-item scale developed for the INSPIRE study. Examples of scale items include “I can tell my healthcare provider who seems caring that I use drugs” and “I can tell my healthcare provider who seems judgmental that I use drugs.” Higher scores indicate greater self-efficacy (Cronbach $\alpha = 0.91$).

Attitudes toward HIV medications were assessed using an 11-item scale developed for the INSPIRE study. Examples of scale items include “I have been feeling better since I started taking HIV medicines” and “The side effects of HIV medicines are not as bad as I thought they would be.” Higher scores represent more positive attitudes (Cronbach $\alpha = 0.70$).

Self-efficacy for taking medicines as prescribed was assessed using a 13-item scale developed for the INSPIRE study. Examples of scale items include “How sure are you that you can or will be able to take your HIV medications exactly the way the doctor tells you to, all the time?”, “...when other people are around?”, and “...when the medicines have been making you feel bad?” Higher scores indicate greater self-efficacy (Cronbach $\alpha = 0.96$).

Participants’ sense of personal responsibility for protecting drug or sex partners from becoming infected with HIV was measured with a 7-item scale adapted from a scaled developed for another study.³⁶ Higher scores indicate greater sense of personal responsibility (Cronbach $\alpha = 0.82$).

Depressive symptoms were assessed using the 7-item depression component of the Brief Symptom Inventory (BSI),

which has demonstrated high validity and reliability,³⁷ including among HIV-infected IDUs.⁴¹ Higher scores indicate greater depressive symptoms (Cronbach $\alpha = 0.88$).

Self-perceived health status was determined by assessing self-reported limitations in the performance of activities of daily living (eg, grooming, bathing, dressing) using the 6-item Physical Functioning subscale of the Medical Outcomes Study (MOS).³⁸ This scale is reverse-coded, such that higher scores signify worse self-perceived health status (Cronbach $\alpha = 0.87$).

Self-efficacy for safer drug use was assessed using a 6-item scale developed for the INSPIRE study. Examples of scale items include “I can clean my needle after use, even if my sharing partner also has HIV,” “...even if I am using with people I don’t know,” and “...even if I am pressured by someone who is dope sick.” Higher scores indicate greater self-efficacy (Cronbach $\alpha = 0.85$).

Social support was measured using a modified version of the measure of social support in community settings developed by Barerra.³⁹ Domains measured included emotional support (ie, listen to personal problems, give advice) and instrumental or financial support (ie, help out with errands, lend money or something valuable). Higher scores indicate greater perceived social support (Cronbach $\alpha = 0.89$).

Finally, sense of personal empowerment was assessed using a 28-item scale⁴⁰ to measure perceived ability to influence one’s environment. Higher scores indicate greater empowerment (Cronbach $\alpha = 0.85$).

Statistical Analysis

We calculated frequencies for each of the independent variables. Categorical variables were expressed as proportions, and continuous variables were expressed as medians. We then examined associations between adherence and medication errors and the independent variables in univariate analyses using the χ^2 or Fisher exact test for categorical variables and the Wilcoxon test for nonnormally distributed data for continuous variables. Logistic regression models were then constructed to investigate the association of each independent variable with the dichotomous outcomes of adherence ($\geq 90\%$ vs. $< 90\%$) and medication errors. Variables that were significant in the univariate analysis at the value of $P < 0.20$ were included in the initial logistic regression models, as were the following person-level covariates: demographic variables (gender, age, race, and education), recent cocaine use, and beliefs about methadone/antiretroviral interactions. Parsimonious models were then developed through manual elimination of variables that did not significantly ($P \leq 0.10$) contribute to the model. The appropriateness of the fitted logistic regression model was tested using Hosmer-Lemeshow goodness-of-fit test. All analyses were performed with the SAS version 8.2 software package (SAS Institute, Cary, NC).

