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Client Attributes and Service
Intervention
Correlates of
Self Reported Viral Load Levels

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Introduction

Among the most important outcomes of HIV medical care is maintaining patient viral loads at undetectable or low levels through combination antiretroviral therapies. A closely associated policy objective, at the system-of-care level, is the reduction in social disparities in medical treatment success. The literature suggests three possible reasons for treatment failure. The first is incomplete adherence to antiretroviral therapy. The second is acquiring a specific drug-resistant strain of HIV at the point of initial viral transmission, and the third is super- or re-infection with a drug-resistant HIV strain. The latter transmission route is generally a consequence of intravenous drug use or unprotected sexual behavior (Levy 2003; Blackard et al. 2002; Ramos 2002; Little et al. 2002). Although there are many plausible ways social factors may pattern the risk for treatment failure, published evidence is lacking for a population-based sample of HIV positive individuals.

This study explores social, behavioral, and service intervention correlates of treatment success using data from the sixth through eighth rounds of interviews with the original CHAIN cohort. For this study treatment success is operationally defined as self-reported viral load below 400 c/ml among individuals experienced with combination therapy. These are CHAIN participants who have reported use of two or more antiretroviral medications at the current or at an earlier interview. Although we have no way to assess drug resistance, the analysis does attempt to separate out whether study variables have direct associations with treatment success or whether they operate through current adherence to Highly Active Antiretroviral Therapy (HAART) and other combination regimens.

Key Findings

- 63 percent of combination-therapy-experienced CHAIN participants reported treatment success (viral loads <400) at the time of their last interview. The success rate increased to 70 percent among cohort members currently on HAART at time of last interview.
- Currently on HAART and completely adherent to HAART were the most salient factors associated with treatment success. Drug holidays – in which individuals purposefully interrupted their treatment regimens – were associated with a significant reduction in treatment success.
- There was minimal and uncertain association between treatment success and other independent factors. The most robust findings indicated that unstable housing and younger age were associated with reduced treatment success.
- The quality of medical care, but not the use of ancillary services, was associated with treatment success. Reports of barriers that impeded timely access to needed medical services lowered the likelihood of treatment success. Use of case management services, drug treatment, mental health, and housing services were all unrelated to treatment

success.

- The large number of observations missing viral load data introduced a degree of uncertainty about the true nature of social influences on treatment outcomes.

Methods

*The CHAIN Sample Design.*¹

At its inception in 1994, the CHAIN Project pursued a recruitment procedure designed to yield a broadly representative sample of people known to be living with HIV in New York City. Study recruitment was conducted collaboratively with 43 randomly selected agencies, stratified to represent roughly equal numbers of medical care and social service sites as well as sites that were and were not recipients of Ryan White Title I grants. At 30 sites, staff contacted a random sample of respondents. The names of clients who indicated an interest in participating were turned over to CHAIN staff for interviews. An open enrollment procedure was implemented at the remaining 13 agencies. All eligible respondents present on a small number of recruitment days were invited by agency providers and CHAIN staff to participate in the CHAIN study. Interviews were then scheduled with interested respondents. A total of 648 individuals recruited from participating agencies completed baseline interviews. The agency-based sample was supplemented with 52 interviews conducted with HIV-positive individuals with little or no connection to medical and social services. These individuals were contacted at outreach sites and through nominations from CHAIN participants. More detailed information on sampling strategy and recruitment may be obtained upon request from MHRA (CHAIN Technical Report #1).

Seven rounds of interviews have been completed since the baseline study was conducted during 1994 and 1995. Intervals between interviews were approximately six to nine months during the early round of interviews, In later rounds of interviews the interval between interviews was lengthened to a year to 15 months. The research team has used a number of resources and strategies to re-contact or confirm the status of individuals lost to follow-up, and occasionally an individual who has been lost to follow-up in an earlier wave is re-contacted and interviewed at a subsequent wave.

