Impact of antiretroviral class switching on cardiometabolic risk: data from the HIV-HEART Aging cohort

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KEY MESSAGES

Changing the ART regimen to another class has no clinically relevant impact on the metabolic and cardiovascular risk profile.

Management of cardiovascular risk factors is becoming increasingly important in the medical care of aging people living with HIV.

Background

- Increasing life expectancy in people with HIV (PWH) leads to a growing burden of cardiometabolic comorbidities, including overweight and obesity, dyslipidaemia, hypertension, and diabetes mellitus
- Cardiovascular risk in PWH is multifactorial: traditional risk factors, chronic immune activation, HIV-related factors, metabolic effects of long-term antiretroviral therapy (ART)
- Increase in integrase strand transfer inhibitor (INSTI)-based regimens: high antiviral efficacy, favourable tolerability, high barrier to resistance
  → concerns: weight gain and potential cardiometabolic consequences after switch to INSTI-based regimens
- real-world longitudinal data are required to determine whether switching ART class is associated with changes of cardiometabolic risk

Objective: To investigate the impact of switching ART regimens to another class, compared with stable ART therapy, on cardiometabolic parameters over a 2.5-year follow-up period in a large cohort.

Study Design and Cohort

- **HIV-HEART Aging Cohort (HIVH):** prospective, longitudinal observational study investigating cardiovascular and metabolic risk factors in PWH in the Ruhr area in Germany since 2004
- **Analysis group (n=1177) (see Figure 1):**
  → participants that attended both the 15-years follow-up (FU15; 2020–2022) and the 17.5-year follow-up (FU17): observation interval of ~2.5 years
  → participants were all on a stable ART drug class for at least six months before FU15 (switches within classes were tolerated)
  → **stable ART class group n=999 (84.9%) vs. ART class switch group n=178 (15.1%)**

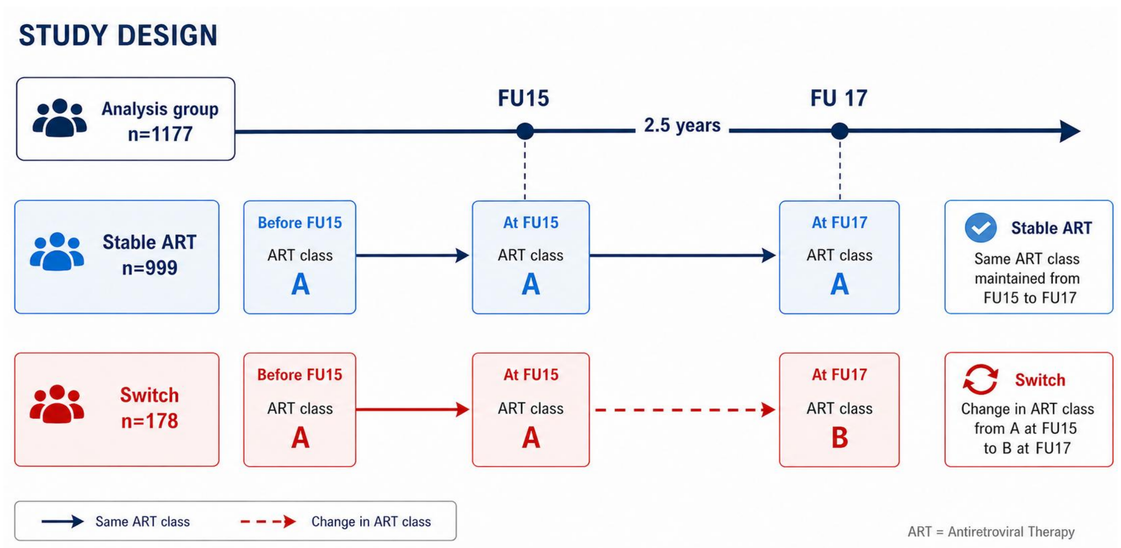

Figure 1: Schematic overview of the study design, showing the 1,177 participants from the HIV-Heart-Aging cohort included in the analysis, divided into stable ART class group and ART class switch group.

