Medically Eligible Women Who Do Not Use HAART: The Importance of Abuse, Drug Use, and Race

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Women are one of the fastest-growing groups infected with human immunodeficiency virus (HIV) in the United States.1 When women with HIV use highly active antiretroviral therapy (HAART), dramatic declines in morbidity and mortality have been reported.²⁻⁵ However, both patient and provider characteristics have been shown to influence HAART use in women. As we have previously shown, African American women, those with a history of injection drug use, and those currently using alcohol and illicit drugs were less likely to report initiating HAART.⁶ Additionally, women with high levels of depressive symptoms are less likely to use HAART, whereas those receiving mental health treatment are more likely to report use of HAART. Further. women receiving care from HIV specialists are more likely to receive recommended antiretroviral therapy.8

As HAART regimens become more varied and convenient, it is important to examine why women who are medically eligible for this therapy remain untreated. We report here on the prevalence and predictors of lack of HAART use in 2000–2001 among medically eligible women enrolled in the Women's Interagency HIV Study (WIHS), a cohort study of women with and at risk for HIV infection, representative of women with HIV in the United States.⁹

METHODS

Subjects

The WIHS is a longitudinal multicenter study funded by the National Institutes of Health, including 6 clinical sites: Bronx/Manhattan and Brooklyn, NY; Chicago, Ill; Washington, DC; and San Francisco and Los Angeles, Calif. After institutional review board approval, participants with or at risk for HIV were enrolled into WIHS between October 1, 1994, and November 30, 1995. Eligible

Objectives. We investigated the prevalence and characteristics of HIV-positive women who do not report highly active antiretroviral therapy (HAART) use.

Methods. We analyzed HAART use among 1165 HIV-positive participants in the Women's Interagency HIV Study.

Results. Between October 1, 2000, and March 31, 2001, 254 women with clinical indications for HAART reported not using it, 635 reported HAART use, and 276 had no clinical indications. In multivariate analysis, using crack/cocaine/heroin and a history of abuse decreased the likelihood of using HAART, whereas being White increased it.

Conclusions. One of 4 women for whom HAART was indicated reported not using HAART. Childhood sexual abuse prevention, more intensive abuse treatment, and continuing drug treatment may enhance HIV disease treatment of women. (Am J Public Health. 2004;94:1147–1151)

women were aged 13 years or older, gave informed consent, were tested for HIV infection, completed an interview in English or Spanish, and had a clinical examination and extensive laboratory testing every 6 months. The study's methodology, training, and quality assurance activities and the cohort's baseline characteristics have been reported previously.

A standardized interview-based survey was used to collect demographics; medical and psychosocial history; history of cigarette smoking; alcohol use, illicit drug use (including intravenous drugs and noninjected heroin, crack, and cocaine), and drug treatment programs; sexual history; and history of medication use and reasons for not taking medications at each 6-month visit. Participants were shown photographs of all antiretroviral medications to help increase accurate reporting. The Center for Epidemiological Studies Depression Scale measured depressive symptoms, with a score of 16 or greater indicative of a probable depressive disorder.

Women were considered to have experienced abuse if they answered affirmatively to any questions about physical, sexual, or emotional coercion. For this analysis, a history of abuse included domestic violence, defined as physical or sexual abuse or coercion by an in-

timate partner or spouse; recent abuse, defined as abuse experienced within the past year; and childhood sexual abuse, defined as sexual abuse that occurred before 18 years of age. Abuse data were not collected at the 2 California sites because of reporting requirements, which would have interfered with participant confidentiality.

WIHS recruited women from HIV care, drug treatment, HIV-testing, and sexually transmitted disease clinic programs. Each research site relates to an HIV care program, to which women are referred if they are not already in care. These comprehensive HIV programs offer obstetric and gynecologic services, and many have on-site or connections to mental health and drug treatment. The WIHS protocol specifically calls for flagging responses to survey questions requiring follow-up or referral to specialized care, particularly for illicit drug use, depression, and domestic violence. 10 This ensures that these issues are openly addressed at the end of the interview session.

