Published in final edited form as:

J Acquir Immune Defic Syndr. 2011 March 1; 56(Suppl 1): S54–S61. doi:10.1097/QAI.0b013e3182097576.

The impact of cocaine use on outcomes in HIV-infected patients receiving buprenorphine/naloxone

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Abstract

BACKGROUND—Cocaine use is common in opioid dependent HIV-infected patients but its impact on treatment outcomes in these patients receiving buprenorphine/naloxone is not known.

METHODS—We conducted a prospective study in 299 patients receiving buprenorphine/naloxone who provided baseline cocaine data and a subset of 266 patients who remained in treatment for greater than or equal to one quarter. Assessments were conducted at baseline and quarterly for one year. We evaluated the association between baseline and in-treatment cocaine use on buprenorphine/naloxone retention, illicit opioid use, antiretroviral adherence, CD4 counts, HIV RNA, and risk behaviors.

RESULTS—Sixty-six percent (197/299) of patients reported baseline cocaine use and 65% (173/266) of patients with follow-up data reported in-treatment cocaine use. Baseline and in-treatment cocaine use did not impact buprenorphine/naloxone retention, antiretroviral adherence,

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CD4 lymphocytes, or HIV risk behaviors. However, baseline cocaine use was associated with a 14.8 (95% CI=9.0–24.2) times greater likelihood of subsequent cocaine use (95% CI=9.0 – 24.2), a 1.4 (95% CI=1.02 – 2.00) times greater likelihood of subsequent opioid use, and higher Log₁₀ HIV RNA ($p \leq .016$) over time. In-treatment cocaine use was associated with a 1.4 (95% CI=1.01–2.00) times greater likelihood of concurrent opioid use.

CONCLUSIONS—Given cocaine use negatively impacts opioid and HIV treatment outcomes, interventions to address cocaine use in HIV-infected patients receiving buprenorphine/naloxone treatment are warranted.

Keywords

Cocaine; HIV; Buprenorphine; heroin dependence; opioid-related disorders

Introduction

Cocaine use is prevalent among patients infected with HIV and those entering treatment for opioid dependence^{1, 2}. It has been reported in 40–46% of patients entering methadone and buprenorphine/naloxone treatment^{34, 5} and is associated with increased rates of psychiatric disorders, HIV risk behaviors, criminal activity and negative social interactions^{6–10} and can predict shorter treatment retention and poorer treatment outcomes^{10–12}. A recent pharmacokinetic study examining the impact of cocaine use on methadone treatment in opioid dependent patients found that methadone-maintained patients who were regularly using cocaine had evidence of lower methadone levels and more rapid methadone clearance¹³. A similar pharmacokinetic study evaluating buprenorphine levels in cocaine using and cocaine non-using cohorts found that cocaine users had lower buprenorphine plasma concentrations¹⁴. A study of patients receiving buprenorphine treatment through a drug treatment program revealed that patients with ongoing cocaine use had more drug use, legal and psychiatric problems¹⁵. In a recent analysis, we found that patients who were using cocaine prior to initiating primary care office-based buprenorphine/naloxone treatment and those who used cocaine while engaged in treatment, were less likely to be retained in treatment and had fewer weeks of continuous opioid-negative urine toxicology tests¹⁶. Notably in this study, over 30% of patients who had no evidence of cocaine use in the 30 days prior to treatment and had no evidence of cocaine use during the first two weeks of treatment, initiated cocaine use during treatment.

While ongoing cocaine use clearly has adverse implications for addiction treatment outcomes in HIV-infected patients, it also adversely affects HIV outcomes. HIV-infected patients who use cocaine have poor access to and utilization of HIV health care services^{17–22}, are less likely to receive antiretroviral therapy compared with those who use other drugs^{19, 22, 23}, have poor adherence to HIV antiretroviral therapy^{24–29}, and appear to have accelerated progression of their HIV disease^{30–33}. Given the growing evidence of the efficacy of buprenorphine/naloxone in treating opioid dependence³⁴, in office-based settings^{4, 35} including HIV clinical settings³⁶, it is critical to evaluate the association between cocaine use and treatment outcomes in opioid dependent HIV-infected patients. Therefore, the purpose of the current study is to evaluate the associations between baseline and in-treatment cocaine use and both substance use and HIV outcomes in a cohort of HIV-infected patients receiving office-based buprenorphine/naloxone treatment.

