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HIV Medication
Regimens & Treatment
Success:
PI-based vs PI-sparing,
in 3 Cohorts

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C.H.A.I.N. REPORT

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Introduction

Since the advent of the first FDA-approved protease inhibitors, twenty antiretroviral medications (ARV's) have been approved for therapeutic use. Combinations of these medications are principally organized around protease inhibitors (PI-based regimens) or non-nucleoside reverse transcriptase inhibitors (NNRTI-based regimens, also known as PI-sparing regimens), with a smaller proportion organized about nucleoside reverse transcriptase inhibitors (NRTI's). In order to tailor these medications for maximal effect, physicians typically consider a number of clinical factors: (1) a patient's current virological and immunological status, (2) his or her treatment history, (3) pre-existing drug resistance to either specific medications or to classes of medications, and (4) pharmacokinetics, particularly drug-drug interactions and co-morbidities such as hepatitis or other liver diseases, which might adversely affect drug absorption. Treatment guidelines also recommend that clinicians consider a constellation of client-centered factors that might influence a patient's adherence to a specific medication regimen. Client-level factors include an individual's presumed tolerance of pill burden, dietary restrictions, and potential side effects of a specific medication regimen; a client's social stability, including the ability to safely manage and store medications; supportive mechanisms in a patient's life, such as familial or other social supports as well as professional supports; and substance and alcohol use as well as such specific transmission risk behaviors as needle-sharing and unprotected sex. The most recently released federal guidelines provide limited guidance regarding specific medication regimens for substance users, suggesting only that clinicians consider ARVs with lower hepatic and neuropsychiatric side effects, simpler dosing, and lack of interaction with methadone.

Much of the research published to date has focused on the epidemiology of HIV and AIDS; the virology of HIV; explorations of effective treatments and appropriate clinical guidelines for initiating or changing therapies; on the role of supportive services; and to a lesser extent, on the disproportionate impact of HIV on selected subgroups. Within the relatively narrow window of a clinical encounter, though, a physician considering various treatment options must be able to synthesize the biological and clinical data at hand, as well as understand the social and behavioral forces that can influence the likelihood of treatment success. Given the prevalence of substance users among HIV-positive adults in care, clinicians must weigh the merits of prescribing the more tolerable NNRTI-based regimens, which if not adhered to can lead to class-wide drug resistance and the potential transmission of drug-resistant viral strains to others, or the more traditional PI-based regimens, which are more resilient to non-adherence but which are harder to tolerate. From a public health perspective, prescription patterns can influence community-wide drug resistance and secondarily therapeutic efficacy, as well as population levels of health, productivity, and service utilization and burden. Policymakers need to be able to estimate the scope of such a problem, and identify policies or programs which can ameliorate or address the factors impeding treatment success or leading to widespread transmission of a drug-resistant virus. There is little in the research literature which has considered these factors in a unified fashion, much less with any established theoretical framework. This research will advance a conceptual framework based on individual, clinical, and contextual factors, within the broad rubric of social disparities theory.

As a preliminary study, the investigators examined HIV treatment success among substance users. First, we characterized the subjects by medication regimen (none, PI-based,

NNRTI-based, NRTI-based). Using data from consecutive interview rounds we constructed a measure of treatment success based on a change of CD4 count and VL from one interview round to the next. As Table 2 illustrates, we identified eight potential changes, and examined how they varied by medication regimen and current substance use. Regardless of medication regimen, substance users on ARVs were less likely to report viral suppression than were non-substance users. When we examined variations in medication regimen by cohort, as illustrated in Table 3, there were significant differences between the two contemporaneous cohorts (NYC II and Tri-County), in that subjects in the NYC cohort were more likely to report NNRTI-based regimens than were subjects in the suburban Tri-County cohort. Table 4 illustrates how treatment success -- characterized as "success, equivocal, or failure" -- was constructed from the change variables, and Table 5 illustrates the mean treatment success rates for the two major medication regimens, taking in to account adherence. As Table 5 illustrates, although there is a slightly larger success rate for NNRTI-based regimens there is also a larger drop-off towards failure among non-adherents, a finding consistent with the research literature. Lastly, we conducted a chi-square analysis of treatment success related to a number of individual, clinical/practice, and social/cultural factors, as illustrated in Table 6. Consistent with a social disparities model, it appears that social advantage is associated with treatment success (white, higher education, higher income, employed, older subjects) as are positive clinical factors (good provider communication, optimal care). While these preliminary findings are suggestive, and in keeping with our conceptual model, they are limited by both self-report and missing data. Current drug users are more likely than non-drug users to have item-missing data on their clinical markers (particularly viral load), thus tempering the findings.

