Published in final edited form as:

AIDS Care. 2013 January ; 25(1): 109–117. doi:10.1080/09540121.2012.687814.

Active cocaine use is associated with lack of HIV-1 virologic suppression independent of non-adherence to antiretroviral therapy: use of a rapid screening tool during routine clinic visits

Daniel A. Rasbach, B.A.^{1,*}, Andrew J. Desruisseau, M.D.^{2,*}, Aaron M. Kipp, Ph.D.^{3,4}, Samuel Stinnette, M.S.¹, Asghar Kheshti, M.S.¹, Bryan E. Shepherd, Ph.D.⁵, Timothy R. Sterling, M.D.^{1,6}, Todd Hulgán, M.D., M.P.H.¹, Catherine C. McGowan, M.D.¹, and Han-Zhu Qian, M.D., Ph.D.^{3,4,**}

¹Division of Infectious Diseases, Department of Medicine, Vanderbilt University School of Medicine, Nashville, Tennessee 37232, USA

²Division of Infectious Diseases, Meharry Medical College, Nashville, Tennessee 37208, USA

³Vanderbilt Institute for Global Health, Vanderbilt University School of Medicine, Nashville, Tennessee 37203, USA

⁴Division of Epidemiology, Department of Medicine, Vanderbilt University School of Medicine, Nashville, Tennessee 37203, USA

⁵Department of Biostatistics, Vanderbilt University School of Medicine, Nashville, Tennessee 37232, USA

⁶Center for Health Services Research, Department of Medicine, Vanderbilt University School of Medicine, Nashville, Tennessee 37232, USA

Abstract

Clarifying the relationship between illicit drug use and HIV-1 virologic suppression requires characterization of both illicit drug use activity and adherence to antiretroviral therapy (ART). We developed a rapid clinical questionnaire to assess prior 7-day illicit drug use and ART adherence in a cross-sectional study among 1,777 HIV-infected persons in care. Of these, 76% were male, 35% were African-American, and 8% reported injection drug use as their probable route of HIV-1 infection. Questionnaire-reported frequencies of cocaine and marijuana use within the previous 7 days were 3.3% and 12.1%, respectively. Over three quarters (77.8%) of participants were on ART, of whom 69.7% had HIV-1 virologic suppression (HIV-1 RNA <48 copies/mL). Univariate analyses revealed that compared to no use, cocaine and marijuana use were both associated with missed ART doses ($P < 0.01$). Multivariable logistic regression analysis adjusting for non-adherence demonstrated that cocaine use was independently associated with failing to achieve virologic suppression (adjusted odds ratio (aOR), 0.46; 95% confidence interval (CI), 0.22–0.98) but marijuana use was not (aOR, 1.08; 95% CI, 0.72–1.62). This result strengthens the evidence of a direct effect of cocaine on virologic control, independent of non-adherence to ART.

Keywords

Drug use; cocaine; marijuana; antiretroviral therapy; HIV-1 virologic suppression

**Corresponding author. 2525 West End Avenue, Suite 750, Nashville, TN 37203, USA. Telephone: (615) 343-3159. han-zhu.qian@vanderbilt.edu.

*These authors contributed equally to this work

1. Introduction

Illicit drug use is an important cofactor in the ongoing human immunodeficiency virus (HIV)-1 pandemic. In the United States, an estimated 1.0–1.2 million persons are living with HIV/AIDS (Centers for Disease Control [CDC], 2008). Drug use is common in this population. Some studies suggest that the prevalence rates of recent cocaine and marijuana use could be as high as over 50% and 30%, respectively (Baum et al., 2009; Cofrancesco et al., 2008; Hessol et al., 2007; Sohler et al., 2007). Although AIDS-related morbidity and mortality have significantly decreased since the introduction of effective antiretroviral therapy (ART) (Mocroft et al., 2003; Walensky et al., 2006), HIV-infected drug users may have less access to ART (Bogart, Kelly, Catz, & Sosman, 2000; Cofrancesco et al., 2008; Lucas, Cheever, Chaisson, & Moore, 2001; McGowan et al., 2011), be less adherent to ART (Arnsten et al., 2002; Hinkin et al., 2007; Mills et al., 2006), have poorer virologic control (Arnsten et al., 2002; Cofrancesco et al., 2008; Lucas et al., 2001), and ultimately have worse clinical outcomes than non-drug users (Hogg et al., 2002; Lima et al., 2009; Lucas, Gebo, Chaisson, & Moore, 2002; Wood et al., 2003; Qian et al., 2011).

