

Supplementary file to

Chammartin F et al. Measures of longitudinal immune dysfunction and risk of AIDS and non-AIDS defining malignancies in antiretroviral treated people with HIV

Table S1. Baseline socio-demographic and clinical characteristics of people with HIV (PWH) in the RESPOND database and PWH included in the analysis

	Overall RESPOND database (n=30816)	PWH included in the analysis (n=19247)
Age [year]		
< 50	21491 (69.7%)	13698 (71.2%)
50-65	7920 (25.7%)	4746 (24.7%)
≥ 65	1405 (4.6%)	803 (4.2%)
Mean age (interquartile range)	44 (36-51)	44 (36-51)
Sex		
Male	23350 (75.8%)	14715 (76.5%)
Female	7466 (24.2%)	4532 (23.5%)
Risk group		
Men having sex with men	14313 (46.4%)	9596 (49.9%)
People who inject drugs	4337 (14.1%)	1921 (10.0%)
Heterosexual	10128 (32.9%)	6544 (34.0%)
Other / unknown	2038 (6.6%)	1186 (6.2%)
Race		
White	22106 (71.7%)	12934 (67.2%)
Other / unknown	8710 (28.3%)	6313 (32.8%)
CD4 cell count [cells/μl]		
<350	5854 (23.5%)	4731 (24.6%)
350-500	5471 (22.0%)	4233 (22.0%)
≥ 500	13594 (54.5%)	10283 (53.4%)
Missing	5897	
CD8 cell count [cells/μl]		
<1000	12545 (65.1%)	12533 (65.1%)
≥ 1000	6721 (34.9%)	6714 (34.9%)
Missing	11550	
CD4:CD8 ratio		
<0.5	7277 (37.8%)	7271 (37.8%)
0.5-1.0	8126 (42.2%)	8119 (42.2%)
≥ 1	3861 (20.0%)	3857 (20.0%)
Missing	11552	
HI viral load [copies/ml]		
<200/detection limit	17320 (69.5%)	12590 (65.4%)
≥200	7609 (30.5%)	6657 (34.6%)
Missing	5887	
Body mass index [kg/m²]		
<30	17177 (55.7%)	12785 (66.4%)
≥30	1471 (4.8%)	1128 (5.9%)
Missing	12168 (39.5%)	5334 (27.7%)
Hepatitis C status		
Negative	17270 (56.0%)	14029 (72.9%)
Positive	4959 (16.1%)	2981 (15.5%)
Unknown	8587 (27.9%)	2237 (11.6%)

Hepatitis B status

Negative	20807 (67.5%)	16029 (83.3%)
Positive	1101 (3.6%)	735 (3.8%)
Unknown	8908 (28.9%)	2483 (12.9%)

Smoking

No	9739(31.6%)	7043 (36.6%)
Yes	8290 (26.9%)	6018 (31.3%)
Unknown	12787(41.5%)	6186 (32.1%)

PWH: people with HIV

Positive hepatitis B = positive surface antigen or detectable DNA; positive hepatitis C = positive antibody test or detectable RNA

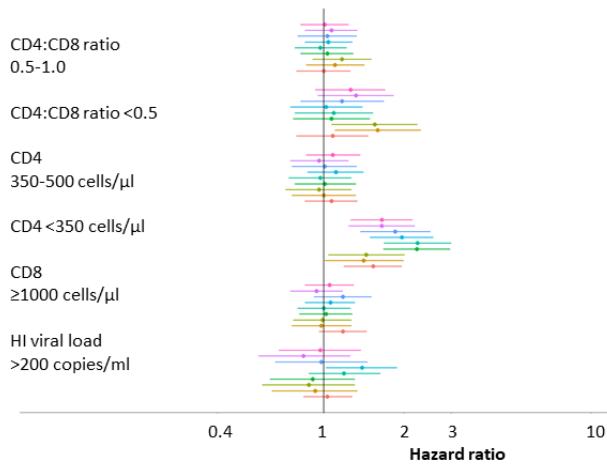
Table S2: Model parameter estimates for non-AIDS and AIDS defining malignancies and composite endpoints of infection-, smoking-, and body mass index-related malignancies

