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TDF and Efavirenz but Not INSTI or TAF Use Are Associated With Weight Gain After cART Initiation.

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Background

Combination antiretroviral therapy (cART) containing integrase strand transfer inhibitors (INSTIs) and/or tenofovir alafenamide (TAF) has been associated with greater weight gain (WG). Yet few studies have jointly adjusted for "anchor" (protease inhibitors [PI], non-nucleoside reverse transcriptase inhibitors [NNRTI] or INSTIs) *and* "backbone" (nucleoside reverse transcriptase inhibitors [NRTI] antiretroviral (ARV) components as well as non-ART factors.

Methods

We examined weight and body mass index (BMI) change in a large HIV clinic in the Southern US from 2008–2022.

We followed all previously ART-naïve patients during their first three years after ART initiation and use of 11 individual ARVs, comparing "anchor" and "backbone" components with each other and jointly adjusting for their use.

We used ANOVA and chi-square tests to compare differences between baseline covariates and generalized estimating equations (GEE) for the relationship between "anchor" and "backbone" use and BMI change during ART, employing Fisher's Least Significant Difference Method to correct for multiple comparisons.

Our models also adjusted for time, baseline demographic and HIV-characteristics, and time-updated HIV and substance use variables.

To gauge the proportion of overall variance explained by different categories of predictors, we used marginal coefficients of determination for a non-linear mixed model containing the main effects of the fully-adjusted GEE model.

Results

- 4,194 patients contributed 20,528 BMI measurements. The majority of patients were black (55%) and male (77%). Median baseline BMI was 24.4 kg/m^2, inter-quartile range (IQR) 21.6–28.2.
- The median BMI gain over 3 years was +1.9 kg/m^2 (IQR 0.1–4.1), corresponding to +5.4 kg (IQR 0.5–12.2 kg).
- Significant and parallel changes in both "anchor" and NRTI ARV use over the observation period show in Figure 1.
- ARV use accounted for only 9% of the predicted BMI change in models.

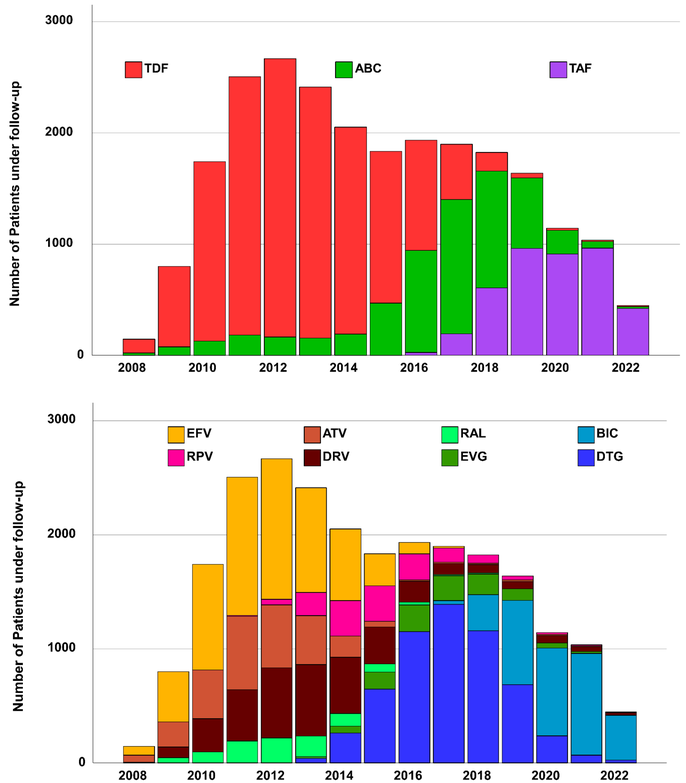

Figure 1. Number of patients using the study ARVs per calendar year

Marginal Means for predicted BMI gain		Model1 Baseline covariates		Model2 Baseline covariates &concomitant ARVs		Model3 Fully adjusted*	
		BMI gain (95% CI)	p-value	BMI gain (95% CI)	p-value	BMI gain (95% CI)	p-value
Anchor Drug	*Dolutegravir*	2.12 (1.91-2.33)	REF	2.18 (1.87-2.49)	REF	2.25 (1.90-2.60)	REF
	Bictegravir	2.36 (2.09-2.63)	0.13	1.99 (1.56-2.43)	0.56	2.19 (1.72-2.66)	0.85
	Elvitegravir	1.79 (1.50-2.08)	**0.05**	1.88 (1.56-2.20)	0.22	2.11 (1.72-2.50)	0.55
	Raltegravir	1.60 (1.21-1.99)	**0.01**	1.90 (1.47-2.33)	0.28	2.05 (1.60-2.51)	0.43
	Darunavir	1.75 (1.49-2.01)	**0.02**	2.00 (1.70-2.31)	0.41	2.26 (1.90-2.62)	0.97
	Atazanavir	1.68 (1.40-1.96)	**0.01**	1.98 (1.63-2.33)	0.38	2.24 (1.83-2.64)	0.96
	Rilpivirine	1.66 (1.35-1.96)	**0.009**	1.95 (1.58-2.32)	0.34	2.01 (1.61-2.41)	0.29
	Efavirenz	1.16 (0.97-1.35)	**<0.0001**	1.49 (1.21-1.77)	**<0.001**	1.68 (1.32-2.03)	**0.003**
Backbone NRTI	*TAF*	2.37 (2.14-2.61)	REF	2.29 (1.88-2.70)	REF	2.39 (1.97-2.82)	REF
	Abacavir	2.13 (1.92-2.35)	0.10	1.90 (1.53-2.26)	0.19	2.13 (1.71-2.56)	0.35
	TDF	1.47 (1.33-1.60)	**<0.0001**	1.58 (1.42-1.75)	**0.004**	1.77 (1.51-2.03)	**0.005**

Table 1. Estimated marginal means for BMI gain during study.
The p-values are relative to DTG and TAF resp(least significant difference method for multiple comparisons).); *includes time-updated covariates and six interaction terms; REF: reference value.

- Among the "anchor" components, only efavirenz (EFV) was associated with lower weight gain and there were no apparent differences between the INSTIs, PIs or rilpivirine (Table 1).
- Within the "backbone" components, only tenofovir disoproxil fumarate (TDF) was associated with lower weight gain, while the difference between TAF and abacavir was not significant (Table 1).

Conclusions

- Our demographically diverse patient population experienced substantial weight gain 3 years after ART initiation.
- Weight gain was accounted for mostly by non-ARV factors.
- Among 11 examined ARVs, only efavirenz and TDF were independently associated with (decreased) weight gain.
- Analyses of weight change associated with individual ARVs should account for concomitant ARVs and non-ARV variables.