

Supplemental Table S1: Unadjusted and Adjusted Hazard Ratios for Diabetes Associated with Baseline Factors Considered in Model 3 SMART Participants Only

Baseline Covariate	Unadjusted		Adjusted*	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Age (per 10 years)	1.64 (1.29 - 2.08)	<.001	1.43 (1.08 - 1.89)	0.013
Female (vs. male)	1.09 (0.64 - 1.85)	0.76	0.67 (0.35 - 1.28)	0.22
White (vs. non-white)	0.62 (0.38 - 1.01)	0.054	0.70 (0.40 - 1.23)	0.21
Hepatitis B or C co-infection	1.42 (0.81 - 2.49)	0.22	2.04 (1.06 - 3.90)	0.032
CD4+ (square root)	1.03 (0.98 - 1.08)	0.28	1.03 (0.97 - 1.08)	0.3
HIV RNA ≤ 500 (vs. > 500)	0.84 (0.51 - 1.38)	0.49	0.64 (0.35 - 1.15)	0.13
Lipid lowering therapy	2.73 (1.64 - 4.53)	<.001	2.20 (1.23 - 3.94)	0.008
BP lowering therapy	3.02 (1.85 - 4.93)	<.001	1.31 (0.77 - 2.23)	0.32
BMI (kg/m ²)	1.10 (1.07 - 1.13)	<.001	1.10 (1.06 - 1.14)	<.001
Smoking	0.54 (0.32 - 0.91)	0.021	0.54 (0.31 - 0.95)	0.034
LDL cholesterol (per 10 mg/dL)	0.99 (0.93 - 1.07)	0.87	0.99 (0.92 - 1.06)	0.77
HDL cholesterol (per 10 mg/dL)	0.89 (0.75 - 1.06)	0.19	1.01 (0.84 - 1.23)	0.88
Triglycerides (per 10 mg/dL)	1.01 (1.00 - 1.02)	0.006	1.01 (1.00 - 1.02)	0.21
No ART	1.08 (0.46 - 2.55)	0.86	0.88 (0.33 - 2.35)	0.8
Stavudine containing regimen	1.75 (0.83 - 3.70)	0.14	1.56 (0.72 - 3.37)	0.26
Zidovudine containing regimen, no Stavudine	1.44 (0.71, 2.88)	0.31	1.52 (0.74 - 3.10)	0.26
Other ART, no Zidovudine or Stavudine (ref.)	--	--	--	--
*Includes all covariates in table plus IL-6 and hsCRP				

Supplemental Table S2: Subgroup analysis for IL-6 with BMI in 3 groups

	No. of diabetes cases	Rate (1000 py)	HR associated with doubling of IL-6		interaction P-value
			HR	95% CI	
Age (years)					0.75
≤45	61	5.38	1.28	(0.97-1.68)	
>45	76	14.02	1.31	(1.05-1.65)	
Gender					0.56
Men	109	8.26	1.33	(1.09-1.63)	
Women	28	7.85	1.08	(0.68-1.72)	
Race					0.20
White	73	6.36	1.38	(1.08-1.76)	
Black	41	13.73	1.13	(0.81-1.57)	
Other	23	10.03	2.06	(1.11-3.78)	
BMI (kg/m²)					0.23
<25	46	4.70	1.30	(0.97-1.75)	
25-29	45	8.72	1.12	(0.81-1.55)	
30+	46	25.52	1.70	(1.23-2.34)	
Smoking †					0.48
Yes	19	7.20	1.22	(0.79-1.86)	
No	49	13.37	1.42	(1.07-1.89)	
Study					0.99
ESPRIT	69	6.60	1.32	(0.98-1.78)	
SMART	68	10.79	1.31	(1.04-1.65)	

Models adjusted for age, gender, race, square root baseline CD4 count, co-infection with hepatitis B or C, viral load, type of ART (stavudine, zidovudine (no stavudine), other ART or no ART), use of lipid lowering drugs, use of blood pressure lowering drugs and BMI. Models are also stratified by study except subgroup analysis by smoking status.