	Non-AIDS defining malignancy	AIDS- defining malignancy	Infection- related malignancy	Smoking- related malignancy	Body mass index-related malignancy
CD4:CD8 ratio lagged 12 months					
≥1.0	1	1	1	1	1
0.5-1.0	1.01 (0.82-1.24)	1.18 (0.53-2.64)	1.09 (0.72-1.63)	1.14 (0.83-1.57)	1.07 (0.71-1.64)
<0.5	1.26 (0.93-1.70)	2.61 (1.10-6.19)	2.03 (1.24-3.33)	1.26 (0.81-1.95)	1.03 (0.55-1.93)
CD4 cell counts lagged 12 months (cells/μl)					
≥500	1	1	1	1	1
350-500	1.08 (0.86-1.37)	1.09 (0.61-1.96)	1.36 (0.94-1.97)	0.98 (0.68-1.42)	0.95 (0.58-1.56)
<350	1.65 (1.26-2.15)	3.48 (2.06-5.86)	2.62 (1.79-3.83)	2.25 (1.56-3.23)	1.74 (1.02-2.97)
CD8 cell counts lagged 12 months (cells/μl)					
<1000	1	1	1	1	1
≥1000	1.05 (0.85-1.30)	1.05 (0.71-1.54)	1.07 (0.79-1.44)	1.09 (0.81-1.47)	0.97 (0.63-1.51)
HI viral load lagged 12 months (copies/ml)					
≤200/lower detection limit	1	1	1	1	1
>200	0.97 (0.68-1.38)	31.71 (20.10- 50.01)	6.33 (4.71-8.51)	1.08 (0.66-1.75)	0.98 (0.47-2.02)
Age (year)	1.07 (1.07-1.08)	1.02 (1.01-1.04)	1.04 (1.03-1.05)	1.08 (1.07-1.09)	1.07 (1.05-1.08)
Sex					
Male	1	1	1	1	1
Female	0.97 (0.78-1.22)	1.31 (0.83-2.06)	0.89 (0.62-1.27)	0.91 (0.67-1.23)	0.89 (0.58-1.37)
Risk group					
Men having sex with men	1	1	1	1	1
People who inject drugs	1.98 (1.57-2.51)	0.62 (0.36-1.10)	0.67 (0.40-1.12)	4.56 (3.31-6.28)	3.95 (2.53-6.17)
Heterosexual	0.93 (0.75-1.14)	0.55 (0.34-0.90)	0.73 (0.53-1.02)	1.20 (0.86-1.67)	1.23 (0.79-1.93)
Other/unknown	1.23 (0.88-1.71)	1.03 (0.55-1.93)	1.14 (0.70-1.83)	1.52 (0.90-2.57)	1.42 (0.69-2.91)
Race					
White	1	1	1	1	1
Other/Unknown	0.83 (0.68-1.01)	1.07 (0.73-1.55)	1.14 (0.70-1.83)	0.79 (0.58-1.09)	1.07 (0.72-1.59)
Hepatitis C status					
Negative			1		
Positive			1.47 (0.97-2.25)		
Unknown			1.41 (0.88-2.26)		
Hepatitis B status					
Negative			1		
Positive			2.10 (1.34-3.29)		
Unknown			1.00 (0.62-1.62)		
Smoking lagged 12 months					
No				1	
Yes				1.77 (1.33-2.37)	
Unknown				1.11 (0.78-1.57)	
Obesity (BMI>30 kg/m²)					
No					1
Yes					1.31 (0.75-2.29)
Unknown					0.59 (0.37-0.93)

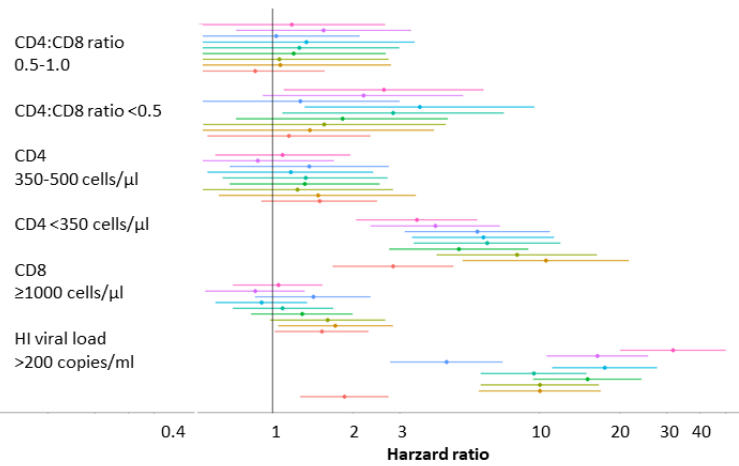
Positive hepatitis B = positive surface antigen or detectable DNA; positive hepatitis C = positive antibody test or detectable RNA