Methods

Study Design

We performed an analysis of patients enrolled in the Buprenorphine and Integrated HIV Care Model Demonstration Project (BHIVES) (Models paper, *JAIDS*) including data contributed by nine sites participating in this national multi-site study. Eligible subjects underwent uniform assessments at each site at baseline and every three months (quarterly) for a year.

Subjects

Subjects met the following eligibility criteria; age ≥ 18 , HIV-infected, DSM-IV criteria for opioid dependence, aspartate transferase (AST) or alanine transferase (ALT) less than five times normal, not dependent on benzodiazepines or alcohol, not pregnant, not acutely suicidal or psychiatrically impaired, able to understand English or Spanish, and willing to participate in the study for one year. The study was approved by the Institutional Review Boards at each site and written informed consent was obtained for all subjects.

Treatment—All patients received daily treatment with buprenorphine/naloxone. Based on the resources available at each site, patients received varying levels of psychosocial counseling as part of their opioid dependence treatment (Models paper, *JAIDS*).

Measures

We collected demographic and clinical data at baseline and at each subsequent quarter. Clinical data included CD4 lymphocyte count, Log_{10} HIV RNA, and HIV drug and sex risk behaviors. HIV medication adherence was measured using the Center for Adherence Support Evaluation (CASE) Adherence Index, a simple composite measure of self-reported antiretroviral therapy adherence with a range of scores from 3–20. A CASE score greater than 10 is associated with 95% HIV antiretroviral medication adherence³⁷. Substance use characteristics as well as self-reported illicit opioid and cocaine use were also collected using the Addiction Severity Index (ASI)-Lite³⁸. Because urine toxicology data were collected for clinical care and not for research purposes in some sites, the study sites were not consistent in their timing or use of urine toxicology analysis. Therefore, urine toxicology data are not included in this analysis. We defined baseline cocaine use as any self-reported cocaine use within 30 days of the baseline assessment. In-treatment cocaine use was defined as any self-reported cocaine use within the 30 days prior to the quarterly interview.

Data Analyses

Because cocaine use prior to entry into treatment (baseline) may be associated with worse outcomes and because patients who are abstinent from cocaine at baseline may initiate cocaine use during treatment (in treatment) we assessed outcomes among two not mutually exclusive groups. The first analysis was conducted in those patients who provided a response at baseline regarding their cocaine use ($N=299$). The second analysis was conducted only in those patients ($N=266$, 89% of baseline sample) who remained in treatment for at least one quarter. Primary outcome measures assessed in both groups included retention in buprenorphine/naloxone treatment and proportion of patients with self-reported cocaine and illicit opioid use across quarters. Retention in buprenorphine/naloxone treatment was defined as the receipt of at least one dose of buprenorphine/naloxone in a given study quarter. Other outcome measures included adherence to HIV antiretroviral medications, changes in CD4 counts and Log_{10} HIV RNA, and needle sharing and condom use risk behaviors. All data were analyzed using SPSS 15.0 for Windows. Using chi square and t-tests, we first conducted preliminary analyses of the comparability of baseline

measures for subjects with and without cocaine use, and the possible need for including baseline variables as covariates in the analyses of treatment outcome data. The effects of cocaine use on buprenorphine retention were analyzed using the Kaplan-Meier product limit method and the generalized Wilcoxon test. Generalized Estimating Equations (GEE) were used to assess changes in dichotomous outcomes over time. Mixed model analysis was applied when the outcome variable was expressed continuously.

