

Success comes at a cost: weight, lipids and metabolic risks in HIV

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Obesity at antiretroviral therapy initiation and long-term risk of cardiovascular disease, cancer, or death in people with HIV: a prospective cohort study

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ABSTRACT

Background: Altered adipose tissue biology plays a key role in the development of cardiovascular disease (CVD) and cancer and contributes to mortality. We assessed the effect of obesity in people with HIV (PWH) at antiretroviral treatment (ART) initiation on the risk of clinical events.

Methods: We included PWH from the Icona study who, at ART initiation, were free from AIDS, CVD and cancer. PWH were grouped by BMI at ART initiation as non-obese (BMI 18.5-29.9) or obese (BMI ≥ 30). Underweight PWH were excluded. We performed a standard survival analysis with time-fixed covariates at baseline with a composite outcome of CVD/cancer/death. We hypothesized that age may be an effect measure modifier: results are presented after stratification by age (young [18-30], middle aged [31-60] and older [>60 years]).

Results: A total of 11,652 PWH (20.7% females, median age 38 years [IQR: 31, 46]) were included: 11,005 (94.4%) were non-obese and 647 (5.6%) obese (Table 1). A total of 837 events were recorded: 122 CVD, 374 cancers and 341 deaths.

By 15 years from ART initiation, the risk of CVD/cancer/death was 19.1% in obese (95% CI: 14.1-24.9%) vs. 12.4% in non-obese (95% CI: 11.3-13.4%, log-rank p=0.006) (Figure 1A,B). After controlling for confounding, the difference was attenuated (adjusted hazard ratio [aHR] 1.28 [95% CI: 0.98-1.67], p=0.073) (Table 2). Although we did not find evidence for interaction (p-value=0.758) there was a clear trend for a larger effect in younger PWH: young (aHR 1.83 [95% CI 0.74, 4.56]), middle aged (aHR 1.49 [95% CI 1.11, 2.00]) and older (aHR 1.20 [95% CI 0.60, 2.41]).

Conclusions: Obesity at ART initiation is associated with an increased risk of CVD/cancer/death and the effect size was larger for PWH younger than 60 years. Addressing obesity in PWH from ART initiation should be integrated into an overall strategy towards improving PWH prognosis.

Table 1. Main characteristics of people with HIV (PWH) at ART initiation, stratified by exposure group (PWH with and without obesity).

Characteristics	PWH without obesity N= 11,005	PWH with obesity N= 647	p-value*	Total N= 11,652
Baseline Characteristics:				
Sex at birth, n(%)			<.001	
Female	2241 (20.4%)	171 (26.4%)		2412 (20.7%)
Age, years			<.001	
Median (IQR)	38 (31, 45)	41 (35, 50)		38 (31, 46)
Nationality, n(%)			0.126	
Not born in Italy	1999 (18.2%)	133 (20.6%)		2132 (18.3%)
Mode of HIV acquisition, n(%)			<.001	
PWID	1685 (15.3%)	86 (13.3%)		1771 (15.2%)
MSM	4926 (44.8%)	205 (31.7%)		5131 (44.0%)
Heterosexual contacts	3995 (36.3%)	332 (51.3%)		4327 (37.1%)
Other/Unknown	389 (3.6%)	24 (3.7%)		423 (3.6%)
Hepatitis co-infection, n(%)			0.434	
HCV-Ab				
No	5726 (52%)	353 (54.0%)		6079 (52.2%)
Yes	1328 (12.1%)	69 (10.7%)		1397 (12%)
Not tested	3951 (35.9%)	225 (34.8%)		4176 (35.8%)
HBsAg			0.247	
No	6916 (62.8%)	422 (65.2%)		7338 (63)
Yes	58 (0.5%)	4 (0.6%)		62 (0.5%)
Not tested	4031 (36.6%)	221 (34.2%)		4252 (36.5%)
Psychiatric diagnosis, n(%)			0.279	
Yes	326 (3.0%)	24 (3.7%)		350 (3.0%)
Diabetes, n(%)			<.001	
Yes	165 (1.5%)	44 (6.8%)		209 (1.8%)
Active injecting drug use, n(%)			0.356	
Yes	389 (4.2%)	27 (5.0%)		416 (4.2%)
Alcohol use, n(%)			0.816	
Abstain	2135 (19.4%)	133 (20.6%)		2268 (19.5%)
Social use	1651 (15.0%)	95 (14.7%)		1746 (15.0%)
Abuse	492 (4.5%)	32 (4.9%)		524 (4.5%)
Unknown	6727 (61.1%)	387 (59.8%)		7114 (61.1%)
Smoking, n(%)			0.001	
No	3179 (28.9%)	230 (35.5%)		3409 (29.3%)
Yes	3008 (27.3%)	160 (24.7%)		3168 (27.2%)
Characteristics at ART initiation:				
Time from HIV diagnosis to ART initiation, months			0.268	
Median (IQR)	3 (1, 42)	4 (1, 46)		3 (1, 42)
Calendar year of ART initiation			0.002	
Median (IQR)	2013 (2004, 2017)	2014 (2008, 2018)		2013 (2004, 2017)
Type of first ART regimen, n (%)			0.033	
3TC+DTG	311 (2.8%)	32 (4.9%)		343 (2.9%)
Pf/r	2980 (27.1%)	172 (26.6%)		3152 (27.1%)
NNRTI	2764 (25.1%)	153 (23.5%)		2917 (25.0%)
INSTI	3063 (27.8%)	173 (26.7%)		3236 (27.8%)
Other	1887 (17.1%)	117 (18.1%)		2004 (17.2%)
CD4 count, cells/mm3			<.001	
Median (IQR)	349 (221, 494)	389 (249, 556)		351 (223, 498)
0-200 cells/mm3, n(%)			0.634	
Median (IQR)	2314 (21, 98%)	113 (18.1%)		2427 (21.7%)
Viral load, log₁₀ copies/mL			<.001	
Median (IQR)	4.71 (4.15, 5.24)	4.58 (3.95, 5.04)		4.71 (4.14, 5.23)
Follow-up, months				
Median (IQR)	84 (32, 135)	83 (32, 132)		84 (32, 135)

