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in Atlanta and Miami

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Master of Science

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M.D., Brown Medical School, 2004

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Abstract

Factors associated with antiretroviral utilization among HIV-infected crack cocaine users in Atlanta and Miami

By Rupali Kotwal Doshi

Despite availability of antiretroviral therapy (ART), HIV-infected drug users, particularly crack cocaine users, continue to have high HIV-related morbidity and mortality. The purpose of this study was to determine factors associated with ART utilization among HIV-infected crack cocaine users. A cross-sectional analysis was conducted using the baseline data for hospitalized HIV-infected crack cocaine users recruited for Project HOPE (Hospital Visit is an Opportunity for Prevention and Engagement with HIV-positive Crack Users) in Atlanta and Miami, who were eligible for ART (reported or documented any lifetime use of ART or CD4 <350 cells/μl). Among 350 eligible participants, mean age was 44.9 years (SD 7.0), 49% were male, 90% were black, and 81% were heterosexual. Median CD4 count was 144 cells/μl, and 78 of 350 (22%) were taking ART. Of the participants taking ART, 60% had undetectable HIV-1 viral load, representing 9% of the eligible population. Multivariable logistic regression was conducted to examine the relationship between homelessness and ART utilization. Current homelessness was negatively associated with ART utilization on bivariate and multivariable analyses (adjusted OR 0.31, 95% CI 0.16-0.60). A model to predict ART utilization was developed for Atlanta participants and tested for generalizability among Miami participants; variables chosen for this model included age, race, gender, insurance, homelessness, depression, crack use frequency, and alcohol use frequency. AUC for Atlanta was 0.814 and Miami was 0.577. When visits to HIV primary care were added to the model, AUC for Atlanta was 0.84 and for Miami was 0.678. Viral load suppression was modeled among ART users. None of the measured covariates, including age, gender, race, city, alcohol use, marijuana use, crack use, depression, HIV knowledge, patient-provider relationship, homelessness, and trust, were independently associated with viral load suppression. For HIV-infected crack cocaine users, structural factors may be as important as individual and interpersonal factors in facilitating ART utilization. Only 9% of HIV-infected crack cocaine users had viral suppression, but among those on ART, 60% achieved viral suppression. Future public health programs in the US should focus on improving uptake of ART and achieving viral suppression among crack cocaine users.

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INTRODUCTION

Antiretroviral therapy (ART) for treatment of HIV has both individual and social benefits. ART dramatically reduces morbidity and mortality among HIV-infected individuals (1), and this includes substance abusers (2, 3). ART also reduces HIV transmission. For example, early data showed that transmission of HIV from mother to child could be reduced by use of zidovudine, the first antiretroviral medication approved for use in treating HIV infection (4). More recent data showed that combination ART can reduce transmission between serodiscordant sexual partners (5).

Despite strong evidence to support ART use to treat HIV, persistent disparities in antiretroviral access and use contribute to unnecessary HIV disease progression and higher mortality among HIV-infected drug users (2, 6). Some of the known barriers to antiretroviral treatment access and utilization include substance use, mental illness, provider communication, medication side effects, low levels of social support, poverty, and homelessness (7-10). These barriers disproportionately burden the HIV-infected urban poor (8).

HIV-infected crack cocaine users

Crack cocaine is a solid form (“rock”) of cocaine powder that is generally smoked (12). Smoking crack cocaine results in euphoria (“high”) within approximately 30-90 seconds (13). Other neuropsychiatric effects include depressed mood and brain hypoperfusion (14). In addition, use of crack cocaine has been associated with hypersexuallity and high-risk sexual behavior (15). Crack cocaine use remains common among HIV-infected persons in some urban settings (16). It is known to contribute to the spread of HIV through high-risk sexual behaviors (17, 18).

HIV-infected crack cocaine users historically have had poor access and use of HIV care (11). In HIV-infected persons, use of crack cocaine is associated with less linkage to HIV primary care after initial diagnosis of HIV (19), irregular engagement in outpatient care (16, 20), reduced antiretroviral adherence (21, 22), accelerated HIV disease progression (23-26), and a greater risk of AIDS-related death (23). Symptoms of mental illness commonly affect HIV-infected crack cocaine users (27) and may additionally compromise access to and retention in HIV primary care as well as medication adherence (21, 28, 29). An improved understanding of the barriers to antiretroviral utilization among this population is needed in order to better design interventions to address these poor outcomes.

Intersecting epidemics: homelessness, substance abuse, and HIV

Homelessness is one major societal factor that affects HIV-infected individuals and particularly those with drug addiction. Homelessness is more prevalent among HIV-infected individuals, and homeless individuals may engage with greater frequency in HIV risk behaviors such as commercial sex work and drug use (30). In a study conducted among HIV-infected individuals in New York City, drug abuse was associated with unstable housing, and unstable housing was associated with decreased use of medical care (31). In a study of HIV-infected injection drug users in Vancouver, Canada, homelessness and frequent heroin use were negatively associated with ART utilization (32). Based on this epidemiology, we sought to explore the relationship between homelessness and ART utilization among a unique population, HIV-infected crack cocaine users.

Factors affecting antiretroviral utilization

Prior studies have emphasized individual-level barriers to antiretroviral utilization. In these studies, ART utilization has been found to be negatively associated with African-American race (33), female gender (34), injection drug use (7, 10, 32), and depressive symptoms (35). Among vulnerable populations, interpersonal-level and structural-level factors have been shown to be predictors of ART utilization as well. For example, among HIV-infected injection drug users in Baltimore, Miami, New York, and San Francisco, better patient-provider communication, higher levels of social support, stable housing, access to drug treatment and medical coverage were associated with improved access to ART (36). Factors associated with ART utilization in the HIV-infected crack cocaine-using population have not been studied to date. A broad approach that acknowledges the potential importance of identifying multilevel individual and societal factors is important to develop interventions that will engage and retain HIV-infected crack cocaine users in HIV primary care and support their use of ART.

For this thesis, we explored multiple ways to measure ART utilization. We also examined the relationship between homelessness and ART utilization among a cohort of HIV-infected crack cocaine users eligible for ART who were recruited from inpatient wards of two safety net hospitals located in the southeastern US. Similar analyses have been conducted in other cohorts of HIV-infected drug users (36, 37). In addition, we attempted to create a clinical prediction tool for ART utilization. Finally, we explored factors associated with viral load suppression among study participants who were taking

ART.

METHODS

Specific aims and hypotheses

Aim 1a: To estimate the prevalence of ART utilization among hospitalized HIV-infected crack cocaine users who are eligible for ART, based on self-report and medical chart data.

