GREATER WEIGHT GAIN AFTER SWITCH TO INSTI-BASED REGIMEN FROM NNRTI VS. PI REGIMENS

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BACKGROUND

The median body mass index (BMI) and prevalence of obesity among persons with HIV (PWH) on stable ART have been steadily increasing.[1]

A higher BMI is associated with increased risk of diabetes and cardiovascular disease in PWH.[2,3]

Recent reports describe greater weight gain among ART-naïve PWH starting integrase strand transfer inhibitor (INSTI)-based ART vs. protease inhibitor (PI) or non-nucleoside reverse-transcriptase inhibitor (NNRTI)-based ART.[4,5]

Many ART-experienced PWH have switched to newer INSTI-based regimens. We hypothesized PWH with sustained viral suppression switched from an NNRTI-based to an INSTI-based regimen would have greater weight gain compared to those switched from a PI-based regimen.

METHODS

Inclusion Criteria:

- **Adult PWH switched from NNRTI- or PI- to INSTI-based ART** between January 1st, 2007 and December 31st, 2014 (before the introduction of tenofovir alafenamide) in the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD).
- HIV-1 RNA <1000 copies/mL for 2 years prior to and following the regimen switch.

Statistical Analysis:

- **Piecewise linear mixed effects models** with random intercepts and slopes estimated pre- and post-switch weight over time.
- **Models adjusted** for age, sex, race, cohort site, HIV acquisition mode, calendar year, pre-switch ART class (NNRTI vs. PI), and CD4+ T cell count and BMI at the time of switch.
- **Interaction terms** for sex, race, and age (<50 vs. ≥50) with regimen and time (separate models).

Outcomes Assessed:

Comparison of pre-switch and post-switch weight slope.

RESULTS

870 PWH switching to INSTI-based regimen and meeting viral suppression criteria

	Combined (n=870)	PI (n=527)	NNRTI (n=343)
Age at switch to INSTI (*years*)	50 (43, 57)	50 (43, 56)	50 (42, 57)
Non-white race	41%	43%	38%
Male sex	83%	80%	87%
Body mass index (*kg/m²*)	26 (24, 30)	27 (24, 30)	26 (24, 30)
CD4⁺ T cell count (*cells/μL*)	620 (453, 822)	608 (438, 820)	638 (480, 822)

Table 1. Clinical and demographic characteristics of study population at time of regimen switch. Continuous variables are described as median (IQR)

INSTI distribution: 870 Total; 431 RAL; 263 EVG; 176 DTG

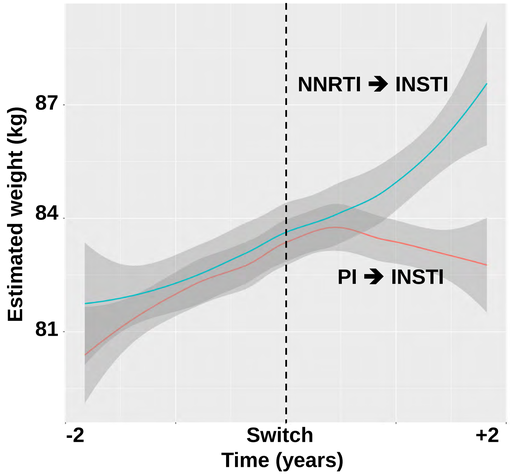

Figure. Unadjusted estimated weight for all persons before and after switch to INSTI by pre-switch regimen

Regimen switch	Pre-switch weight slope (kg/year)	Post-switch weight slope (kg/year)	P-value for slope change
NNRTI ➔ INSTI	**0.63**	**1.13**	**< 0.001**
NNRTI ➔ DTG	0.84	1.73	< 0.001
NNRTI ➔ RAL	0.74	0.97	0.21
NNRTI ➔ EVG	0.56	1.00	0.07
PI ➔ INSTI	**0.80**	**0.34**	**< 0.001**
PI ➔ DTG	0.84	-0.04	< 0.001
PI ➔ RAL	0.74	0.17	< 0.001
PI ➔ EVG	0.56	0.89	0.11

Table 2. Adjusted pre- and post-switch weight slopes by individual INSTI agents

	Females		Males		Non-whites		Whites		Age <50		Age ≥50	
Pre-switch regimen	NNRTI	PI	NNRTI	PI	NNRTI	PI	NNRTI	PI	NNRTI	PI	NNRTI	PI
Weight slope before switch (kg/year)	0.14	0.94	0.72	0.77	0.76	1.04	0.60	0.61	0.97	0.87	0.21	0.70
Weight slope after switch to INSTI (kg/year)	**1.58**	0.49	1.04	0.30	**2.03**	0.44	0.49	0.25	0.89	0.63	**1.38**	0.04
p-value for slope change	**<0.001**	0.07	0.04	**<0.001**	**<0.001**	**<0.001**	0.54	**0.01**	0.69	0.13	**<0.001**	**<0.001**

Table 3. Weight slopes pre- and post-switch to an INSTI-based regimen by sex, race, and age

CONCLUSIONS

1. PWH on stable NNRTI-based ART with long-term viral suppression had higher annualized weight gain after a switch to INSTI regimens compared to person who switched from PI-based ART.
2. Among those switched from NNRTI- to INSTI-based ART, annualized weight gain was greatest for females, non-whites and older PWH.
3. These findings may reflect a heterogenous effect of ART class and agent on body weight regulation that is not limited to the initiation of first regimens in the treatment-naïve.

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