Figure 1. Unweighted (Figure 1A) and weighted (Figure 1B) Kaplan-Meier curves of the main outcome: risk of CVD, cancer or death according to the exposure.

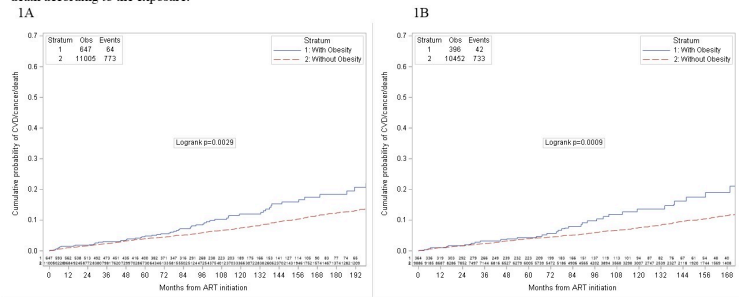


Table 2. Risk of CVD/cancer/death by exposure group (HR - standard Cox proportional hazard regression models): overall, by age strata and by sex assigned at birth.

	Unadjusted HR (95%CI)	P value	Adjusted HR (95%CI)	P value
CVD/cancer/death				
PWH without obesity	1		1	
PWH with obesity	1.47 (1.14, 1.90)	0.003	1.28 (0.98, 1.67)	0.073
Data were adjusted for year of ART initiation, age, sex assigned at birth, mode of HIV acquisition, HIV-RNA and CD4 at ART, hepatitis co-infection, smoking, diabetes, level of education and employment status.				
	Unadjusted HR (95%CI)	Adjusted HR (95%CI)	Interaction p-value	
CVD/cancer/death by age strata				
				Young (18-30 years)
PWH without obesity	1	1		
PWH with obesity	1.76 (0.71, 4.35)	1.83 (0.74, 4.56)		
				Middle age (31-60 years)
PWH without obesity	1	1		
PWH with obesity	1.37 (1.03, 1.83)	1.49 (1.11, 2.00)		
				Older (> 60 years)
PWH without obesity	1	1		
PWH with obesity	1.16 (0.58, 2.30)	1.20 (0.60, 2.41)		
Data were adjusted for year of ART initiation, sex assigned at birth, mode of HIV acquisition, HIV-RNA and CD4 at ART, hepatitis co-infection, smoking, diabetes, level of education and employment status.				
	Unadjusted HR (95%CI)	Adjusted HR (95%CI)	Interaction p-value	
CVD/cancer/death by sex at birth				
				Male
PWH without obesity	1	1		
PWH with obesity	1.59 (1.20, 2.10)	1.38 (1.04, 1.84)		
				Female
PWH without obesity	1	1		
PWH with obesity	1.10 (0.60, 2.02)	1.42 (0.77, 2.62)		
Data were adjusted for year of ART initiation, age, mode of HIV acquisition, HIV-RNA and CD4 at ART, hepatitis co-infection, smoking, diabetes, level of education and employment status.				