



Document Title: Statistical report – CD4 decline

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Study Title: The Canadian Cohort of HIV+ Slow Progressors: A Study of Host and Viral Factors Associated with Disease Progression in Long Term HIV Infected Subjects

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## 1 Executive Summary

We compared the difference in slope of CD4 for the four defined groups using mixed effects regression analysis. The slopes were compared from time of first known CD4 determination (section 4) as well as from the point at which the patients presented to the study (section 5). Since the groups are defined by the behaviour of their viral load over time, it is not necessarily the case that CD4 would show a similar pattern during the period prior to study presentation. The second analysis tells us whether the groups, once identified, progress at different rates of CD4 decline from that point on. Since the slow progressors were defined by a slower decline in CD4 than the controls, it is expected that there would be differences in the slope of CD4 between these two groups in the first analysis.

We also evaluated the effect of a variety of covariates (gender, age at diagnosis, race, mode of transmission, Hepatitis B status, Hepatitis C status and history of cardiovascular related problems) on the CD4 slope and conservatively adjusted for any of these covariates if the p-value was  $< 0.2$ .

Section 4 deals with the slope of CD4 since infection. The values of the slopes reflect the average decline in CD4 per year. The order of the slopes for the four groups is in accordance with what one would expect. Note that the p-values accompanying each slope reflect whether the rate of decline is different than zero. As can be seen in the pairwise comparisons, the differences between the elite controllers and virologic controllers were statistically significant compared to the control group. In addition, the differences between the elite controllers and non-virologic controllers were also statistically significant. Differences between groups were insensitivity to the adjustment of covariates.

Section 5 deals with the slope of CD4 since the time of inclusion in the study. This analysis examines the question of whether these groups, once identified, progress at different rates of CD4 decline prospectively. In this analysis, the magnitude of the slope of the decline is not in the expected order, although it seems like elite and virologic controllers have similar rates of decline which are superior to non-virologic controllers and controls whose rates of decline are greater, though short of statistical significance.

Section 6 looks at time to onset of therapy for the prospective cohort. The curves are in accordance with the hypothesis that progression to onset of therapy should be fastest in the controls and slowest in the elite controllers, with the other groups in between.



## 2 Group definitions

Patients are classified into 4 groups:

- 1) Elite controller:
  - slow progressors (true or potential) with VL at baseline  $<50$
- 2) Virologic controller:
  - slow progressors (true or potential) with VL at baseline between 50 and 3000
- 3) Non-virologic controller:
  - slow progressors (true or potential) with VL at baseline  $>3000$
- 4) Control

### 3 Demographics

Variable	All (n=203) <sup>1</sup>	Elite (n=46)	Virologic (n=69)	Non-virologic (n=33)	Control (n=20)	Exceptions (n=35) <sup>2</sup>
Sex - male, n (%) <sup>3</sup>	145 (72.1)	34 (73.9)	50 (73.5)	26 (81.3)	18 (90.0)	17 (48.6)
Place of birth						
Unknown	4	1	1	2	0	0
Canada	131 (65.8)	29 (64.4)	42 (61.8)	24 (77.4)	14 (70.0)	22 (62.9)
Other	68 (34.2)	16 (35.6)	26 (38.2)	7 (22.6)	6 (30.0)	13 (37.1)
Race, n (%)						
Unknown	4	1	1	2	0	0
Caucasian	135 (67.8)	29 (64.4)	48 (70.6)	23 (74.2)	14 (70.0)	21 (60.0)
Black (Haitian)	19 (9.5)	5 (11.1)	4 (5.9)	3 (9.7)	3 (15.0)	4 (11.4)
Black (African)	19 (9.5)	5 (11.1)	5 (7.4)	2 (6.5)	0 (0.0)	7 (20.0)
Hispanic (Latino)	8 (4.0)	1 (2.2)	2 (2.9)	1 (3.2)	2 (10.0)	2 (5.7)
Asian	5 (2.5)	2 (4.4)	3 (4.4)	0 (0.0)	0 (0.0)	0 (0.0)
Native American	7 (3.5)	3 (6.7)	1 (1.5)	2 (6.5)	0 (0.0)	1 (2.9)
Other	6 (3.0)	0 (0.0)	5 (7.4)	0 (0.0)	1 (5.0)	0 (0.0)
Race, n (%)						
Unknown	4	1	1	2	0	0
Caucasian	135 (67.8)	29 (64.4)	48 (70.6)	23 (74.2)	14 (70.0)	21 (60.0)
Black	38 (19.1)	10 (22.2)	9 (13.2)	5 (16.1)	3 (15.0)	11 (31.4)
Other	26 (13.1)	6 (13.3)	11 (16.2)	3 (9.7)	3 (15.0)	3 (8.6)
Source of income, n (%)						
Unknown	9	1	1	4	2	1
Remunerated employment	114 (58.8)	19 (42.2)	43 (63.2)	16 (55.2)	16 (88.9)	20 (58.8)
Unemployment insurance	7 (3.6)	2 (4.4)	1 (1.5)	2 (6.9)	1 (5.6)	1 (2.9)
Welfare	40 (20.6)	12 (26.7)	14 (20.6)	4 (13.8)	1 (5.6)	9 (26.5)
Other	33 (17.0)	12 (26.7)	10 (14.7)	7 (24.1)	0 (0.0)	4 (11.8)
Annual income, n (%)						
Unknown	20	4	3	9	2	2
<10000	39 (21.3)	10 (23.8)	11 (16.7)	6 (25.0)	4 (22.2)	8 (24.2)
10000-29999	57 (31.1)	18 (42.9)	15 (22.7)	9 (37.5)	6 (33.3)	9 (27.3)
30000-50000	49 (26.8)	6 (14.3)	25 (37.9)	3 (12.5)	6 (33.3)	9 (27.3)
>50000	38 (20.8)	8 (19.0)	15 (22.7)	6 (25.0)	2 (11.1)	7 (21.2)
Highest level of education completed, n (%)						
Unknown	10	3	2	3	2	0
Elementary	39 (20.2)	4 (9.3)	11 (16.4)	11 (36.7)	4 (22.2)	9 (25.7)
Secondary	50 (25.9)	17 (39.5)	12 (17.9)	8 (26.7)	4 (22.2)	9 (25.7)
Professional education	33 (17.1)	6 (14.0)	13 (19.4)	3 (10.0)	9 (50.0)	2 (5.7)
College	27 (14.0)	3 (7.0)	15 (22.4)	2 (6.7)	0 (0.0)	7 (20.0)
University diploma	14 (7.3)	5 (11.6)	4 (6.0)	1 (3.3)	1 (5.6)	3 (8.6)