Results

Characteristics

The demographic and clinical characteristics of the 299 patients who received at least one dose of buprenorphine/naloxone and provided data on baseline cocaine use are listed in Table 1. Of the 299 patients, the mean age was 45 years, 68% were male, 51% were black, and 57% had greater than or equal to a high school education. Their mean years of opioid dependence was 17, the majority of patients reported current injection drug use (60%), they had a mean years of HIV diagnosis of 12 years, and 60% were receiving antiretroviral medication. Sixty-six percent (N=197) of patients reported baseline cocaine use. Baseline cocaine users were more likely to be black ($p=.045$), primarily use heroin, as opposed to other opioids ($p=.01$), were less likely to be receiving antiretroviral medications ($p=.04$), had higher Log_{10} HIV RNA levels ($p=.02$), and were more likely to be engaging in needle sharing ($p=.02$).

Substance Use Outcomes

Treatment Retention

Baseline Cocaine Use: Patients who reported cocaine use at baseline (N=197) as compared with those who reported no cocaine use at baseline had similar rates of treatment retention in all follow-up periods (Table 2 and Figure 1).

In-treatment Cocaine Use: Patients reporting in-treatment cocaine use had lower rates of treatment retention only during the first quarter ($p=.03$) but higher rates of treatment retention at all subsequent follow-up time-points (Table 3).

Illicit Cocaine and Opioid Use

Baseline Cocaine Use: The odds of using cocaine during treatment for those with baseline cocaine use was 14 times higher than those without baseline cocaine use ($\text{OR}=14.76$; $\text{CI}=9.0 - 24.2$; $p<=.05$) (Table 2). A greater proportion of those with baseline cocaine use had illicit opioid use during the first quarter ($p=.02$). Over time, those with baseline cocaine use were 1.4 times more likely to use illicit opioids during treatment than those without baseline cocaine use ($\text{OR}=1.43$; $\text{CI}=1.02 - 2.00$; $p=.04$) (Table 2).

In-treatment Cocaine Use: A greater proportion of patients reporting in-treatment cocaine use as compared with those without in-treatment cocaine use reported illicit opioid use during the first quarter ($p=.02$). Patients with in-treatment cocaine use were 1.4 times more likely to use illicit opioids over time than those patients without in-treatment cocaine use ($\text{OR}=1.42$; $\text{CI}=1.01-2.00$; $p=.04$) (Table 3).

HIV Outcomes

HIV Antiretroviral Medication Adherence

Baseline Cocaine Use: Patients reporting baseline cocaine use had poorer adherence to their HIV antiretroviral medications than those without baseline cocaine use during all four quarters (all $p\text{-values}<.05$). There were no differences in HIV antiretroviral adherence over

time between those with and those without baseline cocaine (Beta= $-.07$; CI= $-1.4-.01$; $p \leq .07$) (Table 2).

In-treatment Cocaine Use: There were no differences in HIV antiretroviral medication adherence in all four quarters (all p -values $>.05$) or over time (Beta = $-.06$; CI= $-1.35-.10$; $p \leq .10$) between patients with in-treatment cocaine use as compared to those without in-treatment cocaine use (Table 3).

CD4 Lymphocyte Counts

Baseline Cocaine Use: While there was a trend towards lower CD4 lymphocyte counts in those patients with baseline cocaine use (except for during the third quarter), there were no differences in CD4 lymphocyte counts in the four quarters (all p -values $>.05$) and over time (baseline use: Beta = -19.8 ; CI= $-80.1 - 40.5$; $p>.05$) (Table 2).

In-treatment Cocaine Use: In contrast, those patients with in-treatment cocaine use had lower CD4 counts in all four quarters and this difference reached statistical significance in the fourth quarter ($p=.02$) (Table 3). Over time there were no differences in CD4 counts (Beta = 15.1 ; CI= $-43.0 - 73.3$; all $p>.05$) (Table 3).

Log₁₀ HIV RNA levels

Baseline Cocaine Use: Those with baseline cocaine use compared with those who reported no baseline cocaine use had higher Log₁₀ HIV RNA levels, except for during the third quarter, but this difference was not significant (Table 2). However, baseline cocaine users had a higher Log₁₀ HIV RNA level, on average 0.26 points higher than non-users, over time (Beta = $.26$; CI = $.05 - .48$; $p \leq .02$).