Aim 1b: To calculate the positive predictive value (PPV) and negative predictive value (NPV) of self-reported ART utilization using the medical chart data as the gold standard.

Aim 2: To estimate the association between homelessness and ART utilization among hospitalized HIV-infected crack cocaine users.

> Hypothesis 2a: Homeless HIV-infected crack cocaine users are less likely to use ART than those who are not homeless.
>
> Hypothesis 2b: The effect of homelessness on ART utilization varies by gender.

Aim 3: To develop a clinical prediction tool to identify HIV-infected crack cocaine users who are most likely to take ART.

Aim 4: To determine the factors independently associated with undetectable viral load among HIV-infected crack cocaine users taking ART.

> Hypothesis 4: More visits to HIV primary care, no homelessness, and strong patient-provider relationship are independently associated with undetectable viral load.

Design

This is a cross-sectional study nested within the parent study, Project HOPE (Hospital Visit is an Opportunity for Prevention and Engagement), a randomized clinical trial that enrolled hospitalized HIV-infected crack cocaine users (NIH/NIDA-funded RO1 5R01DA017612, registered at www.clinicaltrials.gov NCT00447798). The trial tested a multi-component prevention care advocate intervention designed to decrease high risk sexual behavior, improve linkage to HIV primary care, and improve readiness for substance abuse treatment. Data for the current analysis were collected at the baseline study visit for Project HOPE.

Subjects and Enrollment

The study participants were HIV-infected crack cocaine users recruited from the inpatient medical wards of Grady Memorial Hospital, Atlanta, Georgia, and Jackson Memorial Hospital, Miami, Florida, between August 2006 and February 2010. The inclusion criteria for the parent study included: age ≥ 18, HIV-infected, reported use of crack cocaine within the previous 2 years, sexually active within the previous 6 months, hospitalized at the time of enrollment, and ability to speak English. Pregnant patients were excluded.

We chose CD4 <350 cells/µl as one of the eligibility criteria for the current analysis.[1] The cutoff of CD4 <350 cells/µl was chosen because as of 2006, the Department of Health and Human Services recommended starting antiretroviral therapy if CD4 <350 cells/µl. Although more recently the guidelines have been updated to include individuals with higher CD4 levels (up to 500 cells/µl and above 500 cells/µl), the strongest evidence remains for ART use when CD4 <350 cells/µl (38).

HOPE participants considered eligible for ART included those with measured CD4 <350 cells/µl (n=304), were identified in the medical chart as taking ART (additional n=20), or reported prior use of ART (additional n=26), for a total of 350 participants.

Procedure

This study was approved by the institutional review boards of the University of Miami and Emory University and the research oversight committees of Jackson Memorial Hospital and Grady Memorial Hospital. After obtaining informed consent and HIPAA forms (Health Insurance Portability and Accountability Act of 1996), structured interviews were administered to eligible participants upon their enrollment in Project HOPE. Trained interviewers collected interview data at the participant's bedside using a Handheld-Assisted Personal Interview. Data collected from interviews included information on socio-demographics, alcohol and drug use, mental health, sexual

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[1] CD4 cell count is a marker of disease progression for HIV, and lower CD4 cell count indicates more advanced HIV disease. HIV-infected individuals with CD4 <200 cells/µl or evidence of AIDS-related opportunistic infections are considered to have progressed to AIDS.

practices, and medical care.

In addition, data was abstracted from medical charts and pharmacy records for study participants. Participants provided written consent for study participation and release of medical records. They were reimbursed $25 for the baseline interview, which took approximately 2 hours.

Variables

The outcome variables for this analysis were ART utilization (yes vs. no), measured both by self-report and by medical chart data, and HIV-1 viral load (copies/ml) measured within 90 days before or after study enrollment. HIV-1 viral load was dichotomized as undetectable (<400 copies/ml) vs. detectable (≥400 copies/ml). The covariates of interest were organized according to a previously published study of ART utilization among HIV-infected injection drug users into individual-level, interpersonal-level, and structural-level factors (36).

Individual-level variables were categorized into demographic, substance use and mental health, and medical care categories. Demographic variables included age (continuous), sex (male vs. female), race/ethnicity (black vs. white/other), education (≥ vs. < high school diploma/GED), self-reported monthly income (<$100, $100-599, or ≥$600), current employment (yes vs. no), sexual orientation (heterosexual vs. other), and city (Miami vs. Atlanta). Substance use variables included crack cocaine use frequency during the previous 6 months (≥daily, 1-6 days/week, <1 days/week, or none), alcohol use frequency during the previous 6 months (≥daily, less than daily, none), and history of ever using injection drugs (yes vs. no). We used the methods suggested by the Brief Symptom Index (BSI) developers to categorize participants as at risk for depression (yes vs. no) using gender-specific cutoffs from raw scores of the depression component of the BSI-18 (BSI-18 $\geq$ 9 for women and BSI-18 $\geq$ 7 for men were considered at risk for depression) (39, 40). Medical care utilization was measured for reported use of HIV primary care in past 6 months (< vs. $\geq$2 visits) and reported use of drug or alcohol treatment in the past 6 months (yes vs. no).

The interpersonal variables measured were social support and patient-provider relationship. Social support was measured using the Medical Outcomes Study Social Support Survey that assessed domains of emotional support, tangible support, affectionate support and positive social interaction (41). Responses were based on a 5-point scale (1 to 5), with higher scores indicating greater social support. Participants' scores were dichotomized with an average score $\geq$4 indicating high social support and <4 indicating low social support. HIV knowledge was measured through 18 questions about transmission risk, role of antiretroviral therapy, and self-care. Responses were summed and dichotomized into $\geq$80% correct or <80% correct to reflect high or low knowledge. Patient-provider relationship was assessed using the Engagement with Health Care Provider scale, which has been previously validated (42). The scale includes questions such as, "How much did you feel you could….ask this doctor any questions about your medical condition, get this doctor to listen to your concerns, feel helped by seeing this doctor." Responses were highly skewed, with a median score of 2 of a possible range of 0 to 2. Therefore, the measure was recoded as good (2) versus less than good (0-1).

Structural variables included current homelessness (yes vs. no), spent any time in a jail, prison or correctional facility in last 6 months (yes vs. no), insurance coverage (any vs. none), traded sex for money in the last 6 months (yes vs. no). Having any insurance coverage included private insurance, Medicaid, Medicare, veteran's benefits, or AIDS Drug Assistance Program (ADAP) funding.

Sample size calculation

The initial sample size calculations were conducted for the Project HOPE intervention. To achieve a power of 85% for the detection of a 10% reduction in unprotected sexual intercourse in the prior six months, using a one-sided α=0.05, 180 participants were needed in both the control and intervention arms. A total of 413 participants were enrolled in the study. For the purposes of this analysis, 350 participants were included, based on the criteria described above.

