

GREATER WEIGHT GAIN AMONG TREATMENT-NAÏVE PERSONS STARTING INTEGRASE INHIBITORS

VANDERBILT UNIVERSITY
MEDICAL CENTER

Kassem Bourgi^{1,2}, Cathy A. Jenkins¹, Peter F. Rebeiro¹, Jordan E. Lake³, Richard D. Moore⁴, W. C. Mathews⁵, Michael A. Horberg⁶, Amanda Willig⁷, Michelle Floris-Moore⁸, Michael John Gill⁹, Angel M. Mayor¹⁰, Ronald Bosch¹¹, Timothy R. Sterling¹ & John R. Koethe¹, for the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) for IeDEA.



¹ Vanderbilt University, Nashville, TN, USA; ² Indiana University School of Medicine, Indianapolis, IN, USA; ³ University of Texas at Houston, Houston, TX, USA; ⁴ Johns Hopkins University, Baltimore, MD, USA; ⁵ University of California San Diego, San Diego, CA, USA; ⁶ Kaiser Permanente Mid-Atlantic States, Rockville, MD, USA; ⁷ University of Alabama at Birmingham, Birmingham, AL, USA; ⁸ University of North Carolina at Chapel Hill, Chapel Hill, NC, USA; ⁹ Alberta Health Services, Calgary, AB, Canada; ¹⁰ Universidad Central del Caribe, Bayamon, Puerto Rico; ¹¹ Harvard University, Boston, MA, USA

Abstract # 1160

Contact: Kassem Bourgi
E-mail: kbouрги@iu.edu
@KaBourgi

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/m ²)	25 (23, 29)	25 (22, 28)	25 (22, 29)
CD4+ T cell count* (cells/ μ L)	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

