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Conflicts of Interest

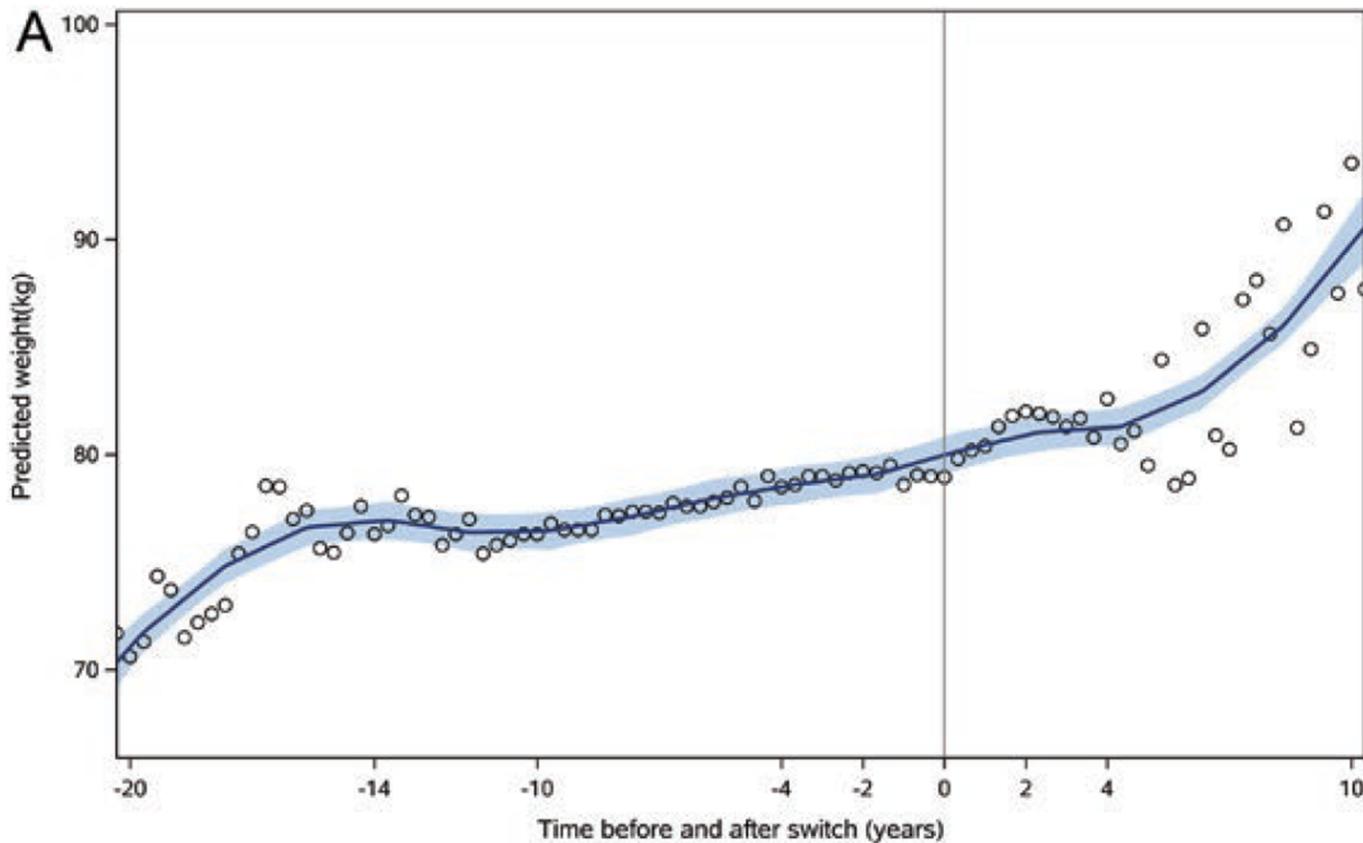
- **Research grants:** ViiV Healthcare, Gilead Sciences, Janssen Cilag
- **Speaker honoraria:** ViiV Healthcare, Gilead Sciences, Janssen Cilag, BMS, MSD
- **Advisory board participation:** ViiV Healthcare, Gilead Sciences, Janssen Cilag, BMS, MSD