Data analysis

SAS (SAS Institute, Cary, NC) was used for all statistical analyses presented here.

Aim 1

The proportion of participants taking ART per self-report and by medical chart was calculated among those eligible for ART. From this data, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated to evaluate how well self-report measured actual ART utilization (considering the medical chart as the gold standard measurement of ART use).

Aim 2

Based on a review of the literature, we constructed a directed acyclic graph (DAG) to explore relationship between homelessness and ART (43). To identify potential confounders, we then conducted bivariate analyses with all covariates with respect to the outcome (ART users vs. nonusers) and the exposure (homeless vs. not homeless). Following this, we conducted a bivariate analysis with calculated crude odds ratios (OR) for each covariate (ART users vs. nonusers). Based on the DAG and potential confounders identified in the bivariate analyses, we created a multivariable logistic regression model and calculated the adjusted prevalence odds ratio (adjusted OR) for ART utilization (homeless vs. not homeless). Details on each variable can be found in the previous section on variables. In particular, substance use variables were ordinal with the following categories: crack cocaine use frequency during the previous 6 months (≥daily, 1-6 days/week, <1 days/week, or none), alcohol use frequency during the previous 6 months (≥daily, less than daily, none), and history of ever using injection drugs (yes vs. no). The multivariable model is given below:

$$Logit\ P(ART\ utilization = 1) = \beta_0 + \beta_1 homeless + \beta_2 gender + \beta_3 race + \beta_4 age + \beta_5 city + \beta_6 crack\_freq + \beta_7 depression + \beta_8 insurance$$

Finally, we examined the interaction between gender and homelessness by creating an interaction term (gender x homeless) and adding it to the multivariable model to calculate adjusted ORs for the effect of homelessness on ART utilization among men and women separately. The multivariable model that includes the interaction term is shown below:

$$Logit\ P(ART\ utilization = 1) = \beta_0 + \beta_1 homeless + \beta_2 gender + \beta_3 race + \beta_4 age + \beta_5 city + \beta_6 crack\_freq + \beta_7 depression + \beta_8 insurance + \beta_9 (gender*homeless)$$

Aim 3

The goals were to, one, develop a logistic regression model to predict ART utilization among one city (Atlanta), based on variables that are often clinically available, and two, assess how generalizable the model was to another city (Miami). The variables included in the model were: age, race, gender, insurance, homelessness, depression, frequency of crack use, frequency of alcohol use. We chose Atlanta as the city in which to develop the model because it had more participants. Receiver operating characteristic (ROC) curves were constructed for each city and compared graphically. Furthermore, an additional variable, visits to HIV primary care, was added to the predictive model for Atlanta, and the new model's performance was assessed among Miami participants. ROC curves for the new model were constructed for each city and compared graphically.

Aim 4

Among the subset of participants who were taking ART according to the medical chart, we examined the frequencies of each covariate between participants who had undetectable versus detectable viral load. If the expected value of a cell was greater than

5, the Chi-square (X^2) p-value was reported. If the expected value was less than 5, the Fisher's exact p-value was reported. Based on a review of the literature, our own clinical experiences, and the comparative frequencies, we chose covariates to enter into the multivariable logistic regression model that included age, gender, race, city, alcohol use (any vs. none), marijuana use (any vs. none), crack use (≥daily vs. <daily), depression, HIV knowledge, patient-provider relationship, homelessness, and trust. Subsequently, stepwise elimination was conducted, keeping variables with a p-value <0.05 in the final model.

RESULTS

Sample description

The study population was predominantly African-American (89%), heterosexual (81%), and poor (90% reported an annual income ≤$10,000). There was an even distribution of men and women, and there were more participants from Atlanta (55%) compared with Miami (45%). A majority of participants (61%) scored ≥80% correct on the HIV knowledge scale.

Overall, 78 of 350 (22%) eligible participants were using ART according to the medical chart. Of the ART users who had viral load data available (n=52), 31 (60%) had undetectable viral load; this represented 9% of the eligible sample.

Aim 1

There were 350 out of 413 (85%) participants who were considered eligible for ART. 108 out of 350 (31%) reported current use of ART (Table 1). According to the medical chart data, 78 of 350 (22%) were taking ART (Table 1). When compared with the gold standard of medical chart data for ART utilization, the sensitivity of self-reported ART utilization was 94% and the specificity was 87%. The positive predictive value of self-reported ART utilization was 68%, and the negative predictive value (NPV) was 98%.

Aim 2

The directed acyclic graph can be found in Figure 2. CD4 count was categorized into standard groupings and ART utilization was compared between the groups (Table 2).

Frequencies of the covariates of interest were compared between ART users and nonusers (Table 3 through Table 7). Individual demographic covariates can be found in Table 3, individual drug use and mental health covariates are in Table 4, medical care covariates are in Table 5, interpersonal covariates are in Table 6, and structural covariates are in Table 7.

The variables around which the outcome differed included city, crack use frequency, alcohol use frequency, use of HIV primary care, drug or alcohol treatment, trust, patient-provider relationship, insurance, and homelessness. Among Atlanta participants, 31% used ART, and among Miami participants, 69% used ART ($p<0.0001$). Crack use in the previous 6 months was less frequent among ART users ($p=0.025$). More of the ART users abstained from alcohol (41% abstinence among ART users vs. 28% abstinence among nonusers, $p=0.0045$). Among ART users, 86% reported at least 2 visits to HIV primary care, while only 47% of nonusers reported at least 2 visits to HIV primary care in the previous 12 months ($p<0.0001$). Reported drug or alcohol treatment in the past 6 months was more frequent among ART user (31%) compared with nonusers (13%) ($p=0.0001$). ART users less frequently (22%) believed that the government had not tested ART drugs enough compared with nonusers (34%) ($p=0.042$). Patient-provider relationship was strong among 70% of ART users compared with 46% of nonusers ($p=0.0002$). Having any insurance was reported by 65% of ART users and only 47% of nonusers ($p=0.0093$). Current homelessness was reported by 23% of ART users, compared with 45% of nonusers ($p=0.0006$).

Comparisons of the frequencies of the covariates for the exposure (homeless and not homeless) are in Table 8 and Table 9. The variables around which the exposure differed included gender, crack use frequency, use of HIV primary care, and insurance. Men were more likely than women to report current homelessness (56% vs. 44%, p=0.039). Homeless individuals were more likely to us crack at least daily compared with non-homeless individuals (p=0.0017). Homeless individuals had a high rate of screening positive for depression (74%) compared with non-homeless individuals (59%) (p=0.0043). Use of HIV primary care (≥2 visits in 12 months) was reported by 46% of homeless participants, compared with 63% of non-homeless participants (p=0.0031). Participants who were homeless were less likely than non-homeless participants to report having any insurance (45% vs. 56%, p=0.05).