Changes to ART Regimens

- **ART class switch group (n=178):**
→ switch in treatment regimens towards another ART class over a 2.5-year period
→ **INSTI-based regimens** increased **from 25.3% (n=45) at FU15 to 87.1% (n=155) at FU17**; **PI- and NNRTI-based regimens declined** substantially; **NRTI-backbone were used by the majority,** but slightly decreased over 2.5 years as well

Substance class (switch)	FU15 (Baseline)	FU17 (2,5 Years)	Trend
INSTI (integrase strand transfer inhibitor)	45 (25.3 %)	155 (87.1 %)	↑ +61.8 %
NNRTI (non-nucleoside reverse transcriptase Inhibitors)	90 (50.6 %)	55 (30.9 %)	↓ -19.7 %
PI (protease inhibitors)	55 (30.9 %)	13 (7.3 %)	↓ -23.6 %
NRTI-Backbone (nucleoside reverse-transcriptase inhibitors)	157 (88.2 %)	145 (81.5 %)	↓ -6.7 %

- **stable ART class group (n=999):**
→ baseline treatment regimens across all substance classes over a 2.5-year period
→ **NRTI-backbone** is used by the majority in the stable ART class group (**92.5%**); **INSTI-based therapies** were used by the **majority of persons in the stable group (73%); NNRTI- and PI-based therapies** accounted for the **smallest share**

Substance class (stable)	FU15 (Baseline)	FU17 (2,5 Years)	Trend
INSTI (integrase strand transfer inhibitor)	729 (73.0 %)	729 (73.0 %)	↔ 0%
NNRTI (non-nucleoside reverse transcriptase Inhibitors)	256 (25.6 %)	256 (25.6 %)	↔ 0%
PI (protease inhibitors)	106 (10.6 %)	106 (10.6 %)	↔ 0%
NRTI-Backbone (nucleoside reverse-transcriptase inhibitors)	924 (92.5 %)	924 (92.5 %)	↔ 0%

Characteristics of the analysis group

- **ART class switch group:**
  → BMI (~26 kg/m²) and overweight/obesity (51.1%) remained unchanged
  → diagnosed hypertension increased (40.5% to 47.2%), while blood pressure remained stable
  → LDL- (138 to 120 mg/dl) and total cholesterol (208 to 183 mg/dl), triglycerides (201 to 167 mg/dl), and hyperlipidaemia (56.7% to 54.5%) decreased; HDL cholesterol remained unchanged
  → HbA1c (5.6 to 6%) and diabetes mellitus prevalence (9 to 12%) increased
  → Smoking prevalence decreased (39.3% to 37.6%)
- **Stable ART class group:**
  → BMI was stable (~27 kg/m²), overweight/obesity decreased from 59.0% to 55.9%
  → diagnosed hypertension increased (39.9% to 46.4%), while blood pressure remained stable
  → Hyperlipidaemia increased (56.6% to 58.8%)
  → HDL cholesterol remained unchanged; LDL- (133 to 122 mg/dl) and total cholesterol (200 to190 mg/dl) and triglycerides (188 to 172 mg/dl) decreased
  → Smoking prevalence remained unchanged
  → HbA1c (5.7 to 5.8 %) and diabetes mellitus pevalence (11.8% to 16.0%) increased

Table 1: *Characteristics of PWH from the HIV-Heart-Aging cohort at FU15 and FU17, grouped by stable ART class regimes and switched ART class regimes over 2.5 years; continuous variables are shown as mean (standard deviation), categoric variables are shown as frequency(percent); each row also shows the number of available data for that specific parameter; [Abbreviations: NRTI=Nucleoside (and Nucleotide) Reverse Transcriptase Inhibitors, NNRTI=Non-Nucleoside Reverse Transcriptase Inhibitors, INSTI=Integrase Strand Transfer Inhibitors , PI=Protease Inhibitors*

