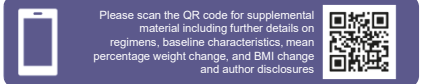


Risk Factors Associated With $\geq \pm 10\%$ Weight Change in Treatment-Naïve and Treatment-Experienced People Living With HIV Initiating or Switching to an NNRTI- or INSTI-Based Antiretroviral Therapy in Four Large Cohort Studies

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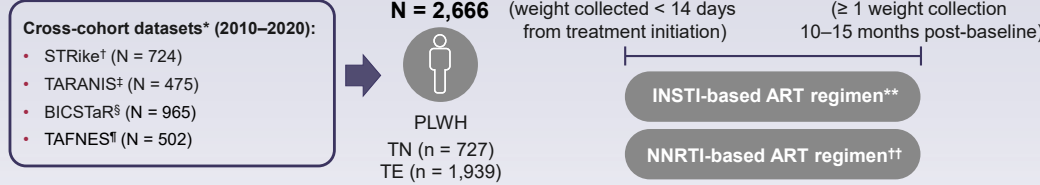
Introduction

- Worldwide, body weight and BMI are increasing in the general population, as well as in PLWH^{1,2}
- Weight change can be multifactorial; some ART regimens have been associated with weight gain but there are also reports of weight loss³⁻⁷
- Factors driving weight changes in PLWH are not well understood
- The aim of this study was to explore risk factors associated with $\geq 10\%$ weight gain and $\geq 10\%$ weight loss in PLWH after initiating or switching NNRTI or INSTI-based ART

Methods

Objective: To estimate adjusted odds ratios for potential risk factors associated with $\geq 10\%$ weight gain or loss from baseline to 12 months of follow-up in PLWH initiating or switching NNRTI- or INSTI-based ART from four study cohorts

Figure 1. Study Design



*Prospective observational cohort studies; participants initiating/switching to an NNRTI- or INSTI-based ART were included; †TN and TE participants initiating EFV/F/TDF; ‡TN and TE participants initiating EVG/COBI/F/TAF or RPV/F/TAF; §TN and TE participants initiating BIC/F/TAF (study ongoing, data as of August 2021); ¶TN and TE participants initiating EVG/COBI/F/TAF, RPV/F/TAF or F/TAF; **Included RAL/F/TAF, EVG/F/TDF, EVG/F/TAF, BIC/F/TAF and DTG/F/TAF; ††Included RPV/F/TDF, RPV/F/TAF, EFV/F/TDF, EFV/F/TAF, NVP/F/TAF and ETR/F/TAF.

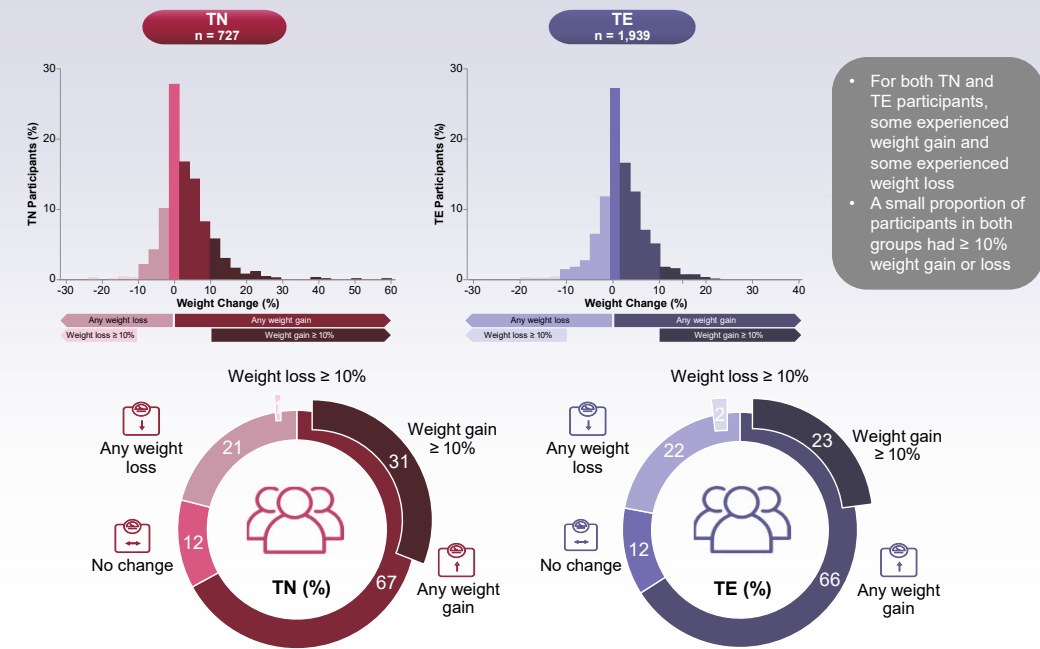
Figure 2. A Multivariate Logistic Regression Model Estimated Adjusted Odds Ratios for Potential Risk Factors Associated With $\geq 10\%$ Weight Change at 12-Month Follow-Up