In-treatment Cocaine Use: Those with in-treatment cocaine use generally had higher Log₁₀ HIV RNA levels than those without in-treatment cocaine use, except for during the third quarter, and this difference reached statistical significance in the fourth quarter ($p=.03$) (Table 3). Over time there were no differences in the Log₁₀ HIV RNA levels (Beta = 0.15 ; CI= $-0.07 - 0.36$; $p>.05$).

HIV Risk Behaviors

Baseline Cocaine Use: There was a higher proportion of baseline cocaine users compared to non-cocaine users who reported needle sharing during the first quarter ($p=.01$). This difference did not persist in the other quarters or over time (Table 2). There were no differences in condom use in each quarter (all p -values $>.05$) or over time based on baseline cocaine use (OR = 0.95 ; CI $0.58/1.54$; $p>.05$).

In-treatment Cocaine Use: There was no difference in needle sharing in each quarter (all p -values $>.05$) or over time (OR = 1.30 ; CI= $0.65 - 2.60$; $p>.05$) based on in-treatment cocaine use. There was no difference in non-condom use in each quarter (all p -values $>.05$) or over time (OR = 1.44 ; CI= $0.85 - 2.46$; $p>.05$) based on in-treatment cocaine use (Table 3).

Discussion

We found that baseline and in-treatment cocaine use in HIV-infected patients who are receiving buprenorphine/naloxone for the treatment of opioid dependence has considerable implications in terms of its association with ongoing illicit drug use during treatment. Patients with baseline cocaine use were significantly more likely to use cocaine during treatment than those without baseline cocaine use. Even more critical and relevant to the

current study examining the treatment of opioid dependence is that there was a very substantial association between both baseline and in-treatment cocaine use and the likelihood of ongoing opioid use during buprenorphine/naloxone treatment. Regarding HIV outcomes, those with baseline cocaine use had poorer medication adherence than those without baseline cocaine use and while this association was statistically significant, it has uncertain clinical significance. We found no association between in-treatment cocaine use and antiretroviral medication adherence. In addition, while cocaine use, either at baseline or during treatment, was associated with lower CD4 counts, cocaine use did not impact CD4 counts over time. Finally those with baseline cocaine use had higher Log₁₀ HIV RNA levels at baseline and over time.

Our results are similar to and contrast with prior research. Similar to a recent study¹⁶ in which we found that patients who were using cocaine at the time of initiating buprenorphine/naloxone treatment and those who with in-treatment cocaine use had fewer weeks of continuous opioid abstinence, the current study found baseline and in-treatment cocaine use associated with an approximately 1.5 times increased risk of self-reported opioid use at follow-up time points. In contrast, while the earlier study revealed a significant impact on treatment retention, the current study did not find this association. This likely reflects the greater medication dispensing requirements (thrice to once per week) and stricter definition of treatment drop-out (off of medication for greater than seven days) used in the earlier randomized, controlled clinical trial³⁵. The rate of observed cocaine use in the current study, 60% of patients at baseline cocaine and 65% of patient during treatment, is similar to rates described in other studies^{1,2}. Similarly, our results demonstrating trends towards poorer medication adherence, lower CD4 counts, and higher HIV RNA levels, are consistent with previous findings. Studies have demonstrated that active cocaine use is associated with poor adherence to antiretroviral therapy²⁴⁻²⁹, and HIV disease progression³⁰⁻³³.

Our study has limitations. First our results are based on self-reported drug use, not confirmed by urine toxicology analyses. This could lead to under-reporting of drug use. Second, since studies were conducted across a number of sites, the study samples and treatment interventions may have differed in ways that we did not evaluate. Third, it is possible that patients using cocaine were differentially retained and the results represent reporting bias. Fourth, since the eligibility criteria for this multi-site study excluded individuals with dependence on sedatives, benzodiazepines, or alcohol and severe or co-occurring untreated psychiatric conditions, our findings may not generalize to HIV-infected patients receiving buprenorphine/naloxone with these comorbidities. Fifth, given that retention in buprenorphine/naloxone treatment was defined as the receipt of at least one dose of medication in a given study quarter, some subjects could be minimally involved in the study for most of each quarter which is a considerably different level of involvement than a full participant. Sixth, our analysis of cocaine use was not time varying, reflecting our desire to categorize patients as baseline and/or in-treatment cocaine users. Finally, the analyses were not corrected for multiple comparisons.

