Assessing HIV Treatment Adherence among Multidiagnosed Clients

Saul Laird, MSW and Ellen Krouss, MSW

Since the introduction of new HIV antiretroviral treatment combinations—highly active antiretroviral treatment (HAART)—many people with HIV have experienced remarkable success. The complexity of treatment regimens, however, remains a challenge and may undermine efficacy. These regimens involve taking multiple medications consistently and at various and frequent intervals, often tied to meals. HIV-positive people with either or both behavioral and psychosocial problems—including substance abuse and psychiatric disorders—may have particular difficulty adhering to these strict guidelines.

Erratic adherence may lead to drug resistance significantly diminishing treatment options and worsening prognosis. In addition, HIV antiretroviral treatments can have severe side effects and may damage the liver, kidneys, and other organs. If used improperly, a person may incur harm without benefit. For society, erratic adherence may result in the creation of resistant strains of HIV that could be transmitted to other people, rendering current medications useless for treating future cases. Finally, the cost of HIV treatment is expensive and, while negligible compared to an individual's health, should not be squandered through ineffective use. This article, anchored by a case study, defines the psychosocial issues clinicians should explore when considering HIV antiretroviral treatment for people with multiple diagnoses, that is, the combination of HIV and either or both psychiatric and substance abuse disorders.

The Case of Mr. J

Mr. J is a 40-year-old heterosexual man with a history of bipolar disorder and polysubstance dependence. Mr. J had a tumultuous upbringing, marred by childhood abuse and poverty. He began using and selling drugs as a teen, which escalated to injection heroin use and crack cocaine dependence, and he continues to use crack daily. Mr. J was diagnosed with HIV in 1993, while serving a sentence in state prison. Mr. J, who is impulsive and concrete, and has difficulty accepting responsibility for his actions, believes he has been dealt a “raw hand.” His psychiatric symptoms—serious depression, including two suicide attempts—contribute to a pattern of instability. However, he has also experienced brief periods of increased motivation and improved social functioning. Mr. J has a history of eviction and homelessness, although he has just secured a room at a single room occupancy (SRO) hotel and plans to spend his limited Social Security check more wisely. As a result, Mr. J’s depressive symptoms have decreased: he says he feels “upbeat and happy.”

Recently, Mr. J’s CD4+ cell count fell below 200, and his viral load rose dramatically. His physician prescribed a triple combination antiretroviral regimen three years ago but discontinued it when Mr. J had trouble regularly taking both antiretroviral and psychiatric medications. Mr. J wants to restart medication. His current medical provider, Dr. C, is considering his request, but is hesitant because of Mr. J’s unstable housing, daily crack cocaine use, and history of nonadherence. Dr. C wants Mr. J to enter a substance abuse treatment program, but Mr. J does not see his drug use as problematic.

Criteria for Treatment

According to a 2001 review of the literature on HIV medication adherence, adherence to any medical treatment is generally poor and, in terms of HIV treatment, studies have failed to consistently identify patient characteristics that predict non-adherence. The review did find that the best predictor of adherence is the initial level of adher-
Editorial: To Treat or Not To Treat
Robert Marks, Editor

In this still-new age of improved HIV antiviral treatment, there is tremendous pressure on people with HIV and their doctors to take advantage of the “miracle” drugs. At the edge of this desire, however, there is a fear that treatment may do more harm than good for the individual and for society, particularly for people with “multidiscagnoses”: HIV plus substance use, a psychiatric disorder, or both.

While side effects are a significant challenge independent of potential medication resistance, it is resistance and what has become its bigger-than-life precursor, non-adherence, that most complicate the decision to treat HIV. There is a growing, if inconclusive, literature on which factors predict HIV treatment adherence and which approaches may improve it.

In this issue of FOCUS, Saul Laird and Ellen Krouss, front-line clinicians, temper the lack of clarity in the research literature with their practical experience in the field working with multidiscagnosed clients. They apply this experience not only in their definition of the issues, but also in the way they model the role of the individual—both the person with HIV and members of his or her treatment team—in developing creative approaches to treatment decision making and adherence support.

