

NNRTI-to-INSTI Switches Across North America May Have Had a Substantial Population

Impact on Weight

Poster 687

Contact
Kassem Bourgi
kbourgi@nashvillecares.org

Kassem Bourgi^{1,2}; Aihua Bian²; John R. Koethe²; Samir Gupta³; Cal Cohen⁴; Jean C. Lee⁴; Timothy R. Sterling²; Richard D. Moore⁵; Jordan E. Lake⁶; Catherine Lesko⁷; Frank J. Palella Jr⁸; Marina Klein⁹; Vincent C. Marconi¹⁰; Samuel Pierre²; Peter R. Rebeiro² for the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD).

¹ Nashville CARES, Nashville, TN, USA; ² Vanderbilt University Medical Center, Nashville, TN, USA; ³ Indiana University School of Medicine, Indianapolis, IN, USA; ⁴ Gilead Sciences, Foster City, CA, USA; ⁵ Johns Hopkins School of Medicine, Baltimore, MD, USA; ⁶ UTHealth, Houston, TX, USA; ⁷ Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA; ⁸ Northwestern University, Chicago, IL, USA; ⁹ McGill University Health Centre, Montreal, QC, Canada; ¹⁰ Emory University School of Medicine, Atlanta, GA, USA.



Background

- INSTI-based ART regimens and TAF have been associated with greater weight gain compared to NNRTIs and older NRTIs, potentially reflecting the weight-suppressive effects of EFV and TDF.
- HIV care in North America has shifted from NNRTI-based regimens (often EFV/TDF/FTC) to INSTI-based regimens, frequently including TAF.
- The weight impact of NNRTI-to-INSTI switching among virologically suppressed, previously treatment-naive PWH is not well defined.

Study Objective

- To assess the impact of switching from NNRTI-based ART to INSTI-based regimens, with or without TAF, on longitudinal weight change among virologically suppressed, previously treatment-naive people with HIV.

Methods

Study population

- Adults with HIV enrolled in the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD)
- On NNRTI-based ART for ≥2 years from 2007 onward with sustained virologic suppression.
- Switched to an INSTI-based regimen with ≥1 post-switch weight measurement.

Measurement

- **Outcome:** Change in body weight over time before and after ART switch
- **Primary analysis:** All switches NNRTI- to INSTI-based ART
- **Subgroup analysis:** EFV/TDF/FTC → INSTI+TAF switch
- **Covariates:** Age, sex, race, baseline weight, CD4 count, HIV-1 RNA, ART initiation year, NRTI backbone, and cohort site.

Statistical Analysis

- Weight trajectories assessed using linear mixed-effects models with random intercepts and slopes
- Compared rates of weight change pre- vs post-switch, with predicted mean weight change over time.
- Models adjusted for demographic, clinical, and treatment-related covariates

Switching from older NNRTI-based regimens to newer INSTI-based treatments was associated with an **acceleration in weight gain** among PWH across the US and Canada. The increase was largest after switches involving **EFV/TDF → INSTI + TAF**. Future studies should evaluate whether this widespread ART switch contributed to rising **obesity** and **cardiometabolic risk** at the population level.

Results

| Characteristic | Overall NNRTI → INSTI (N = 3,452) | EFV/TDF/FTC → INSTI + TAF (N = 1,473) |
|---|---|---|
| Baseline Age*, years | 43 (33–51) | 44 (35–52) |
| Male Sex | 3,092 (90%) | 1,335 (91%) |
| Black Race | 1,468 (43%) | 658 (45%) |
| HIV acquisition risk: MSM | 1,313 (38%) | 437 (30%) |
| ART initiation year* | 2010 (2009–2012) | 2011 (2009–2012) |
| HIV-1 RNA*, log ₁₀ copies/mL | 4.5 (3.8–5.0) | 4.5 (3.9–5.1) |
| Baseline BMI*, kg/m ² | 25.6 (22.9 – 28.8) | 26.0 (23.0 – 29.0) |
| NRTI backbone: TDF/FTC | 3,214 (93%) | 1,473 (100%) |
| NNRTI Core Drug: EFV | 3,109 (90%) | 1,473 (100%) |

Table 1. Baseline Demographic and Clinical Characteristics of Participants Who Switched from NNRTI- to INSTI-Based ART
* Continuous variables reported as median (IQR)

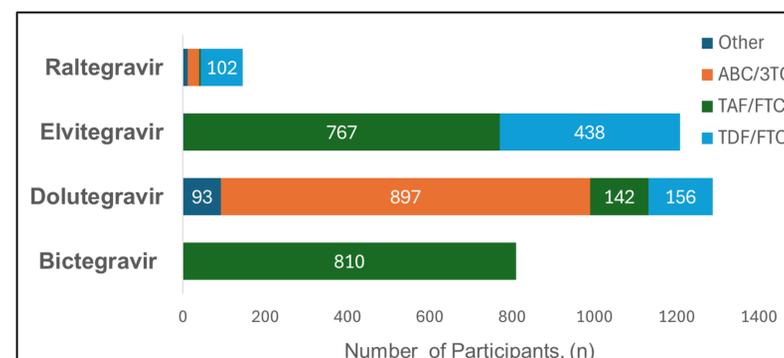
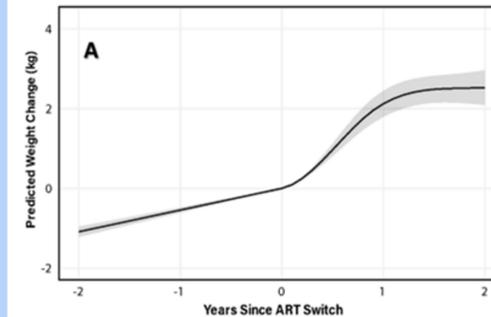


Figure 1. Distribution of Post-Switch INSTI-Based Regimens by Core INSTI and NRTI Backbone

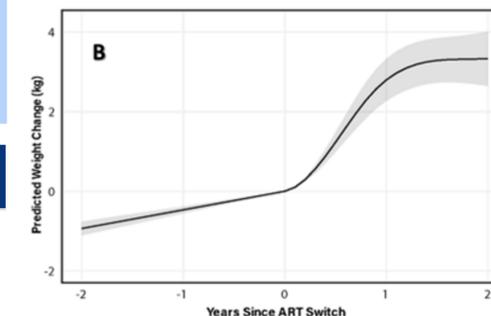
Results (continued)

A. All NNRTI to INSTI Switches (N= 3,452)



Rate of Weight Change:
Pre-switch: 0.6 kg/yr
Post-switch: 1.7 kg/yr
P-value: <0.001
Weight Gain at year 2:
Mean: 2.5 kg
95% CI: 2.1 – 3.0

B. EFV/TDF/FTC to INSTI+TAF Switch (n= 1,473)



Rate of Weight Change:
Pre-switch: 0.5 kg/yr
Post-switch: 2.2 kg/yr
P-value: <0.001
Weight Gain at year 2:
Mean: 3.3 kg
95% CI: 2.7 – 4.0

Conclusions

- Switching from NNRTI- to INSTI-based ART was associated with a marked acceleration in weight gain.
- Weight gain was greatest following EFV/TDF/FTC to INSTI + TAF switch.
- Given the widespread transition from EFV/TDF to INSTI/TAF in the US, these shifts may have had a population-level impact on increasing obesity and cardiometabolic risk among PWH.
- **Limitations:** retrospective cohort study, possibility of unmeasured confounders (dietary habits, concurrent medications), bias from incomplete or missing data ...

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