Research in this area has been problematic and often contradictory because of the heterogeneity of the drug-using population and the difficulty in measuring drug use and adherence to ART. Variation in the reporting and analysis of drug use includes active versus historical use, injection versus non-injection routes, type of drug, and frequency of use (Kapadia, Vlahov, Donahoe, & Friedland, 2005). A recent review of the literature on non-injection drug use and HIV disease progression found great heterogeneity in how active drug use was analyzed (Kipp, Desruisseau, & Qian, 2011). Similarly, ART adherence assessment may differ with regard to duration of recall, self-report versus objective measurement, and the format for self-report: frequency of missed doses, proportion of doses taken correctly, or Likert-type responses concerning ability to take or frequency of taking doses as prescribed (Berg, Wilson, Li, & Arnsten, 2010; Deschamps et al., 2008; Simoni et al., 2006; Wilson, Carter, & Berg, 2009). Recent reports suggest that single item measures may perform as well or better than detailed multi-item measures and have the added benefit of increased feasibility in the clinic setting (Berg et al., 2010; Deschamps et al., 2008). The literature contains a variety of recall periods, often chosen based on research or clinical objectives (Simoni et al., 2006; Wilson et al., 2009). Recall times of 7 days and 30 days are most common (Simoni et al., 2006), and recall over a short, recent time period (e.g. 7 days) is most likely easiest for the patient.

We developed a rapid clinical questionnaire to collect recent drug use and adherence data for informing treatment decisions. The questionnaire was administered at every visit to patients attending an outpatient HIV clinic in Nashville, Tennessee, and assessed prior 7-day drug use and missed ART doses. The purpose of this study was to use questionnaire data to identify factors associated with poor HIV-1 virologic control in our cohort, especially with respect to drug use.

2. Methods

2.1 Study design and data collection

This cross-sectional, observational study utilized data from HIV-1-infected individuals 18 years or older who presented for routine care at the Comprehensive Care Center (CCC) in Nashville, Tennessee, between May 20, 2008 and December 31, 2008. The study was approved by Vanderbilt University Medical Center's Institutional Review Board. ART adherence and drug use data were collected by CCC medical providers using a brief questionnaire (Table 1) modified from previously validated questionnaires (Chesney et al., 2000; Toobert, Hampson, & Glasgow, 2000). Using consecutive sampling at routine clinic

visits, providers first asked patients how many times they missed any ART doses within the last 7 days and secondly, how many times they used drugs (marijuana, cocaine/crack cocaine, amphetamine/crystal methamphetamine, heroin or “other” drugs) within the last 7 days. Responses to both questions were recorded by each provider on a paper form, and were later classified categorically as “yes” or “no,” with the option “Not on ART” for those not prescribed ART at the time their questionnaire was administered.

In addition to questionnaire data, patient data were collected from the CCC electronic medical record. The primary outcome was plasma HIV-1 RNA level obtained 10 days before or after completion of the questionnaire. If patients completed more than one questionnaire, we selected for analysis the first complete questionnaire that had a corresponding plasma HIV-1 RNA measurement. For specimens used in this study, virologic suppression was defined as HIV-1 RNA <48 copies/mL. Other variables obtained from the medical record included sex, race, probable route of HIV-infection (injection drug use vs. other), age at HIV-1 RNA measurement, and type of ART regimen.

2.2 Data analysis

Statistical analyses were conducted using SAS software (version 9.2, SAS Institute, Inc., Cary, NC). Univariate comparisons of socio-demographic factors, and illicit drug use were made between the following groups of patients: those on ART and not on ART; those on ART with and without missed doses; and in a supplemental analysis, those on ART with and without an HIV-1 RNA measurement at the time of their questionnaire. Chi-square tests were used for categorical variables and Wilcoxon tests or ANOVA were used for continuous variables. To further assess the relationship between cocaine and marijuana use, missed doses of ART, and virologic suppression, we used multivariable logistic regression models adjusting for sex, race, age, probable route of HIV infection, and whether or not the patient’s ART regimen included an HIV-1 protease inhibitor (PI). The PI variable was included out of concern that virologic response to this drug class may vary with respect to race (Weintrob et al., 2009). Variables in all analyses were considered statistically significant if two-sided p-values were less than 0.05.

3. Results

3.1 Demographics and illicit drug use of study participants

A total of 3,547 questionnaires were completed by 1,777 unique patients during the study period. Of these patients, 76% were male, 35% were African-American, the mean age was 44 years, and 8% reported injection drug use as their probable route of HIV infection. The prevalence of prior 7-day use of marijuana, cocaine or crack, amphetamine or crystal methamphetamine, heroin, and other drugs was 12.1%, 3.3%, 0.3%, 0%, and 0.3% respectively.

3.2 ART treatment

Of the 1,777 patients, 1,382 (78%) reported that they were supposed to be receiving ART at the time the questionnaire was conducted (Table 2). Females were less likely to receive ART than males, African Americans were less likely than non-African Americans, cocaine users were less likely than non-cocaine users, and younger patients were less likely than older patients. As expected, patients on ART had a higher median CD4 count and were more likely to have HIV-1 virologic suppression than those not on ART (Table 2).