Laird and Krouss and, in the second article in this issue, Sharon Perry and Dan Karasic, present some evidence that substance abuse and depression, for example, affect adherence. But as one study emphasizes, the best predictor of adherence to a treatment regimen is a person’s initial level of adherence to that regimen.

That says two things to me. First, adherence may be an in-the-moment thing, best determined by reviewing, as Laird and Krouss suggest, a client’s current substance abuse and psychological status, motivation, and emotional and social resources.

Second, it may be possible to “test” adherence in that moment. This is encouraging, and not only because it may compensate for what one study suggests is the propensity of doctors to overestimate their patients’ capacity to adhere. It also focuses attention beyond global assumptions and inconclusive studies, and squarely on data founded in the present and within the provider-patient relationship.

The decision of whether to prescribe HIV treatment to individuals who face substance use or psychiatric problems ultimately lies with the individual’s physician. However, the primary care provider may find that a multidisciplinary team approach—including input from mental health providers, substance abuse counselors, and nurses—can help in gathering and processing the information required to make this important decision. The team approach enables the physician to assess beyond the patient’s description of his or her history and current condition and benefits the patient by increasing social support and ongoing monitoring.

A comprehensive psychosocial assessment of current functioning can help determine whether a client will be able to follow the rigid medication instructions involved in HIV treatment. The first area to consider is whether an individual is able to care for his or her basic needs for food, clothing, and shelter. If a person is unsure

References
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where his or her next meal is coming from, for example, it is unlikely that he or she will be able to consistently take medication that must be ingested with food. Similarly, if someone is sleeping on the street, keeping track of medications—particularly those that require refrigeration—will be difficult. Mr. J is often homeless, and when he lives in a SRO, he is without basic amenities such as a kitchen or refrigerator.

Another important factor to consider is psychiatric stability. For example, one review of the literature found that across studies of people with various psychiatric diagnoses, individuals who experience depression tend to be less adherent to medication instructions. Untreated depression may result in “diminished ability to think or concentrate . . . recurrent thoughts of death . . . [and] loss of energy,” this may undermine a client’s motivation to continue treatment. Dr. C should assess whether Mr. J is currently depressed, and whether his depression might affect his motivation to take medications, and his judgment and ability to make decisions. Similarly, psychotic symptoms such as hearing voices or having delusions may impede the ability to follow complex medication instructions. Dr. C will also want to note, if Mr. J stops taking medications, whether this is a sign that depressive symptoms have become more acute.

Finally, the primary medical provider and the treatment team need to consider a client’s current substance use. According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), substance intoxication can be associated with “clinically significant and maladaptive behavioral and psychological changes” including mood lability, cognitive impairment, and impaired judgment. One client survey undertaken by the AIDS Project Los Angeles found that recreational drug use and heavy, frequent drinking are associated with non-adherence to HIV medications. The Center for AIDS Research at UCSF has also found that the correlation between non-adherence and substance use may be a “maladaptive manifestation of stress related to non-compliance.” Interviews with these individuals indicated that alcohol and drugs were being used as a means of coping with stress. In the case of Mr. J, his daily crack use is likely to significantly impair his judgment, sense of time, and ability to consistently take his medications.

Beyond current functioning, providers should consider a client’s historical functioning when deciding whether to prescribe HIV treatment. In particular, the team should assess a person’s ability to maintain stability over time. For example, although Mr. J may currently have housing, his history suggests that he may have difficulty maintaining it. If he is evicted, he will face the significant stressors of homelessness discussed above, which may further affect his level of adherence.

