

Risk Factors associated with Extreme Weight Gain in People with HIV

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BACKGROUND

- Prevalence of obesity increased globally within the last decades^I also in people with HIV (PWH)^{II}
- Weight change is a multifactorial process \rightarrow associated with demographics, diet, exercise, psychological and clinical comorbidities, and co-medications
- Initiation of antiretroviral therapy (ART) & switch to/off certain ART regimen in PWH were associated with weight gain^{III,IV,V}

Here: Evaluation of potential factors for weight gain over 5 years in PWH in the Ruhr-area of Germany

Table 1: Baseline characteristics of participants with a weight gain of $\geq 10\%$ (group A, N=212) versus a stable weight from 0 to $\pm 5\%$ (group B, N=969) within 5 years.

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		ch		with weight gain ≥10% 212)	ch	aracteristics of HIV w (I	ith w n=96	
		Ν	BL	N after 5 years	N	BL	Ν	after 5 years
sex (male)		212	160 (75.5%)		969	821 (84.7%)		
caucasian ethnici	ty (yes)	212	180 (84.9%)		969	847 (87.4%)		1
age (years)		212	45.6±11.0	212 50.8±10.8	969	50.2±11.2	969	55.4±11.0
age at time of HIV infection (years)		210	33.7±9.4		949	36.3±10.4		1
duration of HIV ir	nfection (years)	210	11.9±7.4	210 17.0±7.3	949	13.8±7.4	949	19.0±7.4
weight (kg)		212	77.2±14.8	212 89.8±17.2	969	79.2±15.4	969	79.5±15.8
BMI (kg/m²)			25.2±4.7	212 29.3±5.4	969	25.5 ±4.6	969	25.6±4.6
	underweight (<18.5)		4 (1.9%)	2 (0.9%)		25 (2.6%)		22 (2.3%)
	normal weight (<25)		115 (54.2%)	38 (17.9%)		479 (49.4%)		474 (48.9%)
BMI categories	overweight <30)	212	65 (30.7%)	212 96 (45.3%)	969	332 (34.3%)	969	337 (34.8%)
	obese I (<35)		21 (9.9%)	48 (22.6%)		99 (10.2%)		98 (10.1%)
	obese II (<40)		5 (2.4%)	20 (9.5%)		20 (2.1%)		23 (2.4%)
	obese III (≥40)		2 (0.9%)	8 (3.8%)		14 (1.4%)		15 (1.5%)
			200.7±45.6			206.4±46.5		199.2±45.1
	LDL (mg/dl)		130.1±42.7			128.6±40.0		126.6±40.2
	HDL (mg/dl)		49.9±16.5			50.8±16.6		50.4±14.6
lipid related		206	131 (Q1:113;Q3:230)	203 162 (Q1:114;Q3:230)	942	152 (Q1:103;Q3:232)	905	154 (Q1:107;Q3:227)
parameters	Lipodystrophy (yes)	211	23 (10.9%)			153 (16.1%)		140 (14.5%)
	Lipoatrophy (yes)	202	15 (7.4%)	212 17 (8.2%)	868	110 (12.7%)	969	114 (11.8%)
	Lipohypertrophy							
	(yes)		9 (4.5%)	212 9 (4.3%)	868	51 (5.9%)	969	48 (5.0%)
blood pressure	sys. BP (mmHg)		130.3±17.5	143 136.1±16.0	685	134.2±18.1		137.2±19.3
	dia. BP (mmHg)	201	80.7±10.7	143 84.7±10.1	685	82.8±11.3		84.2±11.6
Hypertension (ye			54 (25.5%)			288 (29.7%)		403 (41.6%)
Hyperlipidaemia	(yes)		105(49.5%)			537 (55.4%)	-	556 (57.4%)
smoking (yes)			95 (46.6%)	206 74 (35.9%)		323 (44.0%)		388 (44.0%)
diabetes mellitus			11 (5.2%)			82 (8.5%)		129 (13.3%)
physical excercise		191	44 (23.0%)	141 28 (19.9%)	594	155 (26.1%)	482	129 (26.8%)
	MSM		127 (59.9%)	_		588 (60.7%)	_	
	Hetero		42 (19.8%)	_		206 (21.3%)	_	
way of	IVDU		11 (5.2%)	_		48 (5.0%)	_	
HIV transmission	transfusion	212	2 (0.9%)	_	969	13 (1.3%)	_	
	epidemic area		19 (9.0%)	_		71 (7.3%)	_	
	other		3 (1.4%)	_		5 (0.5%)	_	
	unknown	_	8 (3.8%)			38 (3.9%)		
imm. CDC WHO			22 (10.5%)	16 (7.5%)		84 (8.8%)	_	68 (7.1%)
HIV state		210	92 (43.8%)		951	401 (42.2%)	-	404 (41.7%)
		_	96 (45.7%)	100 (47.2%)		466 (49.0%)		496 (51.2%)
clinical CDC WHO	HIV A		94 (44.7%)	84 (39.6%)		350 (36.8%)	_	350 (36.8%)
HIV state	HIV B	210	56 (26.7%)		951	293 (30.8%)	968	305 (31.5%)
	HIV C /AIDS	_	60 (28.6%)	60 (28.3%)		308 (32.4%)		353 (36.5%)
ART yes			205 (96.7%)			929 (97.0%)		955 (98.1%)
CD4/CD8 ratio			0.8 (Q1:0.6 Q3:1.2)	· · · · · · · · · · · · · · · · · · ·		0.79 (Q1:0.52 Q3:1.1)		0.84 (Q1:0.57 Q3:1.2)
CD4 cell count (counts/µl)			685.6±321.2			646.2±312.0		704.7±328.3
viral load below o			191 (90.1%)			858 (88.5%)		893 (92.2%)
	NRTI		193 (94.2%)			881 (94.4%)		673 (90.5%)
	NNRTI		86 (42.0%)			332 (36.7%)		224 (30.1%)
ART substance			78(38.1%)			338 (36.2%)		387 (52.0%)
group	PI		51 (24.9%)			315 (33.8%)	-	208 (28.0%)
	Booster		67 (32.7%)			379 (40.6%)		271 (36.4%)
	Entry inhibitor		5 (2.4%)			16 (1.7%)		14 (1.9%)
combination med	lication (yes)	205	104 (50.7%)			551 (59.1%)		274 (36.8%)
Single tablet regi	men (yes)	205	86 (42.0%)	211 155 (73.5%)	933	286 (30.7%)	744	404 (54.3%)
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Note: Categorical variables are presented as frequency (percent), continuous variables are presented as mean (+/-standard deviation) or me (interguartile range).

