Crack Cocaine, Disease Progression, and Mortality in a Multi-Center Cohort of HIV-1 Positive Women

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Abstract

Background—Longitudinal associations between patterns of crack cocaine use and progression of human immunodeficiency virus (HIV-1) disease are poorly understood, especially among women. This paper explores relationships between crack use and HIV-1 disease outcomes in a multi-center cohort of infected women.

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Methods—Subjects were 1686 HIV-seropositive women enrolled at six U.S. research centers in the Women's Interagency HIV Study. Approximately 80% were nonwhite and 29% used crack during the study period. Cox survival and random regression analysis examined bi-annual observations made April 1996 through September 2004. Outcome measures included: death due to AIDS-related causes; CD4 cell count; HIV-1 RNA level; and newly acquired AIDS-defining illnesses.

Results—Persistent crack users were over three times as likely as nonusers to die from AIDS-related causes, controlling for use of highly active antiretroviral viral therapies self-reported at >=95% adherence, problem drinking, age, race, income, education, illness duration, study site, and baseline virologic and immunological indicators. Persistent crack users and intermittent users in active phases showed greater CD4 cell loss and higher HIV-1 RNA levels controlling for the same covariates. Persistent and intermittent crack users were more likely than nonusers to develop new AIDS-defining illnesses controlling for identical confounds. These results persisted when controlling for heroin use, tobacco smoking, depressive symptoms, Hepatitis C virus co-infection, and intravenous drug use.

Conclusions—Use of crack cocaine independently predicts AIDS-related mortality, immunologic and virologic markers of HIV-1 disease progression, and development of AIDS-defining illnesses among women.

Recent research suggests that cocaine may directly affect the pathobiology of HIV by causing immune alterations in different lymphocytes such as helper T cells (CD4), suppressor/cytotoxic T cells (CD8), and natural killer (NK) cells.[1] Studies show that cocaine interferes with the body's ability to defend against infection by inhibiting the effector functions of neutrophils and macrophages, and by suppressing cytokine production, decreasing operation of important immune responses.[2] Cocaine also enhances the replication of HIV in vitro.[3] Cells from chronic cocaine users more readily support HIV replication and development of AIDS-defining opportunistic infections than cells from nonusers, suggesting a direct role for cocaine in the acquisition and progression of AIDS.[2] Recently, cocaine has been shown to cause membrane permeability facilitating endothelial transmigration of infected dendritic cells across the blood brain barrier to the central nervous system.[4] There is also evidence of cocaine-mediated alteration of immune responses and host resistance due to disturbances in the balance of Th1 pro-inflammatory versus Th2 anti-inflammatory cytokines and lipid bioeffectors.[3]

Epidemiologic research confirms that crack users are at high risk for HIV infection and progression.[5-6] In a prospective study of HIV-seropositive drug users, crack use was significantly associated with progression to AIDS.[7] A study of HIV-positive current and former drug users found that active cocaine use was the strongest predictor of failure to maintain viral suppression; 13% of active users maintained suppression vs. 46% of non-users.[8] In a prospective cohort study, compared with nonusers and former users, active cocaine and heroin users experienced smaller median reductions in HIV-1 RNA and smaller median increases in CD4 from baseline, controlling for antiretroviral exposure, adherence, and socio-demographic factors.[9] Compared to nonusers, the risk of AIDS-related opportunistic conditions was greater for persistent users and intermittent users during periods of active use, with no difference during periods of abstinence.[10]

Mixed results characterize studies of drug users in exclusively female U.S. cohorts. In a multi-center cohort of HIV-positive women, injection drug use was not associated with progression to AIDS.[11] Another large multi-site cohort study found that hard drug use (i.e., cocaine, heroin, methadone, or injecting drugs) was significantly associated with AIDS-defining illnesses, but not with change in CD4, HIV-RNA, or mortality.[12] In a third multi-site cohort of HIV+ women, non-injection drug use was associated with time to AIDS-defining event but not with AIDS-related mortality.[13]

While suggestive, these studies and others focusing on injection drug use do not uniformly demonstrate a link between illicit drug use and HIV-1 disease progression.[14-17] Possible reasons include: diverse definitions of illness progression; failure to differentiate between active and nonactive users; and lack of distinction between mortality due to AIDS versus non-AIDS causes.[17] Other reasons include lack of controls for highly active antiretroviral therapy (HAART) use and adherence, and inadequate follow-up periods. We addressed all of these issues by examining patterns of crack use and their association with four distinct measures of HIV/AIDS disease progression in a multi-center cohort over an eight-and-one-half-year period during the HAART era.

