CHANGE IN CARDIOMETABOLIC RISK MARKERS FOLLOWING SWITCH TO INTEGRASE INHIBITORS DIFFERS BY SEX

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Cecile D. Lahiri[1], C. Christina Mehta[1], Qian Yang[1], Julie B. Dumond[2], Maria L. Alcaide[3], Frank Palella[4], Jordan E. Lake[5], Leah H. Rubin[6], Audrey L. French[7], Seble Kassaye[8], Michael Augenbran[9], Anjali Sharma[10], Igho Ofotokun[1], Anandi N. Sheth[1], Jessica A. Alvarez[11]

[1]Emory University School of Medicine, Atlanta, GA, USA; [2]University of North Carolina School of Pharmacy, Chapel Hill, NC, USA; [3]University of Miami, Miller School of Medicine, Miami, FL, USA; [4] Northwestern Feinberg School of Medicine, Department of Medicine, Division of Infectious Diseases, Chicago, IL, USA; [5]UTHealth, Houston, TX, USA; [6]Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA; [7]Stroger Hospital of Cook County Health, Chicago, IL, USA; [8]Georgetown University Medical Center, Washington, DC, USA; [9] SUNY Downstate Health Sciences University, Department of Medicine, Division of Infectious Diseases, Brooklyn, NY, USA; [10] Albert Einstein College of Medicine, Bronx, NY, USA; [11] Emory University School of Medicine, Department of Medicine, Division of Endocrinology, Metabolism, and Lipids, Atlanta, GA, USA

BACKGROUND

- Integrase strand-transfer inhibitor (INSTI)-associated weight gain among people with HIV (PWH) is greater in women than men[1]
- Differences between men and women in cardiometabolic risk markers following INSTI initiation remain unclear, with prior studies not powered to detect sex differences[2,3]

<u>Study AIM</u>: Assess differences in cardiometabolic risk markers by sex up to 5 years following switch to INSTIs

METHODS

MWCCS
MACS/WIHS COMBINED COHORT STUDY

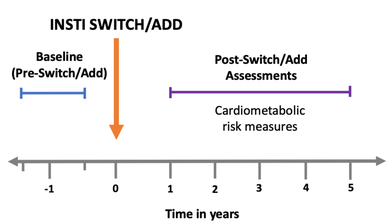


We used data collected between 2007-2020 from men and women enrolled in the MACS/WIHS Combined Cohort Study (MWCCS):

1) **INSTI group:** on ART ≥ 2 years, HIV VL <200 copies/mL and switched to or added an INSTI to ART
2) **Non-INSTI Control**: on ART ≥ 2 years, HIV VL <200 copies/mL and remained on non-INSTI ART
3) **Persons without HIV (PWOH)**

*Excluded study visits where pregnant/within 2 years postpartum, active malignancy or TB, receiving chemotherapy/radiation or PrEP

Figure 1. Study Schema. Cardiometabolic risk markers assessed at baseline and at least annually for up to 5 years following INSTI switch/add. **Note:** "Switch/add" visit was first visit where participant reported taking INSTIs, thus not exact switch date



Outcomes

- Systolic and diastolic blood pressure (SBP, DBP)
- Fasting total cholesterol, triglycerides, HDL, LDL

Analyses

- Linear regression mixed effect models assessed effects of natal sex, group, and time on cardiometabolic risk marker change
- Adjusted for: age, race/ethnicity, socioeconomic status, smoking, alcohol, hypertension or cholesterol medications, BMI

Switching to INSTIs (vs non-switch) was associated with greater increases in blood pressure and decreases in HDL for women but not for men, possibly consequent to greater INSTI-associated weight gain in women.