3.3 ART adherence

Among 1,382 patients who were on ART, 149 (11%) did not have an HIV-1 RNA measurement within 10 days of their questionnaire and were excluded from subsequent

analyses. There were no statistically significant differences in demographic, drug use, or adherence variables between those with HIV-1 RNA measurements and those without (data not shown). ART adherence was measured as having missed no doses in the past 7 days. After excluding six patients who did not respond to the missed doses question, 18% (226/1,227) reported missing at least one dose in the past 7 days (Table 3). African American patients were more likely to report missing doses; use of cocaine, marijuana, and amphetamine were also associated with higher likelihood of missing doses. Additionally, those on an ART regimen containing a PI were more likely to miss doses than those on other regimens. Age and sex were not significantly associated with missing doses.

3.4 Factors associated with lack of HIV-1 virologic suppression

Nearly seventy percent (69.7%, 860/1,233) of patients who were on ART had HIV-1 virologic suppression (plasma HIV-1 RNA level <48 copies/mL) at the time of their questionnaire. Among 373 patients who were on ART and were not suppressed, the median HIV-1 RNA was 430 copies/mL (interquartile range (IQR): 110–5,830 copies/mL).

Univariate analyses revealed that compared to no use, cocaine and marijuana use were both associated with missed ART doses (48.6% vs. 17.6%, $P<0.001$; 26.7% vs. 17.4%, $P<0.006$, respectively). In the multivariable logistic regression model, cocaine use (adjusted odds ratio (aOR), 0.46; 95% confidence interval (CI), 0.22–0.98), missed ART doses (aOR, 0.36; 95% CI, 0.26–0.49), African American race (aOR, 0.64; 95% CI, 0.49–0.84), and use of a PI-containing regimen (aOR, 0.63; 95% CI, 0.48–0.84) were statistically associated with lack of HIV-1 virologic suppression (Table 4). There was no association between virologic suppression and sex, age, or marijuana use.

We repeated the multivariable analysis using virologic failure (HIV-1 RNA <200 copies/mL) as the outcome rather than virologic suppression (HIV-1 RNA <48 copies/mL) (Panel on Antiretroviral Guidelines for Adults and Adolescents, 2011). We found that 992 (80.5%) patients did not have virologic failure (instead of 860 (69.7%) who did have virologic suppression). The associated factors were similar to the original analyses, including the association of cocaine use: OR=2.00 (95% CI: 0.92, 4.35) for virologic failure versus OR=0.46 (95% CI: 0.22, 0.98) for virologic suppression.

4. Discussion

4.1 Summary of findings

Our study using point prevalence data on drug use and adherence obtained through the use of a brief, clinical questionnaire demonstrated that self-reported cocaine use in the past 7 days, self-reported missed ART in the past 7 days, African American race, and use of a PI-containing regimen were independently associated with a lack of HIV-1 virologic suppression at the time the questionnaire was administered. In contrast to cocaine use, marijuana use was not independently associated with detectable HIV-1 RNA levels after controlling for missed doses, even though it was associated with missed doses.

4.2 Cocaine use as an independent factor associated with detectable viremia

As in the present study, use of illicit drugs such as cocaine has previously been correlated with poor ART adherence in HIV-infected individuals (Arnsten et al., 2002; Hinkin et al., 2007), yet it can be difficult to distinguish the physiologic effects of illicit drug use on HIV replication from the effects of ART non-adherence (Kipp et al., 2011). Research has linked HIV disease progression in illicit drug users to incomplete ART adherence (Arnsten et al., 2002; Hinkin et al., 2007; Lucas et al., 2002), but there are also pathophysiologic data to support the direct role of cocaine in HIV disease progression. In vitro studies have reported

increased HIV replication in peripheral blood mononuclear cells treated with cocaine (Bagasra & Pomerantz, 1993; Cabral, 2006; Nair, Chadha, & Hewitt, 2000), with mouse models showing a corroborating increase in circulating HIV-1 RNA (Tashkin, 2005). It has been proposed that cocaine disrupts immune function by modulating the distribution of lymphocytes, and impedes immune response by inhibiting neutrophil and macrophage function and suppressing cytokine production (Cabral, 2006). Regardless of the exact mechanism, our data support the hypothesis that cocaine use plays more than an indirect role in virologic control; recent cocaine use remained strongly associated with unsuppressed HIV-1 RNA even after controlling for self-reported adherence, race, and type of ART regimen in the multivariable model.

