

DOLUTEGRAVIR-BASED REGIMENS ARE ASSOCIATED WITH WEIGHT GAIN OVER TWO YEARS FOLLOWING ART-INITIATION IN ART-NAÏVE PEOPLE

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On behalf of the CNICS Network

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WHAT IS THE NEED?

- Weight gain is common among PLWH after ART initiation
- PLWH who initiate integrase inhibitor (II)-based regimens may gain more weight than those on other regimens
- We leveraged the strengths of the CNICS cohort to re-examine this question as prior studies often had inherent limitations
 - Small
 - Examined classes not individual agents or regimens
 - Combined ART-experienced and naïve PLWH
 - Did not address potential confounders such as anti-psychotic medications which impact weight
 - Used historical controls or only had limited numbers on regimens relevant in the current treatment era
 - Did not assess differences in regimen backbones, such as TDF vs TAF
- This study evaluated short- and long-term weight change among PLWH initiating their first ART regimen with a regimen commonly used in the current ART era

METHODS

CNICS Cohort:

- Geographically and racially/ethnically diverse
 - 8 sites across the US
 - ART naïve, started first ART regimen between 2012-2018
 - This study evaluated short- and long-term weight change among PLWH initiating their first ART regimen
 - CNICS data repository captures comprehensive clinical information from outpatient and inpatient encounters including medication data, diagnoses, and historical clinical information collected at initial clinic visit
- The 10 most common regimens with a minimum of 90 PLWH were included in analyses



REGIMENS

Regimen	Core Class	Drug 1	Drug 2	Drug 3	Drug 4
EFV	NNRTI	Efavirenz	Emtricitabine/Lamivudine	TDF	
RPV	NNRTI	Rilpivirine	Emtricitabine/Lamivudine	TDF	
ATV	PI	Atazanavir	Emtricitabine/Lamivudine	TDF	Ritonavir
DRV	PI	Darunavir	Emtricitabine/Lamivudine	TDF	Ritonavir
RAL	INSTI	Raltegravir	Emtricitabine/Lamivudine	TDF	
EVG/TDF	INSTI	Elvitegravir	Emtricitabine/Lamivudine	TDF	Cobicistat
EVG/TAF	INSTI	Elvitegravir	Emtricitabine/Lamivudine	TAF	Cobicistat
DTG/TDF	INSTI	Dolutegravir	Emtricitabine/Lamivudine	TDF	
DTG/TAF	INSTI	Dolutegravir	Emtricitabine/Lamivudine	TAF	
DTG/ABC	INSTI	Dolutegravir	Emtricitabine/Lamivudine	Abacavir	

ANALYSES

- Change in weight was calculated as the difference in weight between baseline and subsequent visit
- We examined weight changes in both short-term (6 month) and long-term (all) follow-up using linear mixed models
 - Models were adjusted for time on regimen, the interaction between regimen and time on regimen, age, sex, race, hepatitis C and hepatitis B virus coinfection, nadir CD4, smoking, diabetes, anti-psychotic medication use (time-updated), and site
- Weight change was visually evaluated using generalized additive model (GAM) plots to assess linearity and patterns of weight change over time after ART initiation

SHORT-TERM WEIGHT GAIN (6 MONTHS)

Weight gain after 6 months, comparing ART regimens in adjusted analyses

N=2999	n	Δ kg/6 mos	95% CI		P-value
Years on regimen (EFV ref)	415	0.22	-1.00	1.45	0.72
Reg typex Years on regimen					
1: RPV	341	0.13	-1.43	1.69	0.87
2: ATV	95	2.66	0.32	5.00	0.03
3: DRV	258	4.11	2.32	5.90	0.00
4: RAL	95	2.52	0.38	4.66	0.02
5: EVG/TDF	780	2.29	0.88	3.70	0.00
6: EVG/TAF	282	2.46	0.91	4.02	0.00
7: DTG/TDF^a	233	3.11	1.49	4.72	0.00
8: DTG/TAF^b	116	4.88	2.17	7.59	0.00
9: DTG/ABC^c	383	2.83	1.31	4.36	0.00

^a DTG/TDF tested different vs EFV, RPV

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LONG-TERM WEIGHT GAIN (MEAN 2.0 YEARS)

Weight gain after ~2 years, comparing ART regimens in adjusted analyses

N=2999	n	Δ kg/6 mos	95% CI		P-value
Years on regimen (EFV ref)	427	0.38	0.10	0.66	0.01
Reg typex Years on regimen					
1: RPV	349	-0.08	-0.47	0.30	0.67
2: ATV	96	0.62	-0.20	1.44	0.14
3: DRV	263	1.07	0.53	1.61	0.00
4: RAL	99	0.55	-0.13	1.23	0.11
5: EVG/TDF	790	0.24	-0.10	0.58	0.16
7: DTG/TDF^a	235	0.64	0.12	1.17	0.02
9: DTG/ABC^c	383	0.75	0.37	1.14	0.00