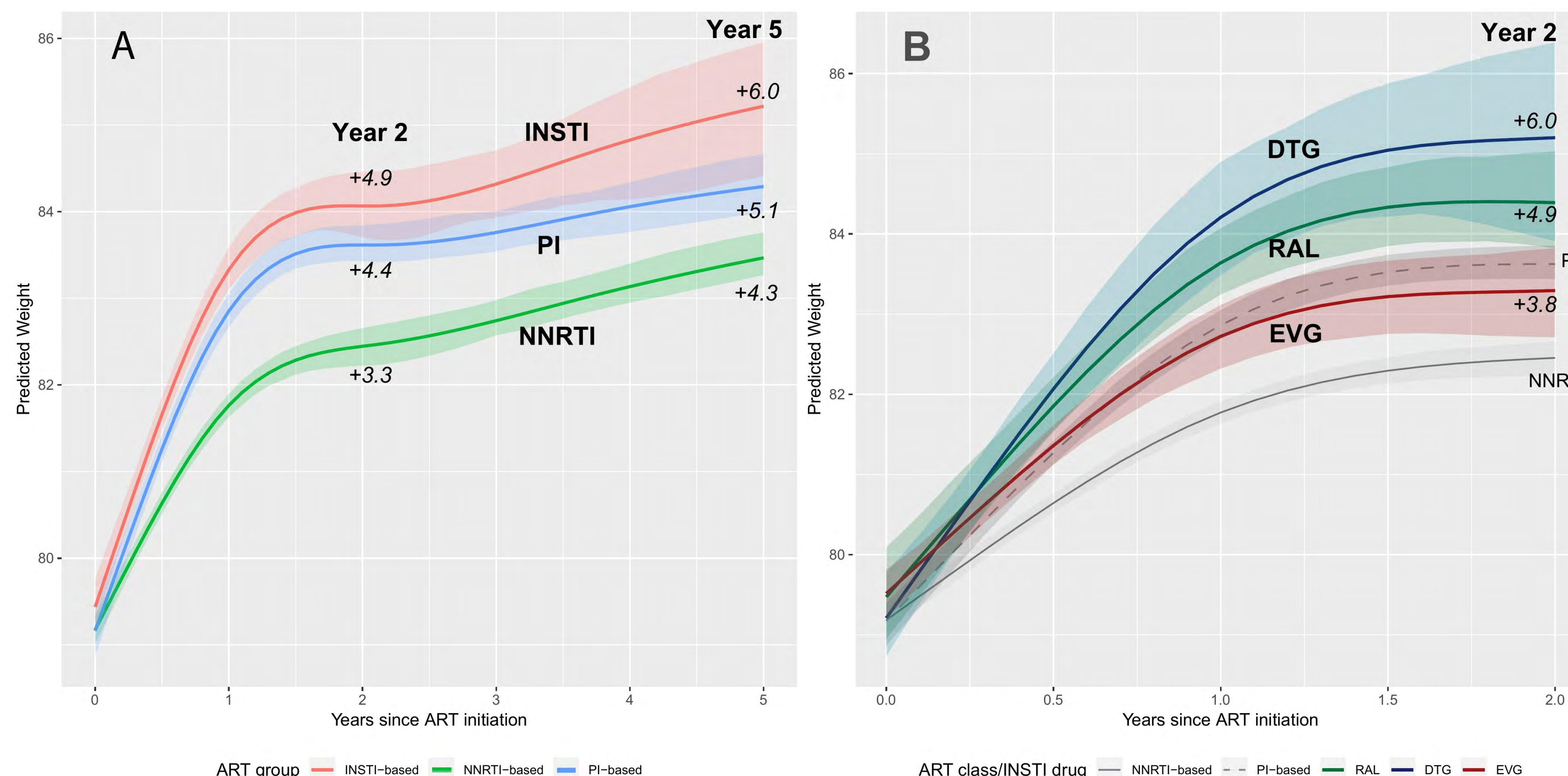


Figure 1. Predicted weight changes within: (A) 5-years of ART initiation by ART class (B) 2-years of ART initiation by INSTI drug and ART class

References:

1. Koethe JR et al. Rising Obesity Prevalence and Weight Gain Among Adults Starting Antiretroviral Therapy in the United States and Canada. *AIDS research and human retroviruses* 2016; 32(1): 50-8.
2. Grant PM et al. Long-term body composition changes in antiretroviral-treated HIV-infected individuals. *AIDS* 2016; 30(18): 2805-13.
3. Koethe JR et al. Higher Time-Updated Body Mass Index: Association With Improved CD4+ Cell Recovery on HIV Treatment. *JAIDS* 2016; 73(2): 197-204.
4. Norwood J et al. Brief Report: Weight Gain in Persons With HIV Switched From Efavirenz-Based to Integrase Strand Transfer Inhibitor-Based Regimens. *JAIDS* 2017; 76(5): 527-31.
5. McComsey GA et al. Body composition changes after initiation of raltegravir or protease inhibitors: ACTG A5260s. *CID* 2016; 62(7): 853-62.
6. Reynes J et al. Lopinavir/ritonavir combined with raltegravir or tenofovir/emtricitabine in antiretroviral-naïve subjects: 96-week results of the PROGRESS study. *AIDS research and human retroviruses* 2013; 29(2): 256-65.