There is evidence of the association between ongoing drug use and adverse health outcomes in HIV-infected patients. There is also growing evidence of the effectiveness of buprenorphine/naloxone treatment to treat opioid dependence in HIV-infected patients^{36, 39}. There are, however, substantial levels of cocaine use in this population and our results provide novel findings that indicate that cocaine use prior to initiation of and during buprenorphine/naloxone treatment is associated with worse substance use and HIV treatment outcomes. These findings also highlight that while buprenorphine/naloxone does not appear to mitigate the impact of cocaine use on outcomes, it does not appear to make these outcomes worse.

There are a number of potential explanations as to how cocaine use could be associated with ongoing illicit opioid use. Patients who continue to use cocaine may be more likely to have access to and use illicit opioids. There may be physiologic explanations for the higher rate of opioid use in cocaine users who are receiving buprenorphine/naloxone treatment. A recent pharmacokinetic study that revealed that patients with concomitant cocaine use had lower buprenorphine plasma concentrations proposed that one mechanism might be that cocaine-induced vasoconstriction might reduce buprenorphine/naloxone sublingual absorption or increase buprenorphine metabolism⁴⁰. These latter mechanisms could reduce buprenorphine and nor-buprenorphine levels and result in illicit opioid use to counteract opioid craving and/or withdrawal. Based on the high rates of cocaine use and the detrimental effects of cocaine use in HIV-infected opioid dependent patients, further research that explores pharmacologic and psychosocial treatments for cocaine, that are feasible and efficacious in office-based settings, will likely help improve substance use and HIV treatment outcomes seen with buprenorphine/naloxone treatment.

Acknowledgments

This publication was supported by grant number 1H97HA03800 from the Health Resources and Services Administration. This grant is funded through the HIV/AIDS Bureau's Special Project of National Significance. The contents of this publication are solely the responsibility of the authors and do not necessarily represent the views of the funding agencies or the U.S. government. Dr. Sullivan is a Robert Wood Johnson Physician Faculty Scholar. Dr. Schottenfeld is supported by the National Institute on Drug Abuse (NIDA K24 DA000445 and R01 DA009803). Dr. Fiellin is supported by the National Institute on Drug Abuse (NIDA R01 DA019511-01, R01 DA025991, R01 DA020576-01A1). (NEED FUNDING SUPPORT FROM ALL AUTHORS)

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Figure 1. Treatment Retention Based on Cocaine Use at Baseline

Baseline Cocaine

—— Use

- - - No Use

Table I

Patient Characteristics (overall and by cocaine use)

Characteristic	All patients N=299	Cocaine Use at Baseline N=197	No Cocaine Use at Baseline N=102	P-value
Age, mean (SD)	45.2 (8.1)	45.6 (7.7)	44.5 (8.7)	NS
% Male	67.9% (203)	65.5% (129)	72.5% (74)	NS
Race/Ethnicity				
% White	23.1% (68)	23.1% (38)	30.3% (30)	0.045
% Black	51.2% (151)	57.2% (112)	39.4% (39)	
% Hispanic	22.4% (66)	22.4% (41)	25.3% (25)	
% Other	3.4% (10)	2.5% (5)	5.0% (5)	
% High school education or greater	57.2% (172)	56.7% (111)	59.8% (61)	NS
% Full-time employed	25.8% (77)	24.9% (49)	27.5% (28)	NS
% Primarily heroin user	39.8% (119)	44.7% (88)	30.4% (31)	0.011
% Primarily prescription opioid user	15.1% (45)	12.7% (25)	19.6% (20)	0.080
% Injection drug use at treatment entry	60.1% (180)	56.9% (112)	66.7% (68)	0.064
Years of opioid dependence, mean (SD)	17.2 (11.1)	17.4 (10.8)	16.6 (11.6)	NS
% Prior methadone maintenance treatment	51.5% (154)	52.8% (104)	49.0% (50)	NS
Years of HIV diagnosis, mean (SD)	12.2 (6.5)	12.3 (6.4)	11.8 (6.8)	NS
% Antiretroviral treatment at treatment entry	60.4% (180)	56.6% (111)	67.6% (69)	0.042
Baseline CD4, mean (SD)	429.6 (823)	410.3 (729.6)	473.5 (1013.5)	NS
Baseline Log ₁₀ HIV RNA, mean (SD)	3.465 (1.051)	3.581 (1.029)	3.248 (1.063)	0.023
% HIV risk behaviors: needle sharing	9.1% (27)	11.8% (23)	3.9% (4)	.017
% HIV risk behaviors: sex without condom	24.6% (73)	24.6% (48)	24.5% (25)	NS