Variable	All (n=203) <sup>1</sup>	Elite (n=46)	Virologic (n=69)	Non-virologic (n=33)	Control (n=20)	Exceptions (n=35) <sup>2</sup>
BA/BSc	19 (9.8)	4 (9.3)	7 (10.4)	4 (13.3)	0 (0.0)	4 (11.4)
MA/MSc	10 (5.2)	3 (7.0)	5 (7.5)	1 (3.3)	0 (0.0)	1 (2.9)
PhD	1 (0.5)	1 (2.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Martial/housing status, n (%)						
Unknown	11	2	3	3	3	0
Single	97 (50.5)	23 (52.3)	34 (51.5)	12 (40.0)	8 (47.1)	20 (57.1)
Couple	58 (30.2)	11 (25.0)	21 (31.8)	11 (36.7)	9 (52.9)	6 (17.1)
Family	24 (12.5)	7 (15.9)	7 (10.6)	3 (10.0)	0 (0.0)	7 (20.0)
With friends	4 (2.1)	0 (0.0)	3 (4.5)	0 (0.0)	0 (0.0)	1 (2.9)
Other	9 (4.7)	3 (6.8)	1 (1.5)	4 (13.3)	0 (0.0)	1 (2.9)
Modes of transmission, n (%) <sup>4</sup>						
Unknown	5	2	1	1	1	0
HIV+ partners	101 (51.0)	19 (43.2)	41 (60.3)	15 (46.9)	9 (47.4)	17 (48.6)
Sex without condom and/or condom break	116 (58.6)	23 (52.3)	45 (66.2)	19 (59.4)	12 (63.2)	17 (48.6)
MSM	109 (55.1)	20 (45.5)	40 (58.8)	19 (59.4)	17 (89.5)	13 (37.1)
Multiple partners	86 (43.4)	18 (40.9)	34 (50.0)	12 (37.5)	9 (47.4)	13 (37.1)
Intravenous drug user	21 (10.6)	6 (13.6)	5 (7.4)	3 (9.4)	1 (5.3)	6 (17.1)
Syringe exchange	18 (9.1)	5 (11.4)	4 (5.9)	3 (9.4)	1 (5.3)	5 (14.3)
Native of endemic country	111 (56.1)	19 (43.2)	34 (50.0)	22 (68.8)	18 (94.7)	18 (51.4)
Modes of transmission, n (%) <sup>4</sup>						
Unknown	5	2	1	1	1	0
Sexual	174 (87.9)	36 (81.8)	61 (89.7)	29 (90.6)	18 (94.7)	30 (85.7)
Intravenous drug user	23 (11.6)	6 (13.6)	5 (7.4)	4 (12.5)	1 (5.3)	7 (20.0)
Native of endemic country	111 (56.1)	19 (43.2)	34 (50.0)	22 (68.8)	18 (94.7)	18 (51.4)
CD4 count at baseline						
Median (IRQ)	650 (499, 780)	725 (612, 928)	650 (549, 740)	650 (518, 740)	435 (342, 469)	630 (450, 759)
Mean (SD)	672.4 (272.7)	803.5 (377.4)	683.7 (208.4)	652.8 (173.6)	426.2 (130.8)	636.7 (260.1)
Range	(230, 2780)	(320, 2780)	(360, 1403)	(395, 1233)	(230, 780)	(240, 1348)
CD8 count at baseline						
# unknown	3 (1.5)	2 (4.3)	0 (0.0)	1 (3.0)	0 (0.0)	0 (0.0)
Median (IRQ)	838 (580, 1165)	720 (485, 1098.5)	856 (605, 1280)	940 (582, 1185)	780 (594, 1155)	826 (656, 999)
Mean (SD)	928.4 (515.2)	846.3 (462.5)	946.6 (475.3)	1100.3 (716.4)	837.3 (366.7)	891.0 (494.4)
Range	(234, 3702)	(260, 2210)	(300, 2840)	(450, 3702)	(310, 1699)	(234, 2900)
BMI						
# Missing/Unknown	18 (8.9)	6 (13.0)	4 (5.8)	4 (12.1)	1 (5.0)	3 (8.6)
Median (IQR)	26.1 (23.7, 31.3)	26.4 (23.8, 31.6)	25.9 (23.7, 29.9)	24.2 (21.4, 29.7)	26.4 (24.1, 32.4)	27.4 (24.1, 32.1)
Mean (SD)	27.3 (5.7)	27.5 (5.1)	26.9 (5.3)	26.5 (7.3)	27.9 (4.8)	28.5 (6.3)
Range	(17.9, 50.5)	(17.9, 39.8)	(18.2, 47.4)	(18.9, 50.5)	(21.4, 35.9)	(19.1, 44.7)
Had cardiovascular related problems <sup>5</sup>	50 (24.9)	17 (37.0)	16 (23.5)	4 (12.5)	2 (10.0)	11 (31.4)
Hepatitis B (On or before study) <sup>6</sup>	65 (34.0)	15 (35.7)	23 (34.8)	11 (34.4)	3 (15.0)	13 (41.9)