METHODS

Study Population

The Women's Interagency HIV Study (WIHS) is a prospective cohort study of HIV disease progression among 2058 HIV-positive women at six consortium centers: Brooklyn, NY; the Bronx, NY; Chicago, IL; Los Angeles, CA; San Francisco/Bay Area, CA; and Washington, DC. Our analysis includes biannual observations from 4/1/96 (commercial availability of protease inhibitors) through 9/30/04.

We analyzed data from cohort members completing two or more study visits (not necessarily consecutive). All women provided institutional review board-approved written informed consent for research participation and use of their medical records. Analyses were adjusted for covariates identified in prior research as being associated with illicit drug use, HIV disease progression, and mortality both in the WIHS cohort[13,18-19] and other cohorts.[9-12, 14-16] These included age, race/ethnicity, education, income, baseline HIV-1 RNA and CD4, year of HIV+ diagnosis, and study site. We also controlled for problem drinking because of research reviewed by Cabral[3] showing that cocaine in combination with alcohol places individuals at increased risk of infection with a number of pathogens, due to additive or synergistic effects resulting in impaired immune function.

Measurements

The first marker of disease progression was time-varying CD4 T lymphocyte levels of less than 200 cells/mm^3. The second was time-varying HIV-1 RNA greater than 100,000 copies/ml. Lymphocyte subsets were determined using flow cytometry at laboratories participating in the AIDS Clinical Trials quality assurance program. Plasma HIV-RNA levels were measured using a nucleic acid sequence-based amplification technique (Organon Teknika, Durham, USA). Third, newly acquired AIDS-defining illnesses were identified through medical record review using a case file abstraction protocol for participants' primary and specialty care records described elsewhere,[20] along with respondent self-report. Conditions were defined according to the Centers for Disease Control and Prevention AIDS definition excluding the criterion of low CD4 cell count.[21] Cause of death was obtained from death certificates and the National Death Index, local death registries, hospital records, physician reports, and information from friends/relatives. Deaths were classified as AIDS-related if the cause was an AIDS-defining illness, or if the stated cause was organ failure or nonspecific infection and the CD4 cell count was below 200 cells/mm,^{3} using procedures described elsewhere.[22]

At each study visit, women reported how often they took their regimens as prescribed during the past 6 months. Responses were classified as taking all drugs as prescribed >= 95% of the time vs. < 95%. This cutoff was based on past adherence research showing that HIV-1 RNA loads of <400 copies/ml occurred 80% of the time in patients with antiretroviral adherence of >= 95%.[23] The construct validity of this measure is supported by WIHS research finding statistically significant relationships between adherence self-reports and subsequent virologic

and immunologic parameters.[24] For analysis, women were classified at each study visit as reporting HAART with >=95% adherence versus all others (i.e., non-adherent HAART use, other antiretroviral therapy use, and no therapy use).

Biannually, respondents reported the occurrence and frequency of alcohol and crack use in the past six months. Using National Institute on Alcohol Abuse and Alcoholism guidelines for women, at-risk drinking was defined as 8 or more drinks per week, and binge drinking as 4 or more drinks per day. Occurrence of either in the past six months was classified as problem drinking.

Following Lucas,[10] four patterns of use were constructed and a value was assigned to the women's reports for each visit, separately for crack and for alcohol use: 1) intermittent use with current abstinence (crack use or problem drinking reported previously with abstinence reported at the current visit), and 2) intermittent but currently active use (use reported at current visit but not all previous ones), 3) persistent use (use reported at every visit), and 4) nonuse (no reports of crack or problem drinking).

Statistical Analysis

Time to AIDS-related death and time to AIDS-defining illness were each examined using Kaplan–Meier survival analysis to test for differences in survival and hazard function according to patterns of crack use. Data from women with non-AIDS-related mortality were retained in the analysis until the date of death, when they were right-censored. Women lost to follow-up were censored at their last interview date. We used the Cox proportional hazards model to examine whether different patterns of crack use were associated with mortality and with AIDS-defining illnesses controlling for illness duration, baseline immunologic and virologic factors, use of HAART at greater than or equal to 95% adherence, socio-demographic characteristics, and study site. We used random effects logistic regression analysis (MIXOR)[25] to examine the effects of different crack use patterns on CD4 cell count and HIV-1 RNA level controlling for the same covariates. Random effects analysis modeled intrasubject associations as a Gaussian process representing an individual's propensity to develop an outcome indicating virologic, immunologic or clinical disease progression. Two random effects, for intercept and slope, fit the data better than one random effect.