RESULTS

Study Participants

Of the 1161 participants in the INSPIRE study, 54.8% ($n = 636$) reported taking antiretroviral medicines and are described in Table 1. Most of those taking antiretrovirals were non-Hispanic black (66%), male (65%), poorly educated (56%

TABLE 1. Demographic, Drug Use, and Clinical Characteristics of INSPIRE Subjects' Self-Reporting Antiretroviral Use in 4 US Cities (Baltimore, Miami, New York, and San Francisco), 2001 to 2005 (N = 636)

Characteristic	N (%)
Male gender	414 (65)
Age >40 years	399 (63)
Race	
Non-Hispanic white	43 (7)
Non-Hispanic black	412 (66)
Hispanic	124 (20)
Non-Hispanic other	42 (7)
High school education or greater	353 (56)
City	
Baltimore	163 (26)
Miami	166 (26)
New York	177 (28)
San Francisco	130 (20)
Income (≥\$10,000)	78 (13)
Homeless during past year	174 (28)
Ever incarcerated	437 (70)
Currently employed	34 (5)
Admitted for inpatient substance abuse treatment or detoxification in past 6 months	202 (32)
Cocaine use in past 3 months	496 (78)
Shared or lent needles/equipment with HIV-negative or unknown status partners in past 3 months	151 (24)
Median duration of HIV infection (years)	9.5
Median duration of antiretroviral therapy (years)	2.4
Baseline CD4 count ≥200 cells/mm ³	399 (65)
Baseline HIV viral load <400 copies/mL	165 (27)
Belief that HIV medicines "eat" methadone	
Strongly disagree or disagree	340 (56)
Strongly agree or agree	267 (44)

did not complete high school) and had low annual incomes. More than one quarter (28%) reported having been homeless at some time in the past year, nearly all were unemployed, and 70% had ever served time in jail or prison.

Nineteen different antiretroviral medication regimens were reported in various combinations. Most (88%) were taking an antiretroviral regimen characterized as strongly recommended or as included in a list of alternative HAART regimens by the US Department of Health and Human Services guidelines in place at the time of the study,⁴² compared with only 12% taking a regimen categorized as antiretroviral therapy. The most commonly reported antiretrovirals were lamivudine plus zidovudine (43%), stavudine (32%), lamivudine (31%), and efavirenz (25%); overall 97% of subjects were taking a nucleoside reverse transcriptase inhibitor (NRTI)-containing regimen, 53% were taking a protease inhibitor (PI)-containing regimen, and 39% were taking a nonnucleoside reverse transcriptase inhibitor (NNRTI)-containing regimen.

Adherence

Most participants (75%, n = 477) who were taking antiretrovirals reported good adherence (≥90%), which was

strongly associated with having an undetectable viral load (odds ratio [OR] = 1.98, 95% confidence interval [CI]: 1.25 to 3.15). Factors associated with good adherence in univariate and multivariate analysis are listed in Table 2. In univariate analysis, 1 demographic variable (being a high school graduate), 2 drug use variables (not using cocaine or sharing needles/works with partners of unknown HIV status), 1 clinical variable (beliefs about antiretroviral/methadone interactions), and 4 psychosocial characteristics (positive attitudes toward HIV medicines, greater self-efficacy for taking medicines as prescribed, sense of responsibility for protecting others from HIV, and fewer depressive symptoms) were associated (P < 0.05) with adherence. In multivariate analysis, good adherence (P < 0.05) was associated with being a high school graduate, not believing that antiretrovirals "eat" methadone, not sharing or lending drug injection equipment with HIV-negative or unknown status partners, and all 4 psychosocial factors listed previously. In addition, we identified a significant interaction between female gender and depressive symptoms. This interaction term indicated that women with more depressive symptoms had poorer adherence than women with fewer symptoms, but the association between depressive symptoms and adherence was not observed in men. Inclusion of this term in the model did not significantly change the magnitude of the other reported associations.

