Published in final edited form as:
AIDS Behav. 2009 February ; 13(1): 145–153. doi:10.1007/s10461-007-9337-1.

Factors Associated with HIV Viral Load in a Respondent Driven Sample in Los Angeles

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Abstract

This study used a modified version of the Behavioral Model for Vulnerable Populations to examine the predisposing, enabling, and need factors associated with detectable viral load (VL). HIV status was measured using saliva and confirmed by blood. Of 835 persons enrolled, 193 were HIV positive and provided VL counts. A multistage logistic regression demonstrated that the predisposing factors of homelessness and recent substance abuse, particularly methamphetamine abuse, had a negative association with VL. The negative association of homelessness was lessened with the introduction of enabling and need utilization factors in the model. In contrast, the negative association with recent substance abuse on VL was sustained in the final model. Provision of HIV care and medications attenuated the negative association of homelessness within this sample. Guided policy to address substance abuse among those who are HIV positive is needed to improve biological outcomes.

Keywords

Homeless; HIV; substance abuse; viral load; respondent driven sampling

INTRODUCTION

Although tremendous gains have been made in the treatment of human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS), disparities in access and subsequent receipt of care continue to be documented (Cunningham *et al.*, 1995, 1998; King *et al.*, 2004). The face of HIV has changed from the early 1980s and is now reflective of the intercalation of poverty and disease (CDC Factsheet, 2006; Cunningham *et al.*, 2005; Diaz *et al.*, 1994; Krueger *et al.*, 1990). Individuals living in poverty are disproportionately affected both by unstable housing and substance use, which are contributors to lower access to and utilization of medical care (Katz *et al.*, 2001; Kushel *et al.*, 2001, 2006; Martens, 2001; Strathdee *et al.*, 1998). These same factors correlate with transmission of HIV and represent possible contributors to HIV prevalence among the homeless that is three times that of the general population (Culhane *et al.* 2001).

Treating persons with multiple diagnoses (HIV, drug abuse, mental illness) is complicated—not only because of the independent and synergistic disease processes but also because of

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disparate access to care, limited or no insurance, and unmet subsistence needs (e.g., food, transportation, child care; Cunningham *et al*., 1999). When homelessness, i.e., persons without stable or permanent housing who may live on the streets, in a shelter or mission, single room occupancy facility, abandoned building or vehicle or 'doubled up' with friends or family members (DHHS/HRSA, 1999) is added to the equation, outcomes of HIV treatment can be even more compromised (Waldrop-Valverde and Valverde, 2005).

The Behavioral Model for Vulnerable Populations (Andersen *et al.*, 2000; Gelberg, Andersen and Leake, 2000) provides a theoretical framework for analyzing health care utilization within vulnerable populations. The model can be used to demonstrate that utilization of health care and subsequent outcomes can be explained by: (1) variables that predispose persons to use care such as demographics and social structure; (2) variables that enable or create barriers to care such as income, insurance and (3) variables that describe the need for health care determined by individual perception or medical professional evaluation. The Andersen/Gelberg model has been well represented in assessing homeless persons' health care utilization and outcomes (Barkin *et al.*, 2003; Herndon *et al.*, 2003; Kim *et al*, 2006; Lewis, Andersen, and Gelberg, 2003; Stein *et al.*, 2000) and has been used to predict the treatment of HIV-positive individuals with highly active antiretroviral therapy (HAART) (Andersen *et al*., 2000).

HAART has reduced morbidity and mortality from HIV (Crum *et al.*, 2006). Adherence to HAART is important as missed dosages can affect viral replication and can lead to drug resistance (Ho *et al.*, 1995; Low-Beer *et al.*, 2000). Several studies indicate that factors such as current substance use and unstable housing impede medication adherence and viral suppression (Arnsten *et al.*, 2002; Duran *et al.*, 2001; Knowlton *et al.*, 2001; Lucas *et al.*, 2001; O' Connell, 2003; Pulvirenti *et al.*, 2003; Turner *et al.*, 2001), leading to more likely transmission of multidrug resistant strains of HIV (Little *et al.*, 2002).