Abbreviations: BL = Baseline, MSM = Men having sex with men, IVDU = intravenous drug users, BP = Blood pressure, LDL = density lipoprotein, HDL = High density lipoprotein, NRTI = nucleos(t)ide reverse transcriptase inhibitor, NNRTI = nonnucleos reverse transcriptase inhibitor, PI = Protease inhibitor, INSTI = Integrase strand transferase inhibitors TDF = Tenofovir disopr fumarate, TAF = Tenofovir alafenamide, EFV = Efavirenz

METHODS area (Germany) since 2004 apart nge ≤5% to ≥-5 (each N=1108) with "no ARV taken at BL and 5-year follow-up (5YFU)" as reference general characteristics triclycerides* systolic blood pressure* diastolic blood pressure* comorbidities smoking diabetes mellitus+ 07;Q3:227) physical activity ----lipoatrophy **___** lipohypertrophy hypertension ----perlipidemia+ **HIV-specific characteristics** duration of HIV... viral load*

CD4/CD8 Ratio*

ART related characteristics	n Odds Ratio [95%CI]	p
NRTI only at BL**	40 0.30 [0.06-1.10]	0.0
NRTI only at 5YFU**	11 1.10 [0.15-5.39]	0.9
NRTI at BL and 5YFU**	1025 0.79 [0.39-1.74]	0.5
TDF only at BL**	351 1.18 [0.83-1.67]	0.3
TDF only at 5YFU**	41 0.45 [0.15-1.11]	0.0
TDF at BL and 5YFU**	185 0.67 [0.41-1.07]	0.0
TAF only at BL**	34 1.82[0.76-4.01]	0.1
TAF only at 5YFU**	- 347 1.55 [1.09-2.20]	0.0
TAF at BL and 5YFU**	· 172 1.38 [0.87-2.15]	0.3
NNRTI only at BL**	148 0.70 [0.26-1.61]	0.4
NNRTI only at 5YFU**	45 1.32 [0.83-2.07]	0.2
NNRTI at BL and 5YFU**	276 1.33 [0.92-1.92]	0.3
EFV only at BL**	90 1.24 [0.69-2.11]	0.4
EFV only at 5YFU**	3 NA	NA
EFV at BL and 5YFU**	56 0.68 [0.28-1.45]	0.3
INSTI only at BL**	13 NA	N
INSTI only at 5YFU**	266 1.33 [0.89-1.99]	0.3
INSTI at BL and 5YFU**	400 1.22 [0.85-1.75]	0.2
PI only at BL**	139 1.02 [0.63-1.61]	0.9
PI only at 5YFU**	22 0.52 [0.12-1.59]	0.2
PI at BL and 5YFU**	224 0.48 [0.29-0.76]	0.0