Medication Errors

Medication errors (Table 3) in doses per day or pills per dose were made by 54% (n = 346) of those taking antiretrovirals and were strongly associated in univariate analysis with viral loads <400 copies/mL (OR = 0.44, 95% CI: 0.30 to 0.63) and CD4 counts >200 cells/mm³ (OR = 0.69, 95% CI: 0.49 to 0.96); they were also associated with nonwhite race; inpatient substance abuse treatment or detoxification in the prior 6 months; believing that HIV medications eat methadone; and the following psychosocial variables: worse attitudes toward HIV medications, worse self-perceived health status, lower self-efficacy for safer drug use or for disclosing drug use to providers, fewer feelings of empowerment, and more depressive symptoms. In multivariate analysis, factors independently associated with medication errors were nonwhite race, lower self-efficacy for safer drug use, worse attitudes toward HIV medications, and depressive symptoms.

DISCUSSION

In this large multisite study, an A-CASI self-reported measure of good adherence (>90%) in the past 1 day was strongly associated with having an undetectable HIV viral load. Among this sample of HIV-infected IDUs, factors independently associated with poor adherence included sharing or lending needles or other drug paraphernalia with HIV-negative or unknown status partners, negative beliefs about antiretroviral-methadone interactions, negative attitudes toward antiretroviral medications, poorer self-efficacy for taking medications as prescribed, less sense of responsibility for protecting others from HIV, and depressive symptoms. In addition, medication errors occurred in 54% of those taking antiretrovirals; were associated with a detectable HIV viral

TABLE 2. Factors Associated With Good Adherence ($\geq 90\%$) in Univariate and Multivariate Analysis (N = 636): INSPIRE Study Conducted in 4 US Cities (Baltimore, Miami, New York, and San Francisco), 2001 to 2005

	Good Adherence N = 477 N (%)	Poor Adherence N = 159 N (%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Male gender	319 (67)	95 (60)	1.36 (0.94 to 1.97)	1.28 (0.83 to 2.00)
Age >40 years	303 (64)	96 (60)	1.14 (0.79 to 1.65)	1.22 (0.79 to 1.89)
Race				
Non-Hispanic white (reference)	35 (8)	8 (5)	—	—
Non-Hispanic black	311 (67)	101 (65)	0.70 (0.32 to 1.57)	0.92 (0.37 to 2.34)
Hispanic	90 (19)	34 (22)	0.61 (0.26 to 1.44)	0.77 (0.28 to 2.11)
Non-Hispanic other	30 (6)	12 (8)	0.57 (0.21 to 1.58)	0.59 (0.18 to 1.93)
High school education or greater	280 (59)	73 (46)	1.66 (1.16 to 2.39)*	1.57 (1.03 to 2.41)*
No cocaine use in past 3 months	116 (24)	24 (15)	1.81 (1.12 to 2.93)*	1.63 (0.92 to 2.89)
Do not believe that HIV medications “eat methadone”	265 (59)	75 (48)	1.51 (1.05 to 2.18)*	1.53 (1.00 to 2.36)*
No sharing/lending needles or drug paraphernalia in past 3 months	370 (80)	98 (63)	2.36 (1.58 to 3.50)*	2.30 (1.46 to 3.62)*
Baseline CD4 count ≥ 200 cells/mm ³	312 (67)	87 (57)	1.57 (1.08 to 2.28)†	—
Baseline HIV viral load <400 copies/mL	138 (30)	27 (18)	1.98 (1.25 to 3.15)†	—
	Mean (SD)	Mean (SD)		
Positive attitude toward HIV medications	2.88 (0.40)	2.70 (0.40)	3.46 (2.09 to 5.73)*	2.04 (1.12 to 3.70)*
Higher self-efficacy for taking medications as prescribed	3.09 (0.67)	2.66 (0.70)	2.47 (1.87 to 3.25)*	2.13 (1.55 to 2.92)*
Depressive symptoms	1.95 (0.79)	2.29 (0.96)	0.64 (0.52 to 0.79)*	0.74 (0.58 to 0.94)*
Greater sense of responsibility for protecting others from HIV	4.32 (0.64)	4.01 (0.75)	1.90 (1.46 to 2.47)*	1.42 (1.04 to 1.93)*

* $P < 0.05$; † $P < 0.05$, variables not used in multivariate analysis.

load and fewer CD4 cells; and were more likely among patients with poorer self-efficacy for safer drug use, negative attitudes toward HIV medications, and depressive symptoms.

