GREATER WEIGHT GAIN AMONG TREATMENT-NAÏVE PERSONS STARTING INTEGRASE INHIBTORS

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BACKGROUND

The median BMI and prevalence of baseline obesity among PLWH initiating ART has been steadily increasing.[1]

Short-term weight gain following ART initiation has been associated with increased risk of diabetes and cardiovascular disease.[2,3]

Previously reported significant weight gain in virologically suppressed PLWH switching from efavirenz- to INSTI-based regimens (esp. DTG).[4]

Several studies have investigated the association between INSTI-based regimens and weight gain (ACTG study A5260, PROGRESS study).[5,6]

However, data exploring differences in short-term weight gain between different INSTI drugs and between these drugs and other PI and NNRTI-based regimens are limited.

METHODS

Inclusion Criteria:

- **ART Naïve patients,** defined as having no prior ART exposure longer than 45 days anywhere on record, starting treatment between January 1st, 2007 and December 31st, 2016
- Initiated a sustained 3-drug ART regimen with an INSTI, PI or NNRTI
- 17 NA-ACCORD Cohorts

Statistical Analysis:

- **Multivariate Linear Mixed Effects Model**
- **Models adjusted** for demographics (age, sex, race); baseline weight; CD4 count; HIV-1 RNA; year of ART initiation & cohort site.
- **Interaction terms** between time from ART start & regimen/drug, time from ART start & sex, time from ART start & race
- 5-knots restricted cubic splines for continuous variables; multiple imputations for missing variables; bootstrapping to generate 95%CI
- **Censoring:** virologic failure, ART switch or loss to follow-up.

Outcomes Assessed:

1. **Weight by ART class** (INSTI, PI, NNRTI) within 5-years of ART initiation
2. **Weight by INSTI drug** (DTG, EVG, RAL) & between INSTI drugs and PI/NNRTI within 2-years of ART initiation

RESULTS

24,001 patients included in our analysis

	NNRTI (n=11,825)	PI (n=7,436)	INSTI (n=4,740)
Age*	43 (32, 52)	42 (32, 50)	39 (29, 50)
Black race*	42%	43%	40%
Male sex*	90%	80%	86%
Year ART start*	2010 (2008, 2012)	2010 (2008, 2012)	2014 (2012, 2015)
BMI* ***(kg/m²)***	25 (23, 29)	25 (22, 28)	25 (22, 29)
CD4⁺ T cell count* ***(cells/μL)***	312 (180, 452)	262 (105, 406)	360 (195, 531)
HIV-1 RNA* ***(log_{10} copies/mL)***	4.6 (4.0 , 5.1)	4.7 (4.1 , 5.2)	4.6 (4.1 , 5.2)

Table 1. Baseline clinical and demographic characteristics of study population. Continuous variables are described in median (IQR) * p-value <0.05

INSTI distribution: 4,740 Total**; 1,681 (35%)** RAL; **2,124 (45%)** EVG; **935 (20%)** DTG

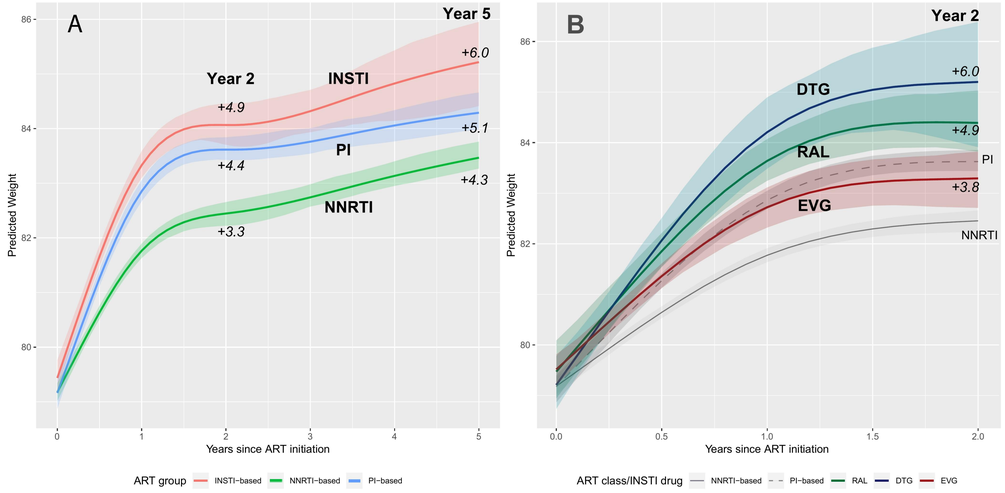

Figure 1. Predicted weight changes within: (A) 5-years of ART initiation by ART class (B) 2-years of ART initiation by INSTI drug and ART class

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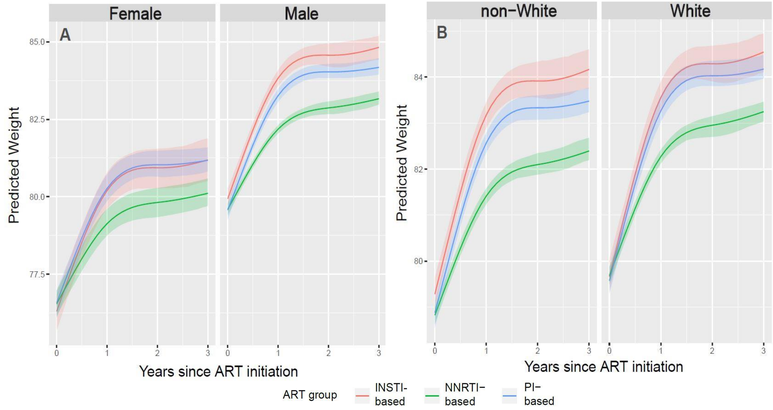

Figure 2. Predicted weight change by ART class: (A) dichotomized by sex; (B) dichotomized by race

CONCLUSIONS

1. Treatment-naïve PLWH starting INSTI, especially DTG and RAL, are at higher risk of weight gain compared to NNRTI-class regimens.
2. Weight gain among patients starting INSTI is not uniform, with PLWH starting RAL and DTG graining significantly more weight than PLWH starting EVG.
3. Weight gain associated with INSTI-based regimens did not vary by sex (male vs. female) or race (white vs. non-white).
4. Further studies are needed to understand the mechanism explaining the difference noted in weight gain among INSTI- based regimens and between these regimens and NNRTI- or PI- based regimens

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