Figure S1: Adjusted hazard ratio of immunological and virological factors for non AIDS defining, AIDS defining, infection-, smoking- and body mass-related malignancies in a sensitivity analysis that considers additional forms of exposures

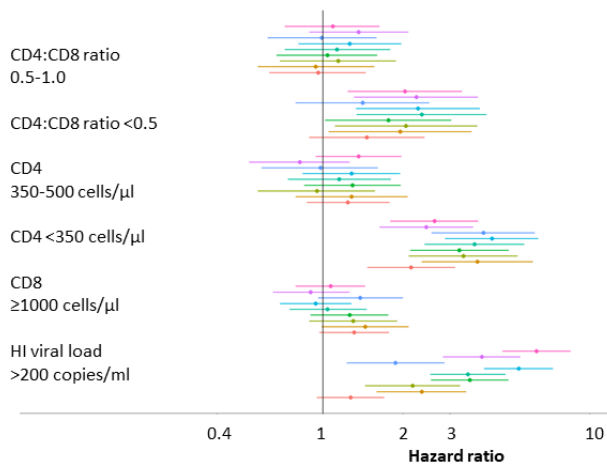
Non-AIDS defining malignancy



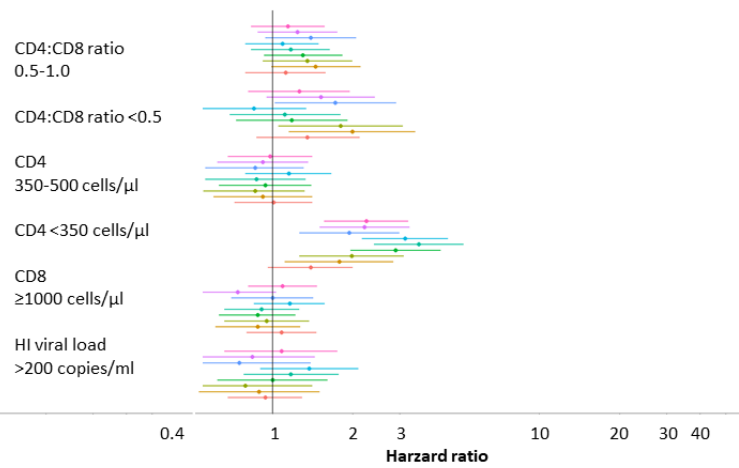
AIDS defining malignancy



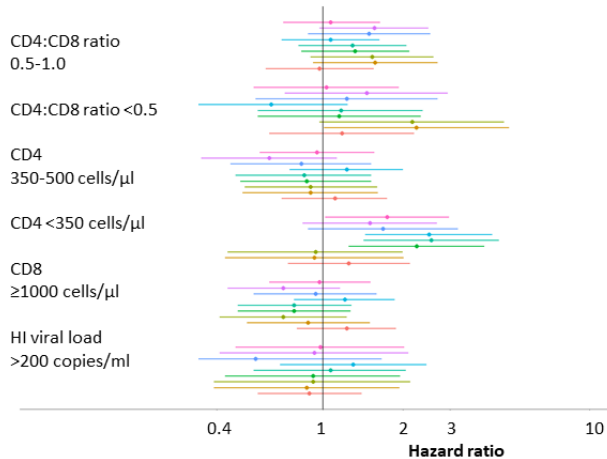
Infection-related malignancy



Smoking-related malignancy



Body mass index-related malignancy

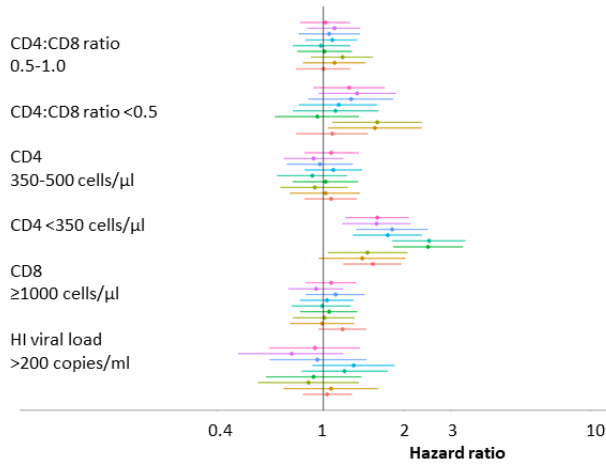


Exposure form

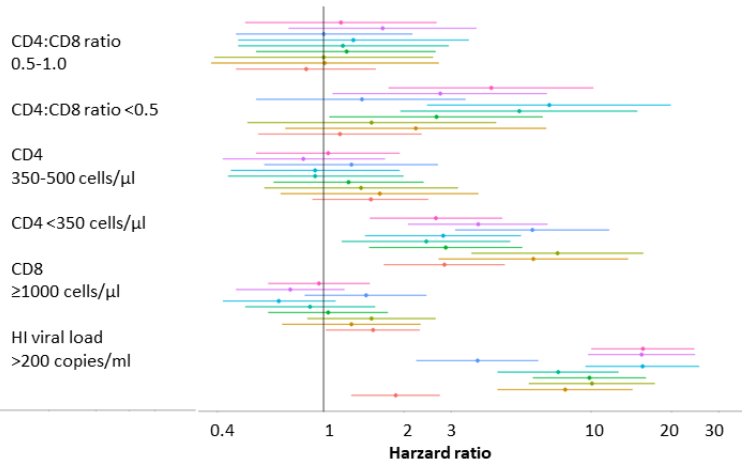


Figure S2: Adjusted hazard ratio of immunological and virological factors for non AIDS defining, AIDS defining, infection-, smoking-, and body mass-related malignancies in a sensitivity analysis that considers additional forms of exposures and restricted extrapolation of immunological and virological factors to 12 months