	FU15				FU17			
Characteristic	**Stable ART drug class**		**ART drug class switch**		**Stable ART drug class**		**ART drug class switch**	
included to comparison group (PWH), n (%)	999	999 (84.9%)	178	178 (15.1%)	999	999 (84.9%)	178	178 (15.1%)
Age, years, mean (SD)	999	53.01 (10.85)	178	54.80 (11.16)	999	56.45 (10.92)	178	58.38 (11.23)
Sex male, n (%)	999	843 (84.38%)	178	145 (81.46%)	999	843 (84.38%)	178	145 (81.46%)
BMI, kg/m², mean (SD)	999	26.72 (4.78)	178	25.78 (5.00)	905	26.81 (4.98)	167	26.11 (5.31)
Underweight, n (%)	13	13 (1.30%)	7	7 (3.93%)	16	16 (1.60%)	9	9 (5.06%)
Normal weight, n (%)	397	397 (39.74%)	80	80 (44.94%)	331	331 (33.13%)	67	67 (37.64%)
Overweight incl. obesity classes I-III, n (%)	589	589 (58.96%)	91	91 (51.12%)	558	558 (55.86%)	91	91 (51.13%)
Since diagnosis of HIV, years, mean (SD)	989	16.99 (8.26)[10]	173	18.27 (7.78)	988	20.43 (8.38)	173	21.85 (7.85)
CD4 cell count, mean (SD)	996	731.82 (315.66)	178	687.54 (294.25)	958	738.28 (311.63)	174	699.20 (289.60)
CD4/CD8 ratio, mean (SD)	996	0.98 (0.60)	178	0.93 (0.47)	959	1.15 (3.26)	174	0.96 (0.49)
Systolic blood pressure, mmHg, mean (SD)	705	135.73 (16.97)	122	137.95 (17.87)	727	134.75 (16.91)	127	136.80 (18.79)
Diastolic blood pressure, mmHg, mean (SD)	705	84.44 (11.02)	122	85.91 (11.27)	727	83.21 (11.04)	127	84.65 (11.46)
HDL-cholesterol, mg/dl, mean (SD)	877	48.83 (14.12)	153	49.95 (15.04)	694	49.81 (14.96)	116	49.14 (14.86)
LDL-cholesterol, mg/dl, mean (SD)	899	133.40 (42.16)	158	138.08 (43.28)	749	121.68 (40.12)	129	120.10 (43.59)
Total cholesterol, mg/dl, mean (SD)	981	199.77 (44.26)	170	207.92 (48.84)	947	189.89 (75.11)	169	182.80 (44.65)
Triglycerides, mg/dl, mean (SD)	980	188.00 (156.92)	170	201.07 (173.57)	947	172.10 (134.49)	169	167.15 (159.25)
Glucose, mg/dl, mean (SD)	980	100.02 (36.01)	174	100.80 (39.03)	661	100.99 (36.17)	111	101.15 (45.61)
HbA1c, %, mean (SD)	835	5.68 (0.99)	139	5.61 (1.00)	542	5.80 (0.92)	78	5.98 (1.49)
Smoking yes, n (%)	999	404 (40.44%)	178	70 (39.33%)	999	405 (40.54%)	178	67 (37.64%)
Diabetes mellitus yes, n (%)	997	118 (11.81%)	177	16 (8.99%)	999	160 (16.02%)	178	22 (12.36%)
Hyperlipidemia yes, n (%)	991	565 (56.56%)	175	101 (56.74%)	985	587 (58.76%)	173	97 (54.49%)
Hypertension yes, n (%)	999	399 (39.94%)	178	72 (40.45%)	999	463 (46.35%)	178	84 (47.19%)

Discussion & Clinical Implications

- In HIVH, switching ART drug classes showed no clinically relevant change in cardiometabolic parameters over 2.5 years
  → majority of participants in the ART class switch group switched from PI-based regimens to INSTI based regimen, while in the stable ART group the majority of participants already used INSTI-based ART regimen
- The switch towards mostly INSTI-based therapy regimens in the ART class switch group did not lead to higher BMI or prevalence of overweight/obesity, lipid and glycaemic parameters remained nearly unchanged
- No differences in blood pressure, glucose, or HbA1c were observed between the stable ART class group and the ART class switch group
- The increasing incidence of hypertension and diabetes mellitus probably reflects the effects of aging in general
- Switching ART drug classes does not substantially reduce or increase cardiovascular risk factors in HIVH
  → Optimal care should combine appropriate ART selection with monitoring and active management of modifiable risk factors, including lifestyle factors (smoking, body weight, physical activity, diet) and metabolic conditions (hypertension, dyslipidaemia, and diabetes)

Limitations:
- The proportion of ART class switchers was small relative to the stable ART class group
- No channeling /selection bias adjustment for neither the ART class switch group, nor the stable ART class group
- The stable ART class group used INSTIs in majority at baseline already, compared to the ART class switch group
- Concomitant medication for cardiometabolic risk factors was not accounted for in this analysis

Conclusion

No changes in cardiometabolic risk following ART class switch: Switching HIV therapy to modern regimens (primarily INSTI-based) does not result in any clinically relevant changes in cardiometabolic parameters.

Former studies suggest a focus on traditional risk management and the prioritizing lifestyle interventions, e.g. targeted treatment of comorbidities and cardiovascular risk factors (e.g., with antihypertensives, statins, and antidiabetic agents) and recommendations regarding physical activity, diet, and smoking cessation.

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Acknowledgement: We want to thank all patients and the whole study team who participated in the HIV HEART Aging Study. The HIV HEART Aging study was supported by Gilead Sciences and ViiV Health Care. The HIV HEART Aging study was registered in ClinicalTrials.gov (NCT04156048) and has been approved by the local ethics committee of the Medical Faculty of the University Duisburg-Essen number 14-5874-BO.