

Weight-Gain in Treatment Naïve Newly Diagnosed HIV-Infected Persons after Initiation on Integrase Strand Inhibitor Based Treatment Regimens

Zsofia Szep¹, Heather Conway², Saishi Cui³, Allison Evans³

Partnership Comprehensive Care Practice, Drexel University College of Medicine¹

Dartmouth-Hitchcock Medical Center²

Drexel University, Dornsife School of Public Health³



Abstract

Objectives: We performed a retrospective cohort study of treatment-naïve patients with newly diagnosed HIV-infection enrolled at an urban university specialty clinic to identify whether INSTI-based ART regimens were associated with greater weight gain compared to NNRTI and PI based regimens in the first 12-18 months of treatment. The secondary aim of this study was to determine differences in weight gain between males and females within each of the three ART classes.

Methods: Differences in weight change and BMI change were compared across ART class using nonparametric tests, specifically the Wilcoxon rank sum test. Nonparametric tests were also used to compare differences in weight change and BMI change between males and females within each ART class. Data were analyzed using R Core Team, 2020.

Results: Among the 348 individuals included in the study, 73% were African American and 79% were male and the median age was 32 years. There were 155 individuals initiating therapy on NNRTI based regimens (44%), 58 were on PI based regimens (17%) and 135 were on INSTI regimens (39%). The median weight at baseline was 170.5 lbs. and the median body mass index was 25.4 kg/m². Median weight increased across all 3 ART regimens within the first 12-18 months of treatment. Median weight gain among the PI group was the greatest, at 6.8 lbs. (p=0.04). Median weight gain among the NNRTI group was the lowest, .88 lbs (p<.01). Median weight gain among those on INSTI based regimens was 4.8 lbs. (p=0.11). Among those on INSTI-based regimens, women had a greater median increase in weight compared to men, 10.1 lbs. compared to 3.2 lbs., (p=0.046).

Conclusion: Overall, among individuals initiating HIV treatment those initiating PI based regimens experienced the most weight gain and individuals initiating INSTI based regimens did not experience a significant weight gain. Women on INSTI based regimens did experience a significant weight gain in comparison to men.. More research is needed to elucidate specific ART regimens' causal role in weight gain and to identify risk factors for ART-associated weight gain.

Background

- Initiation of antiretroviral therapy (ART) has been associated with weight gain¹
- Obesity which heightens the risk of comorbidities such as type 2 diabetes is becoming more prevalent in people living with HIV (PLWH)²
- Integrase strand transfer inhibitors (INSTI) have become the preferred regimen for treatment of HIV
- Several studies have shown increased weight gain in patients who were switched to integrase inhibitor based regimens³
- In a pooled analysis of 8 randomized controlled trials evaluating risk factor for weight gain after ART initiation INSTI based regimens were associated with more weight gain in comparison to PI or NNRTI based regimens⁴
- Few studies have evaluated change in weight in the real-world setting after starting INSTI based regimens in comparison to non-nucleoside reverse transcriptase NNRTI or protease inhibitor PI based regimens

Methods

- Retrospective cohort study of treatment naïve newly diagnosed HIV positive individuals initiating ART between January 1st 2007 and July 1st 2017
- Weight and Body Mass Index (BMI) changes within 12-18 months after initiating ART were compared across three different regimens: nonnucleoside reverse transcriptase inhibitors (NNRTI), protease inhibitors (PI) and integrase strand inhibitors (INSTI)
- Inclusion Criteria:** Adults ≥ 18 years old receiving care at the Partnership Comprehensive Care Practice (PCCP) initiating ART
- Exclusion Criteria:** Pregnancy, End Stage Renal Disease requiring hemodialysis
- Data Analysis:** Differences in change in weight and BMI at 12-18 months were compared across ART class using Wilcoxon Rank Sum Test
- Multivariable logistic regression models determined unadjusted and adjusted odds ratios (ORs) and 95% confidence intervals (Cis) of ≥5% weight gain with INSTI containing regimens versus other regimens
- R Core Team 2020 was used for data analysis

Results

Table 1. Demographic and Clinical Characteristics Overall and by Antiretroviral Regimen