These preliminary studies reinforce the need for more comprehensive collection of key clinical markers, more refined measures of treatment success that take in to account drug resistance and viral fitness, and additional behavioral data that could help explain variation, such as treatment readiness.

Table 1. Profile of substance users in NYC and Tri-County cohorts at baseline

Cohort (enrollment periods):	NYC I (1994, 1998)		NYC II (2002-2003)		Tri-County (2001-2002)		Total	
	n	%	n	%	n	%	n	%
Total Sample	968		693		398		2059	
Drug Use*** (cocaine, crack, heroin, or problem alcohol use)								
Never	210	22%	181	26%	137	34%	528	26%
Past user	458	47%	342	49%	196	49%	996	48%
Current user	300	31%	170	25%	65	16%	535	26%
Type of drug use								
Ever problem drinker***	320	33%	59	9%	36	9%	415	20%
Problem drinker in the past 6 mos*	105	11%	51	7%	30	8%	186	9%
Ever used marijuana/hashish**	740	76%	497[†]	72%	268	65%	1505	73%
Average length of marijuana use at greatest intensity of use***	5.7 years		9.8 years		9.8 years		7.8 years	
Marijuana use in the past 6 mos.	229	23%	156	23%	70	17%	455	22%
Ever used coke/crack***	759	78%	502	72%	261	66%	1522	74%
Greatest frequency of coke/crack use among users***:								
Several times a week	468	67%	367	74%	173	71%	1008	70%
Once a week	101	14%	73	15%	31	13%	205	14%
Several times a month	83	12%	45	9%	28	12%	156	11%
Several times a year	49	7%	10	2%	11	4%	70	5%
Average length of coke/crack use	6.4 years		10.0 years		7.6 years		8.2 years	
Coke/crack use in the past 6 mos***	203	21%	119	17%	40	10%	362	18%
Ever used heroin**	458	47%	272	39%	165	41%	895	43%
Greatest frequency of heroin use among users***:								
Several times a week	347	86%	212	81%	126	82%	685	84%
Once a week	26	6%	25	10%	10	6%	61	7%
Several times a month	21	5%	17	7%	10	6%	48	6%
Several times a year	10	2%	7	3%	8	5%	25	3%
Average length of heroin use	9.8 years		12.2 years		12.7 years		11.1 years	
Heroin use in the past 6 months***	87	9%	31	4%	15	4%	133	6%
Ever intravenous drug use***	425	44%	244	35%	153	38%	822	40%
IVDU in the past 6 months***	71	7%	24	3%	9	2%	104	5%

* p<=.05

** p <=.01

*** p<=.001

† One respondent refused to answer, one response was listed as N/A

†† One response was listed as N/A

Table 2. Measure of Treatment Success by HIV Medication Regimen

					HIV medication regimen ²			
					Total	None	PI	NNRTI
Treatment success measure	Time 1 viral suppression ¹	Time 2 viral suppression ¹	CD4 count ³	n				
Success	yes	yes		791	43%	21%	48%	54%
	no	yes		309	17%	19%	16%	15%
	no	no	increasing	90	5%	6%	5%	4%
Equivocal	no	no	same	284	15%	30%	12%	10%
	yes	no	increasing	44	2%	3%	2%	4%
Failure	no	no	decreasing	122	7%	10%	6%	4%
	yes	no	same	132	7%	7%	8%	4%
	yes	no	decreasing	74	4%	5%	4%	5%
TOTAL (row percentages)				1,846	100%	362 (20%)	1003 (54%)	272 (15%)

Notes on the table

(1) Viral suppression is based on respondent self-report of <400 cells/ml or expressed by their physician as “good” VL. **(2) Medication regimen:** Drawn from respondent self-report of current HIV medications, “Total” refers to all possible regimens, including none, “None” indicates no current HIV medication, “PI” refers to any PI-based regimen with at least one PI, “NNRTI” refers to any NNRTI-based regimen with at least one NNRTI (medication combinations with both a PI and an NNRTI have been characterized as PI-based regimens). The percentages in the Total row are row percentages, illustrating the proportion of the full cohort or substance or non-substance users reporting different medication regimens. The NRTI-based regimen has been left out, and represents the balance. The distribution is statistically significantly different, based on a chi-square analysis. **(3) CD4 count** is drawn from self-reported data, and refers to the change in CD4 count between two subsequent interviews, generally one-year apart. **(4)** Data for this table are drawn from three randomly sampled longitudinal HIV cohorts: CHAIN NYC I cohort, which enrolled 968 HIV+ adults twenty years of age or older between 1994-1998, CHAIN NYC II cohort, which enrolled 693 HIV+ adults between 2002-2003, and CHAIN Tri-County cohort, which enrolled 398 HIV+ adults between 2001-2002 from the surrounding counties of Westchester, Rockland, and Putnam. Among these individuals, there were a total of 1,846 observations in which there was data from two consecutive time periods in which to assess changes in viral status: 924 from NYC I, 400 from NYC II, and 522 from Tri-County.