Due to the limited choice in remaining antiretrovirals for treatment, transmission of resistant HIV has both individual and community health implications. Prior studies on homelessness and HIV seropositive individuals have largely focused on the impact of homelessness and dual diagnoses on utilization of services (Gordon *et al.*, 2006; Kim *et al.*, 2006; Moss *et al.*, 2004). Missing in this work is the extent to which predisposing, enabling and need factors predict successful outcomes from HIV medical care, such as achieving viral load levels that are undetectable.

This manuscript analyzed survey and clinical data from a respondent-driven sample of individuals in Los Angeles County whose behaviors (i.e., being men who have sex with men, drug use) place them at the core of the HIV epidemic. The core refers to a group whose demographic, geographic, and behavioral characteristics contribute to their disproportionate role in the transmission of sexually transmitted infections (Yorke, Hethcote, and Nold, 1978). The objective of this paper is to apply the Behavioral Model for Vulnerable populations to a subset of HIV-seropositive participants enrolled in a larger study to identify factors associated with undetectable viral load. We hypothesized that introducing predisposing vulnerable factors identified in the literature such as homelessness, substance use, and mental illness, would have a negative association with the clinical outcome of viral load. We also hypothesized that introducing factors that enable health care utilization and represent subjective and objective need for health care will decrease and increase, respectively, the differences between HIV positive persons with detectable and undetectable viral loads.

METHODS

Participants

Between August 2005 and August 2006, 835 participants were recruited into the Los Angeles site of the Sexual Acquisition and Transmission of HIV – Cooperative Agreement Program (NIDA's SATH-CAP) using Respondent-Driven Sampling (RDS). RDS is a variant of chain-referral sampling used to reach hidden populations (Heckathorn, 1999, 2002); details of the recruitment method are described elsewhere (Heckathorn, 2002).

Twenty-five "seeds" who met core criteria were recruited via flyers posted at agencies, stores, social organizations, bars, sex clubs, and initiated the referral chains. Sixty- four percent of the 25 seeds were HIV seropositive. They were provided up to seven coupons to recruit individuals from their social network who met core criteria, and from their sexual network. Twenty-one waves were needed to populate the final sample which was comprised of individuals who met the following inclusion criteria: age 18 years and older; resided in Los Angeles County; provided informed consent; identified as either an MSM and/or a DU (powder or crack cocaine, heroin, methamphetamine, or reported injection of any drug in the past six months); a current a sex partner of an MSM or DU in the study; or a sex partner of a sex partner in the study. Forty-seven participants who were women, reported "other" race, or had missing viral load results were excluded from these analyses due to small cell sizes, resulting in a sample of 788. Of these, 193 men were HIV infected and provided labs documenting viral load.

Procedures

All participants underwent a one-hour audio computer-assisted self-interview (ACASI) that included questions about demographics (age, gender, education, race, ethnicity, employment, housing status), medical care access and utilization, sexual practices, sexual partnerships, HIV-related risk behaviors, friendships and social network. Biological data were collected upon completion of the ACASI and included an oral fluid sample tested for HIV antibodies (Oraquik, Orasure Technologies, Bethlehem, PA) and blood specimens (10mL each) to confirm HIV infection (Western Blot) and to assay HIV viral load (Los Angeles County Public Health Department laboratory). Participants received $50 for completing study requirements, and were given coupons to recruit individuals in their social and sexual networks into the study for which they received $20 per successful recruit. The Human Subjects Protection Committee of the University of California, Los Angeles provided oversight of all activities in this project.

Variables

Health status regarding HIV disease was measured by viral load using a qualitative cutoff of 400 copies per mL to classify detectable and undetectable cases (Kushel *et al.*, 2006; Moss *et al.*, 2004).

The following variables were included within the predisposing category: age, number of years being HIV positive; gender, race/ethnicity; relationship status (single, married, separated or widowed); education (high school, some college and above); employment status; self-report of homelessness (yes/no); mental health and substance abuse. Substance use was evaluated as any drug use in the past 30 days; self-reported use of methamphetamine, or cocaine (powder or crack), or heroin, in the previous 30 days.

Variables within the enabling category included health insurance (yes/no) and the type of insurance (health maintenance, private, public: Medicaid, Medicare, Social Security Insurance and Social Security Disability Insurance; Veteran Administration, Champus and other); income during previous 30-day period ($0–500; $501–1000; > $1000); number of physician visits for previous 12 months; current care by a HIV physician specialist.

The final category, perceived and objective need, included current use of HIV medications.