Among this list of factors associated with adherence or medication errors, certain factors are potentially modifiable and should be considered targets for adherence interventions.⁴³ Particularly important among these are depressive symptoms, which have been identified in prior studies to be associated with poor adherence^{10,11} yet are amenable to therapy if properly identified. Negative attitudes toward antiretroviral medications may be targets for health behavior change interventions⁴⁴ that involve correcting deficits in patient’s levels of health behavior-specific information and enhancing health behavior-specific motivation. Self-efficacy for healthier behaviors may also be improved through specific interventions that target complex health behavior-specific skills.⁴³ Finally, discussing beliefs about antiretroviral/methadone interactions (ie, that antiretrovirals eat methadone), although these have been substantiated by drug-drug interaction studies with some PIs and NNRTIs,³⁴ should be an integral part of any adherence intervention for drug users.

Active cocaine use has now been identified in several studies to be associated with poor adherence,^{5,7–11,17,45} but ours is one of the first studies to correlate poor adherence with other HIV risk behaviors (sharing or lending needles or other drug paraphernalia with HIV-negative or unknown status partners) or to identify new psychosocial correlates of adherence among

active IDUs. Less sense of responsibility for protecting others from HIV and sharing drug-using equipment with HIV-negative or unknown status partners may be representative of the same underlying characteristics, as also evidenced by active cocaine use and poor self-efficacy. These characteristics have been hypothesized to include coping strategies that keep one from directly addressing stressful events and allow escape from the reality of being HIV-infected.¹⁷ Greater perceived self-efficacy for taking medications as prescribed was positively associated with adherence among the participants in this study and has been shown to be negatively associated with HAART discontinuation in a recent study of IDUs in Canada.¹³ Interventions promoting health behavior-specific skills, such as perceived self-efficacy to take medication as prescribed, may help to promote adherence to and prevent discontinuation from HAART among drug users.⁴⁶

One specific negative outcome expectancy—the belief that that antiretroviral medications increase methadone metabolism (eat the methadone)—was associated with poor adherence. Outcome expectancies result from observed conditional relations between specific events (eg, taking HAART) and the outcomes the events produce (eg, requiring higher doses of methadone). Approaches to the management of negative outcome expectancies include psychoeducational adherence training providing accurate information about the conditional relations between HAART and health,⁴⁷ including the relation between certain antiretrovirals and methadone metabolism.

TABLE 3. Factors Associated With Medication Errors in Univariate and Multivariate Analysis (N = 636): INSPIRE Study Conducted in 4 US Cities (Baltimore, Miami, New York, and San Francisco), 2001 to 2005

	No Errors N = 290 N (%)	Errors N = 346 N (%)	Univariate Analysis Unadjusted OR (95% CI)	Multivariate Analysis Adjusted OR (95% CI)
Male gender	191 (66)	223 (64)	0.94 (0.68 to 1.30)	0.97 (0.67 to 1.40)
Age >40 years	186 (64)	213 (62)	0.89 (0.65 to 1.24)	0.82 (0.57 to 1.19)
Race				
Non-Hispanic white (reference)	28 (10)	15 (4)	—	—
Non-Hispanic black	187 (66)	225 (67)	2.25 (1.17 to 4.33)*	2.41 (1.17 to 4.96)*
Hispanic	48 (17)	76 (22)	2.96 (1.43 to 6.10)*	3.08 (1.38 to 6.88)*
Non-Hispanic other	20 (7)	22 (7)	2.05 (0.86 to 4.91)	2.04 (0.80 to 5.20)
High school education or greater	171 (59)	182 (53)	0.78 (0.57 to 1.07)	0.98 (0.68 to 1.40)
No cocaine use in past 3 months	68 (23)	72 (21)	0.86 (0.59 to 1.25)	0.96 (0.63 to 1.48)
Do not believe that HIV medications “eat methadone”	167 (61)	173 (52)	0.70 (0.51 to 0.97)*	0.88 (0.62 to 1.26)
Inpatient substance abuse treatment or detoxification in past 6 months	78 (27)	124 (36)	1.53 (1.09 to 2.15)*	—
Baseline CD4 count ≥200 cells/mm ³	195 (69)	204 (61)	0.69 (0.49 to 0.96)†	—
Baseline HIV viral load <400 copies/mL	99 (36)	66 (20)	0.44 (0.30 to 0.63)†	—
	Mean (SD)	Mean (SD)		
Self-perceived health status (higher = worse)	0.82 (0.52)	0.95 (0.51)	1.65 (1.22 to 2.25)*	—
Self-efficacy for disclosing drug use to provider	3.99 (0.87)	3.77 (0.86)	0.75 (0.62 to 0.91)*	—
Positive attitude towards HIV medications	2.93 (0.41)	2.76 (0.39)	0.36 (0.24 to 0.54)*	0.44 (0.28 to 0.69)*
Social support	4.09 (0.86)	3.98 (0.84)	0.85 (0.71 to 1.03)	—
Depressive symptoms	1.90 (0.78)	2.12 (0.88)	1.37 (1.13 to 1.67)*	1.35 (1.09 to 1.68)*
Personal empowerment	2.89 (0.26)	2.83 (0.27)	0.38 (0.21 to 0.71)*	—
Higher self-efficacy for safer drug use	3.64 (1.11)	3.28 (1.17)	0.76 (0.66 to 0.87)*	0.80 (0.69 to 0.93)*

