

Measures of country and site resourcing predict virologic suppression, immunologic response and disease progression in the TREAT Asia HIV Observational Database (TAHOD).

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on behalf of the TREAT Asia HIV Observational Database.

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Introduction

Predictive biomarkers of disease progression include HIV RNA level in plasma (viral load) and CD4 cell count (immune function) [1,2]. In resource-limited settings, access to disease staging diagnostics has lagged behind the availability of anti-HIV medications [3]. Monitoring of patient status via surrogate markers, thereby identifying optimal therapy initiation periods and when treatment should be changed, is not available at a level comparable to developed economies. [4].

Currently, there is little data on how the lack of economic and diagnostic resourcing impacts upon patient health outcomes. In this paper we investigated whether measures of clinical resourcing, such as country income and site-reported availability of diagnostic monitoring, impacted on patient treatment outcomes.



Figure 1: TAHOD Clinical Sites.

Methods

Analyses were based on 2333 (69.7%) HIV infected patients from 17 TAHOD sites who initiated HAART (>= 3 ARVs) from 2000 onwards. 13% of patients were mono/dual ARV experienced.

Sites were categorized on country income criteria and site-reported CD4 and VL (viral load) testing frequency. The four category World Bank criterion, gross national income (GNI) per capita [5] was dichotomized into high (upper-middle/upper) or low (low-middle/low) income. RNA monitoring frequency was classified into 3 categories: >=3 times per year, 1-2 times per year and <1 per year. CD4 monitoring was dichotomized: at least 3 times per year and less than 3 times per year.

Endpoints were VL suppression (<400 copies/ml) and change in CD4 count at 12 months post-HAART, and time to AIDS or death.

Base predictive patient models for each endpoint were determined based on significant demographics (age, gender, HIV exposure), indices of illness severity (CDC classification, baseline CD4 counts and VL), Hepatitis B/C coinfections and first HAART regimen. The impact of measures of resourcing at clinical sites were adjusted for other clinical covariates using these predictive models.

VL<400 copies/ml was analyzed using logistic regression, change in CD4 count using linear regression and time to AIDS or death using Cox proportional hazards. Forward step-wise techniques were used for all regressions.

Results

Patient Characteristics

Selected categories for key patient characteristics are summarized by country income in Figure 2.

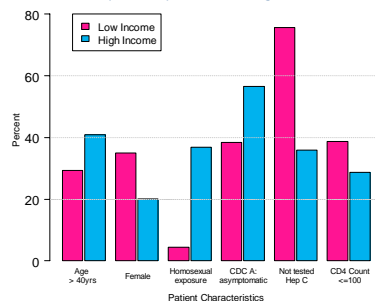


Figure 2: Comparisons of patient characteristics by country income.

Regression Analyses

Of the 2326 patients included in the disease progression analyses, 1120 (48.2 %) of patients had baseline and 12 month CD4 counts data and 785 (33.7%) of patients had 12 month HIV RNA data for contributing to the multivariate linear and logistic regressions, respectively.

Virologic suppression at 12 months following HAART

After adjustment for the base patient model (gender and exposure), the frequency of RNA testing remained statistically significant. Patients at sites reporting less than annual RNA diagnostic testing had a lower probability of being suppressed at 12 months (OR= 0.30, p<0.001).

Table 1: Factors Associated with undetectable HIV at 12 months.

	Total	No. Patients <400 copies/ml	No. (% HIV VL)	Univariate		Multivariate	
				OR	P	OR (95% CI)	P
Gender							
Male	785	651 (82.9%)					
Female	596	487 (81.7%)	1.47	0.109	1.69 (1.0-2.8)	0.038	
Exposure							
Heterosexual	496	417 (84.1%)					
Homosexual	226	197 (87.2%)	1.29	0.280	1.51 (0.9-2.4)	0.090	
Other	63	37 (58.7%)	0.27	0.000	0.28 (0.2-0.5)	0.000	
Frequency of RNA testing							
>=3 per yr	403	349 (86.6%)					
1-2 per yr	297	251 (84.5%)	0.84	0.435	0.91 (0.6-1.5)	0.709	
<1 per yr	85	51 (60.0%)	0.23	0.000	0.30 (0.2-0.5)	0.000	
World Bank							
Low	204	161 (78.9%)					
High	581	490 (84.3%)	1.44	0.078	1.19 (0.8-1.8)	0.449	

Change in CD4 count at 12 months following HAART

After adjustment for the base patient model (age, exposure, baseline CD4), less than annual RNA testing frequency and low income were significantly associated with a higher mean CD4 count response (p<0.001).