Results of the bivariate and multivariable logistic regression models are reported in Table 10. The OR for ART utilization comparing homelessness vs. not homeless was 0.37 (95% CI 0.21-0.67) on bivariate analysis. After adjusting for potential confounders, the odds of prevalent ART use among homeless participants was 0.31 (95% CI 0.16-0.60) times the odds of ART use among non-homeless participants. In addition, the variables that remained significant on the multivariable analysis included city and insurance.

The results for interaction of gender and homelessness are reported in Table 11. The crude OR for ART utilization, homeless vs. not homeless, was 0.16 for women and 0.60 for men. The likelihood ratio test for the gender-homeless interaction term was not significant (p=0.28). However, the adjusted OR for ART utilization, homeless vs. not homeless, was calculated to be 0.16 (95% CI 0.06-0.38) for women and 0.41 (95% CI 0.18-0.94) for men.

Aim 3

The Hosmer-Lemeshow p-value was 0.91, suggesting that the model fit was good. The area under the curve (AUC) for Atlanta was 0.814 and the AUC for Miami was 0.577 (Figure 3). In the second model, the variable for visits to HIV primary care was added into the prediction model. The Hosmer-Lemeshow p-value was 0.54, suggesting a good fit for the model. The AUC for Atlanta was 0.840, and the AUC for Miami was 0.678 (Figure 4).

Aim 4

The frequency of covariates comparing ART users with undetectable vs. detectable HIV-1 viral load can be found in Table 12, Table 13, Table 14, Table 15, and Table 16. Among the covariates, there appeared to be less frequent crack and alcohol use among individuals with undetectable viral load ($p<0.05$). The variables loaded into the multivariable model included: age, gender, race, city, education, alcohol use, marijuana use, crack use frequency, depression, HIV knowledge, patient-provider relationship, trust, and homelessness. None of the examined covariates was independently associated with viral load suppression.

DISCUSSION

The findings from this study provide insight into the correlates of antiretroviral utilization among a unique population, hospitalized HIV-infected crack cocaine users, who have historically had worse health outcomes than others infected with HIV. Non-utilization of ART plays a significant role in the poor health outcomes among this group. In this cross-sectional analysis, only 22% of the eligible participants were taking ART, and only 9% had an undetectable HIV-1 viral load. Both interpersonal and structural factors played significant roles in determining ART use. In particular, homelessness was a distinct factor in determining ART use.

Homelessness was inversely associated with ART utilization in both bivariate (crude OR 0.31) and multivariable (adjusted OR 0.37) analyses. The similarity of point estimates using bivariate or multivariable models suggests that the variables that were controlled did not contribute much to confounding in this sample. The association between homelessness and ART utilization may be due to lack of space to keep medications, lack of personal safety, fear of disclosing HIV status to others, and life priorities that may compete with the activities needed to participate in HIV primary care and take antiretroviral medications. The association between homelessness and ART utilization suggests that provision of stable housing for HIV-infected individuals could increase uptake of ART. Stable housing coupled with case management as an intervention for homeless HIV-infected individuals has been shown to be successful in Chicago (50), but housing alone showed equivocal results in a multicenter trial in

Baltimore, Chicago, and Los Angeles (51). Housing as an intervention to improve ART utilization among HIV-infected crack cocaine users in the Southeast should be explored. The HOPWA (Housing Opportunities for Persons with AIDS) program through the Department of Housing and Urban Development offers incentives and resources for housing for HIV-infected individuals, and results about the effectiveness of this program could be analyzed (52).

Among the other structural factors evaluated, having participated in drug or alcohol treatment in the previous 6 months (crude OR 3.09), having any health insurance coverage (crude OR 2.00), and enrollment in Miami (crude OR 3.64) were associated with ART utilization in the bivariate analysis. In multivariable analysis, city (adjusted OR 3.88) and insurance (adjusted OR 2.03) remained independently associated with ART utilization.

The significance of drug treatment suggests that despite a lack of pharmacologic replacement for cocaine, participation in drug treatment is strongly associated with taking ART. We speculate that drug treatment programs may specifically encourage participation in primary health care or individuals who are motivated to enter drug treatment may also be motivated to take antiretroviral therapy to improve their health. A growing body of literature supports the integration of substance abuse treatment into HIV primary care (44-47), and future studies could consider the benefits specifically for cocaine users. Although pharmacologic therapy for cocaine addiction is not currently available, there are promising therapies that need further study, such as the cocaine vaccine (currently in clinical trials), modafinil, disulfiram, dopamine-beta-hydroxylase inhibitors, selective serotonin reuptake inhibitors (SSRIs), and baclofen (48). In the future, perhaps HIV providers can consider incorporating use of these therapies into the care of HIV-infected cocaine users, in order to improve rates of ART utilization.

The low frequency of insurance coverage in the group (51%) is concerning and reflects challenges in establishing ongoing financing for HIV care in this population. Having any insurance coverage was associated with ART use, which is not surprising, given the high costs associated with primary health care for HIV-infected individuals. Interestingly, this association highlights that existing health care safety nets, such as those supported by the Ryan White Comprehensive AIDS Resources Emergency (CARE) Act, Medicaid, and AIDS Drug Assistance Programs (ADAP) may not reach enough of the HIV-infected population, particularly crack cocaine users (49). The reasons for this could be explored in a future study of health care coverage of HIV-infected crack cocaine users.

Enrollment in Miami was strongly associated with ART utilization; the reasons for this may include fundamental differences in the culture of prescribing physicians, local beliefs of the HIV-infected populations about ART, transportation, or social services between the two cities. These factors were not measured as part of this study but could be the focus of a future investigation.

Among medical care covariates, having at least 2 visits to HIV primary care in the previous 6 months was associated with increased odds of ART utilization in bivariate analysis (crude OR 6.65). It is difficult to obtain antiretroviral therapy without visiting a qualified medical provider. This highlights the importance of engagement and retention in care for HIV-infected crack cocaine users to improve ART utilization rates. Engagement and retention in HIV care have become a main focus for implementation of the "Seek, Test and Treat" public health campaign to reduce HIV incidence in the US (55). Challenges unique to each vulnerable population remain.