A client’s psychiatric history, likewise, is central to this assessment. If, for example, a client becomes suicidal and overdoses on his medications every year on the anniversary of his partner’s death, it may not be prudent to prescribe those HIV antiviral medications that could be lethal in large doses. A history of substance abuse treatment may also reveal HIV treatment barriers. For example, if repeated attempts at substance abuse treatment have been unsuccessful and a client has had a history of multiple substance abuse relapses, his or her current sobriety of two weeks may not be sufficient. Providers may require this client to sustain sobriety over a longer period, for example, 12 months. Alternately, a clinician might request that the client use a harm reduction approach that might allow for the client to decrease his or her use, while increasing the likelihood for medication adherence. Finally, the treatment team should consider how a client has managed his or her health care in the past. If for example, despite psychosocial factors, Mr. J has managed his depression by consistently taking antidepressants, as prescribed, he would probably be a good candidate for HIV antiviral treatment.

In addition to current and historical functioning, providers need to consider a client’s own treatment goals. In this context, motivation, psychological strengths, and social support are relevant. If a client is strongly motivated to overcome psychosocial deficits in order to start an HIV regimen, providers should consider giving him or her the opportunity to try. However, if a client’s motivation stems more from someone else’s desire, for instance, a medical provider or a family member, treatment will probably fail. A client’s strengths may outweigh his or her deficits. For example, if a person demonstrates good judgment or is armed with coping skills, these may balance his or her shortcomings. Lastly, social support from family, friends, or a partner is crucial to relieve stress, reduce isolation,
and provide emotional and practical support—all of which may improve treatment adherence and tolerance.

**Maximizing Treatment Success**

The decision whether to treat is based on balancing all of these factors: medical status, current and historical psychological functioning, and the client’s treatment goals. If a client’s medical condition warrants treatment, a provider should prioritize the client’s current level of functioning over his or her historical functioning, since current functioning is likely the best predictor for medication adherence. While the client’s treatment goals are central and providers should strive to help achieve them, these goals are inherently subjective. In the end, a provider has three options: prescribe HIV treatment while continuing to monitor effectiveness, postpone HIV treatment until client is able to improve his or her current functioning, or refuse to prescribe medication entirely.

To improve the likelihood of treatment success, providers may require clients to access and use relevant psychosocial supports. Among these resources are more frequent medical office visits, inpatient or outpatient substance abuse treatment, psychiatric medication, individual or group therapy, day treatment programming, case management support, housing support, money management, and case management supervision of medication administration.

Given the case of Mr. J, his long history of substance dependence, unstable housing, and unstable mental health, the team might want to recommend that Mr. J demonstrate his motivation for HIV antiviral treatment by agreeing to do something to improve his psychosocial situation. For example, Mr. J might enter a harm reduction substance abuse program to help him decrease his use. He might also undertake a psychiatric evaluation and, if he agrees to use psychiatric medication, his adherence to those drugs could be monitored to determine the prospect he might adhere to HIV medications.

Another option might be to enroll Mr. J in a comprehensive case management program in which social workers would more directly monitor his HIV medication intake. For example, in one San Francisco program, program staff administer daily doses of HIV medications to clients, and this extra medical and psychosocial support has increased the likelihood of adherence. Five months after the program opened, the results are promising: many clients have improved their living conditions, and 76 percent of the clients on HIV antiviral therapy have shown improved viral suppression.5 In cities without a formal medication adherence program, city or county social services may help coordinate patient care.

**Conclusion**

In addition to the medical and psychological issues, HIV treatment of clients with multiple diagnoses raises ethical concerns. Some people argue that everyone, regardless of whether they are able to adhere to the strict guidelines, should be given the opportunity to take HIV medications. Others believe that if a person is unable to take his medication as prescribed, not only would treatment be ineffective, but also it would needlessly subject a person to adverse side effects and long-term bodily harm, waste community resources, and potentially result in the transmission of drug-resistant and cross-resistant virus. The process of treating any client is, therefore, a balancing act: individual strengths, for example, motivation and social support, versus deficits such as substance abuse and homelessness; and a person’s inherent right to the best treatment available versus the community’s right to public health safety and efficiency.