HIV-1 antibody status, HIV-1 RNA, and CD4 T-lymphocyte (CD4) counts were determined at each visit. HIV-1 RNA quantitation was performed using the isothermal nucleic acid sequence-based amplification method in laboratories certified by the National Insti-

tutes of Health (NIH) Virology Quality Assurance program, and CD4 counts were determined using standard flow cytometric techniques at local laboratories certified by the NIH Quality Assurance Program. Baseline hepatitis C antibody assays were performed locally.

HAART use was determined by self-report and defined as (1) 2 or more nucleoside reverse transcriptase inhibitors (NRTIs) in combination with at least 1 protease inhibitor (PI) or 1 non-nucleoside reverse transcriptase inhibitor (NNRTI); (2) 1 NRTI in combination with at least 1 PI and at least 1 NNRTI; (3) a regimen containing ritonavir and saquinavir in combination with 1 NRTI and no NNRTIs; and (4) an abacavircontaining regimen of 3 or more NRTIs in the absence of both PIs and NNRTIs. Combinations of zidovudine (AZT) and stavudine (d4T) with either a PI or NNRTI were not considered HAART. All other antiretroviral regimens were classified as mono or combination therapy. Participants reporting no HAART use may have used the therapy at some time in the past but were not using it at the analyzed study visit.

HAART was considered to be clinically indicated among those women who reported using HAART and those women with a CD4 count less than 350 or a viral load greater than 50 000 (per the published treatment standards in use during the studied visit). ¹¹

Statistical Methods

Analysis of variance was used to test for significant differences between 3 groups of women: those using HAART, those for whom HAART was clinically indicated but who were not using it, and those for whom HAART was not indicated, in terms of a series of respondent background features. Next, multiple logistic regression analysis was used to predict lack of HAART use at study visit 13 (i.e., study visits and interviews occurring between October 1, 2000, and March 31, 2001) among all women for whom HAART was clinically indicated at any time before that study visit. Finally, to study a larger "HAART initiation window," multiple logistic regression analysis was used to model predictors of not using HAART at any of the 3 study visits 11, 12, and 13 among all women for whom

HAART was clinically indicated at study visit 10. This latter analysis was limited to women who had at least 18 to 24 months to initiate HAART, as opposed to the first analysis, in which women could have had a minimum of only 6 months for HAART initiation. As data on abuse were not available from California participants, they were not included in the multivariate analyses. We performed a χ^2 test to examine the association between current drug use and drug treatment.

RESULTS

During the October 2000 through March 2001 study visit, 1219 HIV-infected women were evaluated for their use of antiretroviral therapy. Missing data prevented classification of 54 participants. Of the remaining 1165, 635 women reported using HAART, 254 women for whom HAART was clinically indicated reported not using HAART (130 women were using no therapy, 15 were using monotherapy, and 109 were using combination therapy), and 276 women for whom HAART was not indicated reported using no therapy or mono or combination therapy. Of

the 254 women not using HAART but for whom it was indicated, 163 (64%) had been using HAART at some previous study visit. Of the total 889 women eligible for HAART, 28% reported no HAART use at this study visit.

The demographic and behavioral characteristics for these 3 groups are shown in Table 1. Women in the groups did not differ significantly in median age, in the proportions completing high school, or in having high levels of depressive symptoms. Analysis of variance indicated that a significantly lower percentage of African American women were using HAART, whereas a higher percentage of White women reported using HAART. A lower percentage of women with a history of past and current use of crack, cocaine, or heroin were using HAART. A lower percentage of women with a history of physical or sexual abuse reported using HAART. Similarly, a lower percentage of women with hepatitis C reported using HAART. A higher percentage of women with private insurance and of women currently working reported HAART use.