Being at risk for depression was not associated with ART utilization on bivariate analysis but there was a trend towards significance (crude OR 0.65, 95% CI 0.39-1.09). Endorsement of depressive symptoms has previously been shown to be associated with decreased odds of medication adherence in general populations (56) as well as decreased odds of ART utilization among HIV-infected individuals (57). Treatment of depression in HIV-infected individuals appears improve depression symptoms (58) as well as HIV medication adherence (57, 59), and future studies could specifically consider depression therapy as an intervention to improve ART utilization and achieve viral suppression among HIV-infected crack cocaine users.

Only 9% of the participants eligible for ART in this analysis had undetectable viral load (<400 copies/ml). Given the high frequency of HIV risk transmission behaviors among crack cocaine users (18, 60-64), this figure reinforces the ongoing potential for transmission and the need for interventions that support prevention, including addressing structural and individual barriers to ART access and adherence. Of those taking ART with a viral load available, 60% had an undetectable viral load. This analysis showed that despite ongoing crack use, HIV-infected crack cocaine users had the ability to take medication reliably and to achieve viral suppression, thereby reducing their risk of HIV transmission and improving their HIV-related outcomes. Given the cross-sectional design of this study, it was not possible to determine whether those individuals on ART with detectable viral load (≥400 copies/ml) were in the process of responding or failing therapy or were not adherent to ART.

Based on the ROC curves for the model developed for predicting ART utilization using clinically available variables, the model performed well for Atlanta participants (AUC=0.814) but was not particularly generalizable to Miami participants (AUC=0.577). When the model included the variable for visits to HIV primary care, the model improved for both Atlanta participants (AUC=0.840) and Miami participants (AUC=0.678). Based on the significant difference between the frequency of ART use between the two cities, this finding is not surprising. The poor generalizability of the prediction model between Atlanta and Miami reflects that there may be underlying differences between these cities with respect to ART prescribing practices or barriers to obtaining and taking ART. Further study is needed to elucidate these differences.

Finally, beyond measures of adherence to ART, which were not included in the model, none of the chosen variables (including age, gender, race, city, alcohol use, marijuana use, crack use, depression, HIV knowledge, patient-provider relationship, homelessness, and trust) were independently significant with respect to viral load suppression. The sample size may have been too small to accurately identify significant factors. The lack of significance of any of the selected variables differs from previous literature that suggests that visits to HIV primary care, homelessness, and patient-provider relationship may affect viral suppression. Further inquiry into the factors affecting viral suppression among HIV-infected crack cocaine users should be pursued.

Some of the limitations of this study include the design, context of participant recruitment, generalizability, missing data, and sample size (particularly for the viral load analysis). The cross-sectional analysis precludes any conclusions of causality between the examined variables and the outcome. The study enrolled participants when they were hospitalized for medical reasons, and this context could have influenced the results in several ways. The responses to the baseline questionnaire may have been affected by the environment (hospital room), presence of other medical personnel, concurrent medical illness, and the context of being hospitalized. However, interview staff took all precautions to complete the interview in a private and in a manner respectful of ongoing medical care. The findings may not be generalizable to other HIV-infected drug-using populations since this population lived in urban areas of the southeastern US (Atlanta or Miami) and specifically used crack cocaine. Missing viral load data limits our ability to draw conclusions about correlates of viral suppression. Viral load data was only collected when available in the laboratory tracking systems and was not routinely collected as part of study procedure.

The criteria for determining eligibility may be one more limitation of the study. Part of the eligibility criteria depended on self-report of ART utilization in the past, and previous studies in drug users have used self-report for determining ART use (36). However, self-reported ART use has been shown to be somewhat unreliable, in a general HIV population receiving care, a population of community-recruited injection drug users (65, 66), and the present study. Therefore, it is possible that the group that we considered eligible for ART was an overestimation by 26 participants. If these participants were eliminated from our analysis, the overall prevalence of ART utilization would have increased slightly.

In summary, our data showed that HIV-infected individuals who are active crack cocaine users can engage in HIV primary care, take antiretroviral therapy, and ultimately achieve HIV viral suppression. Multiple structural factors were independently associated with ART utilization, including homelessness, insurance status, and city. These findings suggest that interventions to improve housing and health care coverage could improve ART utilization among this population, and differences between the two cities should be explored further. Medical care covariates, including visits to HIV primary care and drug or alcohol treatment were associated with ART utilization in bivariate analysis; these data suggest that engagement and retention in care for both HIV care and substance abuse treatment are keys to improving ART utilization among this population. Our findings may help to inform policy makers, researchers, administrators, and health care providers in the development of interventions and services to improve access to and utilization of antiretroviral therapy among this disadvantaged population.

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TABLES

Table 1: Comparison of responses to "Are you currently taking HIV medications?" of HOPE participants eligible for ART vs. those verified as taking ART according to medical chart

	ART utilization according to medical chart, Yes	ART utilization according to medical chart, No	Total
Self-reported ART utilization, Yes	73 (94%)	35 (13%)	108
Self-reported ART utilization, No	5 (6%)	237 (87%)	242
Total	78	272	350

Table 2: CD4 category for those taking ART vs. not taking ART determined from medical chart data among eligible HOPE participants (n=342), X^2 p=0.0004

CD4 range (cells/µl)	Not taking ART (n=267) (% for CD4 category)	Taking ART (n=75) (% for CD4 category)
0 – 49	80 (82)	17 (17)
50 – 199	106 (87)	17 (14)
200 – 349	60 (71)	24 (29)
350 – 499	14 (61)	9 (39)
≥500	7 (47)	8 (53)

Table 3: Frequency of individual demographic covariates among those taking ART vs. not taking ART indicated by medical chart data

	Not taking ART (n=272) (%)	Taking ART (n=78) (%)	Total (n=350) (%)	X^2	P-value
Age, mean, years (SD)	44.8 (7.1)	45.1 (6.9)	44.9 (7.0)	N/A	0.74 (pooled T test)
Gender				0.053	0.82
Male	132 (49)	39 (50)	171 (49)		
Female	140 (51)	39 (50)	179 (51)		
Race				4.51	0.10
White	19 (7)	5 (6)	24 (7)		
Black	246 (91)	68 (87)	314 (89)		
Other	5 (2)	5 (6)	10 (3)		
Sexual orientation				0.0025	0.96
Heterosexual	219 (81)	63 (81)	282 (81)		
Any other	53 (19)	15 (15)	68 (19)		
Annual income				0.21	0.65
>$10,000	24 (9)	6 (8)	31 (9)		
≤ $10,000	242 (91)	72 (92)	314 (90)		
City				23.5	<0.0001
Atlanta	168 (62)	24 (31)	192 (55)		
Miami	104 (38)	54 (69)	158 (45)		
HIV knowledge				0.12	0.73
≥80% correct	165 (61)	49 (63)	214 (61)		
<80% correct	107 (39)	29 (37)	136 (39)		

