

Supplementary Figure 1. Flow-chart showing selection of study cohort

Abbreviations: VL, viral load; cART, combination antiretroviral therapy; MACS, Multicenter AIDS Cohort Study

Supplementary Figure 2. Spearman's rank-order correlation matrix for 21 VCY and 3 VL measurements at 12,373 person-visits over the course of 6,736 person-years.

	Overall VCY																						
VCY from cART, 1y	0.76	VCY from cART, 1y																					
VCY from cART, 2y	0.84	0.95	VCY from cART, 2y																				
VCY from cART, 3y	0.88	0.91	0.98	VCY from cART, 3y																			
VCY from cART, 4y	0.91	0.87	0.95	0.98	VCY from cART, 4y																		
VCY from cART, 5y	0.94	0.85	0.93	0.97	0.99	VCY from cART, 5y																	
VCY from cART, 6y	0.96	0.82	0.90	0.94	0.97	0.99	VCY from cART, 6y	-															
VCY from cART, 7y	0.98	0.80	0.88	0.92	0.95	0.97	0.99	VCY from cART, 7y	-														
VCY from cART, 8y	0.99	0.79	0.87	0.91	0.94	0.96	0.99	1.00	VCY from cART, 8y	•													
VCY from cART, 9y	0.99	0.78	0.86	0.90	0.93	0.95	0.98	0.99	1.00	VCY from cART, 9y													
VCY from cART, 10y	1.00	0.77	0.85	0.89	0.93	0.95	0.97	0.99	1.00	1.00	VCY from cART, 10y												
Recent VCY, 1y	0.31	0.27	0.32	0.33	0.34	0.34	0.34	0.33	0.33	0.32	0.32	Recent VCY, 1y											
Recent VCY, 2y	0.36	0.37	0.40	0.40	0.41	0.41	0.40	0.40	0.39	0.38	0.37	0.84	Recent VCY, 2y	1									
Recent VCY, 3y	0.44	0.43	0.47	0.47	0.48	0.48	0.48	0.47	0.46	0.45	0.45	0.79	0.94	Recent VCY, 3y									
Recent VCY, 4y	0.50	0.47	0.51	0.52	0.53	0.53	0.53	0.53	0.52	0.51	0.51	0.74	0.87	0.95	Recent VCY, 4y	1							1
Recent VCY, 5y	0.54	0.49	0.53	0.54	0.55	0.56	0.56	0.56	0.55	0.54	0.54	0.71	0.83	0.91	0.97	Recent VCY, 5y	1						
Recent VCY, 6y	0.58	0.52	0.56	0.57	0.58	0.59	0.59	0.59	0.58	0.58	0.57	0.68	0.79	0.87	0.93	0.97	Recent VCY, 6y						0.4
Recent VCY, 7y	0.61	0.55	0.58	0.60	0.61	0.62	0.62	0.62	0.61	0.61	0.61	0.65	0.76	0.84	0.90	0.95	0.98	Recent VCY, 7y	Danamat				0.1
Recent VCY, 8y	0.67	0.56	0.60	0.63	0.65	0.66	0.67	0.67	0.67	0.66	0.66	0.62	0.72	0.80	0.86	0.91	0.94	0.97	Recent VCY, 8y	Pacant			
Recent VCY, 9y	0.73	0.58	0.63	0.66	0.68	0.70	0.71	0.72	0.72	0.72	0.73	0.57	0.67	0.74	0.81	0.85	0.89	0.91	0.96	Recent VCY, 9y	Pacant		
Recent VCY, 10y	0.79	0.61	0.66	0.70	0.72	0.74	0.76	0.77	0.77	0.78	0.78	0.53	0.62	0.70	0.76	0.80	0.83	0.86	0.91	0.97	Recent VCY, 10y	Most	
Most recent VL	0.28	0.20	0.26	0.28	0.30	0.31	0.31	0.30	0.30	0.29	0.29	0.82	0.67	0.64	0.61	0.59	0.58	0.55	0.53	0.49	0.46	recent VL	First VL
First VL after cART	0.40	0.31	0.37	0.38	0.39	0.39	0.39	0.40	0.40	0.40	0.40	0.22	0.11	0.12	0.14	0.16	0.17	0.19	0.22	0.23	0.25	0.30	after cART
Last pre-cART VL	0.59	0.87	0.79	0.74	0.70	0.68	0.65	0.63	0.62	0.61	0.60	0.17	0.28	0.33	0.36	0.38	0.41	0.43	0.44	0.46	0.47	0.08	0.10