RESULTS

Data from 1686 women were analyzed: 1203 (71.4%) were categorized as nonusers, 429 (25.4%) as intermittent users, and 54 (3.2%) as persistent users of crack. Their characteristics are presented in Table 1.

There were 419 deaths during the follow-up period: 197 (47.0%) were AIDS-related, 138 (33.0%) were non-AIDS related, and 84 (20.0%) were indeterminate. Time to death was assessed with a Kaplan-Meier function (Figure 1). The estimated survival rates at 8.2 years (3000 days) were 89% for nonusers, 90% for intermittent users, and 65% for persistent users (log-rank test=6.6, p<.05). In a Cox proportional hazards model (Table 2) adjusting for age, race, income, education, problem drinking, adherent HAART use, CD4 count < 200 cells/ mm^3 at baseline, HIV-1 RNA level > 100,000 copies/ml at baseline, illness duration, and study site, compared with that for nonusers, the risk of AIDS-related death was significantly higher for persistent users (hazard ratio=3.61, p<.001), but not for intermittent users.

Of the total group of 1686 women, 543 (32.2%) were found to have a newly-acquired AIDS-defining illness during the follow-up period. Significantly higher proportions of intermittent users (42.0%, n=180) and persistent users (38.9%, n=21) reported a new illness during this time period than did nonusers (28.4%, n=342) (chi square=27.6, p<.001). The most frequently

reported AIDS-defining illnesses were bacterial pneumonia (n=98, 18% of all cases), pneumocystis carinii pneumonia (n=52, 10%), herpes simplex virus-non-pulmonary (n=49, 9%), esophogeal candidiasis (n=48, 9%), cryptosporidiasis (n=30, 6%), dementia/ encephalopathy (n=27, 5%), wasting syndrome (n=27, 5%), and tuberculosis (n=20, 4%). Among these, persistent and/or intermittent users were significantly more likely than nonusers to report bacterial pneumonia (chi square=18.8, p<.001), tuberculosis (chi square=16.6, p<. 01), and esophogeal candidiasis (chi square=6.4, p<.05). Time to new AIDS-defining illness was assessed in the three groups with a Kaplan-Meier function (Figure 2). The average days to illness or censoring was 2592 days for nonusers, 2305 days for intermittent users, and 2211 days for persistent users (log-rank test=27.5, p<.001). In a Cox proportional hazards model (Table 2) the risk of AIDS-defining illness was significantly higher for intermittent crack users (hazard ratio=1.57, p<.001) and consistent users (hazard ratio=1.65, p<.05) than for nonusers, adjusting for all covariates.

Figures 3 and 4 present the unadjusted proportions over time by pattern of crack cocaine use of women with CD4 count<200 cells/mm^3, and HIV-1 RNA>100,000 copies/ml. Throughout most of the study period, those reporting persistent crack use had higher viral load concentrations and poorer immune function, while those reporting no use had the lowest HIV-1 RNA levels and best immune health, with intermittent crack users falling in between.

Table 3 presents the results of a time-varying random regression analysis of the effects of persistent and intermittent crack cocaine use on CD4 < 200 and HIV-1 RNA > 100,000. Across both models, persistent crack use, intermittent-active, and intermittent-abstinent crack use were significantly associated with HIV disease progression, controlling for adherent HAART use, problem drinking, women's socio-demographic characteristics, study site, illness duration, baseline viral load (in the CD4 model), and baseline CD4 (in the viral load model). Persistent problem drinking was positively associated with disease progression defined by high viral load but not low CD4. In both models, adherent HAART use was protective against disease progression.

We tested five additional covariates that could account for the relationship between crack use and disease progression, with the same models used in the Cox proportional hazards and random regression analyses. Results (not shown) remained highly similar controlling, separately, for heroin use, intravenous drug use, tobacco smoking, Hepatitis C virus co-infection, and depressive symptoms (using the Center for Epidemiologic Studies-Depression Scale clinical cutoff of 16).[26] The only exceptions were for intermittent-abstinent crack use, which became non-significant in the viral load models when controlling for smoking and for depression.