Despite the intensive effort of the CHAIN field staff, death and other factors resulted in a steady attrition of the cohort available for interviewing. In 1998, coinciding with the fifth round of interviews, the HIV Planning Council approved recruitment of additional participants into the CHAIN study. In consultation with MHRA, the NYC Department of Health, and the HIV Planning Council, CHAIN researchers returned to the original 43 agencies for assistance in recruiting individuals more newly diagnosed with HIV, since 1994. Of the 22 agencies that ultimately agreed to participate in the refresher effort, 19 recruited a random sample of

¹ For further information on CHAIN sample design and data collection methodology, please refer to earlier CHAIN reports.

respondents and 3 agencies conducted an open enrollment, using strategies identical to those employed at the first wave. A total of 267 refresher respondents (including 14 individuals unconnected to medical care) were added to the CHAIN cohort, resulting in a total cohort of 967. More detailed information about the sampling strategy, recruitment, and comparability of the refreshed cohort may be obtained from The Cohort Comparison Report (Update Report #18) and The Unconnected Revisited (Briefing Paper #1).

The sample for this study combines data from the 6th through 8th rounds of interviews. The three rounds of interviews span an observation period from the fourth quarter of 1998 through the second quarter of 2002. During this period, CHAIN staff completed 1,340 interviews with 532 separate CHAIN participants. The study period spans a time when HAART medications had become a routine part of the medical practice. The great majority of CHAIN participants reported having a viral load test and most could recall the value of the most recent viral load test results (see CHAIN Report 2003-3). The sample for this study was restricted to CHAIN participants who were “combination therapy” experienced. These were individuals who reported current use of two or more antiretroviral medications at the current or an earlier interview. (We used data collected on current medications going back to the third round interviews to determine at what interview an individual became “combination therapy” experienced).

Study Variables

Study Outcome: Treatment Success. The outcome measure for this study is treatment success. This variable is constructed from self reported viral load values. From the 5th round of interviews onward, CHAIN participants were asked if they ever had a viral load test and the date and results of the most recent tests. CHAIN Report 2003-3 demonstrated that self-reported viral loads can be reliably grouped into a three-level viral load variable: (1) undetectable or less than 400 c/ml; (2) 401-9,999 c/ml; and (3) 10,000 c/ml and greater. In that earlier report, we operationally defined treatment success as a viral load that is reported to be undetectable or below 400 c/ml among combination therapy experienced individuals. Combination therapy experienced individuals who reported being told by their physician that they had “good” viral loads were classified as treatment successes.

Findings in CHAIN Report 2003-3 raised concerns as to whether people reporting good viral loads should be combined with those in the lowest level. Our data suggest that good viral loads may also be consistent with placement in the 400-9,999 viral load group. For this analysis “good” viral loads will continue to be grouped with the lowest viral load level. We reason that being told that viral loads are good is an indication that the provider is communicating to the patient that the current medical regimen is working, successfully.

We assessed the sensitivity of these findings to alternative definitions of treatment success. We discuss the results in the final section of the report.

Correlates of Treatment Success. The independent variables for this study are listed in

Table 1. They are grouped into three categories. The first group includes factors that are hypothesized to have a direct influence on viral load levels. These variables include the status of combination therapy use at the time of each interview. We distinguished HAART combination from other non-HAART combinations. We also distinguished individuals who were completely adherent from those who were partially adherent to HAART. To assess super-infection hypotheses, various measures of high-risk sexual and injecting drug use behavior were included among the direct influences on viral loads. High risk sex behavior, injecting drug use and any form of substance abuse could also operate indirectly through influence on sustained and current use of HAART. The second group of variables in Table 1 are demographic, behavioral and situational variables that may influence treatment success indirectly, as they may be associated with sustained use of combination therapies and adherent use of HAART. The third group of variables are indicators of service interventions that may possibly operate to enhance treatment success by promoting sustained use of medications and adherent use of HAART.

Logistic regression analysis was used to measure the association between treatment success and each of the independent variables taken separately and in combination. The sequence of models estimated are described in the findings section. Tests of significance were performed after adjusting standard errors for clustering effects associated with combining observations on the same respondent from multiple rounds of interviews.

Table 1: Independent Variables

Variables hypothesized to have direct causal relationship to viral load levels	
Current HAART Use	Not currently on HAART/ Partially adherent/Completely adherent
On combination therapy other than HAART	Yes=1 No=0
On a Drug Holiday	Yes=1 No=0
Drug or alcohol use in last 6 months ²	Yes=1 No=0
Ever injected drug use	Yes=1 No=0
Injected drugs in last six months	Yes=1 No=0
Engaged in unprotected sex in last 6 months	Yes=1 No=0
Number of same sex and heterosexual partners in last six months	Continuous
Indirect demographic, social and situation factors	
Age	Continuous
Gender	Male/Female
Ethnicity	NonHispanic White/ NonHispanic Black/Hispanic
Highest school grade completed	Continuous
Housing status in last six months	1= Unstable housing (doubled up or homeless at some point in last six months), 0=Always had stable housing in last six months.
Mental health functioning	1=Very low functioning ³ 0=Normal Functioning
Parental responsibilities for three or more children under age 18	1=yes 0=No

² A current drug or alcohol user satisfies one or more of the following conditions in the last six month: 1) any use of heroin, cocaine or crack in last 6 months, or 2) drinking problems (having 5 or more drinks weekly or more often or a positive response on drinking problem scale).