† Only available in the SMART study.

Supplemental Table S3: Subgroup analysis for hsCRP with BMI in 3 groups

	No of diabetes cases	Rate (1000 py)	HR associated with doubling of hsCRP		Interaction P-value
			HR	95% CI	
Age (years)					0.78
<45	61	5.38	1.24	(1.06-1.46)	
>45	76	14.02	1.21	(1.05-1.40)	
Gender					0.47
Men	109	8.26	1.25	(1.10-1.41)	
Women	28	7.85	1.13	(0.89-1.44)	
Race					0.009
White	73	6.36	1.31	(1.14-1.51)	
Black	41	13.73	1.01	(0.84-1.23)	
Other	23	10.03	1.71	(1.18-2.47)	
BMI (kg/m²)					0.11
<25	46	4.70	1.24	(1.05-1.47)	
25-29	45	8.72	1.05	(0.87-1.27)	
30+	46	25.52	1.42	(1.15-1.76)	
Smoking †					0.91
Yes	19	7.20	1.24	(0.94- 1.62)	
No	49	13.37	1.17	(0.97- 1.41)	
Study					0.25
ESPRIT	69	6.60	1.30	(1.11-1.52)	
SMART	68	10.79	1.19	(1.03-1.38)	

Models adjusted for age, gender, race, square root baseline CD4 count, co-infection with hepatitis B or C, viral load, type of ART (stavudine, zidovudine (no stavudine), other ART or no ART), use of lipid lowering drugs, use of blood pressure lowering drugs and BMI. Models are also stratified by study except subgroup analysis by smoking status.

† Only available in the SMART study.

Supplemental Table S4: Risk of diabetes in first 3 years of follow-up associated with IL-6 and CRP levels at entry

Type of adjustment	Quartile 1 HR (95% CI)	Quartile 2 HR (95% CI)	Quartile 3 HR (95% CI)	Quartile 4 HR (95% CI)	HR associated with doubling of biomarkers	
					HR (95% CI)	P-value
IL-6						
IL6 range (pg/ml)	(0.15-1.15)	(1.16-1.80)	(1.81-2.82)	(2.83-88.63)	-	-
No-patients with Incident diabetes (n)	7	13	30	37	-	-
Crude Analysis (n=3,965 ; 2.19%)	1.00 (Ref)	1.79 (0.71-4.49)	4.34 (1.90-9.91)	5.12 (2.28-11.48)	1.61 (1.35-1.91)	<0.001
Model 1:	1.00 (Ref)	1.64 (0.65-4.13)	3.52 (1.52-8.17)	3.87 (1.68-8.91)	1.48 (1.23-1.79)	<0.001
Model 2:	1.00 (Ref)	1.33 (0.52-3.40)	2.74 (1.17-6.39)	2.91 (1.25-6.79)	1.45 (1.18-1.79)	<0.001
Model 3:	1.00 (Ref)	1.91 (0.55-6.60)	3.58 (1.15-11.18)	3.58 (1.16-11.06)	1.54 (1.19-1.98)	0.001
hsCRP						
hs-CRP range (µg/ml)	(0.03-0.68)	(0.69-1.56)	(1.57-3.56)	(3.57-98.00)	-	-
No-patients with Incident diabetes (n)	8	12	32	35	-	-
Crude Analysis (n=3,965; 2.19%)	1.00 (Ref)	1.51 (0.62-3.70)	4.00 (1.84-8.68)	4.37 (2.03-9.44)	1.33 (1.18-1.50)	<0.001
Model 1:	1.00 (Ref)	1.47 (0.60-3.61)	3.44 (1.57-7.53)	3.68 (1.69-8.03)	1.30 (1.14-1.47)	<0.001
Model 2:	1.00 (Ref)	1.54 (0.60-3.93)	3.25 (1.41-7.47)	3.21 (1.39-7.38)	1.24 (1.08-1.41)	0.002
Model 3:	1.00 (Ref)	3.54 (0.96-13.07)	4.35 (1.25-15.15)	4.93 (1.42-17.16)	1.27 (1.06-1.51)	0.008

Model 1: Adjusted for age, sex, race, square root baseline CD4 count, co-infection with hepatitis B or C, viral load and type of ART (stavudine, zidovudine (no stavudine), other ART or no ART); stratified by study. 10 participants including 1 event are excluded due to missing baseline covariates.