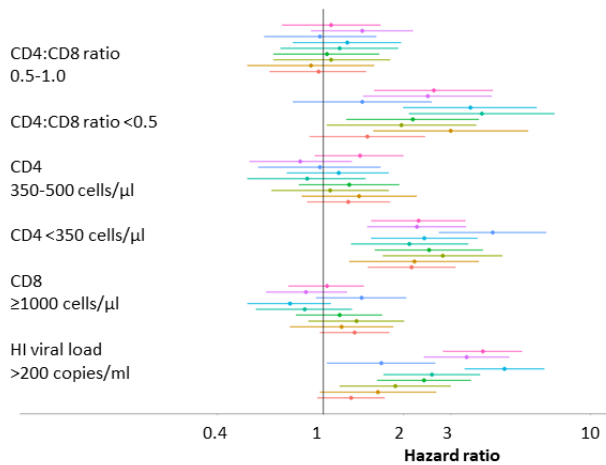
Non-AIDS defining malignancy



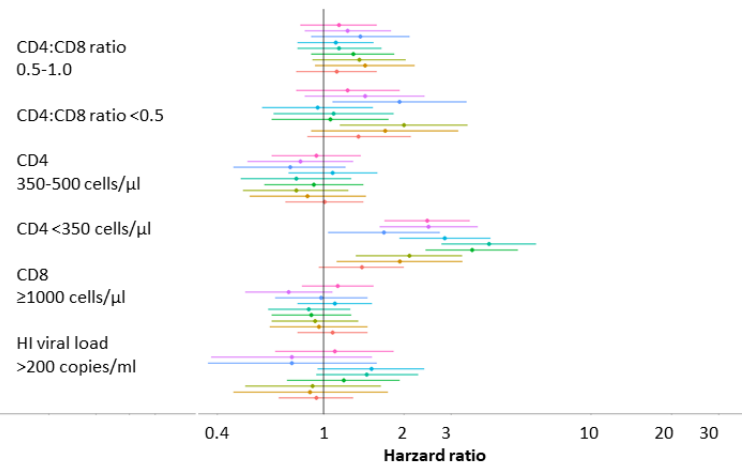
AIDS defining malignancy



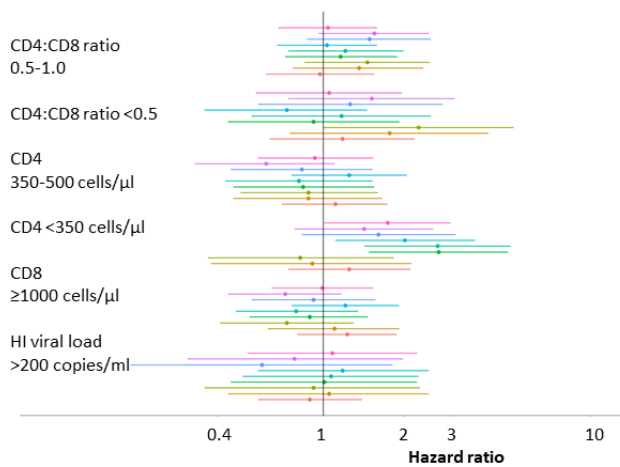
Infection-related malignancy



Smoking-related malignancy



Body mass index-related malignancy



Exposure form

- ◆ lagged 12 months
- ◆ lagged 24 months
- ◆ lagged 36 months
- ◆ Moving average over past 12 months
- ◆ Moving average over past 12 months, lagged 12 months
- ◆ Moving average over past 12 months, lagged 24 months
- ◆ Moving average over past 24 months