³ Very low mental health functioning is a score of 37 or lower on the mental health components summary scale (MCS)

Disclosure of HIV status	0=Disclosed to no one 1=Disclosed to 1-3 persons 2=Disclosed to 3 or more persons
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Service Intervention Variables

Current access to Comprehensive Medical Care ⁴	Yes=1 No=0
Experienced one or more barriers that impede access to medical care ⁵	Yes=1 No=0
Services received in last six months:	
Case management services	Yes=1 No=0
Housing referral or support services	“
Professional mental health services	”
Counseling or support from someone other than a mental health professional	“
Drug treatment therapy	”
Drug self help groups	“

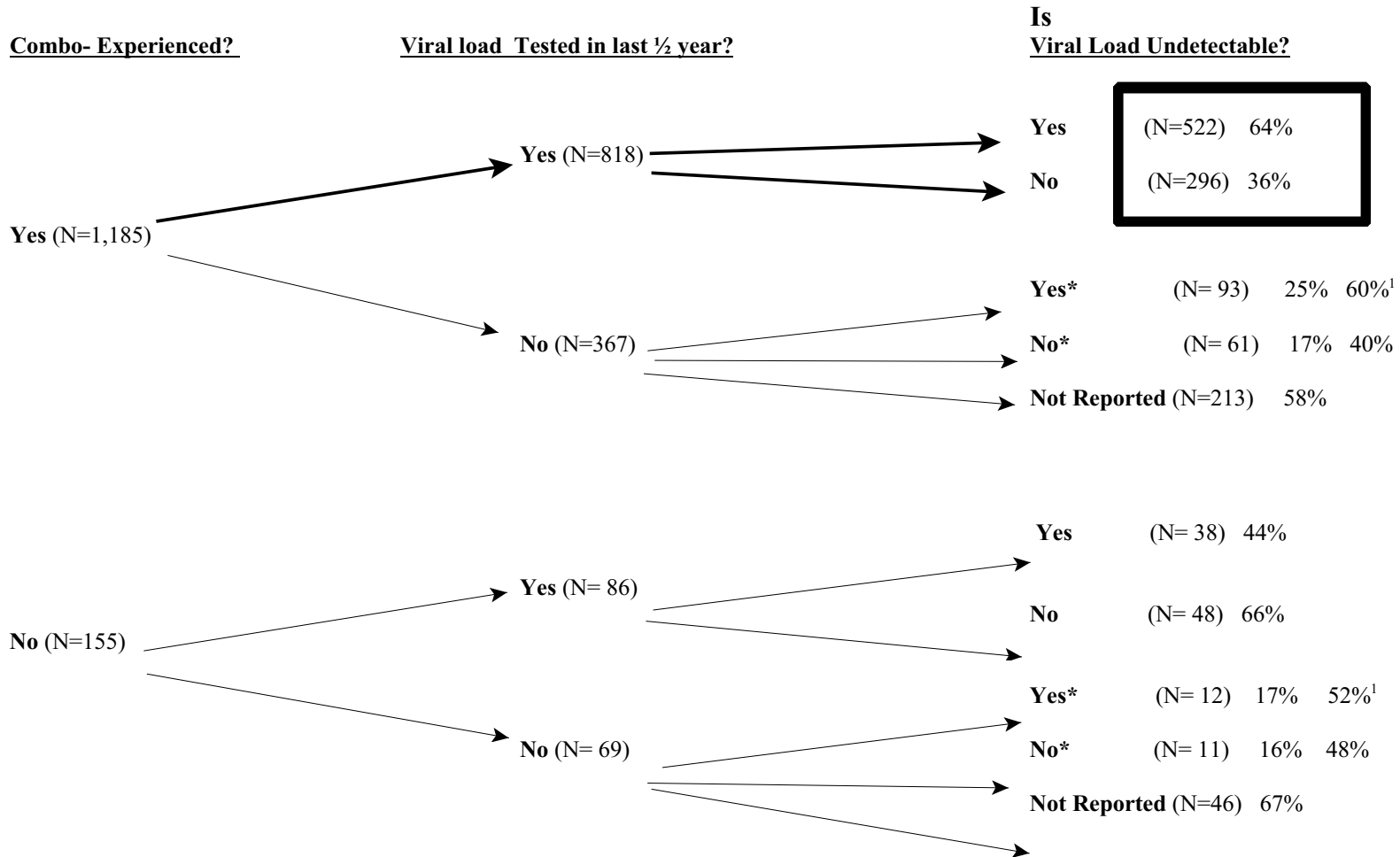
Trends in Treatment Success

Figure 1 displays the disposition of interviews conducted during the study period. For the 6th, 7th and 8th rounds of interviews, 1,340 interviews were completed with 532 participants. Only 818 or 61 percent of the interviews met the dual inclusion criteria: 1) the respondent was combination-therapy-experienced at time of interview, and 2) viral load test results within half a year of the interview were reported. Among the 522 ineligible interviews, 30 percent (155) were with CHAIN participants who had not started on a combination therapy at time of the interview. The remaining 367 ineligible interviews, 31 percent of all interviews with combination-therapy-experienced individuals, were dropped because the respondents either did not have or could not recall results of viral load tests performed within six months of the interview.

⁴ Yes responses are participants reporting that during the last six months they had access to a provider that met all of the following 3 conditions: 1) offers routine medical services, 2) provides information or advice about your health concern and 3) is accessible 24 hours a day for a medical emergency.

⁵ Experienced delays or did not get medical care because of one of 11 logistical or staff interaction problems.

Figure 1: Distribution of 6th through 8th rounds of interviews by combination therapy experience, current viral tests reported and treatment success (Total Interviews=1,340, Study Sample of interviews = 818)