BACKGROUND



Weight increases after switching to an INSTI

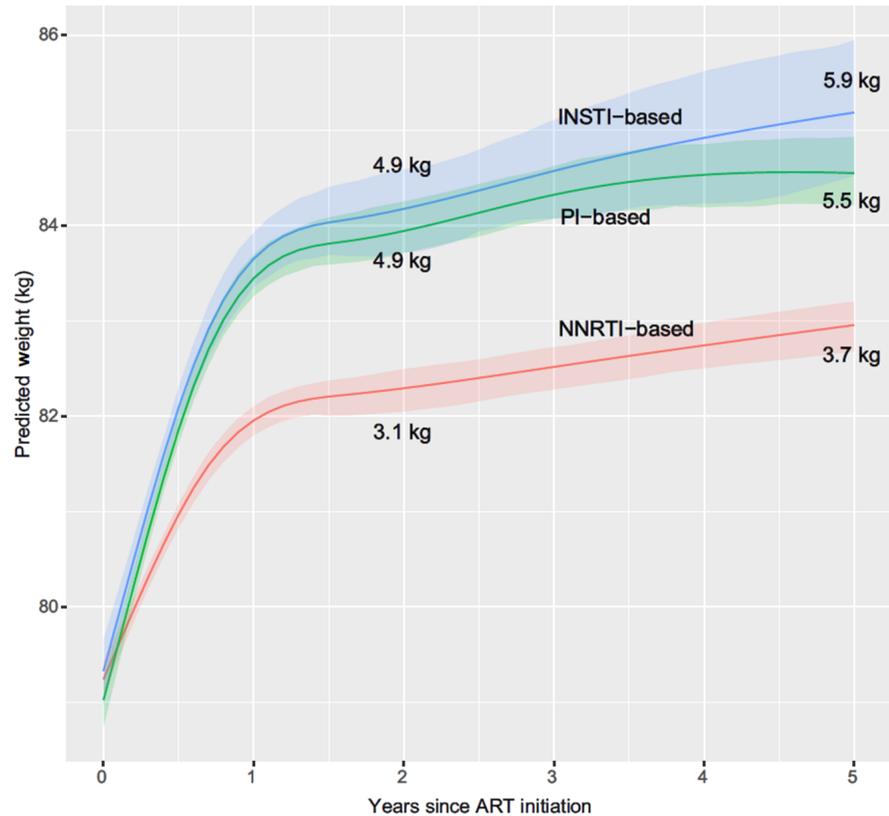
AIDS Clinical Trials Group
Virologically suppressed, ART-experienced (N=972)