Table 2

Substance Use and HIV Treatment Outcomes of HIV+ Patients Receiving Buprenorphine, by Cocaine Use at Baseline (N=299)

	Cocaine Use at Baseline		No Cocaine Use at Baseline		χ	p		
	(N=197)		(N=102)					
	%	n	%	n				
Substance use treatment outcomes by quarter								
Retention in treatment								
Quarter 1	72.1	142	78.4	80	2.49	ns		
Quarter 2	66.0	130	69.6	71	0.11	ns		
Quarter 3	58.9	116	58.8	60	0.36	ns		
Quarter 4	48.7	96	49.0	50	1.08	ns		
Log Rank (Mantel-Cox) Chi-square = 1.908; df 1, p ns								
Percent with cocaine use								
Quarter 1	54.3	76	11.7	80	37.83	.000		
Quarter 2	53.5	68	13.8	71	28.21	.000		
Quarter 3	54.8	63	12.7	60	30.07	.000		
Quarter 4	46.9	60	16.7	50	15.95	.000		
Cross Quarter GEE OR = 14.76; CI 9.01/24.18; p ≤ .001								
Percent with opioid use								
Quarter 1	49.3	69	33.8	26	4.86	.019		
Quarter 2	42.2	54	33.8	22	1.26	ns		
Quarter 3	39.0	46	48.4	31	1.52	ns		
Quarter 4	42.2	54	45.0	27	0.13	ns		
Cross Quarter GEE OR = 1.43; CI 1.02/2.00; p ≤ .039								
	Cocaine Use at Baseline		No Cocaine Use at Baseline		t	p		
	(N=197)		(N=102)					
	Mean	SD	Mean	SD				
HIV outcomes by quarter								
Adherence to HIV medication (CASE Adherence Index Score)								
Quarter 1	10.6	3.4	12.0	3.1	5.58	.020		
Quarter 2	10.3	3.4	11.9	3.4	6.07	.015		
Quarter 3	10.8	3.3	12.1	3.5	3.88	.051		
Quarter 4	10.7	3.3	12.4	3.1	7.55	.007		
Cross Quarter Mixed Model Beta = −0.70; CI −1.4/0.01; p ≤ .075								
CD4 counts								
Quarter 1	371.3	245.4	372.2	205.2	0.0	Ns		
Quarter 2	364.6	274.9	403.3	280.7	0.51	Ns		
Quarter 3	390.1	248.7	383.7	213.7	0.02	Ns		

	Cocaine Use at Baseline		No Cocaine Use at Baseline		χ	p
	(N=197)		(N=102)			
	%	n	%	n		
Quarter 4	335.9	224.3	423.1	207.6	2.46	Ns
Cross Quarter Mixed Model Beta =-19.8; CI -80.1/40.5; p ns						
Log10 HIV RNA levels						
Quarter 1	3.14	0.9	3.01	0.9	0.63	Ns
Quarter 2	3.23	1.0	3.08	0.9	0.61	Ns
Quarter 3	3.03	1.0	3.05	0.8	0.01	Ns
Quarter 4	3.16	1.1	2.98	0.8	0.52	Ns
Cross Quarter Mixed Model Beta = 0.26; CI 0.05/0.48; p $\leq$.0016						
	%	n	%	n	χ	p
Change in HIV risk behavior: needle sharing						
Quarter 1	10.1	14	1.3	1	5.90	.010
Quarter 2	4.7	6	7.7	5	0.72	ns
Quarter 3	3.4	4	3.1	2	0.01	ns
Quarter 4	3.1	4	1.7	1	0.34	ns
Cross Quarter GEE OR =2.12; CI 0.97/4.65; p $\leq$.061						
Change in HIV risk behavior: sex without condom						
Quarter 1	23.0	32	22.1	17	0.03	ns
Quarter 2	18.8	24	23.1	15	0.50	ns
Quarter 3	23.7	28	17.2	11	1.06	ns
Quarter 4	18.0	23	26.7	16	1.88	ns
Cross Quarter GEE OR =0.95; CI 0.58/1.54; p ns						