	Whole Sample (N= 348)	NNRTI (N=135)	PI (N=58)	INSTI (N=155)
Age (median, IQR)	31 (25,45)	32 (24,45) p=0.70	38 (28,45) p<0.05	29 (24,40) p<0.05
Sex (N, % Male)	274 (79%)	112 (83%) p=0.16	29 (50%) p< 0.01	133 (86%) p< 0.01
Race (N, %)				
White	47 (14%)	19 (14%) p= 0.93	4 (7%) p=0.16	26 (17%) p= 0.15
Black	255 (74%)	108 (80%) p<0.05	48 (83%) p= 0.10	99 (64%) p< 0.01
CD4 cell count baseline (cells/mm ³) (median, IQR)	398 (252, 558)	411.0 (262, 528) p= 0.77	298 (129, 433) p< 0.01	416 (287, 584) p<0.05
CD4 cell count at 1 year (cells/mm ³) (median, IQR)	540 (371, 752) N=311	512(345, 639) p<0.01 N= 116	395 (231, 641) p< 0.01 N= 52	593 (447, 826) p< 0.01 N= 143
HIV-1 RNA (copies/mL) (median, IQR)	24,003 (2190, 78,290)	17,706 (1394, 57,940) p= 0.09	7410 (100, 154,442) p= 0.18	34,460 (6025, 85,255) p<0.01
HIV-1 RNA at 1 year (copies/mL) (median, IQR)	20 (20, 48) N= 312	20 (20, 48) N=115 p<0.01	48 (20, 493) N= 52 p< 0.01	20 (20, 30) N= 145 p< 0.01
< 200 copies/mL of HIV-1 RNA at 1 year (N, %)	265 (84.9%) N= 312	100 (74.0%) N= 115 p=0.55	36 (62.1%) N=52 p<0.01	129 (83.2%) N= 145 p=0.09
Hyperlipidemia (N, %)	38 (11.0%)	15 (11.1%) p=1	7 (12.1%) p=0.94	16 (10.3%) p=0.88
Diabetes (N, %)	19 (5.5%)	8 (5.9%) p=0.95	3 (5.2%) p=1	8 (5.2%) p=1
Initial Weight (lbs) (median, IQR)	170.5(149.5, 198.5)	173.4 (154.8, 202.8) p= 0.09	157.3 (138.05, 186.9) p< 0.01	171.0 (149.9, 198.29) p= 0.61
Initial BMI (kg/m ²) (median, IQR)	25.4 (22.4, 28.8) N= 235	25.5 (23.2, 31.0) p= 0.16 N= 69	24.0 (21.8, 27.3) p= 0.09 N= 28	25.6 (22.3, 28.7) p= 0.85 N= 138
BMI ≥30 at ART initiation (N, %)	50 (21.3%) N= 235	20 (29.0%) p=0.008 N= 69	1 (3.6%) p=0.028 N= 28	29 (21.0%) p=1 N= 138
Weight (lbs) at 12-18 month (median, IQR)	174.2 (150.9, 204.7)	173.8 (153.8, 205.5)	166 (142.6, 190.8)	178.8 (151.4, 207.0)
BMI (kg/m ²) at 12-18 months (median, IQR)	26.4 (23.7, 30.6) N=234	26.2 (23.2, 31.2) p=.92 N=89	25.2 (23.7, 29.0) p=.33 N=33	27.2 (23.7, 30.7) p=0.56 N=112
BMI ≥ 30 at 12 – 18 months (N, %)	65(27.8%) N=234	26(29.2%) p=.82 N=89	5(15.6%) p=.12 N=33	34(30.4%) p=.49 N=112