Statistic Analysis

The sample weights created for viral load, the outcome variable, were estimated using RDS Analysis Tool version 5.6.0. (Heckathorn and Volz, 2006). A sensitivity test was conducted for the unweighted data and compared to the results from the weighted data. The point estimates, reported as odds ratios in this study, from two sets of data were not significantly different to each other, and the 95% confidence intervals (CI) although the unweighted estimates tended to be smaller than the weighted estimates. Thus, the unweighted results are presented as they are more conservative than the weighted results.

Univariate analysis comparisons of all predisposing, enabling, and need variables by viral load status (<400 copies per ml or > 400 copies per ml) were performed using analysis of variance (ANOVA) for continuous variables and Chi Square or Fisher's exact test for categorical variables. In order to test our hypotheses in accord with the Behavioral Model, we established three multivariate stepwise models incorporating the predisposing, enabling and need variables sequentially to predict the probability of detectable versus undetectable viral loads in our study population [odds ratios (OR), 95% confidence intervals (CIs)]. These models have been explored for problems of multicollinearity and interactions among the variables in each stepwise model separately.

RESULTS

The Association of Participant Characteristics on Detectable Viral Load

Approximately 55% percent (n=107) of HIV-seropositive participants provided biological samples documenting undetectable viral loads. The predisposing variables showed that HIV-seropositive participants with detectable viral load were significantly more likely to consider themselves homeless (56% vs. 31%, Chi-Square, $p < 0.01$) than those who did not identify as homeless. Participants who reported use of one or more drugs in the past 30 days (62% vs. 46%, Chi-Square, $p < 0.05$), and specifically report recent use of methamphetamine (60% vs. 39%, Chi-Square, $p < 0.05$) were more likely to have detectable viral loads than those who did not report recent drug use. The enabling variables demonstrated that participants who reported seeing a physician for HIV care were significantly less likely to have detectable viral loads (83 % vs. 95%, Chi-Square, $p<0.01$). The need variables associated with viral load such that participants who reported taking their HIV medications were significantly less likely to have detectable viral loads (90% vs. 43%, Chi-Square, $p < 0.001$) (See Table 1).

Multivariate Analysis Results

Table 2 presents the odds ratios for all independent variables in the full model based on logic regression not adjusted for any other independent variables. The next three columns represent the multivariate logistic regression adjusting sequentially for the additional sets of variables. In column 2, the predisposing variables were entered into the first multivariate logistic regression model. Supporting our main hypothesis, participants who considered themselves homeless (Adjusted OR 2.11; 95% CI 0.93, 4.8) or reported using drugs in the past 30 days (Adjusted OR 2.61; 95% CI 1.24, 5.49), were significantly more likely to have detectable versus undetectable viral loads (see Table 2). The association of recent reported methamphetamine use with viral load is about 45% stronger than recent use of other drugs as measured in the crude model (OR 2.36; 95%CI 1.09, 5.08). Participants who considered themselves homeless were more likely to report recent use of methamphetamine (63.3%) than those who did not consider themselves homeless (38.3%), an association that was strongly correlated (R=0.248, p=0.009, Results not in Tables). This significant association precluded inclusion of the methamphetamine variable in the multivariate model as it correlated significantly with any

drug use and with the homelessness variables. Column 3 enters enabling variables after controlling for the predisposing variables. No significant predictors were found among the enabling variables; however, their introduction affected the estimate of the covariate, homelessness, such that it is no longer statistically significant (Adjusted 2.06; 95% CI 0.88, 4.79). The introduction of enabling variables positively associated with reported recent drug use, as participants had higher odds of being detectable (Adjusted OR 2.59; 95% CI 1.22, 5.49). The final model seen in column 4 enters the need variables and controls for the predisposing and enabling variables. As in adjusted model 2, although statistically not significant, the covariate of homelessness has been further negatively affected with lower odds of being detectable compared to the first model. Participants who reported recent drug use, however, were still more likely to have detectable viral loads (Adjusted OR 2.46; 95% CI .99, 6.13) although the estimate becomes less precise.