Variable	All (n=203) <sup>1</sup>	Elite (n=46)	Virologic (n=69)	Non-virologic (n=33)	Control (n=20)	Exceptions (n=35) <sup>2</sup>
Hepatitis C (On or before study) <sup>7</sup>	23 (11.8)	8 (17.8)	7 (10.4)	4 (12.1)	1 (5.0)	3 (10.0)
True slow progressor, n (%)	-	27 (58.7)	40 (58.0)	25 (75.8)	-	-
Transmitter identity known, n (%)	54 (29.8)	8 (18.6)	18 (28.6)	12 (46.2)	5 (33.3)	11 (32.4)
Age at baseline						
# Missing/Unknown	3 (1.5)	0 (0.0)	1 (1.4)	2 (6.1)	0 (0.0)	0 (0.0)
Median (IQR)	42.0 (34.9, 49.3)	45.6 (37.2, 53.2)	41.2 (34.6, 48.5)	45.1 (32.8, 55.3)	37.7 (34.0, 46.8)	40.6 (35.0, 47.8)
Mean (SD)	42.5 (10.0)	45.4 (11.1)	41.5 (9.3)	44.2 (12.2)	40.0 (8.0)	40.7 (7.5)
Range	(23.2, 69.2)	(23.4, 69.2)	(23.2, 65.6)	(23.9, 66.4)	(25.5, 53.6)	(26.1, 53.5)
Age at diagnosis						
# Missing/Unknown	3 (1.5)	0 (0.0)	1 (1.4)	2 (6.1)	0 (0.0)	0 (0.0)
Median (IQR)	33.2 (27.3, 41.2)	35.7 (26.1, 43.9)	35.0 (27.2, 39.8)	33.5 (27.2, 44.4)	32.9 (29.8, 41.4)	30.8 (26.7, 37.5)
Mean (SD)	34.6 (9.5)	36.4 (10.9)	34.1 (7.9)	34.9 (12.5)	35.5 (8.5)	32.4 (7.7)
Range	(7.8, 65.2)	(20.5, 65.2)	(19.2, 49.2)	(7.8, 63.6)	(22.7, 53.2)	(17.6, 51.0)
Year infected at baseline						
Median (IQR)	6.4 (2.9, 11.8)	6.5 (2.4, 17.2)	6.3 (3.2, 10.1)	8.6 (4.0, 14.5)	2.7 (2.1, 3.7)	7.4 (3.7, 11.8)
Mean (SD)	8.1 (6.6)	9.0 (8.2)	7.5 (5.9)	9.8 (6.8)	4.5 (4.8)	8.3 (5.9)
Range	(0.0, 26.8)	(0.0, 26.8)	(0.6, 25.9)	(0.6, 25.1)	(0.3, 16.9)	(0.4, 24.3)
Follow up time, years (since baseline)						
Median (IRQ)	2.6 (1.3, 3.8)	2.5 (1.5, 3.6)	3.0 (1.9, 4.0)	2.5 (1.5, 3.8)	1.6 (1.0, 3.9)	2.5 (0.7, 3.4)
Mean (SD)	2.8 (2.0)	2.6 (1.9)	3.1 (2.1)	2.7 (1.8)	2.3 (2.0)	2.5 (2.2)
Range	(0.0, 8.8)	(0.0, 8.0)	(0.0, 8.8)	(0.0, 6.9)	(0.0, 7.5)	(0.0, 7.9)
Follow up time, years (since first CD4 data)						
Median (IRQ)	8.0 (4.9, 12.4)	7.0 (3.2, 12.9)	8.5 (5.8, 12.4)	9.3 (6.4, 14.0)	5.2 (3.1, 7.2)	9.0 (4.6, 12.2)
Mean (SD)	8.8 (5.4)	8.7 (6.6)	9.2 (5.2)	10.1 (5.6)	5.8 (3.3)	9.0 (4.2)
Range	(0.0, 26.3)	(0.2, 25.6)	(0.0, 25.2)	(1.3, 26.3)	(1.2, 13.1)	(2.6, 20.3)