Mean number of observations per person = 8.9

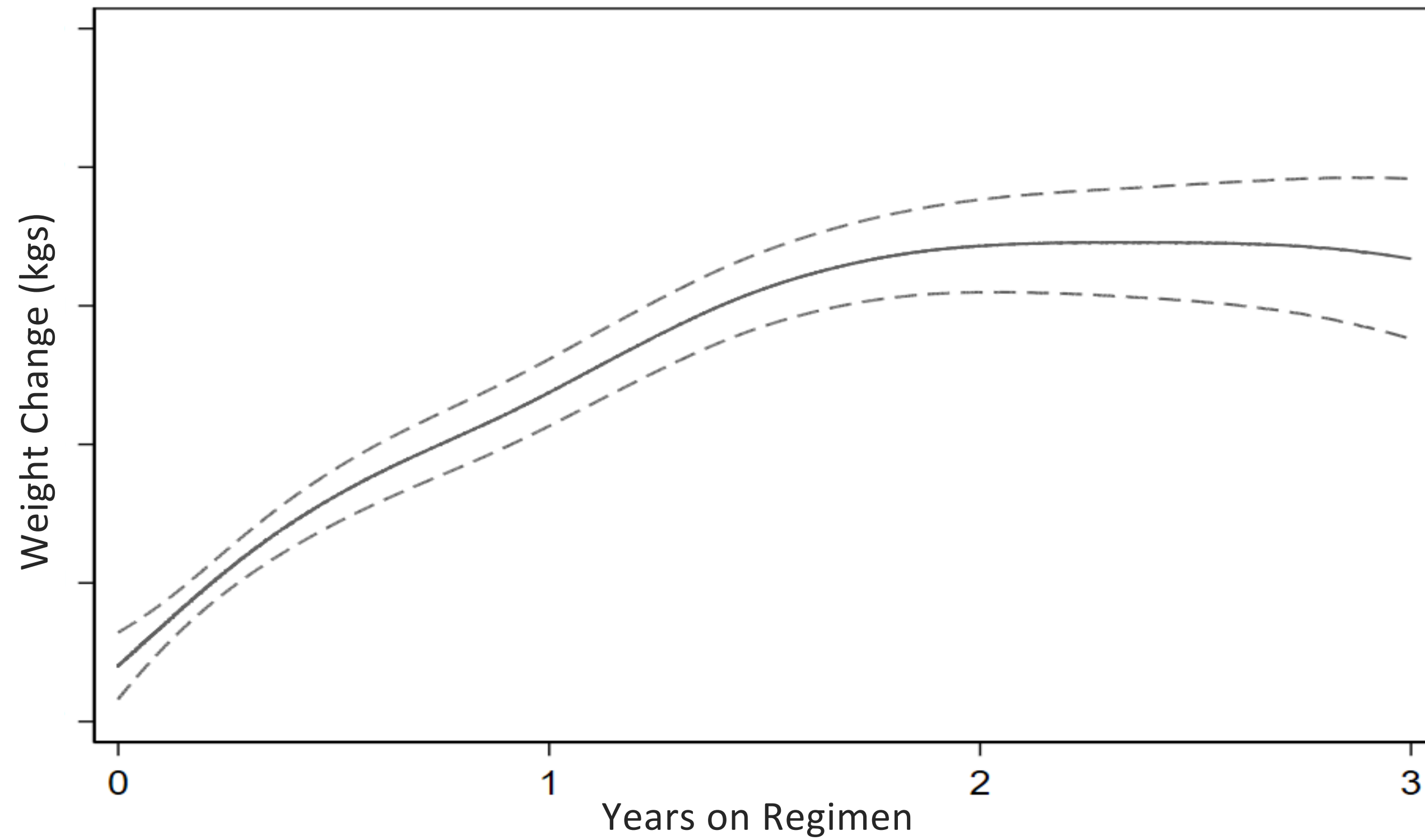
* TAF regimens not included as mean follow up time is shorter due to more recent approval

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^c DTG/ABC tested different vs EFV, RPV, EVG/TDF

GAM PLOT: CHANGE IN WEIGHT IN KG OVER TIME

7: DTG/TDF



LIMITATIONS AND STRENGTHS

Limitations:

- This study had limited follow-up
- ART adherence data was not included
- Bictegravir-based regimens had limited follow-up and therefore not shown

Strengths:

- All participants were ART-naïve at baseline
- The models incorporated anti-psychotic medication use, a known contributor to weight gain
- We compared regimens directly and fairly including regimen backbone which may be particularly important in the current treatment era
- CNICS' large size and comprehensive clinical data allows for comparison of weight changes among PLWH in care by currently used regimens

CONCLUSIONS

- PIs and IIs were associated with greater weight gain than NNRTIs in short-term (6 month) analyses
 - Darunavir was associated with the greatest weight gain of the PIs / NNRTIs
 - Dolutegravir was associated with the greatest weight gain of the IIs
 - Dolutegravir/TAF/FTC was the regimen with the greatest short-term weight gain
 - Some but not all within-class comparisons were statistically significant
- Regimens with TAF appear to show greater weight gain than similar regimens with TDF although longer follow-up will be useful: future studies need to carefully assess both cores and backbones

CONCLUSIONS

- Most weight gain occurs early after ART initiation, then plateaus
 - Supported by GAM plots
 - Greater weight change per 6 months in short-term than long-term analyses
- In long-term analyses
 - Darunavir/TDF/FTC was the regimen with the greatest weight gain
 - Mean weight gain for dolutegravir-based regimens was greater than other II regimens, although not all differences were significant. The differences become smaller with longer follow-up

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