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Change in body mass index (BMI) and association with clinical outcomes after initiation of contemporary HIV antiretroviral (ARV) regimens in EuroSIDA

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INTRODUCTION

- There is increasing evidence that some contemporary antiretroviral (ARV) regimens contribute towards excess weight gain in persons living with HIV (PLWH), in particular, INSTIs, potentially amplified when co-administered with certain NRTIs (e.g. TAF) [1]; however, there are limited data available looking at the clinical implications.
- Earlier studies have linked increases in BMI to cardiovascular disease (CVD)[2] and diabetes mellitus (DM)[2,3,4] and low BMI to CVD, cancer, and mortality[5].
- EuroSIDA, a large prospective observational study, provides more contemporary data, including PLWH with substantial exposure to INSTIs, to study long-term clinical outcomes (CVD, malignancies, DM, all-cause mortality) in relation to BMI changes after initiation of a new ARV in recent years.

METHODS

- PLWH under follow-up were included aged ≥18 years who started a new ARV (baseline) to which they had no prior exposure (first initiation of ART, treatment switch, or addition to existing regimen) during 2010-2019 with baseline and follow-up BMI available.
- Multivariable Poisson regression used to assess the effect of time-updated BMI changes on incidence of clinical outcomes.
- BMI assessments and other time-updated covariates were lagged by 1 year (i.e. proceeded the events by ≥1 year) to minimise reverse causality. Last observation was carried forward.
- Persons with a prior relevant diagnosis and/or <1 year of follow-up from baseline to event/censoring were excluded.

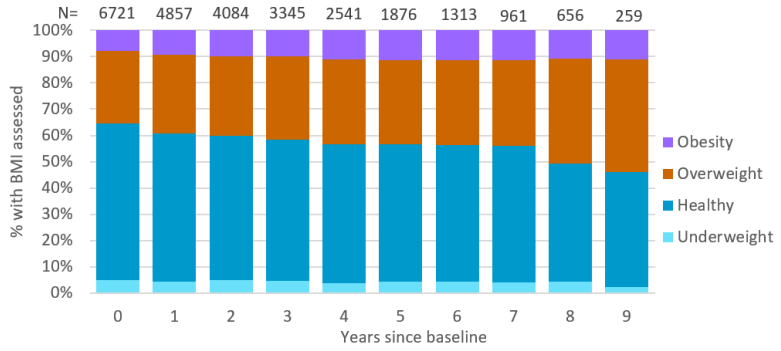
RESULTS

- 6721 PLWH were included with a total of 31420 person-years of follow-up (PYFU). **Table 1** displays baseline characteristics.
- Median follow-up was 4.4 years (IQR 2.6, 6.7) and median number of weight assessments available was 5 (2, 9) per person.

Table 1 Baseline characteristics stratified by baseline BMI category

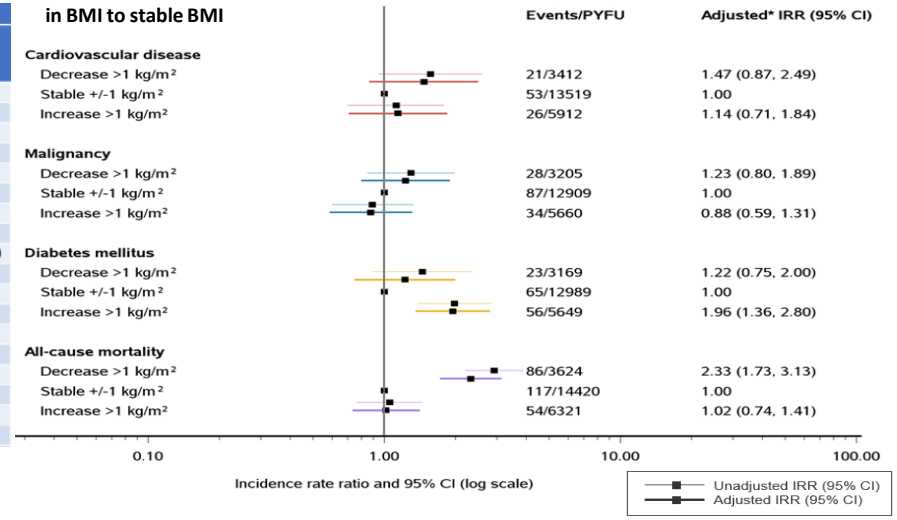
		Total	Baseline BMI category			
			Underweight <18.5 kg/m²	Healthy 18.5 to <25 kg/m²	Overweight 25 to <30 kg/m²	Obesity ≥30 kg/m²
Total, n (%)		6721	338 (5.0%)	4011 (59.7%)	1851 (27.3%)	521 (7.8%)
Male, %		72.3	50.9	71.5	79.7	66.2
Age in years, median (IQR)		48 (40, 55)	49 (38, 55)	48 (39, 55)	49 (42, 56)	50 (43, 55)
Race – white, %		85.5	82.0	86.2	85.8	82.1
HIV infection risk group, %	MSM	38.4	25.4	38.5	42.5	32.2
	IDU	25.2	34.9	27.1	21.2	18.0
Current smoker, %		42.9	60.1	45.8	37.4	29.4
Family history of CVD, %		5.9	5.9	5.5	6.6	6.3
CD4 cells/mm³, median (IQR)		553 (371, 760)	521 (327, 763)	542 (364, 749)	573 (388, 770)	610 (408, 823)
Undetectable HIV RNA<200 copies/L, %		81.6	78.1	81.0	83.4	82.2
Coinfection, %	Hepatitis B	5.5	4.4	5.3	6.1	5.8
	Hepatitis C	38.6	52.4	41.0	33.5	29.0
ART-naïve, %		8.4	7.1	8.7	8.0	8.8
Previously received, %:	NRTIs	91.2	92.9	90.9	91.6	90.4
	PIs	72.6	79.3	72.6	72.5	69.3
	NNRTIs	61.3	63.0	61.1	61.3	61.8
	INSTIs	12.5	12.7	12.0	13.0	14.0
INSTI-containing baseline regimen, %		41.1	45.6	39.3	42.7	45.5

Figure 1 Distribution of BMI categories over time



- Overall, the distribution of baseline BMI categories remained similar over the study period (**Figure 1**); however, 26% experienced an increase and 16%, a decrease at some point over this time.
- **Figure 2** presents number of clinical events and incidence rate ratios.

Figure 2 Incidence rate ratios (IRRs) and 95% CIs comparing changes from baseline in BMI to stable BMI



*The model for each clinical outcome was adjusted for baseline BMI and significant (p>0.1) potential confounders from univariable models, including gender, region, age, prior hypertension and dyslipidaemia at baseline, time-updated previous number of ARVs received, current number in regimen, cumulative exposure to ARV classes, chronic kidney disease, plus other confounders related to but not considered to lie on the causal pathway for the particular outcome.

- After adjustment, differences in incidence of CVD and malignancies between decreased or increased BMI compared to stable were not statistically significant.
- There were consistent findings in sensitivity analyses accounting for the effect of "return to health" and extending lagging time to 2 years to further avoid reverse causality.

LIMITATIONS

- BMI data collected from routine clinic visits - frequency and timing vary.
- Waist:hip ratio may improve accuracy of weight gain but not routinely available. No data collected on diet, exercise, alcohol consumption.
- Clinical event rates are relatively low so power is limited.

CONCLUSIONS

An increase in BMI was found to be associated with DM and a decrease associated with death, but no association was observed for CVD or malignancies.

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