The overall prevalence of reported cocaine use in our cohort (3.3%) was lower than previous studies which ranged from 4.6 % to 40% (Bouhnik et al., 2006; Cofrancesco et al., 2008; Hessol et al., 2007; Purcell, Moss, Remien, Woods, & Parsons, 2005; Sohler et al., 2007; Sullivan, Nakashima, Purcell, & Ward, 1998; Tucker, Burnam, Sherbourne, Kung, & Gifford, 2003). A possible reason is that our questionnaire captured active drug use in the past 7 days as opposed to the past 30 days, previous year, or even longer periods. The 7-day drug use questionnaire captures recent drug use, but may under-represent the prevalence of infrequent cocaine use. Another potential reason for a lower prevalence is that of response bias, since the questionnaire was administered face-to-face by the patients' medical providers. That the questionnaire may under-represent prevalence of cocaine use does not negate its usefulness as a clinical tool for identifying patients with increased risk for detectable viremia. For those identified, medical providers can customize interventions to optimize patient care. As a final note on drug use, though recent marijuana use and recent cocaine use were both significant predictors of missed ART doses, cocaine use alone was a factor associated with unsuppressed virus. This is consistent with reports of both cocaine use and marijuana use affecting ART-taking behaviors (Tucker et al., 2003; Turner et al., 2001), whereas cocaine use alone—and not marijuana use—has a biological impact on disease progression (Cofrancesco et al., 2008; Di Franco et al., 1996; Kipp et al., 2011).

4.3 Association of missed ART with detectable viremia

Since adherence in our study was defined categorically as whether or not patients missed any ART in the previous 7 days it would be difficult to compare directly with other adherence measures which often report percentages of ART doses taken over a period of time. Nevertheless, our results are generally consistent with previous work in this area (Arnsten et al., 2002; Baum et al., 2009; Cook et al., 2008) and our method has the advantage of efficiently capturing active drug use and adherence data at the time of a patient's routine clinic visit and corresponding HIV-1 RNA measurement. Our 7-day questionnaire was favorably perceived by both patients and clinicians and its use has proved to be sustainable in a busy clinical setting, as evidenced by the fact that the CCC is still using it at every patient visit, more than 3 years after it was first implemented. Although the questionnaire has not been formally validated, the observed association between self-reported missed doses and detectable viremia in the present study is consistent with results from studies using more complex measures of adherence (Arnsten et al., 2002).

4.4 Other independent factors

African Americans in the present study were less likely to be prescribed ART than non-African Americans (71% vs. 81 %, $P<0.001$) and were more likely to report missing doses (22% vs. 17%, $P=0.03$). Previous studies at our institution showed that African American patients were slower to initiate ART and were less likely to receive ART while in care at the CCC (Lemly et al., 2009; McGowan et al., 2011). While concerning, these data do not account for the racial difference in virologic suppression found in the present study, since all

patients in the multivariable analysis were on ART and the model adjusted for missed doses. The data corroborate a recent study in a US military cohort which showed that virologic response differs between African Americans and European Americans initiating ART with equal access to care (Weintrob et al., 2009). However, that study did not include a measure of adherence, a limitation which our study has attempted to address.

Of note, treatment with PI-containing ART was associated with missing doses of ART and was also an independent factor of decreased virologic suppression. Several plausible explanations for these findings exist, including that PIs may be given more frequently to patients who are deemed less likely to adhere to treatment or to those who harbor viral resistance mutations.

4.5 Limitations and concluding remarks

It is possible that patients who are actively using drugs might be less likely to present for care (Johnson, Sabin, & Girardi, 2010). We did not have data to test this hypothesis, as ours is an HIV outpatient clinic-based study. A selection bias is possible, but it would be expected that active drug users not presenting at the clinic would also not have virologic suppression due to sporadic care, which is consistent with our findings. In addition to this potential selection bias and response bias mentioned above, our study has several other limitations. First, without strong assumptions it is not possible to make causal inferences from cross-sectional data. Without longitudinal data, we cannot comment on how lack of adherence or drug use affects HIV-1 disease progression. We did not collect information on alcohol use, which is usually more common than use of illicit drugs, but measurement of alcohol use is complicated. In addition, dichotomizing the quantitative adherence and drug use responses into “yes” and “no” variables resulted in a loss of questionnaire specificity. A person who missed one dose of ART was lumped into the same category as a person who missed all 7 days of ART. This method may not bias the results in either direction along the adherence continuum because it is reasonable to consider any missed ART a lack of adherence since the time period in question is so short. However, missing multiple doses is likely associated with a higher probability of detectable HIV-1 RNA and may also be associated with cocaine use. Therefore, we cannot rule out the possibility that among those who reported at least one missed dose of ART, the association between cocaine use and lack of viral suppression was due to cocaine users missing more doses than non-users. Finally, in order for our questionnaire to be administered consecutively to all patients in a busy clinical setting, it was substantially modified from longer validated questionnaires. Thus, in the future, this simple questionnaire requires validation compared to an accepted standard and/or measured medication and drug levels to confirm its usefulness as a rapid screening tool.