Finally, to explore the impact of crack use on immune reconstitution, we conducted a supplementary analysis of associations between patterns of use (nonuse, inactive use, and active use) and immunologic response. Following Lucas and colleagues,[9] for all women remaining in the cohort at the end of the study period (n=1,053), we defined change in HIV-1 RNA ($\log_{10}$ copies/ml) as the difference between the most recent viral load and peak HIV-1 RNA level, and change in CD4 as the difference between the most recent and nadir CD4 lymphocyte counts. We found that the median reduction in HIV-1 RNA level was highest in nonusers, at 1.7 $\log_{10}$ copies/ml, compared to 1.4 $\log_{10}$ copies/ml in inactive crack users and 1.0 $\log_{10}$ copies/ml in active users (F=4.94, df=2/1035, p<.01). The median CD4 increase was highest in nonusers, at 161 cells/mm^3, compared with 123 cells/mm^3 in inactive users, and 100 cells/mm^3 in active users (F=6.99, df=2/1035, p<.01). In multivariate linear regression models (not shown), active and inactive crack use remained significant after adjustment for race/ ethnicity, use of HAART, HAART adherence 95% of time, prior HAART exposure, nadir CD4 count, and peak HIV-1 RNA level. Here, compared with nonusers, active and inactive crack

users had smaller median reductions in HIV-1 RNA from baseline, and smaller median increases in CD4. These results confirm that inferior virologic and immunologic responses are associated with both active and inactive use of crack.

DISCUSSION

Ours is the first study to show that use of crack cocaine in a large, national cohort of HIV-positive women is longitudinally associated with subsequent deterioration in immune status, failure of virologic suppression, development of AIDS-defining conditions, and mortality due to AIDS-related causes, even among those who reported adhering to HAART regimens 95% of the time or more. Likely confounds such as heroin use, intravenous drug use, tobacco smoking, Hepatitis C virus co-infection, and depression do not appear to account for these significant associations, nor do socio-demographic factors, illness duration, or baseline immunologic or virologic indicators. Unlike prior research on a predominantly male sample, [10] we did not consistently find that progression was less likely during periods of abstinence among women crack users, providing support for the notion that effects of cocaine on the immune system may vary by gender, as others have suggested.[3]

Even in the face of this evidence, our analysis does not conclusively demonstrate that crack use causes AIDS-related morbidity and mortality. We have not ruled out other processes that could account for these associations, such as greater sexual risk taking, poorer diet and nutrition, substandard living conditions, and other unknown confounds.

Our findings suggest that a multi-pronged research agenda is needed to understand the effects of crack cocaine on HIV disease progression. In vivo studies can illuminate the specific role of the drug in HIV pathogenesis.[2] In vitro research, such as the human lymphocyte/SCID (huPBL/SCID) mouse model,[1] can shed light on how cocaine upregulates HIV and also acts as a co-factor in HIV pathogenesis.[4] In vitro studies of peripheral blood samples from crack users can examine alterations in T cell and dendritic cell subsets, immune function, cytokine and chemokine expression, indicating predisposition to HIV infection. Studies of alveolar macrophages from the lungs of chronic crack users can help to understand impaired cytokine production[2] and how intrapulmonary accumulation of contaminants may promote chronic lung diseases.[17] However, neither in vivo nor in vitro research can control for the complex interactions that occur in human beings with repeated exposure to crack over time, necessitating rigorous, large-scale epidemiologic studies of morbidity and mortality among HIV+ and at-risk users, and potential differences associated with frequency, quantity, and mode of administration.[17]

While prior research highlights difficulties crack users confront in using the medical care system,[27] this was not true in our cohort. At their last interview, 100% of participants reported seeing a health care provider in the past 6 months: 93% said they saw the same health care provider consistently, including 94% of persistent crack users. Related to this are the findings of a recent study of HIV-positive African Americans in which women crack users reported more positive relationships with their physicians than did male crack users.[28] Use of HAART in the WIHS cohort is significantly related to higher satisfaction with both medical care and with health care providers.[29] This is a foundation on which to build care delivery models that are effective in engaging and retaining women crack users. One recommendation is that women using crack receive sustained follow-up with periodic reevaluations of therapy regimens to promote greater use of and adherence to HAART.[30] Another suggestion is co-location of rapid HIV testing, risk reduction counseling, HIV therapies, psychiatric and substance abuse treatment, and other services to promote successful engagement and seamless access to multiple interventions.[30-31] Finally, the importance of cultural competence is paramount,

calling for diversity in clinical staff, attention to patient-provider communication, and sensitivity to the multiple vulnerabilities faced by these women.[32-33]