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**Clearinghouse: Multidiagnosis and HIV Care**

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Depression, Adherence to HAART, and Survival
Sharon Perry, PHD and Dan Karasic, MD

Adherence to highly active antiretroviral therapy (HAART) has been associated with dramatic reductions in mortality as well as longer survival times for people living with HIV. The benefits of HIV combination treatment, however, are for the most part confined to more stable patient communities in industrialized countries.

Among injection drug users, African Americans, Latinos, women, and the urban poor in the United States, mortality rates continue to resemble pre-HAART levels.1 Due to complex psychosocial barriers, the urban poor living with HIV are also at greater risk of reduced adherence to HAART.2 Among the factors associated with suboptimal adherence, depressive illness may be one of the most common. This article reviews the relationship between depression and HIV, and depression and adherence.

Depression among People with HIV

Estimates vary widely, but the prevalence of depressive disorders among people with HIV may be twice as high as the prevalence among HIV-negative individuals, making depression second only to substance abuse among psychiatric diagnoses in this population. One study of almost 3,000 HIV-positive patients of medical clinics found that, within the prior year, 36 percent had major depression and 27 percent had dysthymia, a syndrome of chronic, less severe depression.3 Elevated symptoms of depression, as measured by self-report instruments, may be even more common. At an inner-city HIV clinic with 44 percent of patients diagnosed with current substance abuse, 54 percent also had a mood disorder.4 Although rates of depression are generally higher among substance users and women, in impoverished groups, sex differences may be less apparent.5

It has been estimated that 50 percent of depressive illness is undetected by primary health care providers. Symptoms of depression may be more difficult to diagnose in HIV-positive people due to overlap with symptoms of medical illness. Among the urban poor, these signs may also be complicated by affective and physical effects of stressful lives, including chronic drug use. Depending upon the stage of HIV illness, HIV-positive patients may have higher scores on the “somatic” subscales of standard depression screening interviews, indicating that some of their symptoms may be related to physical disease or side effects of medications. Careful psychiatric evaluation can identify depressive disorders that may benefit from antidepressant treatment, psychotherapy, or both.

Treatment Of Depression

Studies in HIV settings have demonstrated the efficacy of antidepressant medications, as well as different psychotherapeutic approaches, to treat major depression and dysthymia. Selective serotonin re-uptake inhibitors (SSRIs), such as fluoxetine (Prozac), and tricyclic antidepressants, including imipramine, have been most often used in clinical trials, but all commonly prescribed antidepressants can be used safely among depressed people with HIV, if providers pay attention to potentially adverse side effects and drug interactions.

Unfortunately, relatively few antidepressant trials have included individuals with multiple diagnoses or more complex social barriers to treatment. In a New York study

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5. See also references cited in articles in this issue.

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of HIV-positive, injection drug-using women, 78 percent responded to either fluoxetine or sertraline (Zoloft), but 40 percent failed to complete the trial. Investigators attributed low completion rates to a bias against antidepressants and to structural barriers, including unstable housing, lack of child care, and substance use, rather than ability to tolerate antidepressants.

**Adherence and Depression**

A number of studies have linked symptomatic depression with increased risk of HIV disease progression and mortality. In the pre-HAART era, the San Francisco Gay Men's Health Study linked the severity of depressive symptoms with declining CD4+ cell counts, progression to AIDS, and death. In one of the first post-HAART longitudinal studies, researchers found that women with chronic symptoms of depression had a two-fold increase in risk of death after controlling for declining health status over time. Intermittent depressive symptoms were also associated with mortality.