Our results are consistent with the evolving body of knowledge on adherence, drug use, and race in relation to virologic control, and data were captured together over a very short period of time surrounding a clinic visit. These real-time data, corresponding with “point-in-time” virologic control, set our study apart from others that have not simultaneously considered adherence, drug use, and virologic suppression. The questionnaire is also clinically useful for identifying those with increased risk for detectable viremia and is simple and inexpensive to administer. Further studies that collect more comprehensive longitudinal data on adherence and drug use are needed, as are molecular studies to look at the immunomodulating effects of active cocaine use on HIV-1 replication.

Acknowledgments

The authors would like to thank the Comprehensive Care Center and its patients and medical providers, as well as the Vanderbilt Epidemiology and Outcomes Group for contributions to study design and interpretation of results. This research was supported by National Institutes of Health grants P30 AI54999-09 and K24 AI065298.

References

- Arnsten JH, Demas PA, Grant RW, Gourevitch MN, Farzadegan H, Howard AA, Schoenbaum EE. Impact of active drug use on antiretroviral therapy adherence and viral suppression in HIV-infected drug users. *Journal of General Internal Medicine*. 2002; 17(5):377–381. [PubMed: 12047736]
- Bagasra O, Pomerantz RJ. Human immunodeficiency virus type 1 replication in peripheral blood mononuclear cells in the presence of cocaine. *Journal of Infectious Diseases*. 1993; 168(5):1157–1164.
- Baum MK, Rafie C, Lai S, Sales S, Page B, Campa A. Crack-Cocaine Use Accelerates HIV Disease Progression in a Cohort of HIV-Positive Drug Users. *Journal of Acquired Immune Deficiency Syndromes*. 2009; 50:93–99. [PubMed: 19295339]
- Berg KM, Wilson IB, Li X, Arnsten JH. Comparison of antiretroviral adherence questions. *AIDS and Behavior*. 2012; 16(2):461–8. [PubMed: 21181252]
- Bogart LM, Kelly JA, Catz SL, Sosman JM. Impact of medical and nonmedical factors on physician decision making for HIV/AIDS antiretroviral treatment. *Journal of Acquired Immune Deficiency Syndromes*. 2000; 23(5):396–404. [PubMed: 10866232]
- Bouhnik AD, Preau M, Schiltz MA, Peretti-Watel P, Obadia Y, Lert F, Spire B. VESPA Group. Unsafe sex with casual partners and quality of life among HIV-infected gay men: evidence from a large representative sample of outpatients attending French hospitals (ANRS-EN12-VESPA). *Journal of Acquired Immune Deficiency Syndromes*. 2006; 42(5):597–603. [PubMed: 16773028]
- Cabral GA. Drugs of abuse, immune modulation, and AIDS. *Journal of Neuroimmune Pharmacology*. 2006; 1:280–295. [PubMed: 18040805]
- CDC. HIV Prevalence Estimates- United States, 2006. *MMWR*. 2008; 57(39):1073–1076. [PubMed: 18830210]
- Chesney MA, Ickovics JR, Chambers DB, Gifford AL, Neidig J, Zwickl B, Wu AW. Self-reported adherence to antiretroviral medications among participants in HIV clinical trials: the AACTG Adherence Instruments. *AIDS Care*. 2000; 12(3):255–266. [PubMed: 10928201]
- Cofrancesco J Jr, Scherzer R, Tien PC, Gilbert CL, Southwell H, Sidney S, Dobs A, Grunfeld C. Illicit drug use and HIV treatment outcomes in a US cohort. *AIDS*. 2008; 22(3):357–365. [PubMed: 18195562]
- Cook JA, Burke-Miller JK, Cohen MH, Cook RL, Vlahov D, Wilson TE, Golub ET, Schwartz RM, Howard AA, Ponath C, Plankey MW, Levine AM, Grey DD. Crack cocaine, disease progression, and mortality in a multicenter cohort of HIV-1 positive women. *AIDS*. 2008; 22:1355–1363. [PubMed: 18580615]
- Deschamps AE, De Geest S, Vandamme A, Bobbaers H, Peetermans WE, Van Wijngaerden E. Diagnostic value of different adherence measures using electronic monitoring and virologic failure as reference standards. *AIDS Patient Care and STDs*. 2008; 22(9):735–743. [PubMed: 18754705]
- Di Franco MJ, Sheppard HW, Hunter DJ, Tosteson TD, Ascher MS. The lack of association of marijuana and other recreational drugs with progression to AIDS in the San Francisco Men's Health Study. *Annals of Epidemiology*. 1996; 6(4):283–289. [PubMed: 8876838]
- Hessol NA, Kalinowski A, Benning L, Mullen J, Young M, Palella F, Anastos K, Detels R, Cohen MH. Mortality among participants in the Multicenter AIDS Cohort Study and the Women's Interagency HIV Study. *Clinical Infectious Diseases*. 2007; 44(2):287–294. [PubMed: 17173233]
- Hinkin CH, Barclay TR, Castellon SA, Levine AJ, Durvasula RS, Marion SD, Myers HF, Longshore D. Drug use and medication adherence among HIV-1 infected individuals. *AIDS and Behavior*. 2007; 11(2):185–194. [PubMed: 16897351]
- Hogg RS, Heath K, Bangsberg D, Yip B, Press N, O'Shaughnessy MV, Montaner JS. Intermittent use of triple-combination therapy is predictive of mortality at baseline and after 1 year of follow-up. *AIDS*. 2002; 16(7):1051–1058. [PubMed: 11953472]
- Johnson M, Sabin C, Girardi E. Definition and epidemiology of late presentation in Europe. *Antiviral Therapy*. 2010; 15(Suppl 1):3–8. [PubMed: 20442455]
- Kapadia F, Vlahov D, Donahoe RM, Friedland G. The role of substance abuse in HIV disease progression: reconciling differences from laboratory and epidemiologic investigations. *Clinical Infectious Diseases*. 2005; 41(7):1027–1034. [PubMed: 16142670]