One caveat to our findings is the non-representativeness of our longitudinal cohort, limiting the generalizability of our results. Another study limitation is use of self-report rather than urine or toxicology screening to measure crack cocaine exposure. The same is true for self-reported measures of alcohol use, HAART use, and adherence, which may be subject to distortion due to recall errors or positive response bias. Study intervals were lengthy, number of time-points varied by participant, and respondents entered the study at different stages of illness. The use of death certificates and other administrative records to establish AIDS-related deaths, and reliance on case record review to identify AIDS-defining illnesses also introduced measurement error into our dependent variables. Finally, without direct measures of pathobiology, the effect of crack on disease progression can only be assessed using proxy variables.

The challenges involved in treating crack addiction are well documented, and include high rates of treatment drop-outs, treatment repeaters, and relapse.[34] This suggests the need for models that acknowledge crack users' diverse levels of readiness for change and recognize that work can be done, even with women who are not yet ready to alter their behavior or are just beginning to consider doing so. Helping individuals move from pre-contemplation to readiness for change requires approaches that are assertive and "strengths-based,"[35] building on low-income, minority women's intrinsic resources such as resilience and street smarts.[27,35] Finally, culturally competent care is needed to promote the trust necessary for personal risk taking that accompanies willingness to change through addiction treatment and commitment to antiretroviral regimens.[33,36]