Supplementary Table 1. Adjusted percent changes in survival times for viremia copy-years and cross-sectional viral load measurements in Model B*

	% Change in survival time† (95% CI)					
	VCY measures	Last pre-cART VL	Most recent VL	First post-cART VL		
Overall VCY	-4 (-36, 27)	-0 (-26, 26)	-13 (-28, 1)	-8 (-24, 8)		
VCY from cART, 1y	11 (-44, 66)	-9 (-45, 28)	-14 (-28, -0)	-11 (-29, 7)		
VCY from cART, 2y	1 (-36, 37)	-3 (-31, 25)	-14 (-28, 0)	-9 (-26, 8)		
VCY from cART, 3y	-9 (-40, 22)	2 (-26, 31)	-13 (-27, 1)	-7 (-24, 10)		
VCY from cART, 4y	-11 (-42, 19)	3 (-25, 32)	-13 (-27, 2)	-7 (-24, 10)		
VCY from cART, 5y	-9 (-40, 22)	2 (-26, 30)	-13 (-28, 2)	-7 (-24, 10)		
VCY from cART, 6y	-6 (-37, 26)	0 (-26, 27)	-13 (-28, 1)	-8 (-24, 9)		
VCY from cART, 7y	-1 (-33, 31)	-2 (-27, 23)	-14 (-28, 0)	-9 (-24, 7)		
VCY from cART, 8y	-1 (-32, 31)	-2 (-27, 23)	-14 (-28, 0)	-9 (-24, 7)		
VCY from cART, 9y	-1 (-32, 31)	-2 (-27, 23)	-14 (-28, 0)	-9 (-24, 7)		
VCY from cART, 10y	-1 (-33, 30)	-2 (-27, 23)	-14 (-28, 1)	-8 (-24, 7)		
Recent VCY, 1y	-9 (-29, 11)	-1 (-22, 20)	-8 (-27, 11)	-8 (-23, 7)		
Recent VCY, 2y	-15 (-32, 2)	1 (-21, 23)	-7 (-24, 10)	-6 (-21, 8)		
Recent VCY, 3y	-21 (-37, -6)	5 (-18, 27)	-5 (-22, 11)	-5 (-20, 9)		
Recent VCY, 4y	-20 (-36, -4)	5 (-18, 28)	-7 (-23, 9)	-5 (-20, 10)		
Recent VCY, 5y	-22 (-39, -5)	7 (-17, 31)	-8 (-24, 8)	-5 (-21, 11)		
Recent VCY, 6y	-25 (-43, -6)	9 (-17, 35)	-8 (-23, 8)	-5 (-21, 11)		

Recent VCY, 7y	-24 (-43, -5)	9 (-18, 36)	-8 (-24, 7)	-5 (-21, 12)
Recent VCY, 8y	-22 (-43, -2)	8 (-19, 35)	-9 (-25, 6)	-5 (-22, 12)
Recent VCY, 9y	-17 (-40, 5)	6 (-20, 32)	-11 (-26, 5)	-6 (-23, 10)
Recent VCY, 10y	-17 (-41, 6)	6 (-21, 32)	-11 (-27, 4)	-6 (-23, 11)

- * Model B evaluated each VCY measure jointly with the three cross-sectional VLs (last pre-cART VL, first VL after cART and the most recent VL) after adjusting for demographic and clinical factors, including age (per 10-year increase), non-Caucasian race, most recent CD4+ T cell count (per 100 cells/mm³ increase with linear spline at 200 cells/mm³), baseline CD4+ T cell count (per 100 cells/mm³ increase), AIDS diagnosis prior to cART initiation, MACS study site and cohort enrollment.
- † Percent change in survival times were estimated for each 10-fold increase in the 21 VCY measures (copy-years/mL) and 3 cross-sectional VLs (copies/mL)

Abbreviations: VCY, viremia copy-years; VL, viral load; cART, combination antiretroviral therapy; CI, confidence interval; AIC, Akaike Information Criteria

Supplementary Table 2. Comparing VCY measures with changing assumptions for **undetectable** viral load