- Kipp AM, Desruisseau AJ, Qian H. Non-injection Drug Use and HIV Disease Progression in the Era of Combination Antiretroviral Therapy. *Journal of Substance Abuse Treatment*. 2011; 40(4):386–396. [PubMed: 21353444]
- Lemly DC, Shepherd BE, Hulgán T, Rebeiro P, Stinnette S, Blackwell RB, Bebwaw S, Kheshti A, Sterling TR, Raffanti SP. Race and Sex Differences in Antiretroviral Therapy Use and Mortality among HIV-Infected Persons in Care. *Journal of Infectious Diseases*. 2009; 199(7):991–998. [PubMed: 19220139]
- Lima VD, Harrigan R, Bangsberg DR, Hogg RS, Gross R, Yip B, Montaner JS. The combined effect of modern highly active antiretroviral therapy regimens and adherence on mortality over time. *Journal of Acquired Immune Deficiency Syndromes*. 2009; 50(5):529–536. [PubMed: 19223785]
- Lucas GM, Cheever LW, Chaisson RE, Moore RD. Detrimental effects of continued illicit drug use on the treatment of HIV-1 infection. *Journal of Acquired Immune Deficiency Syndromes*. 2001; 27(3):251–259. [PubMed: 11464144]
- Lucas GM, Gebo KA, Chaisson RE, Moore RD. Longitudinal assessment of the effects of drug and alcohol abuse on HIV-1 treatment outcomes in an urban clinic. *AIDS*. 2002; 16(5):767–774. [PubMed: 11964533]
- McGowan CC, Weinstein DD, Samenow CP, Stinnette SE, Barkanic G, Rebeiro PF, Sterling TR, Moore RD, Hulgán T. Drug use and receipt of highly active antiretroviral therapy among HIV-infected persons in two U.S. clinic cohorts. *PLoS One*. 2011; 6(4):e18462. [PubMed: 21541016]
- Mills EJ, Nachega JB, Bangsberg DR, Singh S, Rachlis B, Wu P, Wilson K, Buchan I, Gill CJ, Cooper C. Adherence to HAART: a systematic review of developed and developing nation patient-reported barriers and facilitators. *PLoS Medicine*. 2006; 3(11):e438. [PubMed: 17121449]
- Mocroft A, Ledergerber B, Katlama C, Kirk O, Reiss P, d'Arminio Monforte A, Knysz B, Dietrich M, Phillips AN, Lundgren JD. EuroSIDA study group. Decline in the AIDS and death rates in the EuroSIDA study: an observational study. *Lancet*. 2003; 362(9377):22–29. [PubMed: 12853195]
- Nair MP, Chadha KC, Hewitt RG. Cocaine differentially modulates chemokine production by mononuclear cells from normal donors and human immunodeficiency virus type 1-infected patients. *Clinical and Diagnostic Laboratory Immunology*. 2000; 7(1):96–100. [PubMed: 10618285]
- Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services; Oct 14. 2011 p. 1-167. Available at <http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf>
- Purcell DW, Moss S, Remien RH, Woods WJ, Parsons JT. Illicit substance use, sexual risk, and HIV-positive gay and bisexual men: differences by serostatus of casual partners. *AIDS*. 2005; 19(Suppl 1):S37–47. [PubMed: 15838193]
- Qian HZ, Stinnette SE, Rebeiro PF, Kipp AM, Shepherd BE, Samenow CP, Jenkins CA, No P, McGowan CC, Hulgán T, Sterling TR. The relationship between injection and noninjection drug use and HIV disease progression. *Journal of Substance Abuse Treatment*. 2011; 41(1):14–20. [PubMed: 21349679]
- Simoni JM, Kurth AE, Pearson CR, Pantalone DW, Merrill JO, Frick PA. Self-report measures of antiretroviral therapy adherence: A review with recommendations for HIV research and clinical management. *AIDS and Behavior*. 2006; 10:227–245. [PubMed: 16783535]
- Sohler NL, Wong MD, Cunningham WE, Cabral H, Drainoni ML, Cunningham CO. Type and pattern of illicit drug use and access to health care services for HIV-infected people. *AIDS Patient Care and STDs*. 2007; 21(Suppl 1):S68–76. [PubMed: 17563292]
- Sullivan, PS.; Nakashima, AK.; Purcell, DW.; Ward, JW. Geographic differences in noninjection and injection substance use among HIV-seropositive men who have sex with men: western United States versus other regions. 1998.
- Supplement to HIV/AIDS Surveillance Study Group. *Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology*. 19(3):266–273.
- Tashkin DP. Evidence implicating cocaine as a possible risk factor for HIV infection. *Journal of Immunology*. 2005; 147(1–2):26–27.