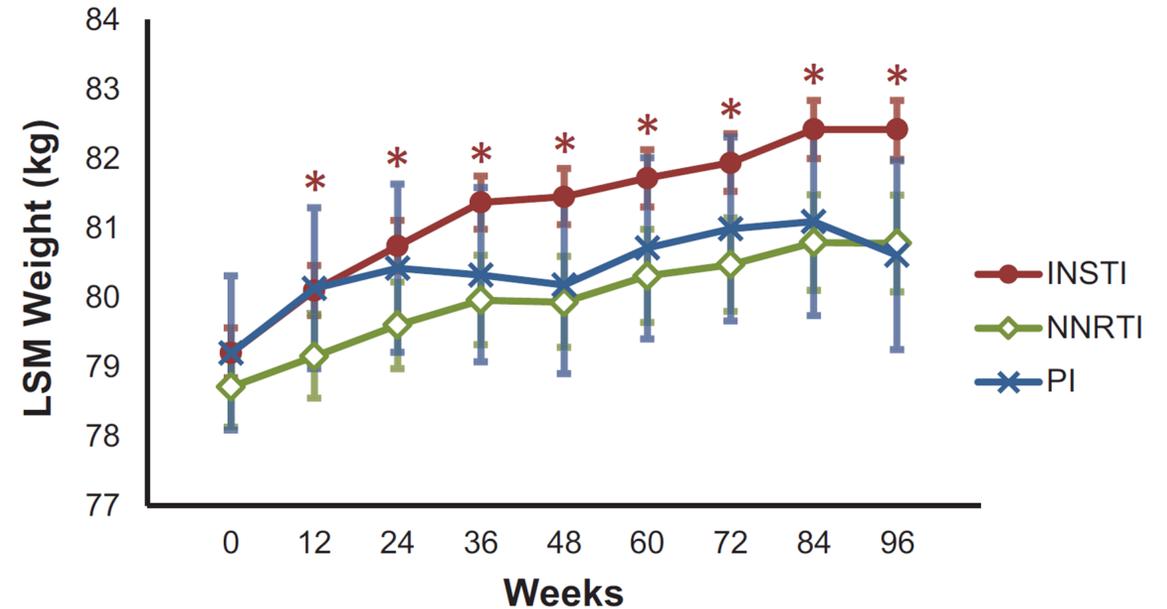
Greater weight increases with INSTI

ART-naïve (N=22,972)
NA-ACCORD



Bourgi, et al. JIAS. 2020.

ART-naïve (N=5,680)
Pooled analysis of 8 RCTs



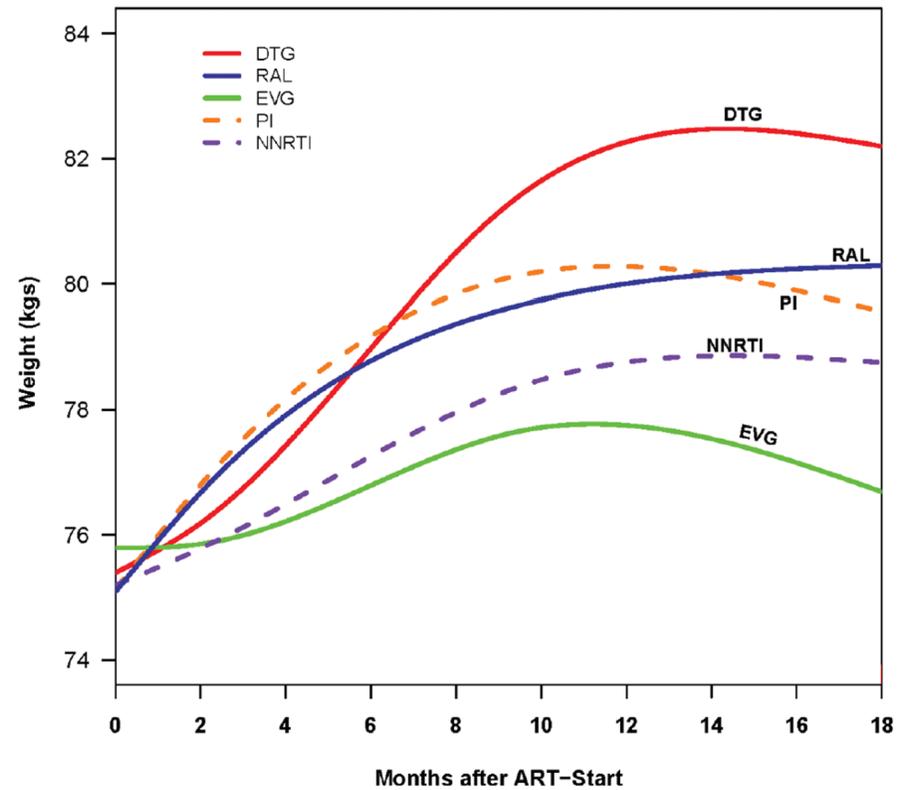
Sax PE, et al. Clin Infect Dis. 2019.