Figure 1. Median Weight Change by Regimen

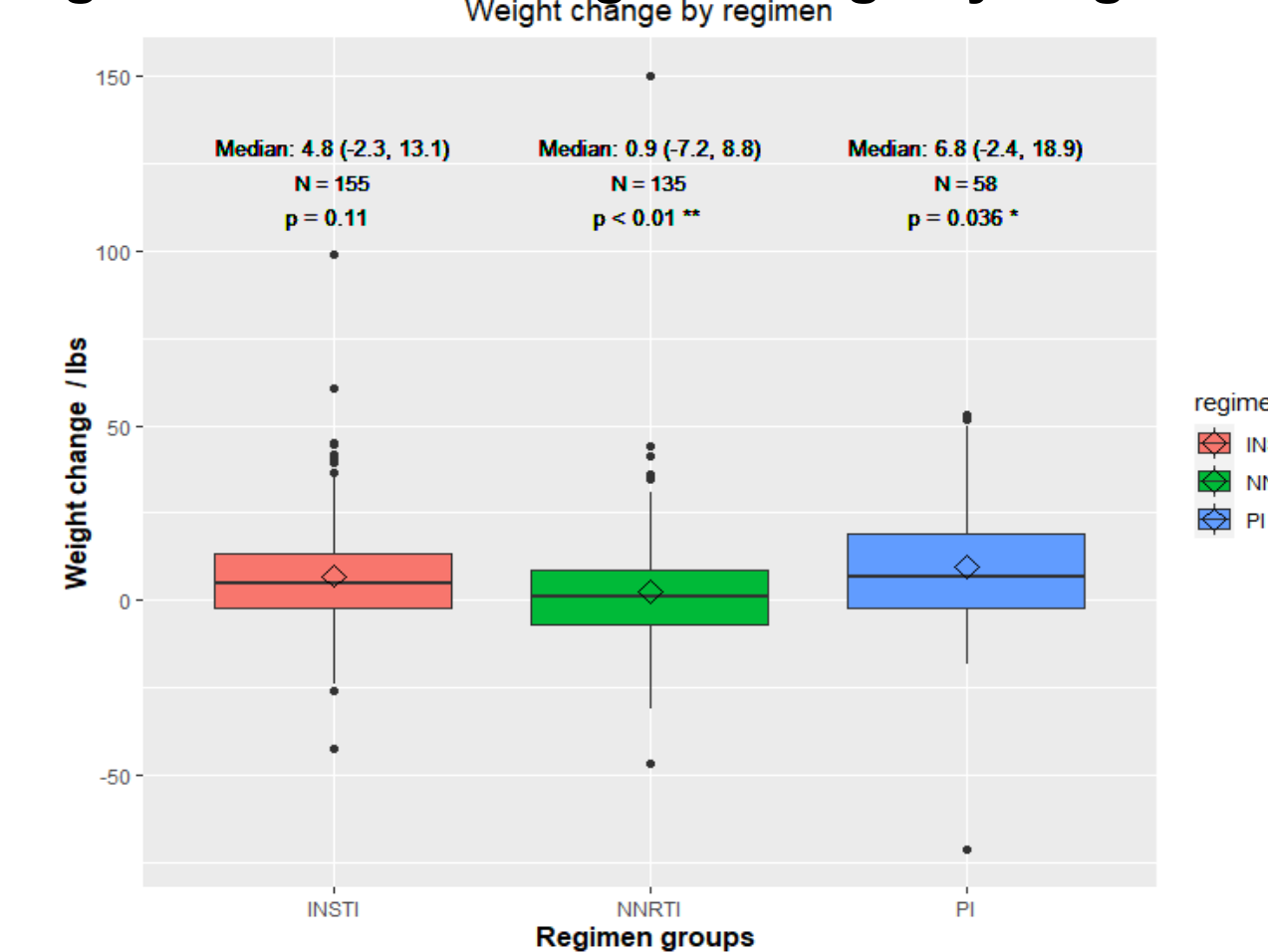


Table 2. Factors associated with ≥ 5% weight gain

Variables	OR	95% CI	p-value
Sex (Female vs Male)	2.47	(1.34, 4.56)	<.01
Race (African America vs Other)	1.14	(0.79,2.50)	.24
Age (<50 vs ≥50)	1.99	(0.95,4.16)	0.07
CD4 (<200 vs ≥200)	5.77	(3.09, 10.78)	<.01
INSTI vs other ART	1.77	(1.06, 2.96)	0.03
Tenofovir vs. other	1.60	(0.88,2.93)	0.12

Results

- Among the 348 individuals included in the study, 73% were African American and 79% were male and the median age was 32 years. (Table1)
- There were 155 individuals initiating therapy on NNRTI based regimens (44%), 58 were on PI based regimens (17%) and 135 were on INSTI regimens (39%). (Table 1)
- Median weight increased across all 3 ART regimens within the first 12-18 months of treatment. Median weight gain among the PI group was the greatest, at 6.8 lbs (p=0.04). Median weight gain among the NNRTI group was the lowest, 0.9 lbs (p<.01). Median weight gain among those on INSTI based regimens was 4.8 lbs (p=0.11). (Figure 1)
- After adjusting for sex, race, age, CD4 count, tenofovir containing regimen, INSTI based regimens were associated with ≥5% weight gain (OR 1.77;95% CI, 1.06-2.96; p=.03) (Table 3)

Discussion

- In our study we did not find a significant weight gain among individuals initiating INSTI based regimens in comparison to PI or NNRTI based regimens
- Individuals starting a PI based regimen did gain significantly more weight (6.8lbs (IQR-2.4, 18.9;p=.04) in comparison to INSTI or NNRTI based regimens
- When adjusting for factors associated with ≥5% weight gain including age, sex, race and CD4 count the association between INSTI based regimen and weight gain remained significant (OR 1.77;95% CI, 1.06-2.96; p=.03)
- Individuals initiating ART are expected to gain weight which is influenced by traditional risk factors and ART regimen
- It is possible that in the more recent ART era PLWH are experiencing more weight gain due to better tolerability and less side effects of the newer ART regimens
- HIV providers need to counsel patients about anticipated weight gain and importance of lifestyle modifications at the time of ART initiation
- Our study was limited by a small sample size which included predominantly males and African American individuals
- Few participants in our study were on tenofovir alafenamide (TAF) based regimens and we were not able to explore the potential relationship of TAF contributing to weight gain with INSTI based regimens
- Further studies of the clinical impact of various ART regimens are needed to better understand the significance of the weight gain related to specific regimens

References

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