Table 2 All-cause mortality among treatment-naive HIV-infected patients according to longitudinal viral load and other viral load measures, 2007–2011
Table 3 All-cause mortality among HIV-infected patients under treatment according to longitudinal viral load and other viral load measures, 2007–2011

Longitudinal Viral Load Predicts Mortality among A Cohort of 3850 HIV-infected individuals

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Background

- Cross-sectional HIV viral load (VL) measurement provides invaluable information for care/treatment and research, but the nature of cross-sectional measures preclude the assessment of longitudinal cumulative plasma HIV burden.
- We examined the association of longitudinal viral load and mortality in a cohort of HIV infected individuals in Washington DC.

Methods

- HIV-infected individuals diagnosed and reported before 2007 to 2011 in Washington DC were included.
- Longitudinal viral load, a time-associated measure of cumulative plasma HIV, was calculated for each patient using the area under the VL curve.
- Cox Proportional model was constructed to analyze the independent association of longitudinal viral load for all-cause of mortality.

Results

- Of 3,850 patients contributing 13,079 person-years of this 4-year longitudinal cohort, the median of the longitudinal viral load was 2.59 log10 copies/mL and 275 patients (7.14%) died.
- When evaluated separately, the 4-year longitudinal viral load (hazard ratio [HR]=2.16 per log10 copies/mL, 95% CI, 1.92–2.43 per log10 copies/mL), the first VL in 2007 (HR=1.43; 95% CI, 1.29–1.58 per log10 copies/mL) and most recent VL (HR=1.69; 95% CI: 1.56–1.82 per log10 copies/mL) were associated with increased mortality, other statistically significant factors include age (HR=1.56; 95%CI: 1.22-2.00), Black (HR=3.74; 95%CI: 2.26-6.21; versus White), other racial/ethnic minorities (HR=2.1; 95%CI:1.01-4.37; versus White), injection drug user (HR=2.43; 95%CI:1.81-3.26; versus men who have sex with men), in-patient facilities (HR=4.17; 95%CI: 2.74-6.35; versus out-patient facilities/private physicians); not engaged in care (HR=2.89; 95%CI: 1.97-4.22), first (HR=8.11; 95%CI:6.39-10.31; <200 versus ≥200 cells/mm^3) and most recent CD4 cell counts (HR=8.99; 95%CI:7.06-11.44 cells/mm^3).
- When simultaneously evaluating VL measures and controlling for other covariates, both longitudinal viral load (HR=1.55, 95%CI: 1.27-1.90 per log10 copies/mL) and most recent VL (HR=1.37; 95% CI: 1.22–1.154 per log10 copies/mL), along with Blacks (HR=1.86; 95%CI: 1.11-3.12), not engaged in care (HR=1.8; 95%CI: 1.23-2.64), and recent CD4 cell counts (HR=4.47; 95%CI: 3.31-6.03; <200 versus ≥200 cells/mm^3), were associated with increased mortality, whereas no cross-sectional first VL measure was independently associated with mortality.

Table 1 Characteristics of the Study Subject from 2007 to 2011

Characteristic	Baseline(N)	Deaths (N)	Person Years	Mortality (/100PYs)	HR (95% CI)	*p*
Participants/observations	3,850	275	13,078.79	2.10		
Age						
< 50	2,804	173	9,492.22	1.82	1.00	
≥ 50	1,046	102	3,586.57	2.84	1.56(1.22, 2.00)	0.0003
Sex						
Male	2,653	180	8,823.82	2.03	1.00	
Female	1,197	95	4,254.97	2.22	1.11 (0.87,1.43)	0.3971
Race/ethnicity						
White	725	16	2,338.45	0.68	1.00	
Black	2,854	246	9,818.68	2.51	3.74 (2.26,6.21)	<0.0001
Other/Unknown	271	13	921.66	1.41	2.10 (1.01,4.37)	0.0465
Transmission Route						
MSM	1,676	29	5,511.99	1.51	1.00	
IDU	785	96	2,649.97	3.62	2.43(1.81,3.26)	<0.0001
Heterosexual Contact	1050	67	3,762.21	1.78	1.21 (0.86,1.67)	0.2502
Other/Unknown	339	29	1,1154.61	2.51	1.68(1.0,2.56)	0.0162
AIDs or HIV/non-AIDs?						
HIV/non-AIDS cases	1,551	59	5,255.57	1.12	1.00	
AIDS cases	2,229	216	7,823.22	2.76	2.47(1.85,3.30)	<0.0001
Reporting Facility Type						
In-patient facilities/Hospitals	1,053	130	3,557.14	3.65	4.17 (2.74, 6.35)	<0.0001
Outpatient facilities/Private Physicians	922	26	2,911.16	0.89	1.00	
Outpatient facilities/Adult HIV Clinics	558	46	1,974.59	2.33	2.69 (1.66,4.35)	0.0092
Other/Unknown Facilities	1,317	73	4,635.89	1.57	1.81 (1.16, 2.84)	<0.0001
Engagement in Care						
Engaged	3,639	245	12,568.37	1.95	1.00	
Not Engaged	211	30	510.42	5.88	2.89 (1.97,4.22)	<0.0001
Referred for Medical Services						
Yes	3,282	239	11,143.19	2.14	1.15 (0.81,1.64)	0.4238
No	568	36	1,935.60	1.86	1.00	
Referred for Substance Abuse Services						
Yes	682	67	2,328.60	2.88	1.49 (1.13,1.96)	0.0045
No	3,168	208	10,750.19	1.93	1.00	

	Hazard Ratio	95%CI	P value
Separate VL models, unadjusted and unweighted *			
Longitudinal viral load, log10 copy, y/mL	2.16	1.92-2.43	<0.0001
First VL, log10 copies/mL	1.43	1.29-1.58	<0.0001
Most recent VL, log10 copies/mL	1.69	1.56-1.82	<0.0001
Combined VL model, unadjusted and unweighted**			
Longitudinal viral load, log10 copy, y/mL	1.55	1.27-1.90	<0.0001
First VL, log10 copies/mL	1.02	0.90-1.16	0.7354
Most recent VL, log10 copies/mL	1.37	1.22-1.54	<0.0001

	Hazard Ratio	95%CI	P value
Separate VL models, unadjusted and unweighted *			
Longitudinal viral load, log10 copy, y/mL	2.22	1.85-2.67	<0.0001
First VL, log10 copies/mL	1.44	1.21-1.70	<0.0001
Most recent VL, log10 copies/mL	1.81	1.60-2.05	<0.0001
Combined VL model, unadjusted and unweighted**			
Longitudinal viral load, log10 copy, y/mL	1.54	1.12-2.11	0.0079
First VL, log10 copies/mL	0.99	0.79-1.23	0.9074
Most recent VL, log10 copies/mL	1.49	1.25-1.78	<0.0001

Conclusion

- Longitudinal VL and most recent viral load predicted mortality independently, suggesting cumulative HIV replication causes harm independent of its effect on the degree of immunodeficiency.
- Longitudinal VL will be a valuable indicator in assessing the disease progress, impact of care program, and dynamics of HIV transmission.
- Further research is needed to better understand the use of the longitudinal viral load.

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