1. Six subjects were excluded due to insufficient data to classify the subject into the groups
2. Also include potential SP that have progressed to CD4<500 within 7 years (n=4)
3. Data missing for 2 subjects
4. Multiple categories can be selected for the same subject.
5. Data missing for 2 subjects. Possible problems include MI, AHD, diabetes, HBP, dyslipidemia, CHD, myocarditis, stroke, CABG, valve replacement and insulin resistance.
6. Data missing for 12 subjects
7. Data missing for 8 subjects



## Non-Nominal information (Transmitter)

Variable	Among those with known transmitter identity					
	All (n=54)	Elite (n=8)	Virologic (n=18)	Non-virologic (n=12)	Control (n=5)	Exceptions (n=11)
Male, n (%)	51 (94.4)	8 (100.0)	16 (88.9)	11 (91.7)	5 (100.0)	11 (100.0)
Place of birth, n (%)						
Canada	29 (53.7)	4 (50.0)	12 (66.7)	5 (41.7)	3 (60.0)	5 (45.5)
Other	22 (40.7)	4 (50.0)	6 (33.3)	5 (41.7)	1 (20.0)	6 (54.5)
Unknown	3 (5.6)	0 (0.0)	0 (0.0)	2 (16.7)	1 (20.0)	0 (0.0)
Age group, n (%)						
18-25	1 (1.9)	0 (0.0)	1 (5.6)	0 (0.0)	0 (0.0)	0 (0.0)
26-35	12 (22.2)	2 (25.0)	2 (11.1)	3 (25.0)	1 (20.0)	4 (36.4)
36-45	8 (14.8)	1 (12.5)	2 (11.1)	2 (16.7)	0 (0.0)	3 (27.3)
>45	7 (13.0)	1 (12.5)	5 (27.8)	0 (0.0)	0 (0.0)	1 (9.1)
Unknown	26 (48.1)	4 (50.0)	8 (44.4)	7 (58.3)	4 (80.0)	3 (27.3)
Mode of transmission <sup>1</sup>						
Unknown	5	0	1	1	1	2
MSM	22 (44.9)	2 (25.0)	7 (41.2)	6 (54.5)	4 (100.0)	3 (33.3)
IDU	7 (14.3)	1 (12.5)	3 (17.6)	2 (18.2)	0 (0.0)	1 (11.1)
Heterosexual relationship	16 (32.7)	4 (50.0)	5 (29.4)	2 (18.2)	0 (0.0)	5 (55.6)
Other	5 (10.2)	1 (12.5)	3 (17.6)	1 (9.1)	0 (0.0)	0 (0.0)
Clinical stage						
Unknown	37 (68.5)	4 (50.0)	11 (61.1)	10 (83.3)	4 (80.0)	8 (72.7)
Chronic (>6 months)	11 (20.4)	3 (37.5)	6 (33.3)	1 (8.3)	0 (0.0)	1 (9.1)
AIDS	6 (11.1)	1 (12.5)	1 (5.6)	1 (8.3)	1 (20.0)	2 (18.2)
CD4 count (among those with AIDS) <sup>2</sup>						
Unknown, n (%)	4 (66.7)					
Median (IRQ)	-					
Mean (SD)	-					
Range	-					
Viral load (among those with AIDS) <sup>2</sup>						
Unknown, n (%)	4 (66.7)					
Median (IRQ)	-					
Mean (SD)	-					
Range	-					

- Multiple categories can be selected for the same subject.
- Summary was suppressed due to insufficient sample size.



## 4 CD4 decline (historical + prospective) – mixed effects regression

The time variable use for modeling will be in terms of *years since the subject became infected*. Two analysis populations were considered. The first one included all subjects, while the second one excluded potential SP.

We first consider testing the significance of the covariates in a univariate manner. Covariates that have a potential impact on the slope of CD4 (p-value<0.2 in any one of the analysis population) will be included in the final model for both analysis population.

Covariate	P-value	
	All subjects	Excluding potential SP
Sex	0.947	0.317
Race	0.283	0.588
Age at diagnosis	<b>0.141</b>	0.487
Modes of transmission		
Sexual	0.860	0.920
IDU	0.472	0.468
Endemic country	0.931	0.766
Hepatitis B (On or before study)	0.342	0.496
Hepatitis C (On or before study)	<b>0.062</b>	<b>0.032</b>
Had cardiovascular related problems	0.242	<b>0.124</b>





Based on mixed effects regression, the estimated CD4 slope for the four groups and the estimated difference between groups are provided below.