*P < 0.05; †P < 0.05, variables not used in multivariate analysis.

Interventions specifically targeted for drug users help to overcome cognitive factors, such as avoidant coping or negative outcome expectancies.

Regarding medication errors, ours is one of the first studies to describe the prevalence of medication errors in a large community-based sample or to determine factors associated with such errors. Although our measure of errors relied on self-report, such errors were strongly associated with HIV viral load and CD4 cell counts, and we therefore believe that our measure was valid. Our observation that errors were associated with recent inpatient substance abuse treatment confirms that patients with unstable substance abuse should be considered at risk for medication errors and poor virologic outcomes. Because medication errors may be contributing to the disparities in HIV outcomes experienced by drug users, it is particularly important to identify errors and provide appropriate counseling to avoid them.

We also observed that participants who thought they could disclose their drug use to their HIV provider were less likely than others in the study to make medication errors. This suggests that there might be an element of enhanced patient/provider communication in these relationships that was not identified by standard measures of patient-provider communication.^{48,49} These findings also suggest that the quality of patient/provider communication affects drug-using

patients’ retention of information about their antiretroviral regimen, and therefore affects HIV virologic outcomes.

Despite its strengths, this study has some limitations. Findings derive from a sample of IDUs recruited from clinic and community sources in 4 US cities; thus, generalizations to other IDUs, especially those only newly initiating HAART, cannot be made with certainty. Additionally, the validity of self-report among drug users is a common concern, but we used computerized data collection methods that have been shown to enhance reporting of sensitive risk behaviors. The possibility of socially desirable responding bias cannot be evaluated, however. Socially desirable responding tendencies would likely result in overestimation of the proportion adherent and underestimation of the proportion making errors. The fact that both of these measures were correlated with the biologic outcomes of HIV viral load and CD4 cell count supports the validity of these self-reported outcome measures. In addition, our measure of medication errors is novel and has not been previously validated. It is possible that some of the errors we observed in reporting medications and dosage were not associated with actual errors in taking the medications. Finally, this analysis was cross-sectional; thus, causal relations cannot be established.

In conclusion, this analysis suggests several avenues for intervention. To improve antiretroviral adherence among

HIV-infected drug users, interventions should focus on (1) enhancing self-efficacy for taking medications as prescribed and (2) managing negative outcome expectancies. In addition, such interventions should work with patients to improve coping strategies and avoid drug use (specifically cocaine use) as a means of coping. To reduce medication errors, adherence interventions for IDUs should promote enhanced patient/provider communication.

