

Supplementary Table 1. Antiretroviral Medication Regimen by Marijuana Use.

	HIV Seroconverters					Chronic HIV				
	Non-users n (%)	Heavy Marijuana n (%)	<i>P</i> Value ^a	Occasional Marijuana n (%)	<i>P</i> Value ^a	Non-users n (%)	Heavy Marijuana n (%)	<i>P</i> Value ^a	Occasional Marijuana n (%)	<i>P</i> Value ^a
Baseline										
Zidovudine (AZT)	37 (46.2)	12 (44.4)	1.00	18 (56.2)	0.405	97 (39.8)	32 (49.2)	0.203	32 (47.8)	0.264
ddI, d4T, ddC	22 (27.5)	4 (14.8)	0.208	13 (40.6)	0.185	77 (31.6)	19 (29.2)	0.765	22 (32.8)	0.883
Protease Inhibitor	24 (30.0)	6 (22.2)	0.621	7 (21.9)	0.486	122 (50.0)	22 (33.8)	0.025	40 (59.7)	0.170
Lamivudine (3TC)	26 (32.5)	12 (44.4)	0.352	14 (43.8)	0.282	162 (66.4)	45 (69.2)	0.767	54 (80.6)	0.025
Abacavir	4 (5.0)	1 (3.7)	0.999	2 (6.2)	0.999	51 (20.9)	15 (23.1)	0.734	14 (20.9)	0.999
Efavirenz	14 (17.5)	9 (33.3)	0.105	6 (18.8)	0.999	82 (33.6)	31 (47.7)	0.043	14 (20.9)	0.052
Time-updated										
Zidovudine (AZT)	14 (23.3)	4 (28.6)	0.734	2 (10.0)	0.333	24 (15.5)	7 (17.5)	0.809	10 (19.2)	0.522
ddI, d4T, ddC	9 (15.0)	3 (21.4)	0.687	1 (5.0)	0.437	5 (3.2)	2 (5.0)	0.634	5 (9.6)	0.126
Protease Inhibitor	28 (46.7)	5 (35.7)	0.557	8 (40.0)	0.796	62 (40.0)	18 (45.0)	0.592	23 (44.2)	0.627
Lamivudine (3TC)	23 (38.3)	4 (28.6)	0.555	4 (20.0)	0.176	43 (27.7)	12 (30.0)	0.844	19 (36.5)	0.294
Abacavir	11 (18.3)	1 (7.1)	0.442	3 (15.0)	0.999	26 (16.8)	7 (17.5)	0.999	8 (15.4)	0.999
Efavirenz	17 (28.3)	5 (35.7)	0.746	9 (45.0)	0.181	66 (42.6)	19 (47.5)	0.596	21 (40.4)	0.871

Self-reported ART medication use. Baseline denotes first ART visit post-seroconversion or baseline visit for HIV seroconverter and chronic HIV cohorts, respectively. Time-updated denotes first incident cardiovascular event after age 40, loss to follow-up, last visit in 2010, or age 60.

Abbreviations: ART, antiretroviral therapy, ddI, didanosine, d4T, Stavudine, ddC, Zalcitabine (dideoxycytidine), HIV, human immunodeficiency virus.

a - Fisher's Exact Test vs. control group.

Supplementary Table 2. Effect of Marijuana Use on HIV Disease Marker Trajectories.