Acknowledgements

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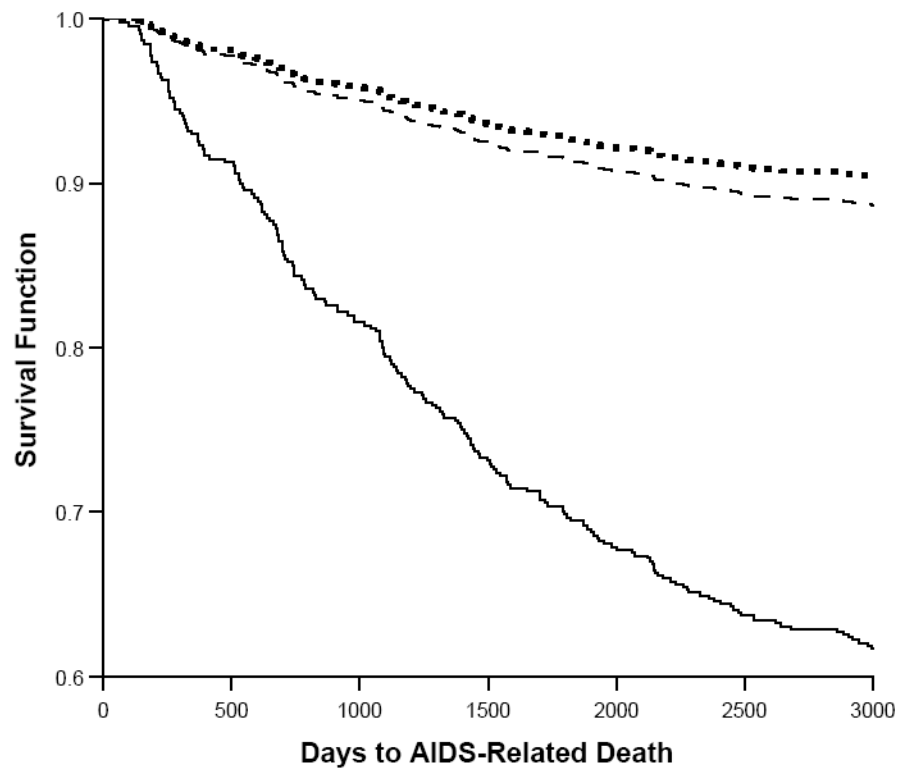
Figure 1.
Survival by patterns of crack use in a cohort of HIV-1 infected women. Compared with nonusers (dashed line), and intermittent users (dotted line), days to death for persistent crack users (solid line) was significantly shorter and survival rates significantly lower (p<.05).
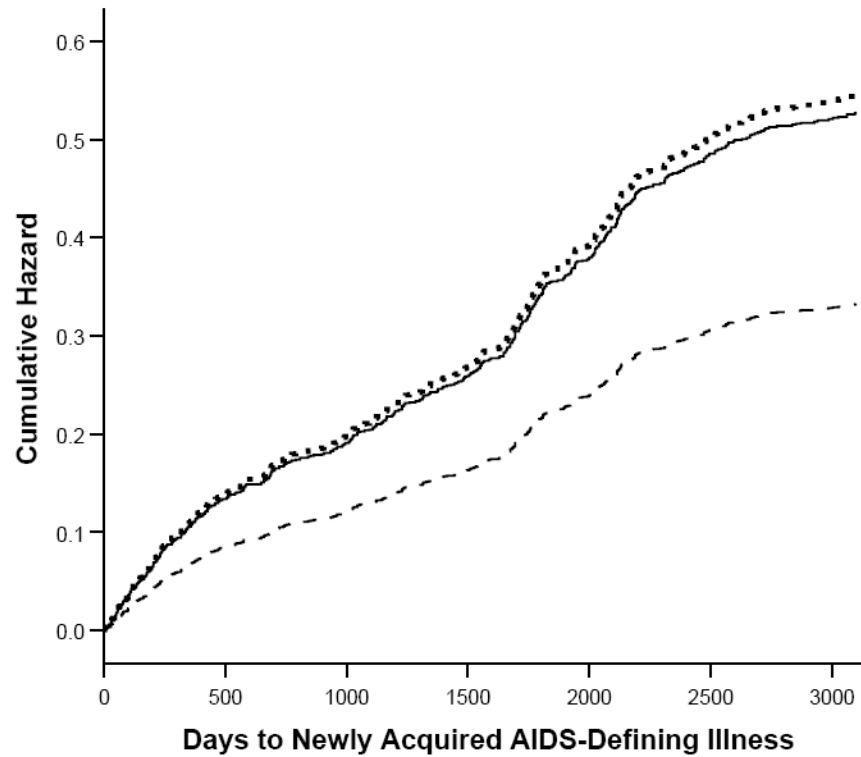
Figure 2.
Time to newly acquired AIDS-defining illness by patterns of crack use in a cohort of HIV-1 infected women. Compared with nonusers (dashed line), days to illness for intermittent users (dotted line) and persistent crack users (solid line) were significantly shorter and hazard rates significantly higher (p<.001).
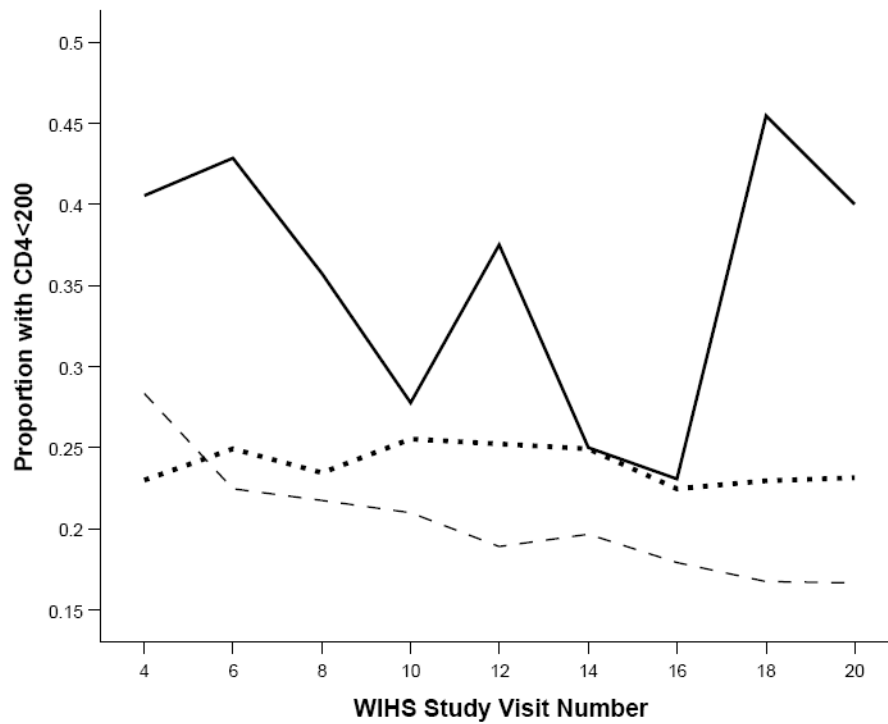
Figure 3.
Unadjusted proportions of women with CD4 lymphocyte count <200 copies/mm3 over 18
semi-annual study visits. Nonusers (dashed line) had generally lower proportions, while
persistent users (solid line) typically had the highest proportions, with intermittent users (dotted
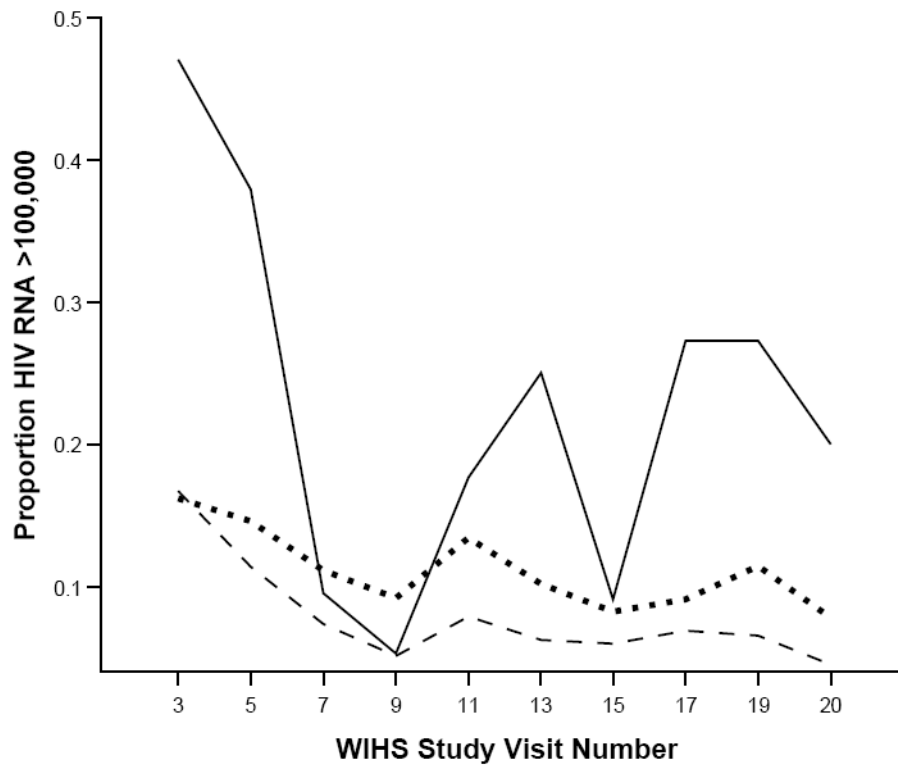line) falling in between.