*Multivariate logistic regression model was not adjusted for race as these data were not collected in the TARANIS dataset – a sensitivity analysis was carried out to adjust for ethnicity; †At least one of hypertension, hyperlipidemia, diabetes mellitus and cardiovascular disease; ‡Insulin, antidiabetics, antidepressants/psychoanaleptics, antipsychotics, antiepileptics, contraceptives, corticosteroids, antihistamines, beta-androgenic blockers; §The comparison group for the $\geq 10\%$ weight gain model excluded those who experienced $\geq 5\%$ weight loss and the comparison group for the $\geq 10\%$ weight loss model excluded those who experienced $\geq 5\%$ weight gain.

Results: Distribution of Participants by Weight Change Category at 12 Months

Figure 3. Proportional Weight Change From Baseline to 12 Months by Baseline Treatment Status



Results: Selected Baseline Demographic and Clinical Characteristics in TN Participants by $\geq 10\%$ Weight Change (Table 1)

Characteristic	Overall (N = 727)	$\geq 10\%$ loss (n = 8, 1%)	$\geq 10\%$ gain (n = 229, 31%)
Age, years, median (Q1, Q3)	38 (30, 46)	40 (31, 50)	38 (30, 46)
Male, %	90	88	90
Studied ART third agent, %			
NNRTI	30	38	15
INSTI	70	63	85**
Studied NRTI, %			
F/TDF	37	38	18
F/TAF	63	63	82***
CD4 count, cells/ μ L, median (Q1, Q3)	386 (251, 541)	502 (248, 578)	377 (158, 544)
Virologic suppression, %†	1	0	1
Late presenters, %‡	44	25	48
Weight, kg, median (Q1, Q3)	73 (65, 82)	80 (75, 94)	71 (65, 79)*
BMI, kg/m ² , median (Q1, Q3)	23.2 (21.5, 25.5)	25.4 (23.9, 30.5)*	22.9 (21.1, 25.3)
Any comorbidity, %§	12	25	11
Comedications, %¶			
Associated with weight gain	11	-	12
Associated with weight loss	4	0	-

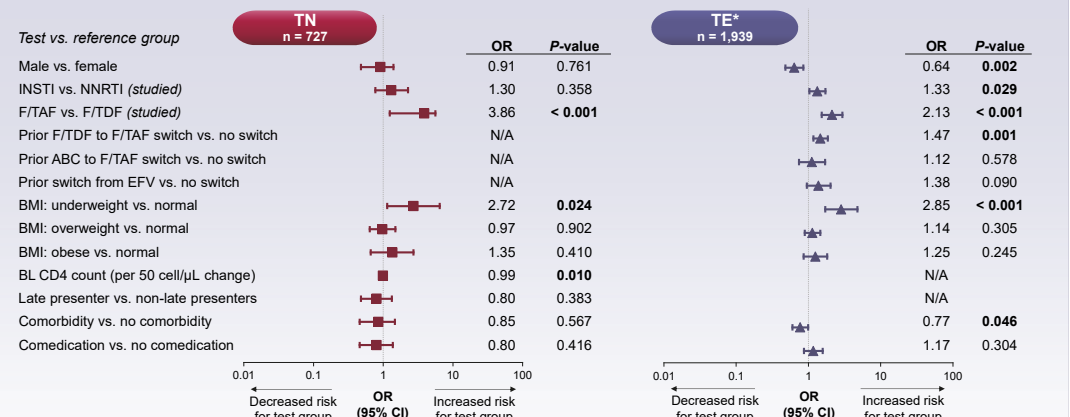
*P < 0.05; **P < 0.01; ***P < 0.001 (P-values compare $\geq 10\%$ loss vs. without $\geq 10\%$ loss or $\geq 10\%$ gain vs. without $\geq 10\%$ gain)
†HIV RNA < 50 copies/mL; ‡CD4 < 350 μ L and/or CDC stage A3, B3 or any C stage; §Associated with obesity: hypertension, hyperlipidemia, diabetes mellitus and cardiovascular disease; ¶Drug classes associated with weight changes included: insulin, antidiabetics, antidepressants/psychoanaleptics, antipsychotics, antiepileptics, contraceptives, corticosteroids, antihistamines, beta-androgenic blockers, antitubercular medication.