Undetectable viral load=400 or lower or MD reported good viral load level

*Viral load for tests taken more than 6 months prior to interview

¹Second column of percentages exclude “Not reported” category from base

Table 2: Rates of treatment success by round of interview

	Rate of Treatment Success
Combination-Therapy Experienced*	
Round 6 (N=256)	58%
Round 7 (N=305)	70%
Round 8 (N=258)	63%
At Last Interview (N=341)	63%
Currently on HAART	
Round 6 (N=164)	66%
Round 7 (N=189)	74%
Round 8 (N=150)	71%
At Last Interview (N=223)	70%

*Taking any combination of antiretroviral therapy at current or prior interviews.

The large majority of CHAIN participants initiated combination antiretroviral therapy during the course of the study period. Among the 532 individuals participating in the 6th through 8th rounds of interviews, 470 (88 percent) were or became combination therapy experienced and 415 (78 percent) progressed to a HAART combination. Table 2 shows that treatment success was sustained at a high level over the four years spanned by the 3 rounds of interviews. Among combination-therapy-experienced participants, 63 percent reported suppressed viral load levels at time of their last interview. Among individuals who were on HAART at the time of their last interview, 70 percent were experiencing treatment success. Rates of treatment success for all treatment-experienced individuals as well as those currently on HAART increased from round 6 to round 7 of interviews, and then declined slightly in round 8. (Table 2)

Subgroup Analysis of Treatment Success

Table 3 summarizes the results of the subgroup analysis. The first column presents unadjusted odds ratios for each independent variable. The next column presents results of a multiple logistic regression analysis in which we included all but the weakest correlates of treatment success. The final column adds in the combination therapy variables. Comparison of odds ratios across the table assists us in understanding the extent to which an association between each variable and treatment success operates directly or indirectly through their association with combination treatment variables.