Estimated CD4 slope

	Slope (counts per year)	All subjects (n=168)			Excluding potential SP (n=112)		
		Estimate	95% CI	p-value <sup>1</sup>	Estimate	95% CI	p-value <sup>1</sup>
No covariate	Elite	-8.71	(-17.62, 0.19)	0.055	-5.85	(-15.04, 3.35)	0.210
	Virologic	-16.05	(-23.01, -9.10)	<0.001	-12.35	(-19.77, -4.93)	0.001
	Non-virologic	-23.23	(-33.02, -13.43)	<0.001	-23.74	(-33.25, -14.24)	<0.001
	Control	-34.70	(-49.59, -19.81)	<0.001	-31.61	(-45.23, -17.98)	<0.001
Adjusted for covariate <sup>3</sup>	Elite	-11.17	(-21.49, -0.85)	0.034	-6.51	(-16.82, 3.79)	0.212
	Virologic	-17.98	(-25.78, -10.18)	<0.001	-12.72	(-21.06, -4.37)	0.003
	Non-virologic	-25.90	(-35.94, -15.86)	<0.001	-23.51	(-33.09, -13.94)	<0.001
	Control	-37.33	(-52.05, -22.61)	<0.001	-34.27	(-47.83, -20.72)	<0.001

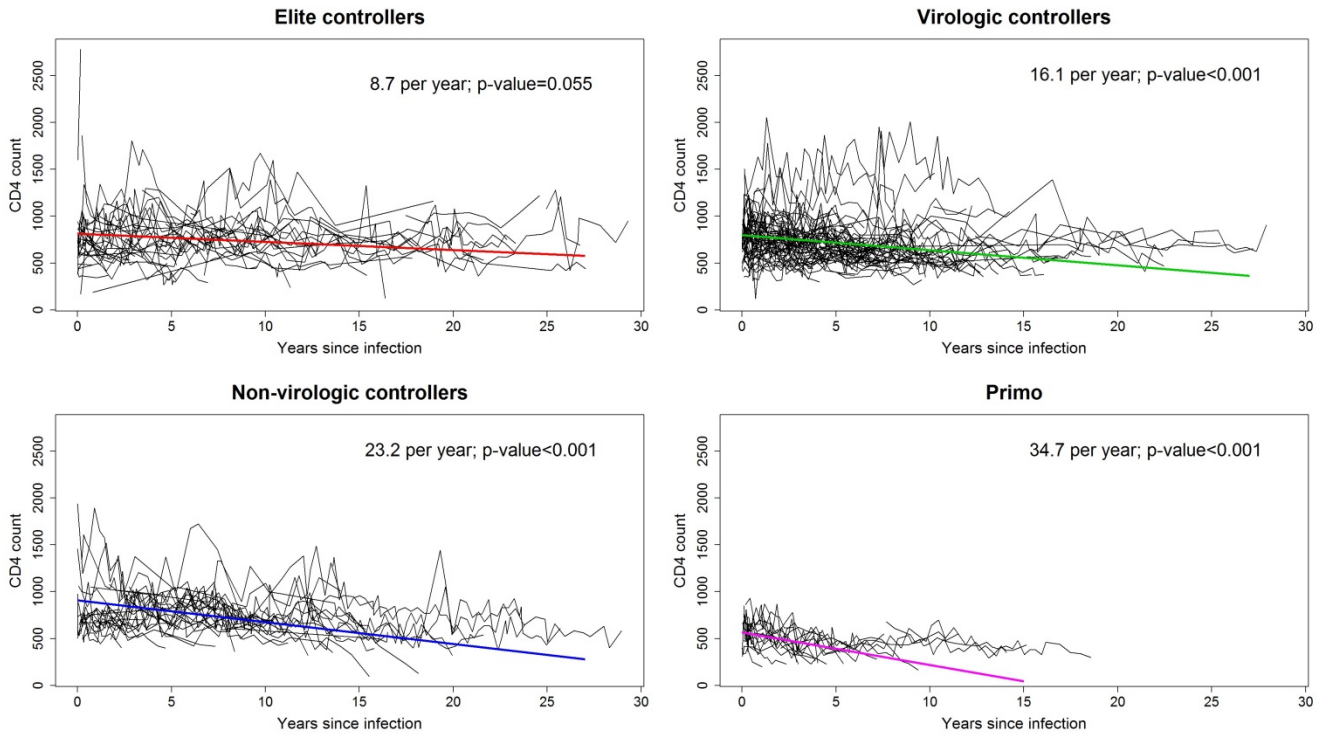
Estimated difference between groups

	Comparison	All subjects (n=168)			Excluding potential SP (n=112)		
		Estimated difference	95% CI	p-value <sup>2</sup>	Estimated difference	95% CI	p-value <sup>2</sup>
No covariate	Elite vs virologic	7.34	(-3.96, 18.64)	0.201	6.50	(-5.31, 18.32)	0.277
	Elite vs non-virologic	14.51	(1.28, 27.75)	<b>0.032</b>	17.90	(4.67, 31.12)	<b>0.009</b>
	Virologic vs non-virologic	7.17	(-4.84, 19.18)	0.239	11.39	(-0.66, 23.45)	0.064
	Elite vs Control	25.99	(8.64, 43.34)	<b>0.004</b>	25.76	(9.33, 42.19)	<b>0.002</b>
	Virologic vs Control	18.65	(2.22, 35.08)	<b>0.026</b>	19.26	(3.74, 34.77)	<b>0.015</b>
	Non-virologic vs Control	11.48	(-6.34, 29.30)	0.205	7.86	(-8.75, 24.47)	0.350
Adjusted for covariate <sup>3</sup>	Elite vs virologic	6.81	(-4.48, 18.11)	0.234	6.20	(-5.13, 17.54)	0.279
	Elite vs non-virologic	14.73	(1.27, 28.18)	<b>0.032</b>	17.00	(3.97, 30.02)	<b>0.011</b>
	Virologic vs non-virologic	7.91	(-4.07, 19.90)	0.193	10.80	(-1.06, 22.65)	0.074
	Elite vs Control	26.16	(8.41, 43.91)	<b>0.004</b>	27.76	(10.97, 44.55)	<b>0.001</b>
	Virologic vs Control	19.35	(2.87, 35.83)	<b>0.022</b>	21.56	(5.84, 37.27)	<b>0.008</b>
	Non-virologic vs Control	11.44	(-6.24, 29.11)	0.203	10.76	(-5.69, 27.22)	0.198