Model 2: Model 1 plus use of lipid lowering drugs, use of blood pressure lowering drugs and BMI; stratified by study. 32 participants including 2 events are excluded due to missing baseline covariates.

Model 3: Model 2 plus cigarette smoking status, LDL, HDL, and triglycerides; SMART participants only. 17 participants including 0 events are excluded due to missing baseline covariates.

Supplemental Table S5: Risk of diabetes after the first 3 years of follow-up associated with IL-6 and CRP levels at entry

Type of adjustment	Quartile 1 HR (95% CI)	Quartile 2 HR (95% CI)	Quartile 3 HR (95% CI)	Quartile 4 HR (95% CI)	HR associated with doubling of biomarkers	
					HR (95% CI)	P-value
IL-6						
IL6 range (pg/ml)	(0.15-1.15)	(1.16-1.80)	(1.81-2.82)	(2.83-88.63)	-	-
No-patients with Incident diabetes (n)	7	14	14	15	-	-
Crude Analysis (n=2,410; 2.07%)	1.00 (Ref)	1.51 (0.61-3.75)	1.51 (0.61-3.75)	1.83 (0.75-4.50)	1.19 (0.90-1.57)	0.22
Model 1:	1.00 (Ref)	1.33 (0.53-3.31)	1.10 (0.43-2.79)	1.31 (0.52-3.33)	1.08 (0.79-1.47)	0.63
Model 2:	1.00 (Ref)	1.22 (0.49-3.05)	0.85 (0.33-2.20)	1.08 (0.42-2.79)	1.01 (0.72-1.42)	0.94
Model 3:	1.00 (Ref)	0.41 (0.08-2.04)	0.23 (0.04-1.31)	0.36 (0.08-1.65)	0.75 (0.41-1.36)	0.34
hsCRP						
hs-CRP range (µg/ml)	(0.03-0.68)	(0.69-1.56)	(1.57-3.56)	(3.57-98.00)	-	-
No-patients with Incident diabetes (n)	2	11	23	14	-	-
Crude Analysis (n=2,410; 2.07%)	1.00 (Ref)	5.55 (1.23-25.03)	11.60 (2.74-49.20)	7.93 (1.80-34.95)	1.30 (1.12-1.52)	<0.001
Model 1:	1.00 (Ref)	4.83 (1.06-21.94)	9.30 (2.18-39.73)	6.03 (1.35-26.92)	1.26 (1.07-1.49)	0.007
Model 2:	1.00 (Ref)	4.28 (0.94-19.56)	7.59 (1.77-32.62)	4.36 (0.96-19.73)	1.21 (1.01-1.45)	0.04
Model 3:	1.00 (Ref)	1.35 (0.22-8.36)	1.22 (0.22-6.92)	0.86 (0.15-5.06)	1.05 (0.77-1.44)	0.75

Model 1: Adjusted for age, sex, race, square root baseline CD4 count, co-infection with hepatitis B or C, viral load and type of ART (stavudine, zidovudine (no stavudine), other ART or no ART); stratified by study. 10 participants including 1 event are excluded due to missing baseline covariates.

Model 2: Model 1 plus use of lipid lowering drugs, use of blood pressure lowering drugs and BMI; stratified by study. 32 participants including 2 events are excluded due to missing baseline covariates.

Model 3: Model 2 plus cigarette smoking status, LDL, HDL, and triglycerides; SMART participants only. 17 participants including 0 events are excluded due to missing baseline covariates.