Figure 4.
Unadjusted proportions of women with HIV-1 RNA viral load >100,000 copies over 18 semi-annual study visits. Nonusers (dashed line) had consistently lower proportions, while persistent users (solid line) generally had the highest proportions, with intermittent users (dotted line) falling in between.

Table 1

Characteristics of 1686 HIV+ women in a multi-site cohort according to longitudinal patterns of crack use, 1996-2004[1]

Variable	Nonusers n = 1,203	Intermittent users n = 429	Persistent users n = 54	Chi Square/ANOVA Significance[2]	Linear Trend Significance
African American	600 (50%)	305 (71%)	36 (67%)	***	***
Hispanic/Latina	331 (28%)	60 (14%)	12 (22%)	***	***
Caucasian/other	272 (23%)	64 (15%)	6 (11%)	**	***
Less than high school education at baseline	414 (34%)	179 (42%)	33 (61%)	***	***
Baseline income <= $12,000/year	651 (55%)	334 (78%)	46 (85%)	***	***
Age in years at baseline	36.5 (8.3)	37.4 (6.6)	38.0 (7.9)	n.s.	--
Baseline CD4 count (cells/mm^3)	364 (264)	433 (305)	257 (194)	***	--
Baseline CD4<200 cells/mm^3	338 (29%)	91 (22%)	20 (40%)	**	**
Baseline CD4 Percentiles					
25th	175	227	70		
50th	328	374	274		
75th	508	564	366		
Baseline HIV-1 RNA level (copies/ml)	89424 (344409)	54815 (157806)	205160 (373550)	**	--
Baseline HIV-1 RNA>100,000 (copies/ml)	164 (15%)	52 (13%)	18 (37%)	***	ns
Baseline HIV-1 RNA Percentiles					
25th	4,000	4,000	4,250		--
50th	8,100	8,950	38,000		
75th	53,250	44,000	265,000		
Baseline log$_{10}$HIV-1 RNA	4.05 (0.93)	4.01 (.090)	4.53 (1.04)	**	**
Baseline log$_{10}$HIV-1 RNA Percentiles					
25th	3.60	3.60	3.63		--
50th	3.91	3.95	4.58		
75th	4.73	4.64	5.42		
Year of HIV+ diagnosis	1991 (2.5)	1991 (2.8)	1991 (2.5)	ns	***
Ever reported HAART	903 (75%)	307 (72%)	17 (32%)	***	***
HAART adherence >=95% at all reports	346 (29%)	69 (16%)	4 (7%)	***	***