DISCUSSION

The Behavioral Model for Vulnerable Populations supported our main hypothesis that predisposing variables such as homelessness and recent drug use would affect the clinical outcome of detectable viral loads in a sample of HIV sero-positive men recruited into a larger study in Los Angeles. Persons who were homeless or reported recent drug use were more than two times more likely to have detectable viral loads compared to those persons not homeless or reporting recent drug use. However, when introducing enabling variables representing factors that facilitate HIV health care utilization (insurance, income and seeing an HIV specialist), the negative association of homelessness and VL was attenuated. Further, when introducing perceived and observed need for health care utilization variables such as taking medications for HIV; the association of homelessness with detectable viral load is further weakened. In our model, although homelessness itself can be predictive of having a detectable viral load, the provision of health care evidenced by having the ability to pay for care, to have an HIV specialist and to take HIV medications can diminish the association of homelessness with the HIV clinical outcome of viral load. This finding is similar to reports from San Francisco showing a high penetration of antiretroviral medical care among the homeless (Riley *et al.*, 2005) and is also consistent with findings that persons who reported access to HIV specialists and adherence to antiretroviral medications were more likely to have better biological outcomes (Riley *et al.*, 2005).

In contrast, participants who reported recent drug use were consistently less likely to have undetectable viral loads even when health care utilization enabling or need variables were introduced into the model. Paradoxically, the negative association of recent drug use on viral load appears to strengthen as enabling and need variables are brought in.

The co-occurrence of homelessness and substance abuse among HIV-seropositive individuals has been shown to worsen health outcomes and increase medical care costs (Aidala *et al.*, 2005; Kim *et al.*, 2006). The strength of the associations of viral load with recent methamphetamine use and viral load with overall recent substance use deserve consideration. Methamphetamine abuse has been identified as a negative predictor of antiretroviral adherence (Halkitis *et al.*, 2005; Moss *et al.*, 2004; Reback *et al.*, 2003) and there are some suggestions that it may have direct immunological effects that could associate with poor biological outcomes (Gavrilin, Mathes, and Podell, 2002; Markowitz *et al.*, 2005).

These analyses have several limitations. First, our sample was recruited using respondent-driven sampling (RDS). While RDS has been proposed as a bias-free sampling methodology to access “hidden” populations, such as MSM and drug users (Ramirez-Valles *et al.*, 2005), its ability to produce representative samples is unclear (Martin *et al.*, 2003). Second, potential self-report bias may have led to an under-reporting of behaviors that are stigmatized or

unpopular such as admitting recent drug use or non-adherence to HIV medication regimens. Third, the single biological outcome variable of viral load, while correlated with control of viral replication, is only one aspect of biological control of HIV disease overall. Use of CD4 counts, which is reflective of overall immune status, would undoubtedly broaden the assessment of biological status for these participants. Fourth, although individuals in the sample who reported taking HIV medications were approximately 92% less likely to have detectable viral loads, we did not have a standardized measure of adherence. There are subpopulations of mutated viruses in which the virus is slow to replicate (Pastori *et al.*, 2006), therefore, persons infected with the delta CCR5 mutation would have lower viral loads, with or without taking medications. However, it is highly improbable that all 107 individuals would have this mutation and is more likely an indirect measure of adherence to medications. Additional analyses of the entire sample from the cooperative agreement (SATH-CAP) need to occur to answer these questions.

Despite these limitations, the Behavioral Model for Vulnerable Populations provided a useful framework in analyzing the association of health care utilization factors on viral load among HIV positive men recruited by RDS sampling. Predisposing factors such as homelessness and reported recent drug use negatively influenced viral load. Enabling factors and need factors such as insurance, visits to an HIV specialist and taking medications had a positive association on viral load for persons who were homeless and HIV positive, but not on those persons who were HIV positive and reported recent substance abuse.

These findings are crucial to understanding factors that correlate with one of the primary biomarkers of HIV disease status in a population with significant healthcare disparities. The use of the Andersen/Gelberg health care utilization model clarified associations between key variables to isolate the relative contribution of homelessness, recent drug use and HIV medication taking on a key marker of HIV medical care. . Findings from this project illustrate the need for policy directed toward emphasizing drug use reduction strategies in groups of HIV-positive, individuals with healthcare disparities to improve HIV and general health outcomes. Further confirmatory studies to analyze the associations between drug use variables and HIV viral load are needed.