	HIV Viral Load (copies/mL, log ₁₀)			CD4 Count (cells/μL, log ₂)			CD8 Count (cells/μL, log ₂)			CD4:CD8 Ratio (log ₂)		
	Estimate	SE	P Value	Estimate	SE	P Value	Estimate	SE	P Value	Estimate	SE	P Value
HIV Seroconverters												
Intercept	4.507	0.409	< 0.0001	9.169	0.242	< 0.0001	9.999	0.191	< 0.0001	-0.846	0.276	< 0.001
Years in study	-0.241	0.032	< 0.0001	-0.130	0.022	< 0.0001	-0.019	0.012	0.119	-0.108	0.020	< 0.0001
Marijuana use												
Daily	-0.049	0.074	0.858	0.264	0.171	0.124	0.143	0.136	0.291	0.145	0.195	0.457
Weekly	0.050	0.038	0.835	0.105	0.050	0.484	0.137	0.118	0.247	-0.012	0.070	0.945
Occasional	-0.042	0.084	0.819	-0.023	0.12	0.839	-0.061	0.088	0.488	0.049	0.127	0.700
Moderate/heavy cigarette smoking ^a	0.079	0.165	0.632	0.032	0.100	0.750	0.009	0.079	0.911	0.007	0.114	0.950
Age at baseline	-0.009	0.009	0.313	0.001	0.005	0.913	-0.008	0.004	0.071	0.009	0.006	0.134
Race												
Black	-0.074	0.17	0.732	-0.170	0.135	0.208	-0.178	0.107	0.098	0.021	0.154	0.891
Other	0.081	0.301	0.787	0.399	0.089	0.036	0.271	0.049	0.072	0.198	0.15	0.357
Education > 12 years	0.021	0.218	0.924	0.053	0.131	0.687	-0.028	0.103	0.787	0.043	0.149	0.771
Chronic HIV												
Intercept	1.951	0.159	< 0.0001	9.308	0.147	< 0.0001	9.534	0.160	< 0.0001	-0.231	0.192	0.227
Years in study	0.056	0.011	< 0.0001	0.010	0.009	0.262	-0.021	0.005	0.0001	0.031	0.009	0.001
Marijuana use												
Daily	0.074	0.094	0.432	-0.170	0.087	0.051	0.160	0.094	0.091	-0.300	0.113	0.009
Weekly	0.048	0.112	0.667	-0.116	0.04	0.267	0.042	0.13	0.711	-0.121	0.036	0.373
Occasional	0.062	0.075	0.408	0.009	0.069	0.897	0.161	0.075	0.031	-0.169	0.089	0.060
Age at baseline	0.036	0.061	0.560	0.062	0.057	0.276	-0.070	0.062	0.256	0.112	0.074	0.132
Moderate/heavy cigarette smoking ^a	-0.006	0.003	0.105	-0.003	0.003	0.345	0.006	0.003	0.060	-0.009	0.004	0.024
Race												
Black	0.123	0.068	0.070	-0.107	0.063	0.091	-0.090	0.068	0.188	-0.027	0.082	0.746
Other	0.037	0.081	0.652	0.073	0.075	0.328	0.093	0.081	0.255	0.002	0.097	0.982
Education > 12 years	0.054	0.069	0.430	0.060	0.064	0.349	-0.019	0.069	0.788	0.078	0.083	0.346

Mixed effects model estimates for post-baseline follow-up, years 0 - 7. Models included a random intercept and slope for each subject.

a - Average ≥ 0.25 packs/day during study period.

Abbreviations: HIV, human immunodeficiency virus; SE, standard error.

Supplementary Table 3. Effect of Marijuana Use and Cigarette Smoking on White Blood Cell and Neutrophil Count Trajectories.