Table 3

Substance Use and HIV Treatment Outcomes of HIV+ Patients Receiving Buprenorphine, by Cocaine Use During Treatment (N=266)

	Cocaine Use During Treatment		No Cocaine Use During Treatment			
	(N=173)		(N=93)		χ	P
	%	n	%	n		
Substance use treatment outcomes by quarter						
Retention in treatment						
Quarter 1	83.8	145	86.0	80	6.87	.032
Quarter 2	78.0	135	74.2	69	1.11	Ns
Quarter 3	69.9	121	62.4	58	1.68	Ns
Quarter 4	59.0	102	50.5	47	1.77	Ns
Not Applicable						
Percent with opioid use						
Quarter 1	49.0	72	33.3	24	4.81	.020
Quarter 2	41.8	56	32.3	20	1.62	Ns
Quarter 3	43.4	56	36.4	20	0.79	Ns
Quarter 4	45.5	61	33.3	18	2.35	.085
Cross Quarter GEE OR = 1.42; CI 1.01/2.00; p ≤ .042						
	Cocaine Use During Treatment		No Cocaine Use During Treatment		t	p
	(N=173)		(N=93)			
	Mean	SD	Mean	SD		
HIV outcomes by quarter						
Adherence to HIV medication (CASE Adherence Index Score)						
Quarter 1	11.3	3.4	11.0	3.5	0.16	ns
Quarter 2	11.1	3.4	10.6	3.7	0.44	ns
Quarter 3	11.1	3.3	11.2	3.7	0.13	ns
Quarter 4	11.4	3.2	11.1	3.7	0.13	ns
Cross Quarter Mixed Model Beta = −0.62; CI −1.35/0.10; p ≤ .096						
CD4 counts						
Quarter 1	364.2	245.8	399.3	206.0	0.66	ns
Quarter 2	370.2	276.9	406.7	273.6	0.44	ns
Quarter 3	371.9	242.4	429.8	205.7	1.37	ns
Quarter 4	327.3	213.6	462.3	207	5.67	0.02
Cross Quarter Mixed Model Beta =15.1; CI −43.0/73.3; p ns						
Log10 HIV RNA levels						
Quarter 1	3.18	1.0	2.88	0.6	3.24	.072
Quarter 2	3.22	1.0	3.09	1.1	0.46	ns
Quarter 3	3.03	0.9	3.04	0.8	0.01	ns

	Cocaine Use During Treatment		No Cocaine Use During Treatment		χ	P
	(N=173)		(N=93)			
	%	n	%	n		
Quarter 4	3.31	1.1	2.74	0.8	4.74	.033
Cross Quarter Mixed Model Beta = 0.15.; CI -0.07/0.36; p ns						
	%	n	%	n	χ	P
HIV risk behavior: needle sharing						
Quarter 1	8.9	13	2.8	2	2.83	.076
Quarter 2	5.2	7	6.5	4	0.12	ns
Quarter 3	4.7	6	0.0	0	2.64	ns
Quarter 4	3.0	4	1.9	1	0.19	ns
Cross Quarter GEE OR =1.30; CI 0.65/2.60; p ns						
HIV risk behavior: sex without condom						
Quarter 1	25.3	37	16.7	12	2.08	.100
Quarter 2	21.6	29	16.1	10	0.81	ns
Quarter 3	22.5	29	18.2	10	0.43	ns
Quarter 4	21.6	29	18.5	10	0.23	ns
Cross Quarter GEE OR =1.44; CI 0.85/2.46; p ns						