We performed a multivariate analysis to determine which of these factors were pre-

TABLE 1—Background Features of HIV-Positive Women by Clinical Indication and HAART Use Status (n = 1165): Women's Interagency HIV Study, October 1, 2000–March 31, 2001

	Using HAART (n = 635)	HAART Indicated, But Not Being Used (n = 254)	HAART Not Indicated (n = 276)
Median age at baseline, y	36.3	36.5	35.6
Race			
African American, %*	52	58	62
White, %*	19	12	14
Latina, %	27	27	21
High school graduate, %	65	59	64
CES-D ≥ 16, %	43	50	42
Illicit drug use			
History of crack, cocaine, or heroin use, %**	66	76	67
Current crack, cocaine, or heroin use, %***	10	20	14
Private insurance*	12	5	15
History of physical/sexual abuse, %**	72	80	80
Income < \$12 000, %*	46	37	46
Hepatitis C antibody positive, %**	37	49	40
Employed, %*	33	26	38

Note. HAART = highly active antiretroviral therapy; CES-D = Center for Epidemiological Studies Depression Scale.

^aFor this variable, n = 750 because abuse items were not included in the protocols of 2 California sites.

*P<.05; **P<.01; ***P<.001; differences significant in 1-way analysis of variance.

TABLE 2—Multiple Logistic Regression Analysis of HAART Nonuse Among Women for Whom HAART Is Clinically Indicated (After Control for Study Site^a) (N = 750): Women's Interagency HIV Study, October 1, 2000–March 31, 2001

	Odds Ratio (95% Confidence Interval)
Current crack, cocaine,	2.11 (1.17, 3.79)
or heroin use*	
History of physical	1.72 (1.07, 2.77)
or sexual abuse*	
Race	
White*	0.45 (0.22, 0.96)
African American	0.73 (0.45,1.17)
Latina	Reference
Private health insurance	0.83 (0.48,1.45)
Income < \$12 000/year	0.82 (0.52,1.28)
Depressive symptoms	0.84 (0.56,1.25)
(CES-D ≥ 16)	
Hepatitis C antibody	1.16 (0.78,1.71)
positive	
High school education	0.69 (0.46,1.02)
or more	
Living in own home	0.65 (0.38,1.13)

Note. HAART = highly active antiretroviral therapy; CES-D = Center for Epidemiological Studies Depression scale.

dictors of lack of HAART use among clinically eligible women. We controlled for high school education; income below poverty level; health insurance; any crack, cocaine, or heroin use; race; study site; age; housing status; depressive symptoms; any history of abuse; and hepatitis C infection. As shown in Table 2, current crack, cocaine, or heroin use, being non-White, and experiencing any physical or sexual abuse increased the likelihood of no HAART use among clinically eligible women. Women who used crack, cocaine, or heroin in the past year were more than twice as likely to report lack of HAART use, even when indicated (odds ratio [OR]=2.1, 95% confidence interval [CI]=1.17, 3.79). Similarly, women with a history of any physical/sexual abuse were

more than 1.5 times more likely to lack HAART (OR=1.72, 95% CI=1.07, 2.77) when clinically eligible. Finally, White women were half as likely to be non-HAART users (OR=0.45, 95% CI=0.215, 0.956).

We next examined lack of HAART use longitudinally over an 18- to 24-month period in a sample of women to determine whether other factors were predictive of HAART use in this group compared with the group studied in the cross-sectional analysis. We identified 159 women who had clinical indications for HAART in 1999 but reported no HAART use for 3 subsequent visits (a total of 18 to 24 months). We used the same multivariate model, which included race, depression, insurance, current drug use, income, hepatitis C, education, housing, abuse, and research site to determine predictors of this continued lack of HAART use (Table 3). Here, too, the model showed that being White predicted using HAART, whereas women with any physical or sexual abuse and with current crack, cocaine, or heroin use were significantly more likely to be HAART nonusers, after we controlled for all other factors.

To determine the availability of drug treatment services for women not using HAART even though it was indicated, we examined reported recent drug use and being in or on the waiting list for a drug treatment program. For the 49 women who had used drugs recently, 41 (84%) were in treatment and 8 (16%) were not in treatment. Another 105 women were in drug treatment but had not used drugs recently.