- ◆ Moving average over past 24 months, lagged 12 months
- ◆ baseline

Figure S3: Adjusted hazard ratio of immunological and virological factors for smoking-related malignancies in a sensitivity analysis that excludes individuals from cohorts with insufficient smoking information

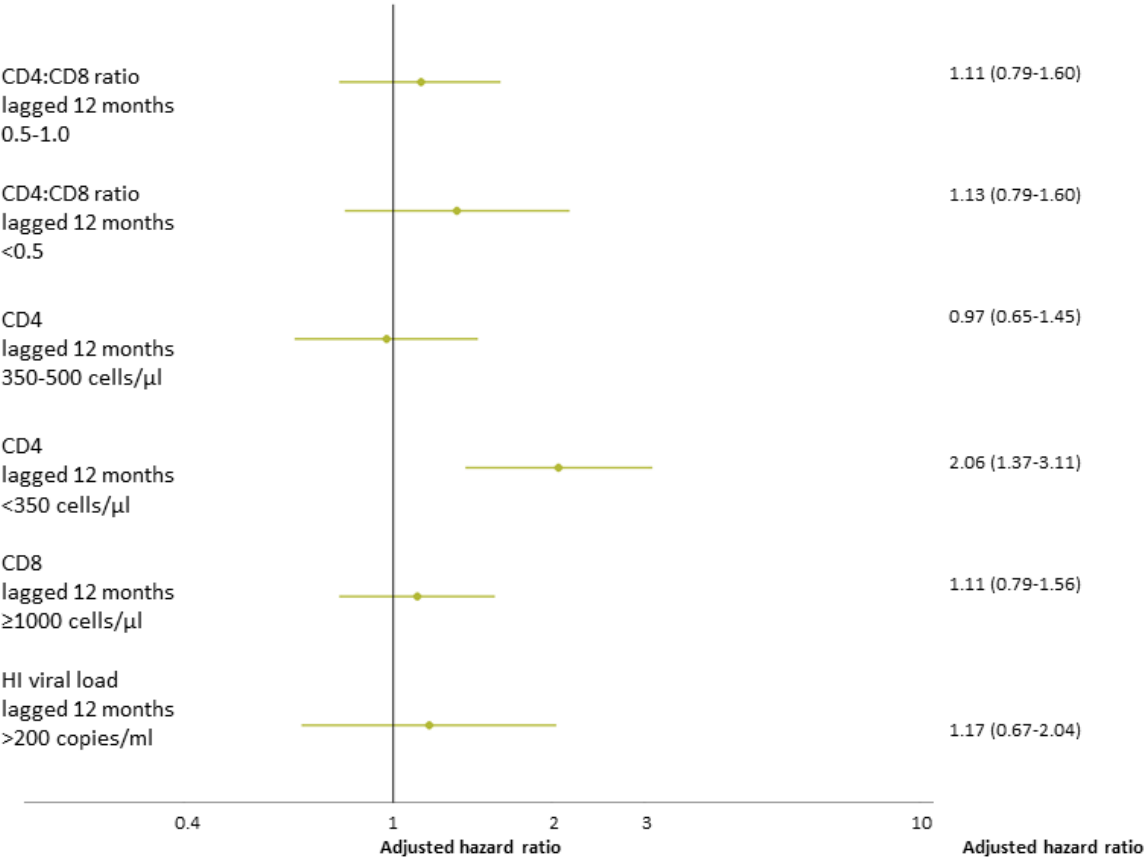


Figure S4: Adjusted hazard ratio of immunological and virological factors for smoking-related malignancies in a sensitivity analysis that excludes individuals from the EuroSIDA cohort that did not routinely collect CD8 cell counts