ACKNOWLEDGMENTS

The INSPIRE Study Team includes the following people: Carl Latkin, Amy Knowlton, and Karin Tobin (Baltimore); Lisa Metsch, Eduardo Valverde, James Wilkinson, and Martina DeVarona (Miami); Mary Latka, Dave Vlahov, Phillip Coffin, Marc Gourevitch, Julia Arnsten, and Robert Gern (New York); Cynthia Gomez, Kelly Knight, Carol Dawson Rose, Starley Shade, and Sonja Mackenzie (San Francisco); David Purcell, Yuko Mizuno, Scott Santibanez, Richard Garfein, and Ann O’Leary (Centers for Disease Control and Prevention); and Lois Eldred and Kathleen Handley (Health Resources and Services Administration).

The authors acknowledge the following people for their contributions to this research: Susan Sherman, Roaina Marvin, Joanne Jenkins, Donny Gann, and Tonya Johnson (Baltimore); Clyde McCoy, Rob Malow, Wei Zhao, Lauren Gooden, Sam Comerford, Virginia Lo Cascio, Curtis Delford, Laurel Hall, Henry Boza, and Cheryl Riles (Miami); George Fesser, Victoria Frye, Carol Gerran, Laxmi Modali, and Diane Thornton (New York); Caryn Pelegrino, Barbara Garcia, Jeff Moore, Erin Rowley, Debra Allen, Dinah Iglesia-Usog, Gilda Mendez, Paula Lum, and Greg Austin (San Francisco); Gladys Ibanez, Hae-Young Kim, Toni McWhorter, Jan Moore, Lynn Paxton, and John Williamson (Centers for Disease Control and Prevention); and Lee Lam, Jeanne Urban, Stephen Soroka, Zilma Rey, Astrid Ortiz, Sheila Bashirian, Marjorie Hubbard, Karen Tao, Bharat Parekh, and Thomas Spira (Centers for Disease Control and Prevention Laboratory).

REFERENCES

1. Gifford AL, Groessl EJ. Chronic disease self-management and adherence to HIV medications. *J Acquir Immune Defic Syndr.* 2002;31(Suppl 3): S163–S166.
2. Descamps D, Flandre P, Calvez V, et al. Mechanisms of virologic failure in previously untreated HIV-infected patients from a trial of induction-maintenance therapy. Trilege (Agence Nationale de Recherches sur le SIDA 072) Study Team. *JAMA.* 2000;283:205–211.
3. Wainberg MA, Friedland G. Public health implications of antiretroviral therapy and HIV drug resistance. *JAMA.* 1998;279:1977–1983.
4. Havlir DV, Hellmann NS, Petropoulos CJ, et al. Drug susceptibility in HIV infection after viral rebound in patients receiving indinavir-containing regimens. *JAMA.* 2000;283:229–234.
5. Lucas GM, Chaisson RE, Moore RD. Highly active antiretroviral therapy in a large urban clinic: risk factors for virologic failure and adverse drug reactions. *Ann Intern Med.* 1999;131:81–87.
6. Bangsberg DR, Perry S, Charlebois ED, et al. Non-adherence to highly active antiretroviral therapy predicts progression to AIDS. *AIDS.* 2001;15: 1181–1183.
7. Ingersoll K. The impact of psychiatric symptoms, drug use, and medication regimen on non-adherence to HIV treatment. *AIDS Care.* 2004;16:199–211.