Table 3. Medication regimen, by cohort (CHAIN data, 1998-2005, n=3,013 obs)

	NYC I (1998-2001)	NYC II (2002-2005)	Tri-County (2001-2005)
<i>n</i>	1,476	770	767
<i>PI-based</i>	73%	53%	63%
<i>NNRTI-based</i>	14%	32%	20%
<i>NRTI-based</i>	13%	15%	17%

Note: the “n” represents repeated observations of 1,729 individuals; the table excludes observations of individuals not on therapy.

Table 4. Operationalizing Treatment Success Based on CD4+ and VL change scores

Success (2)	VL suppressed at Time 2, regardless of whether or not suppressed at Time 1 VL not suppressed at Time 1 or Time 2, but CD4+ increasing
Equivocal (1)	VL dropped from suppressed to not suppressed, but CD4+ increasing VL not suppressed at Time 1 or Time 2, but CD4+ remained the same
Failure (0)	CD4+ decreasing CD4+ remained the same, but VL went from suppressed to not suppressed

Table 5. Mean Treatment Success, by medication regimen & adherence (CHAIN data, 1998-2004, n=1504 obs.)

	Medication regimen	
	PI-based	NNRTI-based
<i>Incomplete adherence</i>	1.36	1.37
<i>Complete adherence</i>	1.35	1.47
TOTAL	1.36	1.44

Note: Treatment success measured as 0 = Failure, 1 = Equivocal, 2 = Success; the “n” represents 1,504 repeated observations of 935 individuals, excluding those with missing values for items of interest

Table 6. Treatment success, by Individual, Social, & Clinical Factors (CHAIN 1998-2004)

		Treatment Success (row percentages)			
		n	Failure	Equivocal	Success
Race/Ethnic* p=0.014	<i>White</i>	321	15%	35%	50%
	<i>Black</i>	1,306	17%	32%	51%
	<i>Latino</i>	664	22%	33%	45%
Education* p=0.022	> HS	1,309	18%	31%	52%
	< HS	1,012	19%	35%	46%
Gender p=0.378	Female	1,085	18%	31%	50%
	Male	1,228	18%	34%	48%
Income p=0.197	<\$10k	1,388	19%	33%	48%
	\$10 - 25k	623	19%	32%	49%
	>\$25k	267	13%	33%	54%
Drug Use** p=0.005	Never	544	17%	31%	52%
	Past	1,306	18%	31%	51%
	Current	471	21%	38%	41%
Work status p=0.158	Not emp	1,780	19%	33%	48%
	Emp	541	16%	33%	52%
Partnered p=0.944	Single	1,135	18%	33%	49%
	Partner	1,186	18%	32%	49%
Age* P=0.041	20-34	303	17%	37%	46%
	35-49	1,458	19%	33%	48%
	50+	560	16%	29%	54%
Pt-provider communication*** p=0.001	Poor	878	19%	37%	46%
	Good	1,443	17%	29%	51%
Comprehensive medical care* p=0.017	Poor	656	16%	37%	46%
	Good	1,660	19%	31%	50%
Preferred practice guidelines p=0.501	Not met	528	18%	35%	47%
	Met	1,793	18%	32%	50%

* p<=.05

** p <=.01

*** p<=.001

Table 7. Treatment success, by Individual, Social, & Clinical Factors, Comparing NYC II and Tri-County (CHAIN 2001-2005)

		Treatment Success (row percentages)			
		n	Failure	Equivocal	Success
Race/Ethnic*	<i>White</i>	310	15%	35%	51%
	<i>Black</i>	1,247	17%	33%	50%
	<i>Latino</i>	612	22%	33%	45%
Education**	> HS	1,234	18%	31%	52%
	< HS	962	19%	36%	45%
Gender	Female	1,037	18%	31%	50%
	Male	1,153	18%	34%	48%
Drug Use**	Never	504	16%	62%	52%
	Past	1,246	18%	31%	51%
	Current	446	20%	39%	41%
Partnered	Single	1,074	18%	34%	48%
	Co-resident partner	538	19%	31%	50%
	Non co-resident Partner	584	17%	34%	49%
Age*	20-34	289	18%	37%	45%
	35-49	1,394	19%	33%	48%
	50+	513	16%	30%	54%
Comprehensive medical care*	Poor	632	16%	37%	47%
	Good	1,559	19%	31%	50%
Preferred practice guidelines	Not met	494	18%	35%	47%
	Met	1,702	18%	32%	50%

* p<=.05

** p <=.01

*** p<=.001