Results: Selected Baseline Demographic and Clinical Characteristics in TE Participants by $\geq 10\%$ Weight Change (Table 2)

Characteristic	Overall (N = 1,939)	$\geq 10\%$ loss (n = 40, 2%)	$\geq 10\%$ gain (n = 451, 23%)
Age, years, median (Q1, Q3)	47 (38, 54)	49 (36, 55)	47 (37, 55)
Male, %	85	83	79***
Studied ART third agent, %			
NNRTI	37	33	28
INSTI	63	68	72***
Studied NRTI, %			
F/TDF	23	25	13
F/TAF	77	75	87***
Pre-switch NRTI, %			
F/TDF to F/TAF – no	45	50	37
F/TDF to F/TAF – yes	47	45	55
ABC/3TC to F/TAF – yes	8	5	9**
Pre-switch EFV	8	10	10
CD4 count, cells/ μ L, median (Q1, Q3)	610 (412, 815)	654 (458, 784)	606 (410, 834)
Virologic suppression, %†	87	80	85**
Weight, kg, median (Q1, Q3)	75 (67, 85)	89 (75, 105)**	74 (65, 84)
BMI, kg/m ² , median (Q1, Q3)	24.3 (22.0, 27.0)	27.6 (24.8, 31.6)*	24.2 (21.7, 27.2)
Any comorbidity, %‡	29	23	28
Comedications, %§			
Associated with weight gain	16	-	18
Associated with weight loss	5	13*	-

*P < 0.05; **P < 0.01; ***P < 0.001 (P-values compare $\geq 10\%$ loss vs. without $\geq 10\%$ loss or $\geq 10\%$ gain vs. without $\geq 10\%$ gain)
†HIV RNA < 50 copies/mL; ‡Associated with obesity: hypertension, hyperlipidemia, diabetes mellitus and cardiovascular disease; §Drug classes associated with weight changes included: insulin, antidiabetics, antidepressants/psychoanaleptics, antipsychotics, antiepileptics, contraceptives, corticosteroids, antihistamines, beta-androgenic blockers, antitubercular medication.

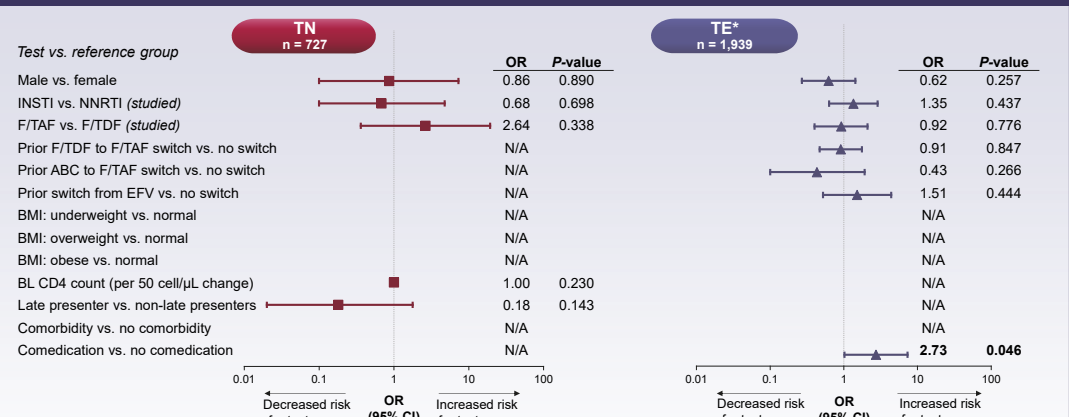
Key Results: Risk Factors Associated With $\geq 10\%$ Weight Gain in Participants Initiating/Switching ART (Figure 4)