8. Crisp BR, Williams M, Timpson S, et al. Medication compliance and satisfaction with treatment for HIV disease in a sample of African-American crack cocaine smokers. *AIDS Behav.* 2004;8:199–206.
9. Sharpe TT, Lee LM, Nakashima AK, et al. Crack cocaine use and adherence to antiretroviral treatment among HIV-infected black women. *J Community Health.* 2004;29:117–127.
10. Arnsten JH, Demas PA, Grant RW, et al. Impact of active drug use on antiretroviral therapy adherence and viral suppression in HIV-infected drug users. *J Gen Intern Med.* 2002;17:377–381.
11. Tucker JS, Burnam MA, Sherbourne CD, et al. Substance use and mental health correlates of nonadherence to antiretroviral medications in a sample of patients with human immunodeficiency virus infection. *Am J Med.* 2003;114:573–580.
12. Howard AA, Arnsten JH, Lo Y, et al. A prospective study of adherence and viral load in a large multi-center cohort of HIV-infected women. *AIDS.* 2002;16:2175–2182.
13. Kerr T, Marshall A, Walsh J, et al. Determinants of HAART discontinuation among injection drug users. *AIDS Care.* 2005;17:539–549.
14. Cunningham WE, Markson LE, Andersen RM, et al. Prevalence and predictors of highly active antiretroviral therapy use in patients with HIV infection in the United States. HCSUS Consortium. HIV Cost and Services Utilization. *J Acquir Immune Defic Syndr.* 2000;25:115–123.
15. Escaffre N, Morin M, Bouhnik AD, et al. Injecting drug users’ adherence to HIV antiretroviral treatments: physicians’ beliefs. *AIDS Care.* 2000;12: 723–730.
16. Berg KM, Demas PA, Howard AA, et al. Gender differences in factors associated with adherence to antiretroviral therapy. *J Gen Intern Med.* 2004;19:1111–1117.
17. Halkitis PN, Kutnick AH, Slater S. The social realities of adherence to protease inhibitor regimens: substance use, health care and psychological states. *J Health Psychol.* 2005;10:545–558.
18. Cook RL, Sereika SM, Hunt SC, et al. Problem drinking and medication adherence among persons with HIV infection. *J Gen Intern Med.* 2001;16: 83–88.
19. Vlahov D, Galai N, Safaean M, et al. Effectiveness of highly active antiretroviral therapy among injection drug users with late-stage human immunodeficiency virus infection. *Am J Epidemiol.* 2005;161:999–1012.
20. Carrieri MP, Chesney MA, Spire B, et al. Failure to maintain adherence to HAART in a cohort of French HIV-positive injecting drug users. *Int J Behav Med.* 2003;10:1–14.
21. Chesney M. Adherence to HAART regimens. *AIDS Patient Care STDS.* 2003;17:169–177.
22. Broadhead RS, Heckathorn DD, Altice FL, et al. Increasing drug users’ adherence to HIV treatment: results of a peer-driven intervention feasibility study. *Soc Sci Med.* 2002;55:235–246.
23. Glass TR, De GS, Weber R, et al. Correlates of self-reported non-adherence to antiretroviral therapy in HIV-infected patients: the Swiss HIV Cohort Study. *J Acquir Immune Defic Syndr.* 2006;41:385–392.
24. Gray J, Hicks RW, Hutchings C. Antiretroviral medication errors in a national medication error database. *AIDS Patient Care STDS.* 2005;19: 803–812.
25. Bangsberg DR, Bronstone A, Hofmann R. A computer-based assessment detects regimen misunderstandings and nonadherence for patients on HIV antiretroviral therapy. *AIDS Care.* 2002;14:3–15.
26. Parienti JJ, Verdon R, Bazin C, et al. The pills identification test: a tool to assess adherence to antiretroviral therapy. *JAMA.* 2001;285:412.
27. Chesney MA, Ickovics JR, Chambers DB, et al. Self-reported adherence to antiretroviral medications among participants in HIV clinical trials: the AACTG adherence instruments. Patient Care Committee and Adherence Working Group of the Outcomes Committee of the Adult AIDS Clinical Trials Group (AACTG). *AIDS Care.* 2000;12:255–266.
28. Simoni JM, Kurth AE, Pearson CR, et al. Self-report measures of antiretroviral therapy adherence: a review with recommendations for HIV research and clinical management. *AIDS Behav.* 2006;10:227–245.
29. Kohli R, Lo Y, Howard AA, et al. Mortality in an urban cohort of HIV-infected and at-risk drug users in the era of highly active antiretroviral therapy. *Clin Infect Dis.* 2005;41:864–872.
30. Purcell DW, Metsch LR, Latka M, et al. Interventions for seropositive injectors—research and evaluation: an integrated behavioral intervention with HIV-positive injection drug users to address medical care, adherence, and risk reduction. *J Acquir Immune Defic Syndr.* 2004;37(Suppl 2): S110–S118.