Table 4: Frequency of individual drug use and mental health covariates among those taking ART vs. not taking ART indicated by medical chart data (n=350)

	Not taking ART (n=272) (%)	Taking ART (n=78) (%)	Total (n=350) (%)	X^2	P-value
Crack use, past 6 months				9.39	0.025
≥ Daily	98 (37)	29 (37)	127 (36)		
1-6 days/week	101 (38)	24 (31)	125 (37)		
<1 day/week	55 (21)	14 (18)	69 (20)		
None	12 (5)	11 (14)	23 (7)		
Alcohol use, past 6 months				13.09	0.0045
≥ Daily	51 (19)	12 (15)	63 (18)		
1-6 days/week	100 (37)	14 (18)	114 (33)		
<1 day/week	44 (16)	20 (26)	64 (18)		
None	77 (28)	32 (41)	109 (31)		
Injection drug use				0.54	0.46
Ever	59 (22)	14 (18)	73 (21)		
Never	212 (78)	64 (82)	276 (79)		
At risk for depression				2.69	0.10
Yes	177 (67)	43 (56)	220 (63)		
No	88 (33)	33 (43)	121 (35)		

Table 5: Frequency of medical care covariates among those taking ART vs. not taking ART indicated by medical chart data (n=350)

	Not taking ART (n=272) (%)	Taking ART (n=78) (%)	Total (n=350) (%)	X^2	P-value
HIV primary care, past 12 months				35.68	<0.0001
≥2 visits	129 (47)	66 (86)	195 (56)		
<2 visits	143 (53)	11 (14)	154 (44)		
Drug or alcohol treatment, past 6 months				14.40	0.0001
Yes	34 (13)	24 (31)	58 (17)		
No	236 (87)	54 (69)	290 (83)		

Table 6: Frequency of interpersonal covariates among those taking ART vs. not taking ART indicated by medical chart data (n=350)

	Not taking ART (n=272) (%)	Taking ART (n=78) (%)	Total (n=350) (%)	X^2	P-value
Believe the government has not tested ART enough				4.14	0.042
Agree	85 (34)	17 (22)	102 (29)		
Disagree	162 (66)	60 (78)	222 (63)		
Patient-provider relationship				13.41	0.0002
Strong	111 (46)	53 (70)	164 (47)		
Not strong	132 (54)	23 (30)	155 (44)		

Table 7: Frequency of structural covariates among those taking ART vs. not taking ART indicated by medical chart data (n=350)

	Not taking ART (n=272) (%)	Taking ART (n=78) (%)	Total (n=350) (%)	X^2	P-value
Insurance				6.76	0.0093
Any	129 (48)	50 (65)	179 (51)		
None	139 (52)	27 (35)	166 (47)		
Currently homeless				11.7	0.0006
Yes	120 (45)	18 (23)	138 (39)		
No	149 (55)	60 (77)	209 (60)		
Incarceration in the past 6 months				1.00	0.31
Yes	71 (26)	25 (32)	96 (27)		
No	199 (74)	53 (68)	252 (72)		

Table 8: Frequency of individual demographic and medical care covariates among those who are currently homeless vs. not currently homeless (n=350)

	Not currently homeless (n=209) (%)	Currently homeless (n=138) (%)	Total (n=350) (%)	X^2	P-value
Age, mean, years (SD)	44.6 (6.9)	45.3 (7.3)	44.9 (7.0)	N/A	0.33 (pooled T test)
Gender				4.25	0.039
Male	93 (45)	77 (56)	170 (49)		
Female	116 (55)	61 (44)	177 (51)		
Race				4.29	0.12
White	10 (5)	14 (10)	24 (7)		
Black	194 (93)	119 (86)	313 (89)		
Other	5 (2)	5 (4)	10 (3)		
Sexual orientation				1.20	0.27
Heterosexual	172 (82)	107 (78)	279 (80)		
Any other	37 (18)	31 (22)	68 (19)		
Annual income				1.62	0.20
>$10,000	22 (11)	9 (7)	31 (9)		
≤ $10,000	186 (89)	128 (93)	314 (90)		
City				0.0013	0.97
Atlanta	114 (55)	75 (54)	189 (54)		
Miami	95 (45)	63 (46)	158 (45)		
Crack use, past 6 months				15.09	0.0017
≥ Daily	61 (30)	66 (49)	127 (36)		
1-6 days/week	88 (43)	37 (27)	125 (36)		
<1 day/week	40 (19)	27 (20)	67 (19)		
None	17 (8)	6 (4)	23 (7)		
Alcohol use, past 6 months				2.56	0.46
≥ Daily	34 (16)	29 (21)	63 (18)		
1-6 days/week	67 (32)	45 (33)	112 (32)		
<1 day/week	37 (18)	27 (20)	64 (18)		
None	71 (34)	37 (27)	108 (31)		
At risk for depression				8.17	0.0043
Yes	119 (59)	101 (74)	220 (63)		
No	84 (41)	36 (26)	120 (34)		

Table 9: Frequency of medical care, interpersonal and structural covariates among those who are currently homeless vs. not currently homeless (n=350)

	Not currently homeless (n=209) (%)	Currently homeless (n=138) (%)	Total (n=350) (%)	X^2	P-value
HIV primary care, past 12 months				8.76	0.0031
≥2 visits	130 (63)	64 (46)	194 (55)		
<2 visits	78 (38)	74 (54)	152 (43)		
Drug or alcohol treatment, past 6 months				0.37	0.54
Yes	37 (18)	21 (15)	58 (17)		
No	172 (82)	117 (85)	289 (83)		
Patient-provider relationship				3.19	0.074
Strong	109 (55)	54 (45)	163 (47)		
Not strong	88 (45)	66 (55)	154 (44)		
Believe the government has not tested ART enough				0.12	0.73
Agree	60 (30)	40 (32)	100 (29)		
Disagree	137 (70)	84 (68)	221 (63)		
Insurance				3.84	0.05
Any	116 (56)	62 (45)	178 (51)		
None	91 (44)	75 (55)	166 (47)		
Incarceration in past 6 months				3.68	0.055
Yes	50 (24)	46 (33)	96 (27)		
No	159 (76)	92 (67)	251 (72)		

Table 10: Crude and adjusted odds ratios for ART utilization (*Not included in multivariable model)