Variable	Nonusers n = 1,203	Intermittent users n = 429	Persistent users n = 54	Chi Square/ANOVA Significance[2]	Linear Trend Significance
Baseline problem alcohol use[3]	123 (10%)	114 (27%)	17 (32%)	***	***
Number study visits completed	12 (6)	13 (5)	6 (6)	***	--
Date of first study visit (mo/year)	8/96	9/96	9/96	**	--
Follow-up time, (months)	86 (20)	85 (18)	66 (33)	***	--
Deceased during study (all cause mortality)	278 (23%)	104 (24%)	37 (68%)	***	***

**
  $p < .01$,

***
  $p < .001$,

n.s.= not statistically significant

[1]Values are expressed as frequency (%) for discrete variables and as mean (standard deviation) for continuous variables.

[2]For discrete variables, significance refers to chi-square and linear by linear associations, for continuous variables, to analysis of variance.

[3]Problem alcohol use is defined as >7 drinks/week and/or >=4 drinks per day

Source: Women's Interagency HIV Study: 1994-2004

Table 2

Cox proportional hazards models of effects of patterns of crack use on AIDS-related mortality and AIDS-defining illnesses, N=1686: Models control for study site.

Variable	Dependent variable: AIDS-related mortality (200/1686 = 11.9%) Hazard Ratio	Dependent variable: Newly acquired AIDS-defining illness[1] (543/1686 = 32.2%) Hazard Ratio
Crack Use	***	***
Intermittent	0.93	1.57***
Persistent	3.61***	1.65*
Problem Drinking[2]	**	
Intermittent	0.54**	1.05
Persistent	0.38	0.69
HAART & >=95% adherent	0.52**	1.13
CD4 lymphocyte count <200 cells/mm^3 at baseline	5.70***	1.05
HIV-1 RNA >100,000 copies/ml at baseline	2.46***	0.94
Year of HIV+ diagnosis	0.99	1.05**
African American	1.44	0.90
Latina	1.16	1.01
Low income (<$12K/yr)	1.27	1.06
Less than high school education	1.16	1.10
Age (10 year increments)	1.04	1.01

*
p<.05,

**
p<.01,

***
p<.001

[1] Defined in accordance with the Centers for Disease Control and Prevention 1993 clinical surveillance conditions, excluding the criterion of low CD4 cell count (CDC, 1993).

[2] Problem drinking defined as = >7 drinks per week and/or binge drinking >=4 drinks per day.

Source: Women's Interagency HIV Study: 1994-2004

Table 3

Random regression analysis of effects of time-varying patterns of crack use on markers of HIV disease progression, N=1686: Models control for study site.

Variable	Dependent Variable: Time Varying CD4<200 cells/mm³ Estimate[1]	Dependent Variable: Time Varying HIV-1 RNA > 100,000 copies/ml Estimate[1]
Intercept	1.87	-1.00
Time (study visit number)	0.05***	0.03***
Crack use		
Crack use intermittent – abstinent	0.67***	0.45**
Crack use intermittent – active	0.98***	0.58***
Crack use - persistent	0.82**	2.24***
Problem drinking[2]		
Problem drinking intermittent - abstinent	-0.18	-0.22
Problem drinking intermittent – active	0.08	-0.01
Problem drinking – persistent	-1.08	1.91*
CD4 lymphocyte count <200 cells/mm³ at baseline	--	2.21***
HIV-1 RNA >100,000 copies/ml at baseline	2.60***	--
Year of HIV+ diagnosis	-0.09***	-0.04
HAART >=95% adherence	-1.10***	-2.13***
Caucasian	--	--
African American	0.24	0.16
Latina	0.69***	-0.16
Low income (<$12K/yr)	0.20**	0.26**
Less than high school education	-0.10	0.22
Age (10 year increments)	0.42***	-0.05

*
p<.05,

**
p<.01,

***
p<.001

[1] Effect shown as unstandardized parameter estimate where negative sign indicates that outcome was less likely and positive sign indicates that outcome was more likely.

[2] Problem drinking defined as >= 7 drinks per week and/or binge drinking >= 4 drinks per day.

Source: Women's Interagency HIV Study: 1994-2004