Acknowledgements

The research team would like to thank Dr. Ronald Andersen for his advice and expertise in the adaptation of the Andersen/Gelberg model and the following individuals for their assistance in the development of this manuscript: Mr. Gregory D. Victorianne; Ms Uyen Kao This project was funded by National Institute of Drug Abuse U01DA17394 (Shoptaw, PI); Minority supplement (Shoptaw PI./King)

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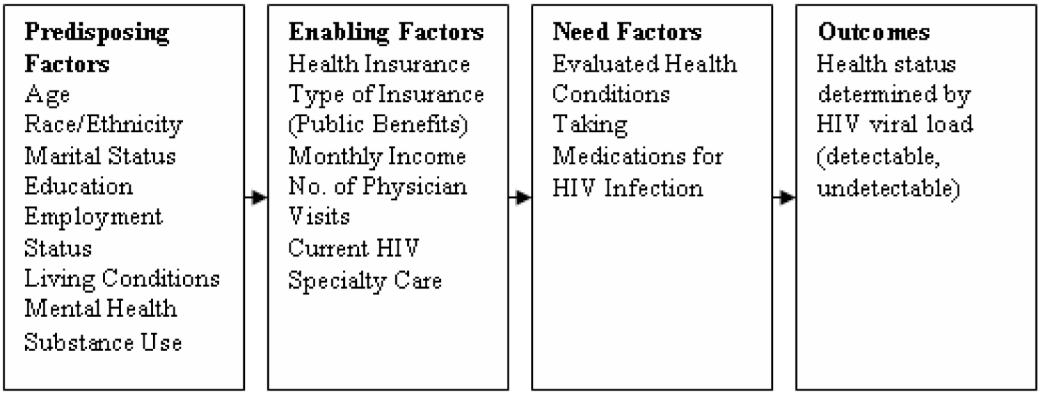

Figure 1.
Behavioral Model for Vulnerable Populations

Table 1

Predisposing, Enabling and Need Variable by Viral Load (n=193).

Variable	Viral load <400 (n=107)[a]		Viral load >=400 (n=86)[a]	
	N or M	% or (SD)	N or M	% or (SD)
A. PREDISPOSING VARIABLES				
Age (in years)	43.14	(8.2)	41.45	(6.7)
Years have been HIV-positive	11.29	(6.7)	10.76	(6.9)
Race-Ethnicity				
Black	49	38%	42	49%
Hispanic/Latino	54	50%	34	40%
White	12	11%	10	11%
Marital				
Single (never married)	74	70%	65	76%
Married, Partnered/Living together	13	12%	8	9%
Separated, Divorced, Widowed	18	17%	12	14%
Education				
High school and less	96	90%	78	91%
Some college and above	11	10%	8	9%
Employment				
Unemployed	85	79%	73	85%
Employed	22	21%	13	15%
Consider Self homeless				
No	74	69%	38	44%*
Yes	33	31%	48	56%
BSI [b]				
Low	42	44%	42	55%
High	53	56%	34	45%
Any drug use in past 30 days?				
No	57	54%	33	38%*
Yes	48	46%	53	62%
Past 30 day use of amphetamine/meth?				
No	33	61%	22	40%*
Yes	21	39%	33	60%
Past 30 day use of cocaine/crack?				
No	44	61%	39	57%
Yes	28	39%	29	43%
Past 30 day use of heroin by itself?				
No	53	84%	45	90%
Yes	10	16%	5	10%
Past 30 day use of other drugs?				
No	22	71%	23	77%
Yes	9	29%	7	23%

Variable	Viral load <400 (n=107)[a]		Viral load >=400 (n=86)[a]	
	N or M	% or (SD)	N or M	% or (SD)
B. ENABLING VARIABLES				
Health insurance				
No	42	39%	42	49%
Yes	65	61%	44	51%
Insurance type				
HMO, Private				
No	101	94%	82	98%
Yes	6	6%	2	2%
Medicaid, Medicare, SSI, SSDI				
No	54	50%	48	57%
Yes	53	50%	36	43%
VA, CHAMPUS				
No	104	97%	83	99%
Yes	3	3%	1	1%
Other types of insurance				
No	96	90%	81	96%
Yes	11	10%	3	4%
Income				
$0 to $500 per month	54	50%	54	63%
$501 to $1000 per month	32	30%	21	24%
$1000 per month and above	21	20%	11	13%
Seeing an MD for HIV				
No	5	5%	13	17%*
Yes	94	95%	63	83%
Times of doctor visit in past 12 months	5.34	(4.2)	5.65	(6.0)
C. NEED AND HEALTH BEHAVIOR VARIABLES				
Taking meds for HIV				
No	10	10%	43	57%*
Yes	89	90%	33	43%

[a] Column totals may not equal total number of participants due to missing values.