Table 3: Summary of Correlates of Treatment Success: bivariate and adjusted odds ratio of treatment success (Number of Observations=818)

	Unadjusted odds ratios	Adjusted odds ratios	
	(1)	(2)	(3)
Male	1.02		
Race/Ethnicity			
Black	1.58	1.48	1.52
Latino	.94	1.02	1.04
(reference group whites)			
Low Mental Health Functioning at previous interview	.63+	.71	.78
Unstably housed	.44*	.48*	.49*
Parenting Responsibility for 3+ children	.65	.65	.83
Disclosed HIV status to 3 or more individuals	.99		
Age	1.04*	1.02	1.02
Grades completed	1.04		
Current drug use	.66	.76	.80
Injection drug user	1.39		
Injection drug user within six months interview	.83		
Number of sex partners last six months	.94		
Any unsafe sex practices	1.81		
Current Medication Status:			
Adherent to HAART	4.66 **		4.10**
On HAART not completely adherent	2.57*		2.50**
On nonHAART combination	2.28*		2.10*
(reference: Treatment experienced not currently taking medications)			
Drug holiday	.34*		.33**

+p<.1 *p<.05 **p<.01

Table 3 underscores the indisputable importance of sustained HAART use, particularly complete adherence to HAART regimens to treatment success. Nearly 3/4 of respondents (74 percent) completely adherent to HAART at time of interview were succeeding with their therapies. Treatment success dropped to 65 percent among those currently on but not completely adherent to HAART and was only slightly lower, 61 percent, among those currently on a nonHAART combination. Treatment success dropped sharply to 40 percent for individuals who had ceased taking combination therapy of any form.

There are very few behavioral or social factors associated with treatment success. The most robust factor is unstable housing. Individuals experiencing unstable housing during the last six months exhibit a 52 percent treatment success compared to 66 percent for the stably housed. Older age also appears to be related to treatment success (see Table 4). Current drug use is associated with reduced treatment success, but this variable's effect is largely a consequence of its association with unstable housing. Although the association is weaker, the data are suggestive that low mental health functioning is associated with reduced treatment success. Our indicators of possible direct exposure to drug resistant strains, unsafe sex practices and current or past injection drug use are not related to treatment success. Finally, contrary to our expectation, the addition of the combination therapy variables had little or no effect on mediating the influence of the few participant characteristics associated with treatment success.

Table 4: Selected Subgroups and Treatment Success Rates

	Treatment Success
Unstably housed	52%
Stable housing	66%
Age less than 35	56%
Age 35-50	63%
age 51+	71%

Service Intervention and Treatment Success

Table 5 presents the association of medical and social service interventions with treatment success. The first column are unadjusted odds ratios for each of the service intervention variables. The second column adjusts service intervention variables for respondent characteristics and the third column presents a model that includes the antiretroviral therapy variables. The most robust finding is that treatment success is lower among CHAIN participants who report experiencing barriers that delayed or caused them not to get needed medical care services. Access to comprehensive medical care is associated with an increase in treatment success, but this association is attenuated and loses statistical significance when it is included in a model with other variables.

Table 5: Summary of Correlates of service interventions: odds ratio of treatment success (Number of Observations=818)

	Bivariate odds ratios	Multiple logistic regression, adjusted odds ratios	
	(1)	(2)	(3)
In the last six month, services were received for			
Case management	.60+	.75	.74
Housing services	.80	1.06	1.07
Formal drug treatment	.89	.94	.94
Self help groups	1.41	1.61	1.45
Professional mental help services	.89	1.05	1.04
Lay counseling	.63+	.64+	.56*
Has access to comprehensive medical care	1.56+	1.36	1.34
Barriers to timely access of medical care	.59*	.59*	.65+
Low Mental Health Functioning at previous interview		.70	.76
Unstably housed		.47*	.47*
Age		1.03*	1.03*
<u>Current Medication Status</u>			
Adherent to HAART			4.65**
On HAART not completely adherent			2.72**
On nonHAART combination			2.26*
(reference: Treatment experienced not currently taking medications)			
On drug holiday			.31**

+p<.1 *p<.05 **p<.01

Analysis not shown here indicates that access to comprehensive primary care loses its statistical significance once we adjust for the reduced access to comprehensive primary care among the unstably housed. Table 5 also indicates that use of other services has little or no bearing on treatment success. The rightmost model in Table 5 includes the service intervention variables, participant characteristics and the HAART treatment variables. It shows that both older age and housing instability continue to be associated with treatment success, independent of current use of HAART.

Sensitivity analysis

The definition of treatment success is not without its shortcomings. We have included a small number of CHAIN cohort members whose success is based on a qualitative response of “good” viral

load as opposed to reporting an exact number. We have also chosen to exclude cases in which viral load test results were older than a half year prior to the survey. Finally, our outcome measure, treatment success, is an imperfect proxy for the outcome of most interest to clinicians: individuals with failing medical regimens because of drug-resistant virus.