- Toobert DJ, Hampson SE, Glasgow RE. The summary of diabetes self-care activities measure: results from 7 studies and a revised scale. *Diabetes Care*. 2000; 23(7):943–950. [PubMed: 10895844]
- Tucker JS, Burnam MA, Sherbourne CD, Kung FY, Gifford AL. Substance use and mental health correlates of nonadherence to antiretroviral medications in a sample of patients with human immunodeficiency virus infection. *American Journal of Medicine*. 2003; 114(7):573–580. [PubMed: 12753881]
- Turner BJ, Fleishman JA, Wenger N, London AS, Burnam MA, Shapiro MF, Bing EG, Stein MD, Longshore D, Bozzette SA. Effects of drug abuse and mental disorders on use and type of antiretroviral therapy in HIV-infected persons. *Journal of General Internal Medicine*. 2001; 16(9): 625–633. [PubMed: 11556944]
- Walensky RP, Paltiel AD, Losina E, Mercincavage LM, Schackman BR, Sax PE, Weinstein MC, Freedberg KA. The survival benefits of AIDS treatment in the United States. *Journal of Infectious Diseases*. 2006; 194(1):11–19. [PubMed: 16741877]
- Weintrob AC, Grandits GA, Agan BK, Ganesan A, Landrum ML, Crum-Cianflone NF, Johnson EN, Ordóñez CE, Wortmann GW, Marconi VC. IDCRP HIV Working Group. Virologic response differences between African Americans and European Americans initiating highly active antiretroviral therapy with equal access to care. *Journal of Acquired Immune Deficiency Syndromes*. 2009; 52(5):574–580. [PubMed: 19755913]
- Wilson IB, Carter AI, Berg KM. Improving the self-report of HIV antiretroviral medication adherence: is the glass half full or half empty? *Current HIV/AIDS Reports*. 2009; 6(4):177–186. [PubMed: 19849960]
- Wood E, Montaner JS, Yip B, Tyndall MW, Schechter MT, O'Shaughnessy MV, Hogg RS. Adherence and plasma HIV RNA responses to highly active antiretroviral therapy among HIV-1 infected injection drug users. *Canadian Medical Association Journal*. 2003; 169(7):656–661. [PubMed: 14517122]

Table 1**Clinical questionnaire on drug use and adherence to HIV antiretroviral therapy (ART)**

-
1	In the last week (7 days), how many times did you miss any of your HIV medications (antiretroviral therapy only)? ____ days
2	In the last week (7days), how many times did you use any of these substances?
	a. Marijuana;
	b. cocaine/crack;
	c. amphetamines/crystal meth;
	d. heroin;
	e. other
-

Table 2

Participant characteristics by receipt of antiretroviral therapy (ART) among 1,777 patients

Variable	N (n=1,777) ^a	On ART ^b (n=1,382)	Not on ART ^b (n=395)	P- value [‡]
Sex				0.001
Female	427	308 (72.1%)	119 (27.9%)	
Male	1,350	1,075 (79.6%)	275 (20.4%)	
Race				<0.001
Non-African American	1,160	942 (81.2%)	218 (18.8%)	
African American	616	439 (71.3%)	177 (28.7%)	
Age (mean ± SD), year	1,777	45.2±9.1	38.7±10.2	<0.001
Injection drug use as route of infection				0.28
Yes	145	118 (81.4%)	27 (18.6%)	
No	1,632	1265 (77.5%)	367 (22.5%)	
Marijuana use				0.79
Yes	214	165 (77.1%)	49 (22.9%)	
No	1,556	1212 (77.9%)	344 (22.1%)	
Cocaine use				0.02
Yes	58	38 (65.5%)	20 (34.5%)	
No	1,711	1340 (78.3%)	371 (21.7%)	
Amphetamine use				0.10
Yes	6	3 (50.0%)	3 (50.0%)	
No	1,761	1372 (77.9%)	389 (22.1%)	
Use of any other drugs				0.19
Yes	6	6 (100.0%)	0 (0.0%)	
No	1,630	1262 (77.4%)	368 (22.6%)	
CD4 count (median, IQR ^c), cells/mm ³	1,525	470, 295–683	438, 303–621	0.05
Proportion with HIV-1 virologic suppression	1541	69.2% (860/1233)	3.2% (10/308)	<0.001
HIV-1 RNA among those without virologic suppression (median, IQR), copies/mL	671	430; 110–5,830	14,265; 2,530–45,250	0.002