[b] Converted the row scores for the BSI 18 symptom dimensions to standardized area T scores and stratified by the distribution of 50% of community norms.

* $p < 0.05$

Table 2

Selected Multivariate Logistic Regression Model of Factors Associated with Detectable Viral Load: Un-weighted Crude (OR) and Adjusted (aOR) Odds Ratios.

Variable	Category	Crude model (n= 193)		Adjusted model 1 [a](n=141)		Adjusted model 2 [a](n=142)		Adjusted model 3 [a](n=132)	
		OR	95% CI	aOR	95% CI	aOR	95% CI	aOR	95% CI
A. PREDISPOSING VARIABLES									
Age		0.97	(0.93, 1.01)	0.97	(0.91, 1.02)	0.97	(0.91, 1.03)	0.98	(0.92, 1.05)
Years have been HIV+		0.99	(0.94, 1.04)	1.00	(0.94, 1.06)	1.00	(0.94, 1.06)	1.03	(0.96, 1.11)
Race	Non-Hispanic black vs. Non-Hispanic white	1.23	(0.48, 3.16)	1.10	(0.33, 3.7)	1.01	(0.29, 3.51)	1.24	(0.29, 5.28)
	Hispanic vs. Non-Hispanic white	0.76	(0.29, 1.94)	0.78	(0.25, 2.48)	0.75	(0.23, 2.49)	0.91	(0.22, 3.79)
	Hispanic vs. Non-Hispanic black	0.61	(0.33, 1.13)	0.71	(0.29, 1.76)	0.74	(0.29, 1.89)	0.74	(0.25, 2.18)
Marital (Ref.=single)	Married, partnered, living together	0.76	(0.34, 1.69)	0.46	(0.16, 1.35)	0.43	(0.14, 1.3)	0.35	(0.09, 1.4)
	Separated, Divorced, Widowed	0.7	(0.27, 1.8)	0.94	(0.31, 2.85)	1.00	(0.32, 3.12)	1.04	(0.29, 3.76)
Education	Some college and above vs. less than college	0.9	(0.34, 2.33)	0.45	(0.11, 1.9)	0.44	(0.1, 1.94)	0.44	(0.09, 2.22)
Employment	Employed vs. Unemployed	0.69	(0.32, 1.46)	0.85	(0.31, 2.34)	0.84	(0.3, 2.38)	1.08	(0.32, 3.58)
Consider Self homeless		2.83	(1.57, 5.12)*	2.11	(0.93, 4.8)*	2.06	(0.88, 4.79)	1.39	(0.49, 3.93)
BSI	50%+ vs 0–50%	0.64	(0.35, 1.18)	0.59	(0.28, 1.26)	0.57	(0.27, 1.22)	0.49	(0.19, 1.23)
Use drug in past 30 days		1.91	(1.07, 3.41)*	2.61	(1.24, 5.49)*	2.59	(1.22, 5.49)*	2.46	(0.99, 6.13)
Use methamphetamine in past 30 days [1]		2.36	(1.09, 5.08)*	-		-		-	
B. ENABLING VARIABLES									
Health insurance		0.68	(0.38, 1.2)			0.64	(0.27, 1.49)	0.63	(0.23, 1.71)
Income	$501–$1000 vs $0–$500	0.52	(0.23, 1.19)			0.84	(0.27, 2.6)	0.49	(0.12, 2.04)
	$1000+ vs $0–$500	0.66	(0.34, 1.28)			1.18	(0.46, 2.98)	1.12	(0.39, 3.18)
Seeing an MD for HIV		0.26	(0.09, 0.76)*			1.01	(0.14, 7.1)	12.22	(1.17, 128.09)
C. NEED AND HEALTH BEHAVIOR VARIABLES									
Taking meds for HIV		0.09	(0.04, 0.19)*					0.05	(0.01, 0.2)*

[1] Because of multicollinearity, the separate multivariate analyses done with the variable set to isolate the individual contribution of methamphetamine on viral load in this sample were not showed.

[a] Sample size changed due to missing data.

* $P<0.05$