	WBC count (cells/ μ L) (\log_2)						Neutrophil count (cells/ μ L) (\log_2)					
	Adjusted Model 1			Adjusted Model 2			Adjusted Model 1			Adjusted Model 2		
	Estimate	SE	P Value	Estimate	SE	P Value	Estimate	SE	P Value	Estimate	SE	P Value
Intercept	12.611	0.181	< 0.0001	12.595	0.181	< 0.0001	11.530	0.069	< 0.0001	11.51	0.071	< 0.0001
Heavy marijuana use	-0.121	0.062	0.051				-0.102	0.083	0.221			
Moderate/heavy cigarette smoking	0.153	0.037	< 0.0001				0.262	0.048	< 0.0001			
Stratified marijuana use & cigarette smoking												
Mj- Sm+				0.199	0.055	< 0.001				0.359	0.074	< 0.0001
Mj+ Sm-				-0.076	0.089	0.393				-0.070	0.120	0.559
Mj+ Sm+				0.023	0.080	0.773				0.190	0.107	0.078
Age ^a	-0.005	0.002	0.042	-0.004	0.003	0.173	0.004	0.003	0.192	0.007	0.004	0.061
Age at first visit	-0.003	0.004	0.539	-0.002	0.004	0.546	-0.0011	0.005	0.035	-0.011	0.005	0.035
Race												
Black	-0.199	0.043	< 0.0001	-0.203	0.043	< 0.0001	-0.310	0.056	< 0.0001	-0.316	0.056	< 0.0001
Other	-0.031	0.054	0.560	-0.029	0.054	0.592	-0.003	0.071	0.969	0.002	0.071	0.979
Education > 12 years	-0.040	0.046	0.386	-0.037	0.046	0.415	-0.054	0.060	0.374	-0.050	0.060	0.409
Total cholesterol (mg/dL)												
180-229	0.022	0.010	0.027	0.022	0.010	0.028	0.007	0.016	0.649	0.007	0.016	0.669
\geq 230	0.030	0.013	0.024	0.030	0.013	0.024	-0.003	0.021	0.899	-0.003	0.021	0.901
HIV viral load \geq 400 copies/mL	-0.123	0.013	< 0.0001	-0.123	0.013	< 0.0001	-0.183	0.02	< 0.0001	-0.183	0.020	< 0.0001
Age * marijuana use	0.02	0.006	< 0.0001				0.021	0.007	0.004			
Age * Stratified marijuana use & cigarette smoking												
Age * Mj- Sm+				-0.004	0.005	0.405				-0.010	0.007	0.140
Age * Mj+ Sm-				0.019	0.008	0.012				0.024	0.010	0.017
Age * Mj+ Sm+				0.018	0.008	0.020				0.013	0.010	0.205

Mixed effects model estimates with \log_2 -transformed WBC and neutrophil count as the dependent variables for the merged HIV+ cohort with follow-up between ages 40-60. Models included a random intercept and slope for each subject. * indicates interaction. Mj+ denotes heavy marijuana users, Mj-, occasional or non-users, Sm+, moderate or heavy smokers (\geq 0.25 packs/day, average), Sm-, light or non-smokers.

Abbreviations: HIV, human immunodeficiency virus; Mj, marijuana; SE, standard error; Sm, smoking; WBC, white blood cells

a - Time-varying covariate, centered at age 40.

Supplementary Table 4. Baseline and Updated Characteristics of the Merged HIV+ Cohort.

	Non- and Occasional Marijuana Use (n=343)	Heavy Marijuana Use (n=71)	P Value ^a
Cohort			0.840
HIV Seroconverters	104 (30.3)	23 (32.4)	
Chronic HIV	239 (69.7)	48 (67.6)	
Length of follow-up, mean (SD), years	6.38 (3.75)	6.07 (3.95)	0.536
Baseline age, median (IQR)	41.5 (40.0-45.5)	41.0 (40.0-47.2)	0.756
Endpoint age, median (IQR)	50.0 (45.8-54.6)	47.0 (44.0-54.0)	0.005
Racial/ethnic group			0.510
White	230 (67.1)	44 (62.0)	
Black	66 (19.2)	18 (25.4)	
Other	47 (13.7)	9 (12.7)	
Education > 12 years	279 (81.3)	58 (81.7)	0.999
Heavy/binge alcohol use ^b	79 (23.0)	19 (26.8)	0.600
Moderate/heavy cigarette smoking ^c	104 (30.3)	38 (53.5)	<0.001
Hypercholesterolemia risk factor ^d	125 (36.4)	21 (29.6)	0.334
Diabetes risk factor ^e	24 (7.0)	1 (1.4)	0.127
Hypertension risk factor ^f	138 (40.2)	25 (35.2)	0.513
Statin use ^g	87 (25.4)	17 (23.9)	0.920
BMI (kg/m ²), mean (SD)	26.2 (3.9)	25.4 (4.7)	0.136
Hemoglobin (gm/dL), mean (SD)	14.8 (1.4)	14.7 (1.5)	0.571
Platelet count (1,000 cells/μL), median (IQR)	215 (180-244)	225 (185-259)	0.312
CD4 count (cells/μL), mean (SD)	637 (288)	715 (341)	0.045
HIV viral load ≥ 400 copies/mL	54 (16.9)	14 (21.2)	0.510
ART adherence at ≥ 95% of visits ^h	226 (67.3)	47 (68.1)	0.999
One or more cardiovascular events	30 (8.7)	14 (19.7)	0.012

Data are n (%) unless otherwise specified at first incident cardiovascular event after age 40, loss to follow-up, last visit in 2010, or age 60.