Women for whom HAART was indicated but who were using no therapy were asked to list the main reason they were not using any therapies. Only 15% reported, "My doctor did not prescribe them," whereas the rest answered that they felt too healthy, wanted to wait, were afraid of side effects, or had difficulty taking the medicines.

DISCUSSION

When queried in late 2000 and early 2001, 1 of 4 women in WIHS for whom HAART was medically indicated reported not using this therapy. Even after 5 years of continued proof of the efficacy of antiretroviral

TABLE 3—Multiple Logistic Regression Analysis Predicting Women's Clinical Eligibility for HAART But Not Using HAART for Final 3 Study Visits After Indication (After Control for Study Site^a) (n=750): Women's Interagency HIV Study, October 1, 1999–March 31, 2001

Variable	Odds Ratio (95% Confidence Interval)	
Current crack, cocaine,	2.04 (1.18, 3.60)	
or heroin use*		
History of physical	1.72 (1.10, 3.05)	
or sexual abuse*		
Race		
White*	0.45 (0.21, 0.95)	
African American	0.83 (0.46,1.50)	
Latina	Reference	
Private health insurance	0.82 (0.37,1.79)	
Income <\$12000/year	0.96 (0.55,1.70)	
Depressive symptoms	0.86 (0.51,1.45)	
(CES-D ≥ 16)		
Hepatitis C antibody	0.88 (0.52,1.49)	
positive		
High school education	0.53 (0.21,1.18)	
or more		
Living in own home	0.75 (0.36,1.57)	

Note. HAART = highly active antiretroviral therapy; CES-D = Center for Epidemiological Studies Depression Scale.

therapy, with the development of more antiretroviral agents and more convenient regimens, and greater opportunity for access to these medications, a significant number of women remained without the benefits of HAART. History of physical/sexual abuse, current drug use and non-White race were all associated with lack of HAART use.

A history of physical, sexual/childhood abuse is common in women with HIV infection, with up to two thirds reporting a lifetime experience with abuse. ^{12–14} Considering this high prevalence of abuse, our finding that women who had been abused were more than 1.5 times more likely to report not using HAART is sobering. This association of abuse and not using HAART has not been reported in previous studies. Felitti et al. ¹⁵ have shown

^aTwo of 6 sites were excluded from the analysis because they did not include abuse items in their study protocols.

^{*}P<.05.

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the association of childhood sexual abuse and other adverse childhood exposures to increased health risks for alcoholism, drug abuse, depression, and suicide, as well as to the presence in adulthood of heart disease, cancer, lung disease, skeletal fractures, and liver disease. We can now add suboptimal HIV treatment to this list.

Studies have demonstrated that women with a history of abuse characterize their relationships with medical providers as less satisfactory than women without a history of abuse. 16 They are more likely to consider the provider as judgmental, annoyed, and disrespectful and find it difficult to discuss private and emotional issues with their providers. Thus, women with a history of abuse rarely acknowledge this abuse during their medical encounters. These less than satisfactory relationships may explain in part why women with HIV and a history of abuse are more likely not to use HAART. In addition, experiences of abusive relationships may be responsible for damaged self-image, which may become an obstacle to efficacious self-care practices. Leenerts¹⁷ describes how "lingering images" of a damaged self grow out of abuse and can produce disconnection from self-care. This combination of an inability to trust health providers and the personal barriers to effective self-care associated with abuse and the sequelae of posttraumatic stress disorder may lead women to decline HAART when it is offered. It is also possible that medical providers may not offer HAART to these women because of concerns regarding emotional instability/adherence to HAART. Certainly the relationship between a woman with a history of abuse and her medical provider requires more investigation if the impact of abuse on HAART use is to be fully understood.