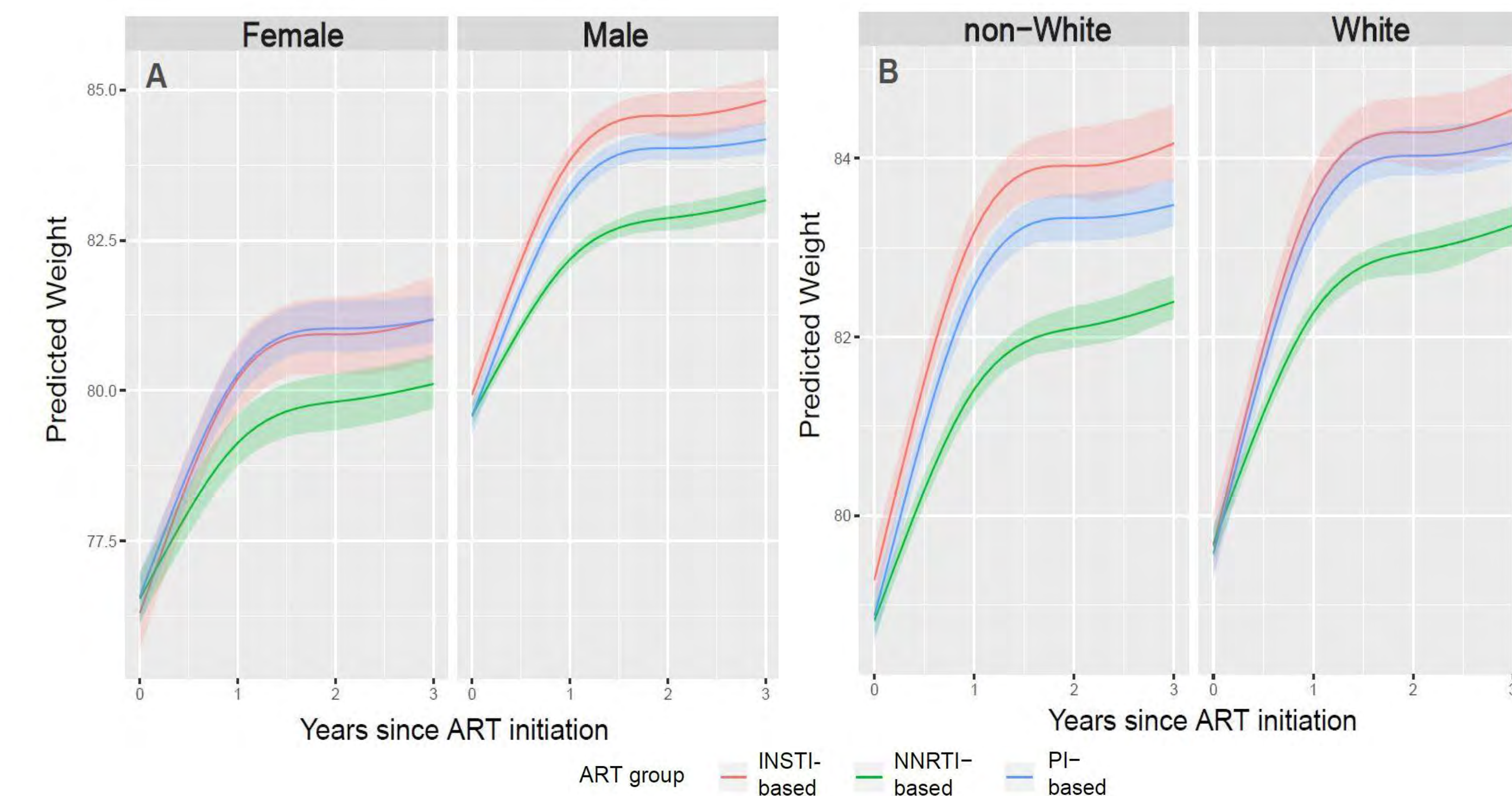


Figure 2. Predicted weight change by ART class: (A) dichotomized by sex; (B) dichotomized by race

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 gaining 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

Acknowledgments:

The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. This work was supported by National Institutes of Health grants U01AI069918, F31AI124794, F31DA037788, G12MD007583, K01AI093197, K01AI131895, K23EY013707, K24AI118591, K24DA000432, KL2TR000421, M01RR000052, N01CP01004, N02CP055504, N02CP091027, P30AI027757, P30AI027763, P30AI027767, P30AI036219, P30AI050410, P30AI094189, P30AI110527, P30MH62246, R01AA016893, R01CA165937, R01DA011602, R01DA012568, R01 AG053100, R24AI067039, U01AA013566, U01AA020790, U01AI031834, U01AI034989, U01AI034993, U01AI034994, U01AI035004, U01AI035039, U01AI035040, U01AI035041, U01AI035042, U01AI037613, U01AI037954, U01AI038855, U01AI038858, U01AI042590, U01AI068634, U01AI068636, U01AI069432, U01AI069434, U01AI103390, U01AI103397, U01AI103401, U01AI103408, U01DA036229, U01HD032632, U10EY008057, U10EY008052, U10EY008067, U24AA020794, US4MD007587, UL1RR024131, UL1TR000083, UL1TR000454, UM1AI035043, Z01CP010214 and Z01CP010176; contracts CDC-200-2006-18707 and CDC-200-2015-63931 from the Centers for Disease Control and Prevention, USA; contract 90047713 from the Agency for Healthcare Research and Quality, USA; contract 90051652 from the Health Resources and Services Administration, USA; grants CBR-86906, CBR-94036, HCP-97105 and TGF-96118 from the Canadian Institutes of Health Research, Canada; Ontario Ministry of Health and Long Term Care; and the Government of Alberta, Canada. Additional support was provided by the National Cancer Institute, National Institute for Mental Health and National Institute on Drug Abuse. **Disclosures:** Supported by an Investigator Sponsored Research grant from Gilead Sciences