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Weight gain and metabolic complications in a large prospective cohort of overweight and obese people with HIV.

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Purpose

To describe the factors associated with weight gain and metabolic complications in people with HIV (PWH) who are overweight or obese.

Methods

This was a multicentre prospective study enrolling overweight and obese PWH in two observational cohorts: the Overweight and oBese people with

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HIV (OBHIV) and Surveillance Cohort Long-Term Toxicity Antiretrovirals (SCOLTA) cohorts. People with at least one year of follow up were included. Weight change was analysed using a linear model adjusted for observation time. Factors associated with incident diabetes and dyslipidaemia were estimated using a Cox proportional hazards model.

Results

1401 overweight (75%) or obese (25%) PWH were enrolled. The mean age was 51 years (SD± 11.6) and 78.6% were male (**Table 1**).

The mean weight change observed in this cohort was +0.03 kg/month in overweight (95%CI 0.0; 0.05) and -0.13 kg/month in obese PWH (95%CI -0.21; -0.04). After multivariable adjustment, which also considered the type of treatment, two variables were associated with the likelihood of significant weight loss: ART experience (-0.09 kg/month SE 0.03, p= 0.0092) and obesity at baseline (-0.09 kg/month SE 0.04, p= 0.0367). No factor was associated with weight gain.

The incidence of diabetes was 2.06/100 PYFU and that of dyslipidaemia was 3.12/100 PYFU.

Incident diabetes was more probable in PWH who were obese (aHR 2.4, 95%CI 1.5;3.9), older (aHR 1.04 per year, 95%CI 1.02;1.07) with steatosis (aHR 2.3, 95%CI 0.9;5.6) and detectable viremia (aHR 3.8 for HIV RNA 50-200 copies/mL, 95%CI 1.7-8.4 and aHR 2.7 for HIV RNA> 200 copies/mL, 95%CI 0.99-7.5). People with a shorter duration of exposure to INSTI appeared to be at higher risk (aHR 5.7 for exposure below the median, 95%CI 2.2-15.05) (**Table 2**).

No risk factor was instead associated with incident dyslipidaemia.

Table 1. Baseline characteristics of 1401 overweight and obese people participating in the study.

	BMI class				All	
	Overweight		Obese			
	N	%)	N	%	N	%
Cohort						
- OBHIV	117	11.2	53	14.8	170	12.1
- SCOLTA	927	88.8	304	85.2	1231	87.9
Female	197	18.9	103	28.9	300	21.4
Caucasian	936	89.7	309	86.6	1245	88.9
Risk factor for HIV						
- VDU	136	13.0	45	12.6	181	12.9
- Sexual exposure	801	76.7	266	74.5	1067	76.2
- Other/Unknown	107	10.2	46	12.9	153	10.9
ART naive	132	12.6	30	8.4	162	11.6
CDC Stage						
- A	570	54.6	208	58.3	778	55.5
- B	243	23.3	78	21.8	321	22.9
- C	200	19.2	58	16.2	258	18.4
- missing	31	3.0	13	3.6	44	3.1
Comorbidities at baseline						
- Diabetes	74	7.1	37	10.4	111	7.9
- Liver steatosis	38	3.6	19	5.3	57	4.1
- Hypertension	289	27.7	126	35.3	415	29.6
- Dyslipidaemia	665	63.7	240	67.2	905	64.6
ART at enrolment in the cohort						
- PI	54	5.2	8	2.2	62	4.4
- INSTI	926	88.7	289	81.0	1215	86.7
- NNRTI	385	36.9	142	39.8	527	37.6

ART: antiretroviral therapy; **BMI:** body mass index; **INSTI:** integrase inhibitors; **IVDU:** intravenous drug use; **NNRTI:** non-nucleoside reverse transcriptase inhibitors; **PI**: protease inhibitors.

Table 2. Factors associated with incident diabetes in 1338 overweight and obese people with HIV.