Our study also found that women who were current users of crack, cocaine, or heroin were twice as likely to report not using HAART when medically indicated. The relation of drug use to lack of HAART has been noted in earlier studies. ^{18–20} The need to encourage physicians to offer all patients appropriate life-extending therapy while providing resources and plans to address barriers to HIV adherence remains a pressing concern. ²¹ Although those in drug treatment programs and those with previous drug use seem to re-

spond to HAART similarly to those who have never used illicit drugs, current injection drug users and cocaine users require intensive support to adhere to HAART.^{22,23} Studies of women with both drug use and abuse consistently show poorer drug treatment outcomes and the need for more tailored and intensive dual-directed therapy.²⁴

In its 2001 discussion of health system challenges, the Institute of Medicine reported: "Some problems-such as substance abuse, AIDS, and domestic violence-are so interrelated that they appear to require a comprehensive rather than problem-by-problem approach." 25(p134) Although residential drug treatment programs for HIV-infected women are available, the pattern of drug addiction often means that women relapse even when treatment has been available. And although advocacy related to abuse and history of child sexual abuse are available, very few intensive residential treatment programs for abuse exist. Mental health services within the public sector (where most of the women with HIV get their care) are also notoriously inadequate.

The WIHS was designed to allow women to honestly report behaviors they might not otherwise disclose and to provide referrals for identified problems. The remarkably high adherence rates to study visits, more than 80% after 5 years,26 attest to the success of this approach. WIHS staff continually provide opportunities for advocacy and treatment for psychosocial problems as shown by the high percentage of drug users in treatment programs. For some women, competing priorities prevent them from choosing these options. Thus, even when an observational cohort is followed within the context of women-centered HIV comprehensive programs and is provided with advocacy and treatment referrals for domestic violence and drug use, we found a continuing significant impact of these issues on women using HAART.

Being non-White was also significantly associated with not using HAART when medically indicated. With the burden of HIV in US women borne by African Americans and Latinas, it is particularly striking to document that race remains predictive of lack of appropriate therapy.²⁷ This predictable but hardly acceptable finding cries out for more effective strategies to overcome this racial gap in

HAART use, especially considering that the primary goal of The Healthy People 2010 Initiative is to eliminate disparities in health care in our country. Recent data confirm that the average life expectancy of African Americans is 6 years less than that of Whites in the United States, with HIV infection, hypertension, diabetes, and trauma responsible for most of this disparity. People 2010 Initiative in the united States, with HIV infection, hypertension, diabetes, and trauma responsible for most of this disparity.

There are some limitations to our study. The data provided are from self-reports and not confirmed by chart review or provider surveys. We cannot tell from our database if there were other medical or nonmedical conditions that providers considered contraindications to the participants' HAART use. The first cross-sectional analysis only allowed us to evaluate HAART use in 1 time period, from 2000 through 2001, and some of these women had been using HAART in the past and discontinued their medications before the studied visit. However, in the second analysis, we evaluated data longitudinally in the subset of women who were not using HAART between 1999 and 2001, and our conclusions are strengthened by the fact that both analyses vielded similar results.

In conclusion, our study suggests that a history of childhood or adult sexual/physical abuse; current crack, cocaine, or heroin use; and racial status are important predictors of appropriate HIV medication use. Through acknowledgment of these challenges and innovative collaborations with mental health, substance use, and abuse experts, HIV providers have an opportunity to more effectively treat all women with HIV infection. But the public health community has an obligation, as well, to assist these efforts by advocating for more comprehensive drug treatment programs, new intensive residential abuse programs, and more successful childhood sexual abuse prevention campaigns.

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Contributors

M.H. Cohen conceived the study, synthesized analyses, and led the writing. J.A. Cook and D. Grey completed the analyses. M. Young, L.H. Hanau, P. Tien, A.M. Levine, and T.E. Wilson assisted with the study and interpretation of analyses. All authors helped to conceptualize ideas, interpret findings, and review drafts of the article.

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Human Participant Protection

We obtained informed consent from the participants in accordance with procedures and consent materials reviewed and approved by the committee on human experimentation at each of the collaborative institutions.

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