Variable	Crude odds ratio (95% CI)	Adjusted odds ratio (95% CI)
Current homelessness (yes vs. no)	0.37 (0.21 – 0.67)	0.31 (0.16 – 0.60)
Age (per year)	1.01 (0.97 – 1.04)	1.00 (0.96 – 1.04)
Race (black vs. not black)	0.72 (0.33 – 1.56)	0.61 (0.24 – 1.53)
Gender (male vs. female)	1.06 (0.64 – 1.76)	1.35 (0.76 – 2.42)
City (Miami vs. Atlanta)	3.64 (2.12 – 6.23)	3.88 (2.10 – 7.13)
Crack use, past 6 months		
≥ Daily	0.32 (0.13 – 0.81)	0.44 (0.16 – 1.24)
1-6 days/week	0.26 (0.10 – 0.66)	0.29 (0.10 – 0.79)
<1 day/week	0.28 (0.10 – 0.76)	0.35 (0.12 – 1.06)
None	Reference	Reference
Alcohol use, past 6 months		N/A*
≥ Daily	0.57 (0.27 – 1.20)	
1-6 days/week	0.34 (0.17 – 0.68)	
<1 day/week	1.09 (0.56 – 2.14)	
None	Reference	
At risk for depression (yes vs. no)	0.65 (0.39 – 1.09)	1.04 (0.57 – 1.88)
Visits to HIV primary care in past 6 months (≥2 vs. <2)	6.65 (3.37 – 13.15)	N/A*
Drug or alcohol treatment in the past 6 months (yes vs. no)	3.09 (1.69 – 5.62)	N/A*
Any insurance (yes vs. no)	2.00 (1.18 – 3.38)	2.03 (1.10 – 3.74)

Table 11: Interaction between homelessness and gender (LRT for gender-homeless interaction p-value = 0.28)

	WOMEN		MEN	
	Not taking ART n=138	Taking ART n=39	Not taking ART n=131	Taking ART n=39
Not currently homeless	81	35	68	25
Currently homeless	57	4	63	14
Crude OR for ART utilization	0.16		0.60	
Adjusted OR for ART utilization (95% CI)	0.16 (0.06 – 0.38)		0.41 (0.18 – 0.94)	

Table 12: Frequency of individual demographic variables among ART users comparing those who have undetectable vs. detectable viral load, *X^2 p-value, †Fisher's exact p-value, ‡Pooled T test

	Detectable viral load (n=21) (%)	Undetectable (n=31) (%)	Total (n=52) (%)	P-value
Age, mean, years (SD)	43.7 (8.3)	44.4 (6.4)	44.1 (7.1)	0.75‡
Gender				0.080*
Male	7 (33)	18 (58)	25 (48)	
Female	14 (67)	13 (42)	27 (52)	
Race				0.40†
Black	19 (90)	24 (77)	43 (83)	
White / Other	2 (10)	7 (23)	9 (17)	
Sexual orientation				0.32†
Heterosexual	18 (86)	22 (71)	43 (83)	
Any other	3 (14)	9 (29)	12 (23)	
Annual income				0.67†
>$10,000	1 (5)	3 (10)	4 (8)	
≤ $10,000	20 (95)	28 (90)	48 (92)	
City				0.94*
Atlanta	7 (33)	10 (32)	17 (33)	
Miami	14 (67)	21 (68)	35 (67)	
HIV knowledge				0.059*
≥80% correct	11 (52)	24 (77)	35 (67)	
<80% correct	10 (48)	7 (23)	17 (33)	

Table 13: Frequency of individual drug and alcohol use variables among ART users comparing those who have undetectable vs. detectable viral load, *X^2 p-value, †Fisher's exact p-value

	Detectable viral load (n=21) (%)	Undetectable viral load (n=31) (%)	Total (n=52) (%)	P-value
Crack use, past 6 months				0.039†
≥ Daily	9 (43)	8 (26)	17 (33)	
1-6 days/week	5 (24)	10 (32)	15 (29)	
<1 day/week	2 (10)	9 (29)	11 (21)	
None	5 (24)	4 (13)	9 (17)	
Alcohol use, past 6 months				0.01†
≥ Daily	6 (29)	2 (6)	8 (15)	
1-6 days/week	0 (0)	9 (29)	9 (17)	
<1 day/week	5 (24)	8 (26)	13 (25)	
None	10 (48)	12 (39)	22 (42)	
Injection drug use				0.49*
Ever	2 (10)	5 (16)	7 (13)	
Never	19 (90)	26 (84)	45 (87)	
At risk for depression				0.73*
Yes	11 (55)	18 (60)	29 (56)	
No	9 (45)	12 (40)	21 (40)	

Table 14: Frequency of medical care covariates among ART users with undetectable vs. detectable viral load, *X^2 p-value, †Fisher's exact p-value

	Detectable viral load (n=21) (%)	Undetectable viral load (n=31) (%)	Total (n=52) (%)	P-value
HIV primary care, past 12 months				0.69†
≥2 visits	19 (90)	26 (84)	45 (87)	
<2 visits	2 (10)	5 (16)	7 (13)	
Drug or alcohol treatment, past 6 months				0.49*
Yes	8 (38)	9 (29)	17 (33)	
No	13 (62)	22 (71)	35 (67)	

Table 15: Frequency of interpersonal variables among ART users comparing those who have undetectable vs. detectable viral load, *X^2 p-value, †Fisher's exact p-value

	Detectable viral load (n=21) (%)	Undetectable viral load (n=31) (%)	Total (n=52) (%)	P-value
Social support				0.74*
High (>75)	12 (60)	20 (65)	32 (62)	
Not high (<75)	8 (40)	11 (35)	19 (37)	
Believe the government has not tested ART enough				0.32†
Agree	6 (29)	5 (16)	11 (21)	
Disagree	15 (71)	26 (84)	41 (79)	
Patient-provider relationship				
Strong	11 (52)	22 (76)	33 (63)	0.08*
Not strong	10 (48)	7 (24)	17 (32)	

Table 16: Frequency of structural variables among ART users comparing those who have undetectable vs. detectable viral load, *X^2 p-value, †Fisher's exact p-value

	Detectable viral load (n=21) (%)	Undetectable viral load (n=31) (%)	Total (n=52) (%)	P-value
Insurance				0.36*
Any	11 (55)	21 (68)	32 (62)	
None	9 (45)	10 (32)	19 (37)	
Currently homeless				0.72†
Yes	3 (14)	6 (19)	9 (17)	
No	18 (86)	25 (81)	43 (83)	
Incarceration in the past 6 months				0.94*
Yes	7 (33)	10 (32)	17 (33)	
No	14 (67)	21 (68)	35 (67)	

FIGURES

Figure 1: HIV-1 $\log_{10}$ viral load distribution for ART users (1) vs. nonusers (0)