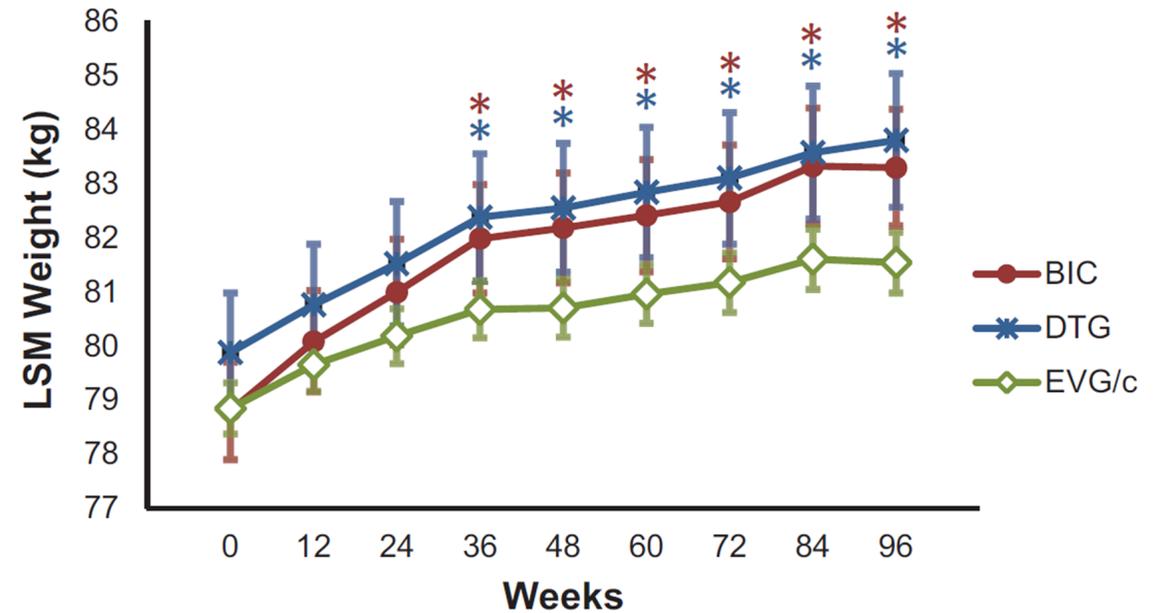
Greater weight increases with DTG

ART-naïve (N=1,152)
Vanderbilt Comprehensive Care Clinic



Bourgi, et al. Clin Infect Dis. 2020

ART-naïve (N=5,680)
Pooled analysis of 8 RCTs



Sax PE, et al. Clin Infect Dis. 2019.