31. Gill CJ, Hamer DH, Simon JL, et al. No room for complacency about adherence to antiretroviral therapy in sub-Saharan Africa. *AIDS*. 2005;19:1243–1249.
32. Arnsten JH, Demas PA, Farzadegan H, et al. Antiretroviral therapy adherence and viral suppression in HIV-infected drug users: comparison of self-report and electronic monitoring. *Clin Infect Dis*. 2001;33:1417–1423.
33. Cance-Katz EF, Rainey PM, Friedland G, et al. The protease inhibitor lopinavir-ritonavir may produce opiate withdrawal in methadone-maintained patients. *Clin Infect Dis*. 2003;37:476–482.
34. Cance-Katz EF. Treatment of opioid dependence and coinfection with HIV and hepatitis C virus in opioid-dependent patients: the importance of drug interactions between opioids and antiretroviral agents. *Clin Infect Dis*. 2005;41(Suppl):S89–S95.
35. Bakken S, Holzemer WL, Brown MA, et al. Relationships between perception of engagement with health care provider and demographic characteristics, health status, and adherence to therapeutic regimen in persons with HIV/AIDS. *AIDS Patient Care STDS*. 2000;14:189–197.
36. Wolitski RJ, Bailey CJ, O'Leary A, et al. Self-perceived responsibility of HIV-seropositive men who have sex with men for preventing HIV transmission. *AIDS Behav*. 2003;7:363–372.
37. Derogatis LR, Spencer PM. *The Brief Symptom Inventory (BSI): Administration, Scoring, and Procedural Manual*. Baltimore, MD: John Wiley; 2006.
38. Stewart AL, Greenfield S, Hays RD, et al. Functional status and well-being of patients with chronic conditions. Results from the Medical Outcomes Study. *JAMA*. 1989;262:907–913.
39. Barrera MA. A method for assessing social support networks in community survey research. *Connections*. 1980;3:8–13.
40. Rogers ES, Chamberlin J, Ellison ML, et al. A consumer-constructed scale to measure empowerment among users of mental health services. *Psychiatr Serv*. 1997;48:1042–1047.
41. Mizuno Y, Purcell D, Borkowski TM, et al. The life priorities of HIV-seropositive injection drug users: findings from a community-based sample. *AIDS Behav*. 2003;7:395–403.
42. Dybul M, Fauci AS, Bartlett JG, et al. Guidelines for using antiretroviral agents among HIV-infected adults and adolescents. *Ann Intern Med*. 2002;137:381–433.
43. Simoni JM, Pearson CR, Pantalone DW, et al. Efficacy of interventions in improving highly active antiretroviral therapy adherence and HIV-1 RNA viral load. A meta-analytic review of randomized controlled trials. *J Acquir Immune Defic Syndr*. 2006;43(Suppl):S23–S35.
44. Fisher JD, Cornman DH, Norton WE, et al. Involving behavioral scientists, health care providers, and HIV-infected patients as collaborators in theory-based HIV prevention and antiretroviral adherence interventions. *J Acquir Immune Defic Syndr*. 2006;43(Suppl):S10–S17.
45. Moss AR, Hahn JA, Perry S, et al. Adherence to highly active antiretroviral therapy in the homeless population in San Francisco: a prospective study. *Clin Infect Dis*. 2004;39:1190–1198.
46. Nieuwkerk PT, Oort FJ. Self-reported adherence to antiretroviral therapy for HIV-1 infection and virologic treatment response: a meta-analysis. *J Acquir Immune Defic Syndr*. 2005;38:445–448.
47. Godin G, Cote J, Naccache H, et al. Prediction of adherence to antiretroviral therapy: a one-year longitudinal study. *AIDS Care*. 2005;17:493–504.
48. Knowlton A, Arnsten J, Eldred L, et al. Individual, interpersonal, and structural correlates of effective highly active antiretroviral therapy use among urban active injection drug users. *J Acquir Immune Defic Syndr*. 2006;41:486–492.
49. Dawson RC, Shade SB, Lum PJ, et al. The health care experience of HIV positive injection drug users. *Journal of Multicultural Nursing and Health*. 2005;11:23–30.