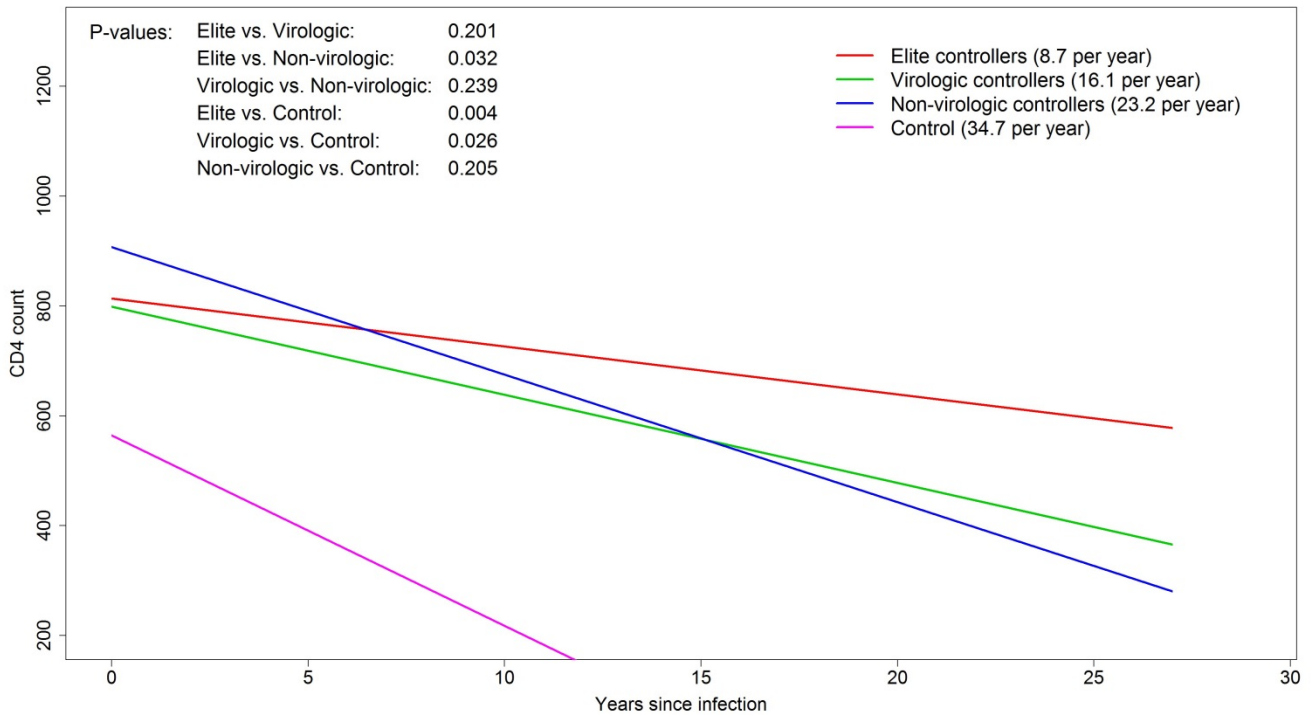
1. For the null hypothesis of slope=0
2. For the null hypothesis of no difference in the slope between the two groups
3. Adjusted for Hepatitis C status, history of cardiovascular related problems and age at HIV diagnosis. Estimated slope is for subject with no Hepatitis C (on and before study), no cardiovascular related problem (pre baseline) and diagnosed at age 35. Hepatitis C, no cardiovascular related problem and older at diagnosis are associated with greater CD4 decline (however, all p<0.05 except for Hep C).



### Unadjusted for covariates (Estimated decline and individual CD4 profile)



### Unadjusted for covariates (Estimated decline and p-value from pairwise comparisons)





## 5 CD4 decline (prospective only) – mixed effects regression

The time variable use for modeling will be in terms of *years since baseline*. The number of years infected (at baseline) will be included as a covariate in the model. Two analysis populations will be considered. The first one included all subjects, while the second one excluded potential SP.

We first consider testing the significance of the covariates in a univariate manner. Covariates that have a potential impact on the slope of CD4 (p-value<0.2 in any one of the analysis population) will be included in the final model for both analysis population.

Covariate	P-value	
	All subjects	Excluding potential SP
Sex	<b>0.112</b>	<b>0.055</b>
Race	0.726	0.660
Age at diagnosis	<b>0.154</b>	<b>0.175</b>
Modes of transmission		
Sexual	0.758	0.594
IDU	<b>0.123</b>	0.324
Endemic country	0.819	0.767
Hepatitis B (On or before study)	0.494	0.844
Hepatitis C (On or before study)	0.774	0.653
Had cardiovascular related problems	<b>0.065</b>	<b>0.091</b>



Based on mixed effects regression, the estimated CD4 slope for the four groups and the estimated difference between groups are provided below.