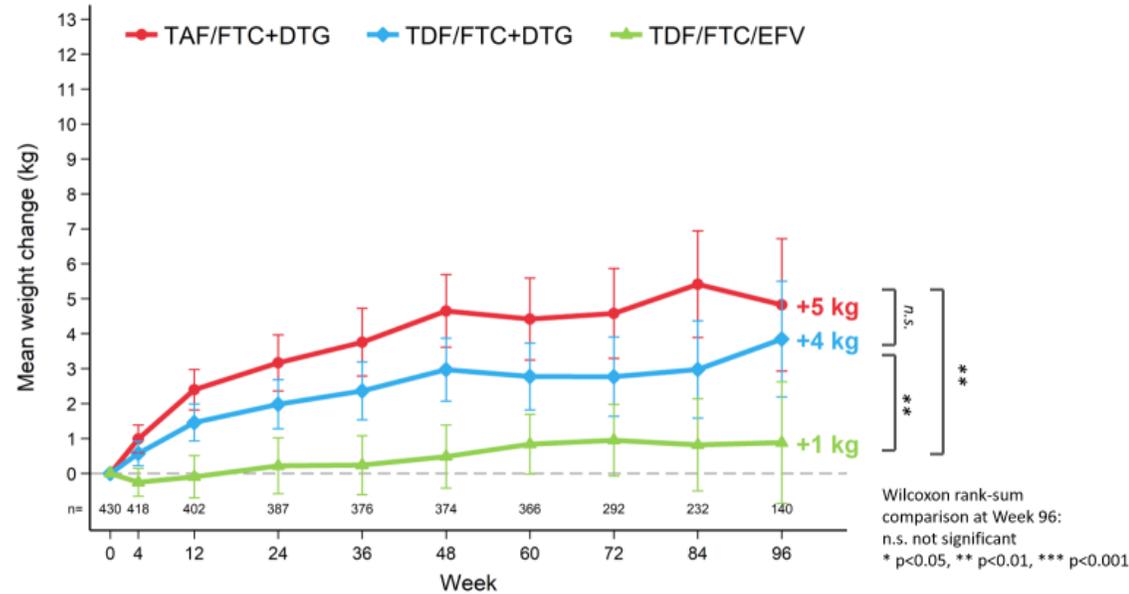




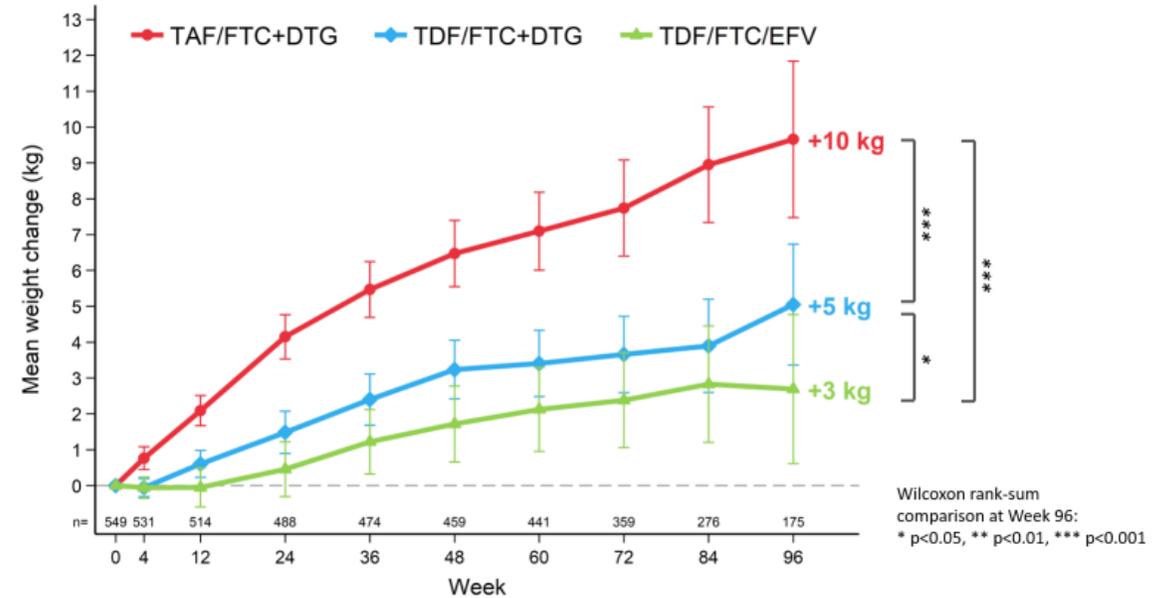
Weight increases with DTG and TAF

ADVANCE trial
ART-naïve (N=1,053)

Men



Women



Venter, et al. IAS Conference. 2019.
Venter, et al. NEJM. 2019.