Abbreviations: BMI, body mass index; HIV, human immunodeficiency virus; IQR, interquartile range; SD, standard deviation.

a - Chi-Squared, ANOVA, or Kruskal-Wallis Rank Sum Test, for categorical, normally-distributed continuous, and non-normally distributed continuous variables, respectively.

b - Highest use at ≥ 2 visits: Heavy, > 14 drinks/week; Binge, 5 or more drinks/occasion at least monthly.

c - Average ≥ 0.25 packs/day in 10 years prior to endpoint.

d - Mean total cholesterol at two most recent visits > 240, or use of cholesterol-lowering medications for at least one year in the 10 years prior to endpoint.

e - Mean total HgA1c at two most recent visits ≥ 6.5%, or use of diabetes medications for at least one year in the 10 years prior to endpoint.

f - Mean total systolic blood pressure > 140 or diastolic blood pressure > 90 at two most recent visits, or use of antihypertensive medications for at least one year in the 10 years prior to endpoint.

g - Reported use for one year or more in the 5 years prior to endpoint.

h - Adherence at visits once ART initiated.

Supplementary Table 5. Association between Cardiovascular Events and Additional Risk Factors.

Predictor	Cardiovascular Events		Unadjusted Models	
	Controls (n=370) n (%)	Cases (n=44) n (%)	OR (95% CI)	P Value
Hypercholesterolemia risk factor ^a				
No	242 (65.4)	26 (59.1)	1.00 (Ref.)	--
Yes	128 (34.6)	18 (41.9)	1.31 (0.69, 2.48)	0.408
Diabetes risk factor ^b				
No	351 (94.9)	38 (86.4)	1.00 (Ref.)	--
Yes	19 (5.1)	6 (13.6)	2.92 (1.1, 7.75)	0.032
Hypertension risk factor ^c				
No	228 (61.6)	23 (52.3)	1.00 (Ref.)	--
Yes	142 (38.4)	21 (47.7)	1.47 (0.78, 2.75)	0.232
Statin use ^d				
No	278 (75.1)	32 (72.7)	1.00 (Ref.)	--
Yes	92 (24.9)	12 (27.3)	1.13 (0.56, 2.29)	0.728
BMI (kg/m ²), mean (SD)	25.9 (4.0)	26.4 (4.9)	1.03 (0.95, 1.11)	0.485
CD4 count (cells/μL), mean (SD) ^e	643.7 (296.8)	705.8 (311.3)	1.07 (0.97, 1.18)	0.190
Hemoglobin (gm/dL), mean (SD)	14.7 (1.4)	14.7 (1.2)	0.99 (0.78, 12.5)	0.922
Platelets (1,000 cells/μL), median (IQR) ^e	213 (179-244)	235 (198-276)	1.07 (1.02, 1.12)	0.004

Time-updated values from the merged HIV+ cohort at first incident cardiovascular event after age 40, loss to follow-up, last visit in 2010, or age 60. Models were fit using logistic regression.

Abbreviations: BMI, body mass index; CI, confidence interval; OR, odds ratio; SD, standard deviation.

a - Mean total cholesterol at two most recent visits > 240, or use of cholesterol-lowering medications for at least one year in the 10 years prior to endpoint.

b - Mean total HgA1c at two most recent visits ≥ 6.5%, or use of diabetes medications for at least one year in the 10 years prior to endpoint.

c - Mean total systolic blood pressure > 140 or diastolic blood pressure > 90 at two most recent visits, or use of antihypertensive medications for at least one year in the 10 years prior to endpoint.

d - Reported use for one year or more in the 5 years prior to endpoint.

e - CD4 and platelet count model estimates expressed as increase in odds per 100 cells/μL and 10,000 cells/uL, respectively.