Table 2: Factors Associated with 12 month change in CD4 counts.

	Total	No. Patients	Change in CD4 (cells/mL)	Univariate		Multivariate	
				Coefficient	P	Coefficient	P
Age (yrs) at entry							
<30	1120	1120	161.1		0.000		0.000
30-40	205	178.4		-2.44	0.848	-2.69 (-27.8, 22.4)	0.833
>40	384	314		-46.98	0.001	-47.22 (-73.6, -20.8)	0.000
Exposure							
Heterosexual	852	162.9			0.033		0.043
Homosexual	159	175.4		-12.41	0.358	19.11 (-6.1, 46.3)	0.169
Other	109	128.5		-36.87	0.021	-29.37 (-46.5, 1.7)	0.004
Baseline CD4 count							
<= 100	567	163.4			0.082		0.003
100-200	308	176.4		13.02	0.239	16.60 (-4.9, 38.1)	0.130
>200	245	135.6		-28.81	0.026	-29.45 (-53.4, -5.5)	0.000
Frequency of RNA testing							
>=3 per yr	328	139.0			0.000		0.000
1-2 per yr	307	148.2		9.22	0.455	19.38 (-5.8, 44.6)	0.130
<1 per yr	485	184.3		45.26	0.000	53.60 (29.5, 77.7)	0.000
World Bank							
Low	613	174.9			0.001		0.001
High	507	144.5		-30.46	0.001	-32.05 (-51.7, -12.4)	0.001

Progression to AIDS or death

After adjustment for the base patient model, lower frequencies of RNA testing were associated with higher rates of disease progression (HR: 1.35 ; p = 0.033).

Table 3: Factors associated with disease progression.

	Total	No. Patients	Rate per 100 person-years	Univariate		Multivariate	
				HR	P	HR (95% CI)	P
Gender							
Male	2226	1646	6.7				
Female	680	5.2	0.71	0.004	0.78 (0.6-1.0)	0.040	
CDC classification							
Category A	1055	4.7		0.000		0.002	
Category B	255	6.6	1.21	0.328	1.06 (0.7-1.6)	0.759	
Category C	1016	9.0	1.84	0.000	1.42 (1.1-1.8)	0.003	
Hepatitis C							
Negative	830	6.2		1.79	0.009	1.76 (1.1-2.7)	0.011
Positive	98	11.6		1.12	0.324	1.11 (0.9-1.4)	0.334
Not tested	1400	6.7			0.000		0.000
Baseline CD4 count							
<= 100	813	9.7		0.42	0.000	0.48 (0.3-0.7)	0.000
100-200	462	4.0		0.34	0.000	0.41 (0.3-0.6)	0.000
>200	367	3.2		0.77	0.022	0.81 (0.6-1.0)	0.079
Unknown	684	7.1			0.002		0.033
Frequency of RNA testing							
>=3 per yr	701	4.9			0.028	1.22 (0.9-1.6)	0.155
1-2 per yr	646	6.4		1.35	0.028	1.22 (0.9-1.6)	0.155
<1 per yr	979	8.8		1.49	0.002	1.35 (1.0-1.8)	0.032
World Bank							
Low	1421	7.8			0.017	0.8 (0.6-1.0)	0.066
High	905	5.3					

Discussion

Site-reported VL testing less than annually is associated with poorer VL suppression, possibly reflecting sites with low capacity using VL testing to confirm treatment failure rather than for routine patient monitoring. Larger CD4 increases at these sites may be attributable to patients commencing therapy with greater immunodeficiency [6].

Less than annual VL testing is also associated with increased risk of disease progression supporting the acceleration of facilitated access to virologic diagnostics for monitoring HIV infection in resource-limited settings.

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