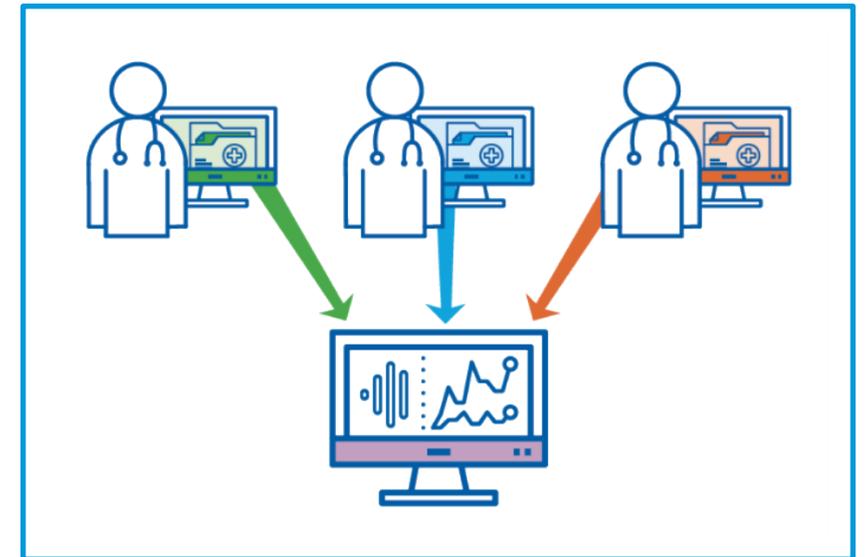
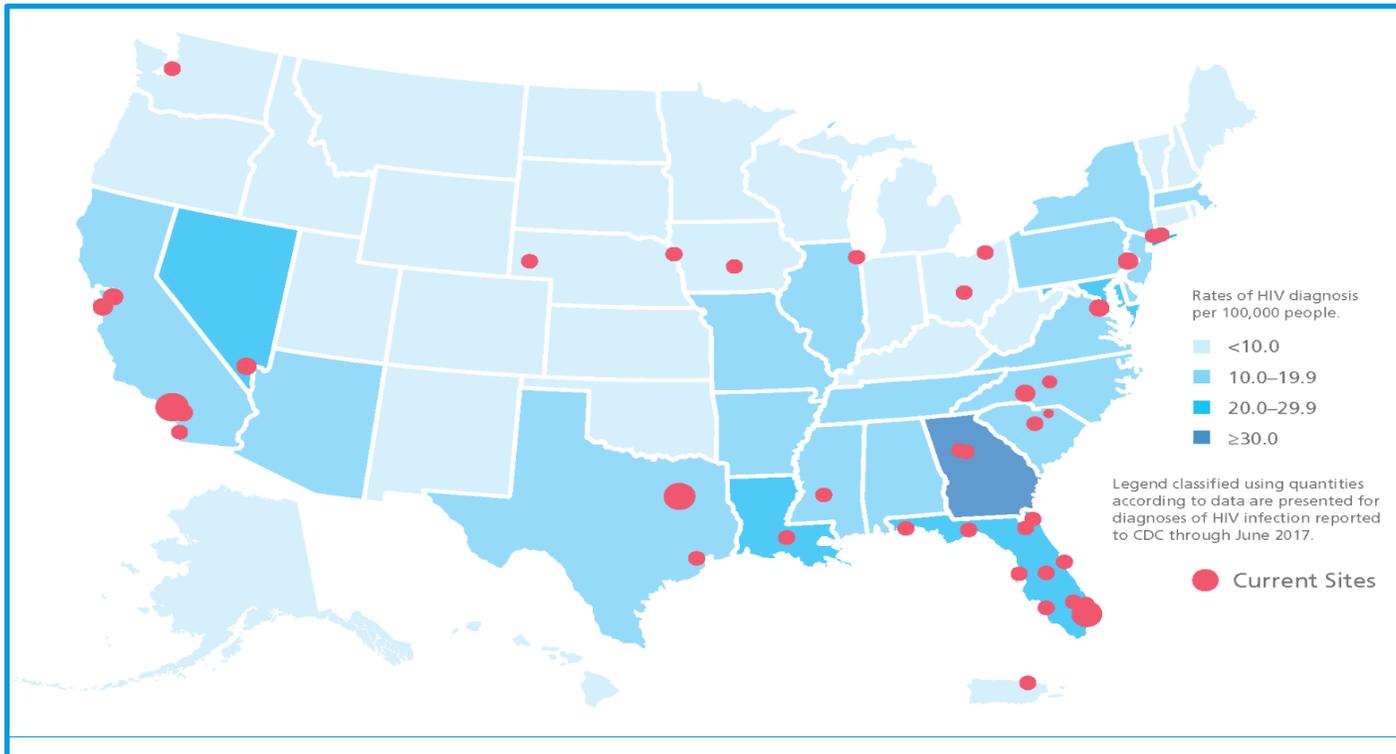