	Model A*		Model A + 3 cross-sectional		
			VLs*		
	% Change in survival	AIC	% Change in survival	AIC	
	time† (95% CI)	7 0	time (95% CI)	7.110	
Overall VCY	-18 (-39, 4)	456.2	-4 (-36, 27)	458.5	
Overall VCY (undetectable VL = 0)	-18 (-38, 1)	455.5	-10 (-38, 18)	458.1	
Overall VCY (undetectable VL = 10)	-18 (-38, 2)	455.8	-8 (-38, 21)	458.3	

† Percent change in survival times were estimated for each 10-fold increase in VCY measures. Abbreviations: VCY, viremia copy-years; VL, viral load; CI, confidence interval; AIC, Akaike Information Criteria

^{*} Model A was adjusted for age (per 10-year increase), non-Caucasian race, most recent CD4+ T cell count (per 100 cells/mm³ increase with linear spline at 200 cells/mm³), baseline CD4+ T cell count (per 100 cells/mm³ increase), clinically defined AIDS diagnosis prior to cART initiation, MACS study site and enrollment cohort. Three cross-sectional VLs included baseline VL, first VL after cART initiation and the most recent VL.

Supplementary Table 3. Adjusted percent changes in survival times for viremia copy-year measurements among 432 cART-initiators with no prior exposure to antiretroviral mono- or dual-therapy

	Model A*		Model A + 3 cross-sectional VLs*			
	% Change in survival time† (95% CI)	AIC	% Change in survival time† (95% CI)	AIC		
<u>-</u>						
Overall VCY	-10 (-37, 18)	131.3	20 (-53, 92)	134.7		
VCY from cART, 1y	-4 (-33, 24)	131.5	65 (-81, 210)	134.4		
VCY from cART, 2y	-4 (-31, 23)	131.5	57 (-61, 175)	134.3		
VCY from cART, 3y	-15 (-38, 9)	131.2	10 (-56, 76)	134.9		
VCY from cART, 4y	-14 (-38, 10)	131.2	16 (-55, 86)	134.9		
VCY from cART, 5y	-13 (-39, 12)	131.2	19 (-54, 92)	134.8		
VCY from cART, 6y	-9 (-36, 18)	131.4	36 (-45, 116)	134.5		
VCY from cART, 7y	-6 (-34, 21)	131.4	41 (-36, 117)	134.3		
VCY from cART, 8y	-7 (-34, 20)	131.4	34 (-40, 109)	134.4		
VCY from cART, 9y	-7 (-34, 20)	131.4	33 (-40, 106)	134.4		
VCY from cART, 10y	-8 (-36, 19)	131.4	25 (-48, 98)	134.6		
Recent VCY, 1y	-12 (-34, 10)	130.8	7 (-41, 55)	134.9		
Recent VCY, 2y	-11 (-32, 10)	131.0	3 (-34, 40)	134.9		
Recent VCY, 3y	-31 (-42, -20)	126.2	-30 (-45, -15)	131.3		
Recent VCY, 4y	-27 (-40, -13)	128.4	-24 (-43, -6)	133.1		
Recent VCY, 5y	-24 (-40, -8)	129.3	-21 (-43, 2)	133.9		
Recent VCY, 6y	-29 (-45, -12)	128.7	-26 (-49, -4)	133.4		
Recent VCY, 7y	-25 (-44, -6)	129.6	-21 (-48, 7)	134.2		
Recent VCY, 8y	-22 (-43, -0)	130.3	-14 (-47, 18)	134.6		
Recent VCY, 9y	-17 (-41, 7)	130.8	-6 (-46, 33)	134.9		
Recent VCY, 10y	-22 (-43, -1)	130.5	-13 (-49, 23)	134.8		

* Model A was adjusted for age (per 10-year increase), non-Caucasian race, most recent CD4+ T cell count (per 100 cells/mm³ increase with linear spline at 200 cells/mm³), baseline CD4+ T cell count (per 100 cells/mm³ increase), clinically defined AIDS diagnosis prior to cART initiation, MACS study site and enrollment cohort. Three cross-sectional VLs included baseline VL, first VL after cART initiation and the most recent VL.