We re-ran many of the analyses reported above using alternative specifications of treatment success. These resulted in only minor changes in findings. Results are essentially unchanged when treatment success is expanded to include all individuals reporting viral loads below 10,000 c/ml. When interviews with viral load test results more than six months before the interview are included in the analysis, they strengthen the statistical association of variables previously identified as correlated with treatment success, and in the fully specified model, current drug use is associated with a marginally significant ($p < .1$) decline in treatment success.

The large number of observations lacking usable viral load data is the most serious threat to the validity of study findings, since viral load data are not missing at random. In particular, African Americans, current drug users and participants with low mental health functioning are more likely to have missing viral load data. To investigate the sensitivity of our findings to missing viral load data, we estimated regression models under the most conservative assumption that all ineligible observations among combination-therapy-experienced participants were treatment failures. The introduction of these additional “failed” observations strengthens the effects of current drug use on reduced treatment success, while diminishing the previous strong effect of unstable housing. When observations with missing viral load data are included as treatment failure, the negative effects of low mental health functioning strengthens and the influence of access to health care services on treatment success is altered. The beneficial effect of access to comprehensive medical care is strengthened as is the benefit of professional mental health services. In contrast the effects of barriers to services are somewhat attenuated.

Discussion

Roughly two-thirds of combination-therapy-experienced CHAIN participants reported viral load levels consistent with treatment success at time of last interview. This relatively high percentage must be tempered by the large number of CHAIN participants who did not report usable viral load data. A small but non-negligible number of CHAIN participants, 136 were treatment experienced but did not provide usable viral load data at most recent interview and another 61 participants did not report ever using a combination therapy. Setting aside the 61 individuals who had never reported using combination therapy, just 46 percent of the combination-therapy-experienced individuals ($N=471$) provided positive evidence for treatment success, another 27 percent were failing on medication, and the treatment status for the remaining 27 percent could not be ascertained at time of last interview.

The second major finding of the study is that, with the not-surprising exception of current use of combination therapy, treatment success was minimally associated with a long list of hypothesized social, behavior and situational factors. Housing instability and younger age were the only robust social correlates of treatment failure. This analysis offered no support that either unsafe sexual activity or injection drug use were related to treatment failure and consequently a reservoir of super-infectivity.

As for service interventions, lowered treatment success was associated with barriers to timely

access to medical care, and to a lesser extent, lack of access to comprehensive primary medical care. The various ancillary services were unrelated to treatment success. Study results also failed to confirm the possible dynamics in which participant characteristics were related to treatment success through their association with current use of medication and adherence. The addition of the treatment variables generally had minimal effect on the odds ratio of the few variables with evidence of an influence on treatment success. The study clearly affirms that adherent use of HAART is the single most important factor associated with treatment success, although incomplete adherence and even use of nonHAART combination appear to have some, if reduced, benefits. The negative effect of drug holidays on treatment success also underscores that this practice may do some harm.

Apart from the obvious importance of sustained adherence to HAART regimens, the results of this study are best interpreted to be suggestive of a cluster of other factors that appear to pattern CHAIN participants' level of treatment success for consideration in future research in this area. In summary, the findings of this analysis offer some basis for speculation that recent spells of homelessness, young age, and possibly current drug use may be linked to reduced chances of treatment success. Besides the possible benefits of access to high quality medical services and ease of access to services, the direct benefits of ancillary services on treatment success remain to be demonstrated. Further research is necessary, particularly efforts to obtain better and more complete viral load information, if we are to draw more confident conclusions about the determinants of treatment success.

References

- Blackard, JT, Cohen DE, Mayer KH. HUMAN Immunodeficiency Virus superinfection and recombination: current state of knowledge and potential clinical consequences. *Clin Infect Dis* 2002, 34: 1108-14
- Levy JA. Is HIV superinfection worrisome? *Lancet* 2003: 361 98-99
- Liitle SJ, Holte S, Routy JP, Daar Es Markowitz M et al. Anitretroviral-drug resistance among patients recently infected with HIV. *New England J Med* 2002: 347: 385-94
- Ramos, A Dale JH, Nguyen L, Phan Ko, Vanichseni S, Promadej N et al. Intersubtype Human Immunodeficiency Virus Type I superinfection following seroconversion to primary infection in two injection drug users. *J of Virology* 2002; 76 :74444-7452.