Estimated CD4 slope (for subjects infected for 8 years at baseline)

	Slope (counts per year)	All subjects (n=162)			Excluding potential SP (n=111)		
		Estimate	95% CI	p-value <sup>1</sup>	Estimate	95% CI	p-value <sup>1</sup>
No covariate	Elite	-23.67	(-44.61, -2.72)	0.027	-21.01	(-50.00, 7.98)	0.151
	Virologic	-24.50	(-41.07, -7.93)	0.004	-20.08	(-42.40, 2.24)	0.077
	Non-virologic	-59.85	(-85.40, -34.31)	<0.001	-59.63	(-90.05, -29.21)	<0.001
	Control	-46.08	(-83.13, -9.03)	0.016	-50.47	(-90.86, -10.09)	0.015
Adjusted for covariate <sup>3</sup>	Elite	-20.60	(-44.98, 3.78)	0.096	-12.93	(-52.04, 26.19)	0.507
	Virologic	-21.60	(-40.61, -2.58)	0.027	-16.72	(-43.33, 9.90)	0.211
	Non-virologic	-49.49	(-75.89, -23.08)	<0.001	-48.98	(-81.40, -16.56)	0.004
	Control	-41.70	(-77.13, -6.27)	0.022	-46.77	(-86.50, -7.04)	0.022

