Table S1. Contributing NA-ACCORD cohorts, 1996-2009

Cohort	N (%)	Calendar years of observation
AIDS Link to the IntraVenous Experience	452 (0.6%)	1996-2007
Case Western Reserve University Immunology Unit Patient Care and Research Database	1,471 (1.9%)	1997-2009
HIV Research Network	8,040 (10.3%)	2000-2007
HAART Observational Medical Evaluation and Research	4,184 (5.4%)	1996-2008
HIV Outpatient Study	3,843 (4.9%)	1996-2009
Johns Hopkins HIV Clinical Cohort	3,591 (4.6%)	1996-2008
Kaiser Permanente Northern California	6,747 (8.7%)	1996-2008
Multicenter AIDS Cohort Study	1,339 (1.7%)	1996-2008
Second Multicenter Hemophilia Cohort Study	33 (0.04%)	2001-2005
Montreal Chest Institute Immunodeficiency Service Cohort	1,810 (2.3%)	1997-2009
Study of the Consequences of the Protease Inhibitor Era	701 (0.9%)	2000-2008
Southern Alberta Clinic Cohort	1,662 (2.1%)	1996-2009
University of North Carolina, Chapel Hill HIV Clinic	1,465 (1.9%)	1999-2008
University of Alabama at Birmingham 1917 Clinic Cohort	2,366 (3.0%)	1996-2009
University of Washington HIV Cohort	2,742 (3.5%)	1996-2009
Veterans Aging Cohort Study Virtual Cohort	32,118 (41.3%)	1996-2008
Vanderbilt-Tennessee CFAR Cohort	2,864 (3.7%)	1997-2007
Women's Interagency HIV Study	2,268 (2.9%)	1996-2008
Total	77,696	1996-2009

Table S2. Baseline characteristics of persons contributing observation time according to follow-up time (at least 1,260 days of follow-up versus fewer than 1,260 days of follow-up), NA-ACCORD, 1996-2009

	N (%)			
Characteristic	At least 1,260 days of follow-up (N = 51,220)	Fewer than 1,260 days of follow-up (N = 26,476)		
Sex	, ,	,		
Male	43,359 (84.7%)	22,502 (85.0%)		
Female	7,861 (15.3%)	3,974 (15.0%)		
Race/ethnicity	, = = ( = = = = )	2,2 ( 2 2 2 )		
White	22,951 (44.8%)	10,964 (41.4%)		
Black	21,504 (42.0%)	10,170 (38.4%)		
Hispanic	3,083 (6.0%)	2,225 (8.4%)		
Other	1,505 (2.9%)	983 (3.7%)		
Unknown – imputed	2,177 (4.3%)	2,134 (8.1%)		
Age (years)	2,111 (1.070)	2,101(0.170)		
18-29	5,171 (10.1%)	3,183 (12.0%)		
30-39	17,061 (33.3%)	7,927 (29.9%)		
40-49	19,138 (37.4%)	9,170 (34.6%)		
<u>40-49</u> ≥50				
	9,850 (19.2%)	6,196 (23.4%)		
Calendar period	00.050 (44.00()	5.004 (40.00()		
1996-1998	22,856 (44.6%)	5,004 (18.9%)		
1999-2001	14,369 (28.1%)	4,164 (15.7%)		
2002-2004	11,746 (22.9%)	4,235 (16.0%)		
2005-2007	2,249 (4.4%)	10,202 (38.5%)		
2008-2009	0 (0.0%)	2,871 (10.8%)		
Combination antiretroviral therapy naïve				
No	13,998 (27.3%)	7,686 (29.0%)		
Yes	37,222 (72.7%)	18,790 (71.0%)		
CD4 cell count (cells/µL)				
<50	5,188 (10.1%)	3,734 (14.1%)		
50-99	3,606 (7.0%)	2,068 (7.8%)		
100-199	7,469 (14.6%)	3,861 (14.6%)		
200-349	11,803 (23.0%)	5,701 (21.5%)		
350-499	10,107 (19.7%)	4,808 (18.2%)		
≥500	13,047 (25.5%)	6,304 (23.8%)		
Viral load (copies/mL)	, ,	, , ,		
≤500	13,685 (26.7%)	7,010 (26.5%)		
501-9,999	12,306 (24.0%)	5,086 (19.2%)		
10,000-99,999	15,834 (30.9%)	8,401 31.7%)		
≥100,000	9,395 (18.3%)	5,979 (22.6%)		
HIV risk group	0,000 (10.070)	3,313 (22.370)		
Injection drug use	6,899 (13.5%)	3,407 (12.9%)		
Men who have sex with men	12,769 (24.9%)	8,050 (30.4%)		
Heterosexual	7,443 (14.5%)	4,321 (16.3%)		
Other		394 (1.5%)		
	745 (1.5%)	, ,		
Unknown – imputed*	2,993 (5.8%)	2,099 (7.9%)		
Unknown – not imputed*	20,371 (39.8%)	8,205 (31.0%)		

Smoking status		
Ever	30,351 (59.3%)	10,971 (41.4%)
Never	9,586 (18.7%)	3,863 (14.6%)
Unknown – imputed*	5,498 (10.7%)	5,976 (22.6%)
Unknown – not imputed*	5,785 (11.3%)	5,666 (21.4%)

<sup>\*</sup>For HIV risk group and smoking, we did not perform imputation for cohorts with a high proportion of unknowns, or with 100% of knowns being ever smokers (for smoking). Thus, we had two categories of unknowns: those with and without imputed values.