RESULTS

Table 1. Baseline (pre-switch) cohort characteristics, n=3464

Median (Q1, Q3) or n(%)	INSTI N=634			Non-INSTI N=1121			Persons without HIV N=1709		
	Men N=223	Women N=411	P value	Men N=412	Women N=709	P value	Men N=891	Women N=818	P value
Age, years	55 (49, 62)	51 (45, 57)	<0.001	52 (45, 58)	48 (41, 53)	<0.001	58 (50, 64)	46 (37, 53)	<0.001
Black race	50 (22)	270 (66)	<0.001	121 (29)	427 (60)	<0.001	183 (21)	561 (69)	<0.001
<HS Education	9 (4)	153 (37)	<0.001	34 (8)	247 (35)	<0.001	33 (4)	292 (36)	<0.001
BMI, kg/m^2	25 (23, 29)	29 (25, 35)	<0.001	26 (23, 28)	29 (25, 35)	<0.001	27 (24, 30)	31 (26, 37)	<0.001
CD4, cells/mm^3	610 (476, 841)	701 (519, 874)	0.010	648 (483, 855)	602 (446, 791)	0.005	*n/a*	*n/a*	*n/a*
Undetectable HIV RNA	197 (88)	349 (85)	ns	369 (90)	614 (87)	ns	*n/a*	*n/a*	*n/a*
TAF use	12 (5)	16 (4)	ns	14 (3)	5 (1)	0.001	*n/a*	*n/a*	*n/a*
NNRTI use	117 (53)	180 (44)	0.037	243 (59)	363 (51)	0.010	*n/a*	*n/a*	*n/a*
Time on ART, years	13 (10, 17)	11 (7, 16)	<0.001	11 (5, 14)	10 (5, 14)	0.0537	*n/a*	*n/a*	*n/a*

2A.



2B.

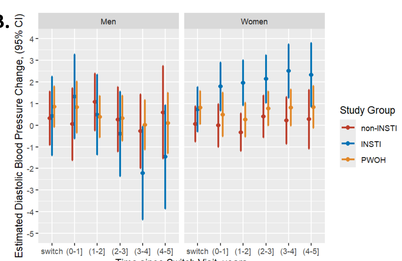


Figure 2. Model-estimated mean change in systolic (A) and diastolic (B) blood pressure from baseline among men and women with and without HIV in the MWCCS, stratified by study group and years since switch.

At 4-5 years, women switching to INSTIs had +8.1 mm Hg increase in SBP and +2.3 mm Hg increase in DBP compared to +3.1 and -1.5 mm Hg in men switching to INSTIs, respectively.

RESULTS

Fig 3.

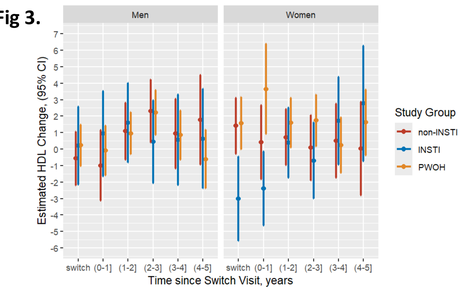


Figure 3. Model-estimated mean HDL change from baseline among men and women with and without HIV, stratified by study group and years since switch. Women switching to INSTIs experienced transient decrease in HDL during the first year whereas men switching to INSTIs did not. Sex*group*years interaction term, p=0.007.

CONCLUSIONS

- **INSTI switch (vs non-switch) was associated with greater increases in BP and decreases in HDL for women but not for men, possibly consequent to greater INSTI-associated weight gain in women.**
- **Further research is needed to understand the implications of INSTI-induced changes on cardiovascular outcomes in persons with HIV and support sex-specific preventative and therapeutic intervention strategies**

ADDITIONAL KEY INFORMATION

References

[1]Lahiri et al, CID 2024, online ahead of print, PMID 39324701
[2]Rupasinghe et al, CID 2025, Feb 24; 80(2): 404-416, PMID 39117341
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Author Contact Information

Cecile D. Lahiri, MD, MSc
cdelill@emory.edu

CFAR Emory Center for AIDS Research
NIH NIDDK
NIH NHLBI

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