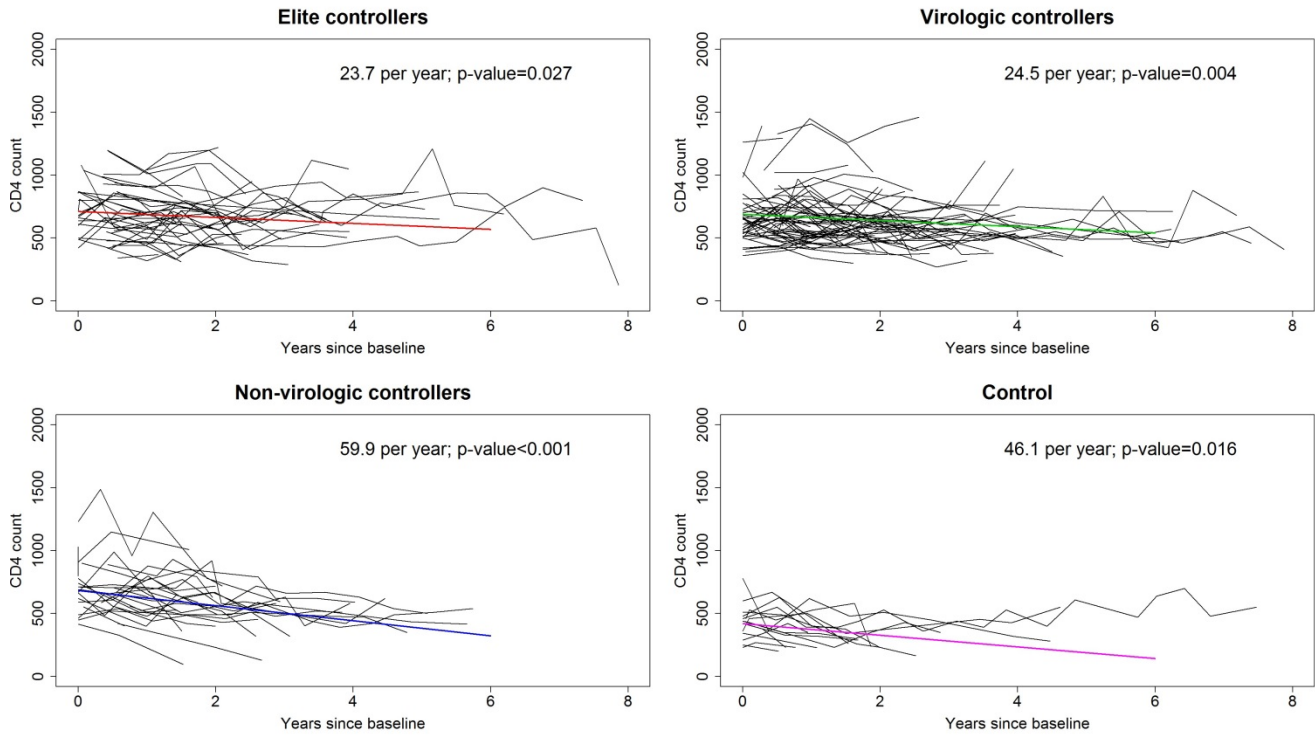
Estimated difference between groups

	Comparison	All subjects (n=162)			Excluding potential SP (n=111)		
		Estimated difference	95% CI	p-value <sup>2</sup>	Estimated difference	95% CI	p-value <sup>2</sup>
No covariate	Elite vs virologic	0.84	(-25.97, 27.64)	0.951	-0.93	(-36.63, 34.77)	0.958
	Elite vs non-virologic	36.19	(3.38, 68.99)	<b>0.031</b>	38.62	(-1.37, 78.60)	0.058
	Virologic vs non-virologic	35.35	(4.72, 65.98)	<b>0.024</b>	39.55	(2.52, 76.58)	<b>0.037</b>
	Elite vs Control	22.41	(-20.46, 65.29)	0.300	29.47	(-22.09, 81.02)	0.256
	Virologic vs Control	21.58	(-18.77, 61.92)	0.289	30.40	(-16.36, 77.15)	0.197
	Non-virologic vs Control	-13.77	(-59.40, 31.86)	0.549	-9.15	(-61.15, 42.84)	0.725
Adjusted for covariate <sup>3</sup>	Elite vs virologic	1.00	(-25.43, 27.42)	0.940	3.79	(-34.29, 41.87)	0.841
	Elite vs non-virologic	28.89	(-3.63, 61.40)	0.081	36.05	(-7.73, 79.84)	0.104
	Virologic vs non-virologic	27.89	(-1.92, 57.70)	0.066	32.26	(-5.10, 69.62)	0.089
	Elite vs Control	21.10	(-21.29, 63.49)	0.323	33.84	(-23.58, 91.27)	0.241
	Virologic vs Control	20.10	(-18.86, 59.06)	0.305	30.05	(-17.67, 77.78)	0.210
	Non-virologic vs Control	-7.79	(-51.66, 36.09)	0.723	-2.21	(-54.02, 49.60)	0.932

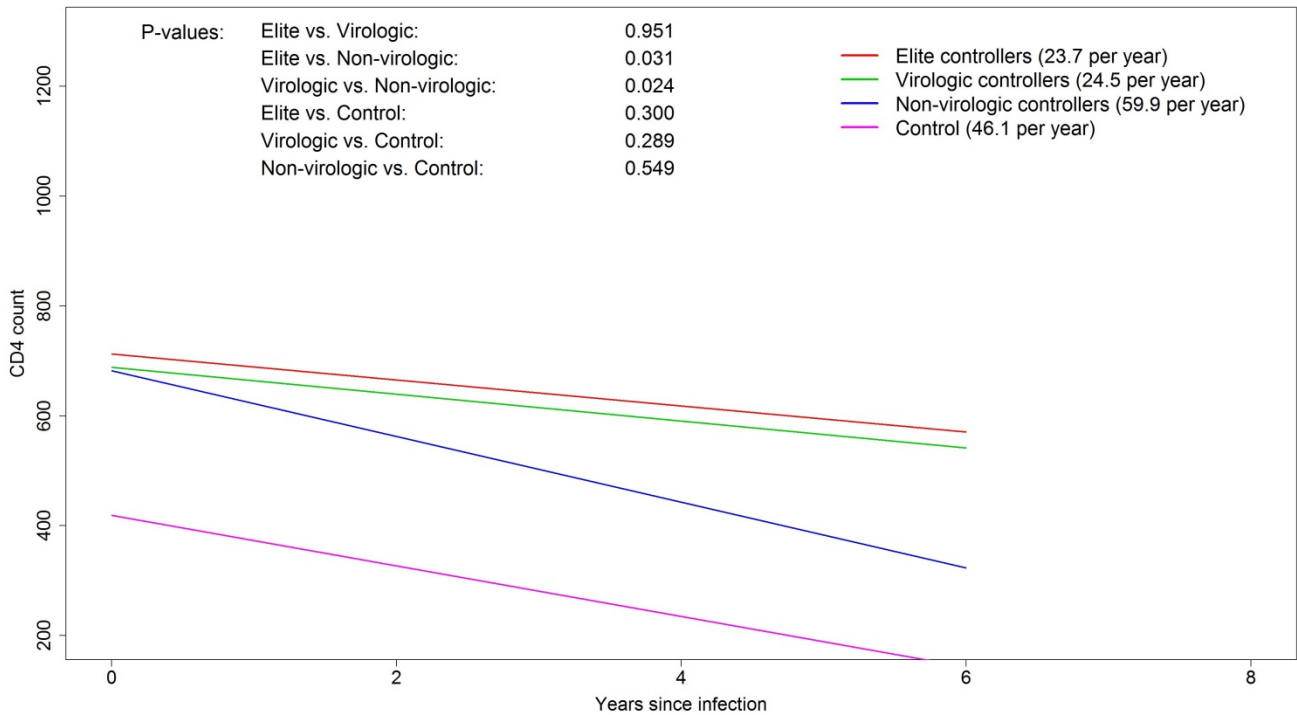
1. For the null hypothesis of slope=0
2. For the null hypothesis of no difference in the slope between the two groups
3. Adjusted for sex, IDU as mode of transmission, history of cardiovascular related problems and age at HIV diagnosis. Estimated slope is for subject infected for 8 years at baseline, male, non-IDU as mode of transmission, no cardiovascular related problem (pre baseline) and diagnosed at age 35. Female, IDU as mode of transmission, no cardiovascular related problem and younger at diagnosis are associated with greater CD4 decline (however, all p<0.05).



### Unadjusted for covariates (Estimated decline and individual CD4 profile)



### Unadjusted for covariates (Estimated decline and p-value from pairwise comparisons)





## 6 Time to start of ART (prospective only)

Kaplan–Meier curve