^aThe sample size may vary by variable due to missing data;^bPercentages shown in this column are row percentages;^cIQR, interquartile range^d†Using Chi-square test except t-test for the continuous variables (age, CD4 count, and HIV-1 RNA)

Table 3

Factors associated with missing at least one dose in the past 7 days among 1,233 patients who received antiretroviral therapy (ART)

Variable	N (n=1,227) ^a	Missed 1 dose ^b (n=226)	No missed doses ^b (n=1,001)	P-value [‡]
Sex				0.17
Female	278	59 (21.2%)	219 (78.8%)	
Male	949	167 (17.6%)	782 (82.4%)	
Race				0.03
Non-African American	832	140 (16.8%)	692 (83.2%)	
African American	394	86 (21.8%)	308 (78.2%)	
Injection drug use as route of infection				0.52
Yes	101	21 (20.8%)	80 (79.2%)	
No	1,126	205 (18.2%)	921 (81.8%)	
ART regimen contains a PI ^c				<0.001
Yes	792	175 (22.0%)	618 (78.0%)	
No	423	51 (12.1%)	372 (87.9%)	
Marijuana use				0.006
Yes	146	39 (26.7%)	107 (73.3%)	
No	1,078	188 (17.4%)	890 (82.4%)	
Cocaine use				<0.001
Yes	35	17 (48.6%)	18 (51.4%)	
No	1,189	209 (17.6%)	980 (82.4%)	
Amphetamine use				<0.001
Yes	3	3 (100.0%)	0 (0.0%)	
No	1,219	220 (18.1%)	999 (81.9%)	
Use of any other drugs				0.35
Yes	6	2 (33.3%)	4 (66.7%)	
No	1,124	207 (18.4%)	917 (81.6%)	
Age (mean ± SD), year	1,227	44.4±10.0	45.4±8.8	0.14

^aThe sample size may vary by variable due to missing data;

^bPercentages shown in this column are row percentages;

^cPI, Protease inhibitor;

[‡]Using Chi-square test except t-test for the continuous variable (age)

Table 4

Multivariable logistic regression analysis of factors associated with HIV virologic suppression among 1,233 patients who received antiretroviral therapy (ART)

Covariate	No. of participants	No. with virologic suppression (%) ^a	Crude OR 95% CI ^b	P- value	Adjusted OR 95% CI ^b	P- value
Sex				0.80		0.15
Female	282	195 (69.1%)	1.0		1.0	
Male	951	665 (69.9%)	1.03 (0.78–1.34)		0.79 (0.58–1.09)	
Race				<0.001		0.002
Non-African American	835	612 (73.3%)	1.0		1.0	
African American	397	247 (62.2%)	0.60 (0.47–0.77)		0.64 (0.49–0.84)	
Age, 1 year increase	1,233	860 (69.7%)	1.01 (1.00–1.03)	0.06	1.01 (1.00–1.03)	0.10
Injection drug use as route of infection				0.42		0.59
No	1130	793 (70.1%)	1.0		1.0	
Yes	102	67 (65.7%)	0.82 (0.53–1.25)		0.88 (0.56–1.39)	
Regimen contains a PI ^c				<0.001		0.002
No	424	329 (77.6%)	1.0		1.0	
Yes	795	529 (66.5%)	0.57 (0.44–0.75)		0.63 (0.48–0.84)	
Marijuana use				0.42		0.72
No	1082	758 (70.1%)	1.0		1.0	
Yes	148	99 (66.9%)	0.86 (0.60–1.24)		1.08 (0.72–1.62)	
Cocaine use				<0.001		0.04
No	1193	843 (70.7%)	1.0		1.0	
Yes	36	15 (41.7%)	0.30 (0.15–0.58)		0.46 (0.22–0.98)	
Missed 1 dose in the past 7 days				<0.001		<0.001
No	1001	747 (74.6%)	1.0		1.0	
Yes	226	111 (49.1%)	0.33 (0.24–0.44)		0.36 (0.26–0.49)	

^aPercentages shown in this column are row percentages;

^bOR, odds ratio, 95% CI, 95% confidence interval;

^cPI, protease inhibitor