In the post-HAART era, depression may reduce survival time by decreasing medication adherence. Adherence to medication can be measured subjectively, by asking patients to report the number of pills they have taken over an interval, or objectively, either by counting the number of pills taken over spaced intervals or by using an electronic recorder placed on a pill bottle to record number of doses taken over an interval. Effective HAART is thought to require adherence levels of at least 80 percent, and levels greater than 90 percent may be necessary to maintain viral load suppression. In a variety of community studies, however, normative adherence levels tend to average 60 percent to 80 percent. In a preliminary report, the San Francisco REACH Cohort Study has reported that poor adherence, averaging around 65 percent in their sample as determined by pill count, is a significant predictor of progression to AIDS or death. Other studies have associated suboptimal adherence with various factors, including lack of stable housing, mental illness, drug use, poor health literacy, and side effects, and, consistently, with depressive symptoms.

A growing number of studies have documented a significant association between self-reported measures of depressive symptoms and poor adherence, interruption of HAART, and missed medical appointments. In addition to quality of adherence, the ability to sustain the HAART regimen continuously over extended periods of time is important to delay progression of disease. Among the urban poor, patterns of sporadic adherence and extended interruptions may be extremely common. In the San Francisco REACH Cohort Study, more than 50 percent of participants have reported at least one episode of severe depressive symptoms during the prior two years. Although subjects with elevated depression scores were as likely as others to have initiated HAART, they had significantly shorter courses of current HAART in addition to lower average pill counts. A few studies have reported a significant reduction in depressive symptoms after HAART initiation; however, no studies have looked prospectively at whether treatment of depression improves HAART adherence outcomes.

**Conclusion**

In a wide variety of populations, symptoms of depression are known to modify medical attendance or medication adherence, and use of adjunctive antidepressant therapy is increasingly common in the treatment of major chronic illness. Although the interaction of social environment, depression, and AIDS survival is complex, use of HAART can dramatically improve quality of life.

The REACH Cohort Study is currently undertaking a randomized controlled trial to evaluate whether adjunctive use of antidepressant therapy can improve HIV treatment adherence and viral load outcomes. Among the issues the study will address are acceptance and tolerance of antidepressants within the HAART regimen, adherence to antidepressants, and the role of medication support programs. Because depression may be a modifiable barrier to effective use of HIV antiviral therapies, diagnosis and treatment of depressive conditions may play a strategic role in bringing the benefits of life-saving therapies to the critical urban core of the epidemic.

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**Recent Reports**

**Drugs, Mental Disorders, and HAART Use**


Drug abuse-related factors formed a greater barrier to the use of HIV antiretroviral treatment than mental disorders, according to a large population-based probability sample of people in care for HIV disease. These factors, however, did not determine the type of therapy among individuals who did access treatment.

Of 4,042 participants selected by researchers, 2,245 individuals completed one initial and two follow-up interviews gathering information on mental disorders, substance abuse (including the “severity” of abuse, as defined by type of drug and number of different types), and self-reported HIV antiretroviral treatment. Only 10 percent reported no antiviral medication. Of those receiving treatment, 69 percent were on a highly active antiretroviral therapy (HAART) regimen, while the remaining 31 percent reported monotherapy or a non-HAART combination. Almost half of the participants reported substance abuse within the year preceding the interview. Only 10 percent, however, reported high severity drug abuse, and 9 percent reported drug dependence.

Thirty-eight percent of participants reported a probable mental disorder, with 20 percent reporting more than one mental disorder. The most common mental disorder was depression. Among drug-dependent participants, 64 percent reported a probable mental disorder, compared to 35 percent for those without dependency. Of participants with high severity drug abuse, 52 percent had mental disorders compared to 36 percent of those with lower severity abuse.

**Drug-dependent individuals, cocaine or heroin abusers, and individuals with a history of injection drug use were significantly less likely than other participants to be on HAART.**

Drug-dependent individuals, cocaine or heroin abusers, and individuals with a history of injection drug use were significantly less likely than other participants to be on HAART. Amphetamine abusers, however, reported a substantially higher use of HAART than other participants. In addition, compared to all other participants, drug-dependent individuals were 60 percent less likely and individuals who had contracted HIV from injection drug use were 50 percent less likely to receive any HIV antiviral treatment, HAART or otherwise.