† Percent change in survival times were estimated for each 10-fold increase in the 21 VCY measurements (copy-years/mL)

Abbreviations: VCY, viremia copy-years; VL, viral load; cART, combination antiretroviral therapy; Cl, confidence interval; AIC, Akaike Information Criteria

Supplementary Table 4. Adjusted percent changes in survival times for AIDS and non-AIDS-related mortality

	Model A: % Change i	n survival time (95% CI)	Model B: % Change in survival time (95% C		
	AIDS deaths	Non-AIDS deaths	AIDS deaths	Non-AIDS deaths	
Overall VCY	-33 (-59, -6)	-6 (-42, 30)	-4 (-42, 34)	-5 (-57, 46)	
VCY from cART, 1y	-25 (-46, -3)	-2 (-38, 34)	13 (-56, 81)	16 (-84, 115)	
VCY from cART, 2y	-32 (-54, -10)	2 (-35, 39)	-13 (-53, 26)	30 (-52, 113)	
VCY from cART, 3y	-36 (-58, -13)	-3 (-38, 33)	-20 (-54, 14)	9 (-52, 70)	
VCY from cART, 4y	-37 (-61, -14)	-4 (-39, 31)	-23 (-58, 12)	4 (-52, 60)	
VCY from cART, 5y	-37 (-62, -13)	-4 (-40, 31)	-21 (-56, 14)	2 (-52, 56)	
VCY from cART, 6y	-38 (-63, -13)	-2 (-38, 33)	-22 (-57, 14)	7 (-49, 62)	
VCY from cART, 7y	-36 (-62, -10)	-2 (-37, 34)	-15 (-52, 23)	8 (-47, 62)	
VCY from cART, 8y	-36 (-62, -10)	-2 (-37, 34)	-13 (-50, 25)	7 (-46, 60)	
VCY from cART, 9y	-34 (-61, -8)	-2 (-38, 33)	-9 (-47, 28)	5 (-47, 57)	
VCY from cART, 10y	-34 (-60, -7)	-3 (-38, 32)	-7 (-44, 31)	3 (-49, 55)	
Recent VCY, 1y	-26 (-40, -12)	-1 (-28, 25)	-11 (-36, 13)	5 (-42, 51)	
Recent VCY, 2y	-30 (-44, -16)	1 (-27, 29)	-21 (-41, -1)	8 (-32, 49)	
Recent VCY, 3y	-34 (-48, -20)	-8 (-34, 18)	-27 (-45, -9)	-8 (-39, 22)	
Recent VCY, 4y	-32 (-48, -16)	-13 (-38, 13)	-21 (-42, -0)	-16 (-44, 12)	
Recent VCY, 5y	-31 (-48, -13)	-21 (-44, 3)	-17 (-40, 6)	-27 (-53, -2)	
Recent VCY, 6y	-34 (-52, -15)	-23 (-48, 2)	-20 (-44, 3)	-32 (-59, -4)	
Recent VCY, 7y	-32 (-53, -12)	-24 (-49, 0)	-17 (-43, 9)	-35 (-62, -9)	

Recent VCY, 8y	-35 (-55, -14)	-22 (-49, 5)	-19 (-46, 7)	-32 (-61, -3)
Recent VCY, 9y	-33 (-56, -11)	-18 (-47, 12)	-16 (-45, 13)	-26 (-59, 7)
Recent VCY, 10y	-33 (-56, -10)	-19 (-49, 10)	-14 (-44, 16)	-31 (-62, 1)

- * Model A was adjusted for age (per 10-year increase), non-Caucasian race, most recent CD4+ T cell count (per 100 cells/mm³ increase with linear spline at 200 cells/mm³), baseline CD4+ T cell count (per 100 cells/mm³ increase), AIDS diagnosis prior to cART initiation, MACS study site and cohort enrollment
- † Model B evaluated each VCY measure jointly with the three cross-sectional VLs (last pre-cART VL, first VL after cART and the most recent VL) after adjusting for all demographic and clinical factors included in Model A. Among the three cross-sectional VLs, adjusted percent change in survival times are only shown for the most recent VL.
- ‡ Percent change in survival times was estimated for each 10-fold increase in the 21 VCY measures (copy-years/mL)

 Abbreviations: VCY, viremia copy-years; VL, viral load; cART, combination antiretroviral therapy; MACS, Multicenter AIDS

 Cohort Study; CI, confidence interval