Table S3. Hazard ratios for Kaposi sarcoma risk in relation to proportion of time on combination antiretroviral therapy (ART) during the 1,080 day time window lagged by 180 days among persons who were ART-naïve at baseline, NA-ACCORD, 1996-2009 (N = 35,804;\* KS cases = 119)

		HR (95% CI)		
Proportion of time on ART	KS cases	Model 1‡	Model 2§	Model 3II
0%	32	5.8 (2.7 to 12.3)	8.6 (3.9 to 18.9)	1.6 (0.7 to 3.9)
>0% to ≤25%	20	5.8 (2.6 to 13.0)	7.4 (3.3 to 16.8)	1.2 (0.5 to 2.9)
>25% to ≤50%	22	5.9 (2.7 to 13.0)	6.9 (3.1 to 15.3)	1.4 (0.6 to 3.4)
>50% to ≤75%	14	3.1 (1.3 to 7.1)	3.4 (1.4 to 7.9)	1.0 (0.4 to 2.7)
>75% to <100%	22	3.1 (1.4 to 6.9)	3.3 (1.5 to 7.2)	1.9 (0.8 to 4.3)
100%	9	1.0 (ref)	1.0 (ref)	1.0 (ref)
Per 20% of time on ART		0.77 (0.70 to 0.85)	0.71 (0.64 to 0.79)	0.96 (0.85 to 1.09)
P-trend		< 0.0001	<0.0001	0.53

ART, antiretroviral therapy; HR, hazard ratio; KS, Kaposi sarcoma; 95% CI, 95% confidence interval.

‡Adjusted for sex, race/ethnicity (white, black, Hispanic, other), cohort, and baseline age (18-29, 30-39, 40-49, and ≥50 years) and calendar period (1996-1998, 1999-2001, 2002-2004, 2005-2007, 2008-2009).

§Adjusted for sex, race/ethnicity, cohort, baseline age and calendar period, and confounding by CD4 cell count (i.e., CD4 cell count at the start of the time window if the person was ART-naïve at the start of the time window or CD4 cell count at ART initiation if the person initiated ART before the start of the time window).

llAdjusted for sex, race/ethnicity, cohort, baseline age and calendar period, confounding by CD4 cell count, and the CD4 cell count and viral load measures in the final model (i.e., CD4 cell count lagged by 180 days, viral load lagged by 180 days, and viral load time-weighted mean during the 1,080 day time window lagged by 180 days).

<sup>\*</sup>Persons with >1 observed viral load ≤500 copies/mL before reported start of antiretroviral therapy (whether or not combination) were censored on the date of first observed viral load ≤500 copies/mL.

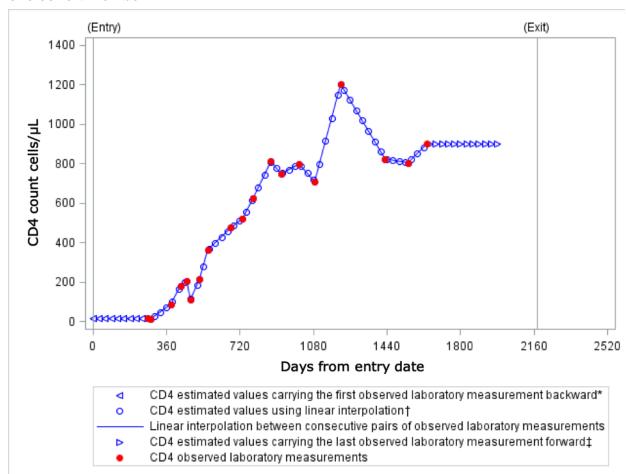


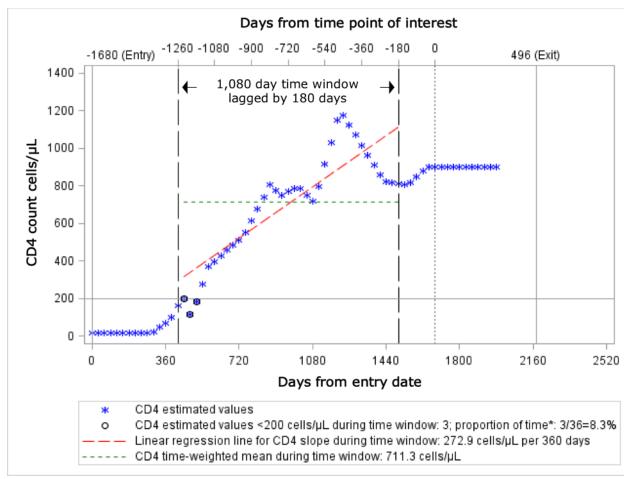
Figure S1. CD4 cell count observed laboratory measurements and estimated values for one cohort member

\*We carried the first observed laboratory measurement backward 360 days or to the entry date, whichever was reached first. For this cohort member, the entry date was reached first, at 270 days.

†We used linear interpolation between consecutive pairs of observed CD4 laboratory measurements to estimate CD4 values at 30-day intervals, assuming a linear relationship.

‡We carried the last observed laboratory measurement forward 360 days or to the exit date, whichever was reached first. For this cohort member, 360 days was reached first. Note that for this cohort member the exit date was the last observed CD4 laboratory measurement plus 540 days. There was no need for estimated CD4 values during the 180 days prior to the exit date because we lagged CD4 by at least 180 days in all analyses.

Figure S2. CD4 slope, proportion of time CD4<200 cells/ $\mu$ L, and CD4 time-weighted mean during one 1,080 day time window lagged by 180 days for a single time point for one cohort member



<sup>\*</sup>Proportion of time CD4<200 cells/µL during time window