**Differential HIV Treatment for Drug Users**


A large Italian study found that injection drug users with HIV are less likely to receive protease inhibitors than other people with HIV, despite free access to prescription medications provided to all Italian citizens.

Researchers recruited 815 participants enrolled in seven Italian clinical centers between October 1997 and April 1998, and scheduled for visits at six month intervals. At each visit, participants completed a patient satisfaction questionnaire. There were no significant differences in prescription rates on the basis of age, gender, homelessness, education, income, or clinical center visited. It was difficult to determine the number of patients who were offered treatment but declined.

While Italian guidelines recommend protease inhibitor regimens for people with CD4+ cell counts of less than 300, 32 percent of eligible patients did not receive these treatments. In addition to injection drug use, factors significantly associated with not receiving protease inhibitors were: having access to less information from providers, having a CD4+ cell count of greater than 200, and having early stage HIV disease.
Prescription rates might differ due to a perception by physicians that injection drug users would be less likely to adhere to the treatment—despite the U.S. National Institutes of Health Panel’s claim that no group of people can be identified as unable to adhere to HIV antiviral treatment. It is also possible that physicians reserved protease inhibitors for the most severe cases, because the limited national health care budget does not provide treatment for all eligible patients.

**HIV Nonadherence and Methadone Treatment**


A study of HIV-positive individuals beginning methadone maintenance treatment found that severity of addiction and continuing drug abuse were not significantly related to adherence to HIV antiviral treatment. Significant predictors of nonadherence included low levels of education and poor emotional functioning.

Of the 42 participants surveyed, 69 percent were men, 38 percent were White, 48 percent were African American, and 14 percent were Hispanic. The mean age was 41 years. All of the participants met criteria for opioid dependence and cocaine abuse, and had been using heroin for an average of 19 years and cocaine for 15 years. Adherence to HIV medication was self-reported weekly during the first four weeks of methadone stabilization and compared to charted medication regimens. Illicit drug use was assessed three times per week using urine screens for opiates and cocaine metabolites.

At entry into the methadone program, 36 percent of participants reported less than 80 percent adherence to their medication regimens; by the fourth week, only 14 percent reported less than 80 percent adherence. Although participants were often prescribed a range of drugs that included HIV antiviral drugs, adherence did not differ significantly by medication class. Without a no-methadone control or an objective measure of adherence, however, more research is needed to confirm these benefits.

**Refusal of HIV Treatment**

Maisels L, Steinberg J, Tobias C. An investigation of why eligible patients do not receive HAART. AIDS Patient Care and STDs. 2001; 15(4): 185–191. (Boston University; and East Boston Neighborhood Health Center.)

The most common reasons eligible HIV-positive individuals refused HIV antiviral treatment was belief that they would not adhere to complex medication regimens and that they experience adverse side effects, according to a series of patient interviews.

Researchers identified 88 community health care center patients who met the United States Public Health Service guidelines for highly active antiretroviral treatment (HAART) eligibility in 1999 (a CD4+ cell count of less than 500 or a viral load of more than 10,000). A registered nurse or administrator from the clinic reviewed medical charts and conducted structured interviews with the 28 patients who did not undergo HAART.

Nine individuals did not receive HAART because their physicians did not recommend it. For these physicians, active drug use was the most common reason for not recommending HAART after discussing it with the patient (even though other studies have shown that physicians cannot accurately predict a patient’s ability to adhere). For three of the nine patients, physicians did not even discuss the HAART option.

Of the patients who were offered HAART but declined, 44 percent said that they were not prepared for the complex regimen and 38 percent said they were afraid of side effects. Follow-up interviews found that 25 percent of the participants who had previously declined treatment had then initiated a HAART regimen; among these individuals, the most common reason for starting treatment was to ameliorate their current symptoms of HIV infection. Other reasons included physician recommendations and pregnancy.
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