	BMI class			All		
Variable	**HR**	**95% CI**	**P value**	**Adjusted hazard ratio**	**95% CI**	**P value**
Age (by 1 year)	**1.04**	**1.02-1.07**	0.0002	**1.04**	**1.01-1.06**	0.0012
Sex (ref. M)	1.14	0.65-2.01	0.6370			
Obesity (ref. overweight)	**2.46**	**1.52-3.99**	0.0002	**2.36**	**1.39-4.00**	0.0015
Risk factor for HIV acquisition (ref. sexual)						
IDU	1.54	0.83-2.86	0.1691			
Other/unknown	1.59	0.82-3.07	0.1710			
steatosis	2.26	0.91-5.64	0.0790			
hypertension	0.61	0.37-0.99	0.0457			
dyslipidemia	0.48	0.30-0.78	0.0031			
CDC Stage (ref. A)						
B	0.94	0.52-1.72	0.8434			
C	1.31	0.73-2.37	0.3624			
HIVRNA (ref. <50 copies/mL)						
50-199 copies/mL	**3.80**	**1.73-8.36**	0.0009	**4.25**	**1.91-9.45**	0.0004
>200 copies/mL	2.71	0.98-7.48	0.0542	2.76	0.85-8.93	0.0903
Ongoing statin (ref. no)	**2.40**	**1.40-4.10**	0.0014	**1.43**	**0.83-2.46**	0.1958
Liver steatosis	0.52-1.72	3.6	19	5.3	57	4.1
ART duration (by 1 year)	1.01	0.99-1.04	0.3076			
Treatment with TAF	1.14	0.70-1.85	0.5992			
Treatment of NRTI	1.002	1-1.005	0.1643			
Months of NRTI (median value 80 months)	1.002	1.00-1.005	0.0760			
< median value	2.58	0.9-7.42	0.0786			
>= median value	2.81	0.98-8.04	0.0537			
missing	2.52	0.77-8.25	0.1277			
Treatment with NNRTI	1.29	0.78-2.13	0.3171			
Months of NNRTI (median value 0 months)	1.00	1.00-1.005	0.1643			
</= median value	1.23	0.61-2.48	0.5630			
> median value	1.83	1.02-3.3	0.0439			
missing	1.90	0.82-4.39	0.1329			
Treatment with PI	1.65	0.66-4.11	0.2836			
Months of PI (median value 0 months)	1.003	0.99-1.006	0.1463			
</= median value	1.54	0.78-3.04	0.209			
> median value	1.65	0.87-3.11	0.127			
missing	2.13	1.09-4.15	0.026			
Treatment with INSTI ref. Never exposed	0.61	0.33-1.11	0.1073			
Months of INSTI (median value of 13 months)	0.97	0.96-0.98	<0.0001			
< median value	**5.71**	**2.17-15.05**	0.0004	**5.539**	**1.95-15.76**	0.0013
>/= median value	1.40	0.53-3.69	0.496			
missing	**5.66**	**1.84-17.38**	0.0025	**4.094**	**1.21-13.90**	0.0238
Cohort (ref. SCOLTA)						
OBHIV	1.82	0.97-3.42	0.0611			

95% **CI:** 95% Confidence Interval; **ART:** antiretroviral therapy; **HR:** Hazard Ratio; **IDU:** intravenous drug use; **INSTI:** integrase inhibitors; **NNRTI:** non-nucleoside reverse transcriptase inhibitors; **PI:** protease inhibitors; **PWH:** people living with HIV; **TAF:** tenofovir alafenamide. Variables were included in the multivariate model through a forward model selection with p value set at 0.2

Conclusions

We observed modest weight changes in overweight and obese PWH. ART experience and obesity at baseline were associated with the likelihood of significant weight loss. The type of antiretroviral treatment was not associated with weight gain or loss. Regarding metabolic complications, we observed that obesity, age, steatosis and detectable HIV-RNA were associated with higher incidence of diabetes, suggesting that not only traditional risk factors but also uncontrolled viral replication and inflammation could be linked with incident diabetes.

Also, a shorter duration of exposure to INSTI appeared to be a risk factor, possibly linked with the choice of INSTI use in people with uncontrolled viral replication. No risk factor was instead associated with incident dyslipidaemia.

These findings suggest that the type of antiretroviral therapy is not associated with weight gain and metabolic complications in people with HIV (PWH) who are overweight or obese in this cohort. The results also suggest that the primary objective is to regulate viral replication also in order to achieve a favourable metabolic outcome. ■