*All estimates were calculated by excluding the pre-switch F/TDF to F/TAF variable because of collinearity with the NRTI (F/TAF vs. F/TDF) variable. The adjusted OR for pre-switch F/TDF to F/TAF was calculated including all covariates but excluding current NRTI (F/TAF vs. F/TDF).

- F/TAF backbone (vs. F/TDF) and being underweight (vs. normal) were associated with weight gain $\geq 10\%$ in TN and TE participants
- Additional risk factors were low baseline CD4 (vs. higher) in TN participants, and being a female (vs. male), F/TDF to F/TAF switching, and not having a comorbidity in TE participants
- In a sensitivity analysis (data not shown), after restricting the sample to participants with information on ethnic origin, ethnicity was not found to be a predictor for weight gain

Key Results: Risk Factors Associated With $\geq 10\%$ Weight Loss in Participants Initiating/Switching ART (Figure 5)



*All estimates were calculated by excluding the pre-switch F/TDF to F/TAF variable because of collinearity with the NRTI (F/TAF vs. F/TDF) variable. The adjusted OR for pre-switch F/TDF to F/TAF was calculated including all covariates but excluding current NRTI (F/TAF vs. F/TDF).

Except for comedication in TE participants, no risk factors for $\geq 10\%$ weight loss were identified

Conclusions

- TN participants:**
- 67% experienced weight gain over 12 months; 31% had $\geq 10\%$ weight gain
 - Factors associated with $\geq 10\%$ weight gain were F/TAF-based ART (vs. F/TDF), low baseline CD4 count and being underweight
 - 21% experienced weight loss; 1% experienced $\geq 10\%$ weight loss
 - No risk factors were associated with $\geq 10\%$ weight loss
- TE participants:**
- 66% experienced weight gain over 12 months; 23% had $\geq 10\%$ weight gain
 - Factors associated with $\geq 10\%$ weight gain were INSTI- (vs. NNRTI) or F/TAF- (vs. F/TDF) based ART, switching from F/TDF to F/TAF (vs. no switch), being female, being underweight at baseline, and not having a comorbidity
 - 22% experienced weight loss; 2% experienced $\geq 10\%$ weight loss
 - The only risk factor associated with $\geq 10\%$ weight loss was being on comedication known to cause weight change

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Abbreviations
3TC, lamivudine; ABC, abacavir; ART, antiretroviral therapy; BIC, bictegravir; BL, baseline; BMI, body mass index; CD4, cluster of differentiation 4; CDC, Centers for Disease Control and Prevention; CI, confidence interval; COBI, cobicistat; DTG, dolutegravir; EFV, efavirenz; ETR, etravirine; EVG, elvitegravir; F, emtricitabine; INSTI, integrase strand transfer inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside/nucleotide reverse transcriptase inhibitors; NVP, nevirapine; OR, odds ratio; PLWH, people living with HIV; Q1, first quartile; Q3, third quartile; RAL, raltegravir; RPV, rilpivirine; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; TE, treatment experienced; TN, treatment naïve

Acknowledgments
Medical writing support was provided by Joanna Nikitorowicz-Buniak, PhD and Emma McConnell, PhD (Aspire Scientific Ltd, Bollington UK), and funded by Gilead.

Disclosures
Data were sourced from cross-cohort datasets: STRiKe (GX-DE-177-0125), TARANIS (GS-FR-292-4043), BICSTaR (GS-EU-380-4472, GS-CA-380-4574, GS-IL-380-5535, GS-JP-380-5065, GS-TW-380-5727), TAFNES (GS-DE-292-1912). Full disclosures can be found in the supplement.