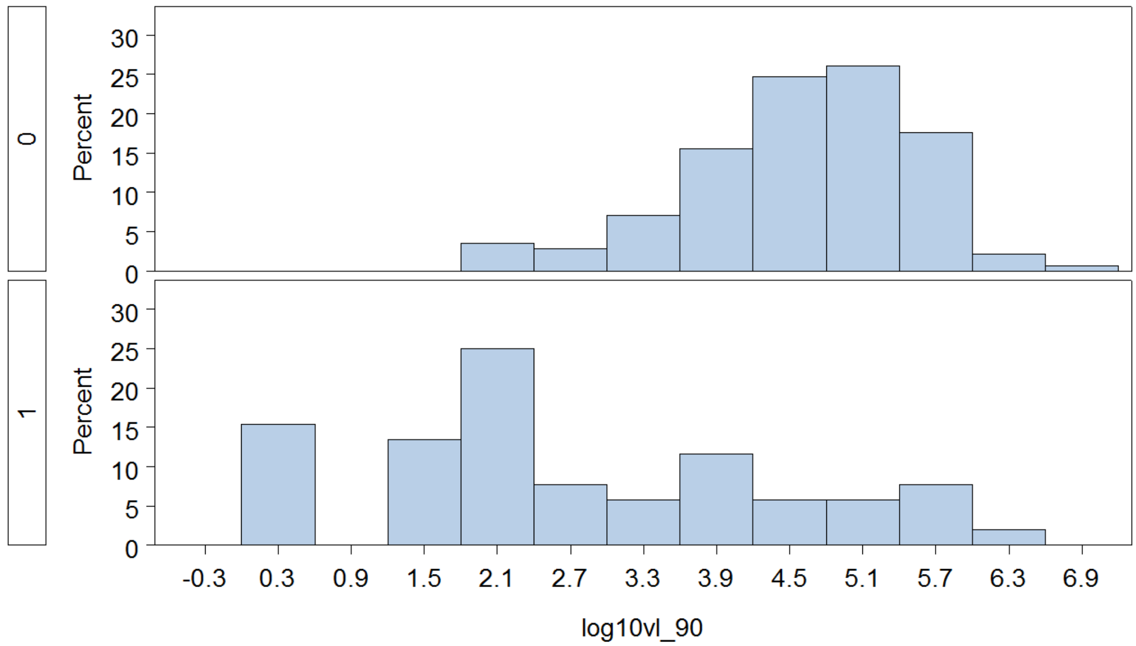

Figure 2: Directed acyclic graph exploring the relationship between homelessness and ART utilization

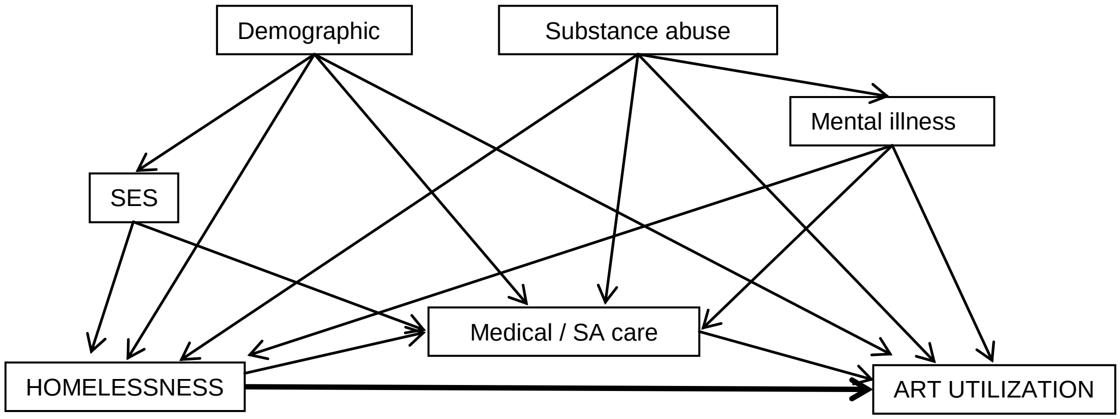

Figure 3: Predicting ART utilization, Hosmer-Lemeshow goodness-of-fit p=0.91, AUC Atlanta = 0.814, AUC Miami = 0.577

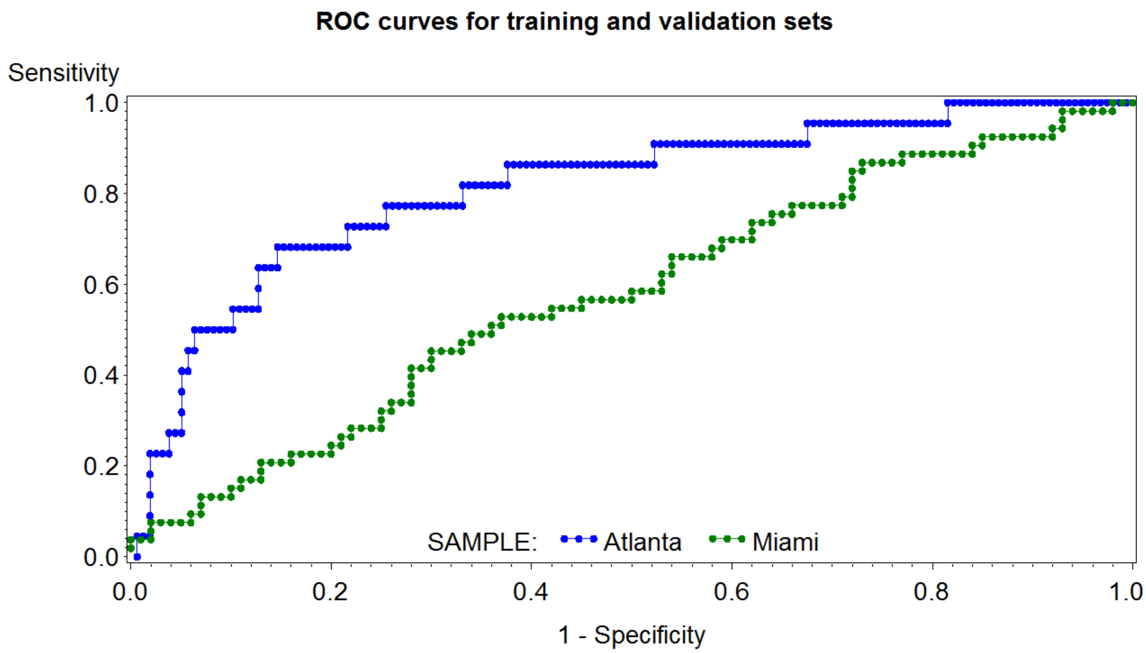

Figure 4: Predicting ART utilization with visits to HIV primary care included in the model, Hosmer-Lemeshow goodness-of-fit p=0.54, AUC Atlanta = 0.840, AUC Miami = 0.678