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Main findings <u>Association with higher risk of >10% weight gain within 5 years in PWH:</u> younger age & higher CD4/CD8 ratio at baseline, switching to TAF, switching off TDF (trend)

<u>Association with lower risk of >10% weight gain within 5 years in PWH</u>: lipoatrophy at baseline, continuous use of PIs

HIV-HEART Aging (HIVH) cohort: Prospective study assessing cardiovascular risk of PWH in the Ruhr

Analysis population: PWH from HIVH with weight measurements at two different time points 5 years

Risk factor assessment: Logistic regression (adj. for baseline age, sex, duration of HIV) comparing weight gain of ≥10% (group A, N=212) with stable weight from 0 to ±5% (group B, N=974) in 5 years Odds ratios (OR) & corresponding 95% confidence limits (CI) for variables at baseline (BL) are shown (Continuous variables: OR per standard deviation (SD); Antiretrovirals (ARV): dummy variables

n	Odds Ratio [95%CI]	p value
1164	0.97 [0.95-0.99]	<0.001
980	1.15 [0.97-1.36]	0.116
1058	0.92 [0.77-1.09]	0.327
1132	0.88 [0.74-1.04]	0.21
877	0.89 [0.75-1.06]	0.196
877	0.88 [0.74-1.04]	0.123
930	1.10 [0.79-1.52]	0.576
1164	0.66 [0.31-1.27	0.226
781	0.78 [0.52-1.16]	0.221
1058	0.55 [0.29-0.98]	0.042
1054	0.66 [0.29-1.35]	0.267
1164	1.16 [0.79-1.67]	0.451
1164	1.06 [0.77-1.47]	0.707
1159	0.89 [0.74-1.06]	0.195
1153	0.93 [0.75-1.08]	0.403
1148	1.28 [1.10-1.49]	0.001

Figure 1: Logistic regression models of potential risk factors for $\geq 10\%$ weight gain over 5 years. Estimates are presented Odds ratio and as corresponding 95% confidence limit (CI). All variables are considered at baseline (BL).

*) per standard deviation +) covariate diabetes mellitus combines diabetes diagnosis or anti-diabetes medication, Hyperlipidemia combines hyperlipidemia and lipid diagnosis lowering medication

Figure 2: Logistic regression models of potential risk factors for $\geq 10\%$ weight gain over 5 years. Estimates are presented as Odds ratio and corresponding 95% confidence limit (CI). INSTI use only at BL and EFV only at 5 year follow-up (5YFU) could not be shown (NA) because of low number of persons in this subgroup.

++) for all ARV variables the reference group is ARV not used at BL and 5YFU



RESULTS

• **1186 participants:** mean age 49.4±11.3 years, 16.9% females, 87% Caucasian, 2% ART naïve

Mean weight change within 5 years:

- Group A: 77.2±14.8 to 89.8±17.2kg
- Group B: 79.2±15.7 to 79.5±15.8kg

Regression models in Figure 1 & 2:

- Increasing age: OR 0.97 [95%CI 0.95-0.99]
- Prevalent lipoatrophy: OR 0.55 [95%Cl 0.29-0.98]
- Increasing CD4/CD8 ratio: OR 1.28 [95%CI 1.10-1.49]
- Pls at BL & 5YFU vs. no Pls at BL & 5YFU:
- OR 0.48 [95%CI 0.29-0.76]
- CD4/CD8 ratio increased from 0.8±0.5 (BL) to 1.0±3.1 (after 5 years) within this group
- Lipoatrophy changed from 15.8% (BL) to 14.3% (after 5 years) within this group

Specific NRTIs:

- Switch to TAF after BL: OR 1.55 [95%CI 1.09-2.20] TDF at BL & 5YFU: OR 0.67 [95%CI 0.41-1.07]
- 80.7% of TAF group switched from TDF at BL to TAF during the observation period

CONCLUSION

- Younger age & increasing CD4/CD8 ratio at BL with $\geq 10\%$ weight gain within 5 years; associated Lipoatrophy at BL associated with lower risk of weight gain within 5 years
- Continuous use of Pis associated with a lower risk of weight gain
- No association of NNRTI or INSTI intake with ≥10% weight gain over 5 years
- Switching off TDF: Trend towards increased weight gain Switching to TAF after BL associated with increased risk for $\geq 10\%$ weight gain.

ADDITIONAL KEY INFORMATION

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