METHODS



OPERA[®]

The Longitudinal Cohort



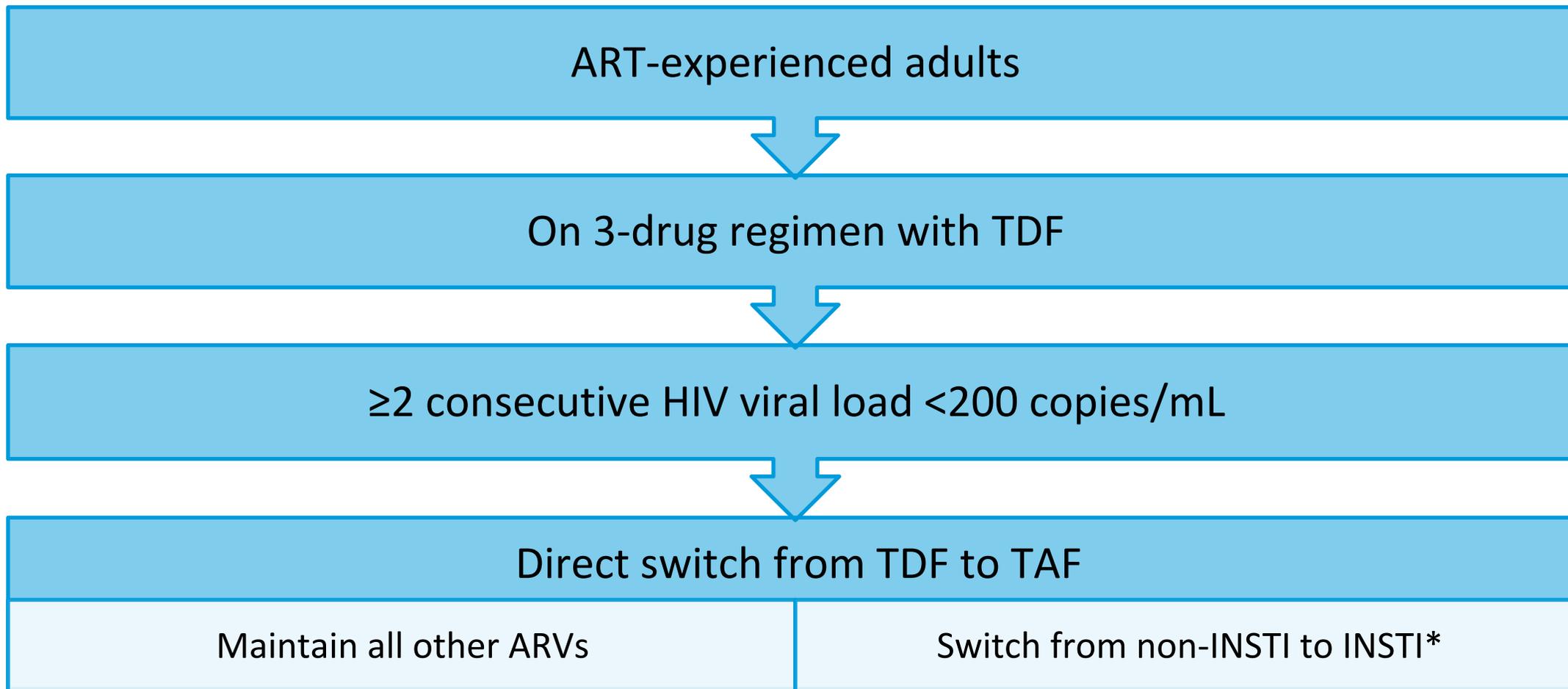
Prospectively captured,
routine clinical data from
electronic health records

>60 publications

~ 8% of all PLWH receiving care in the US
115,000+ PLWH, 65 Cities, 19 States, 1 US Territory



Study Population



* Never exposed to an INSTI prior to switch



Statistical analyses

Linear mixed models (random intercepts)

Covariates: age, sex, race, (age-sex, race-sex interactions), BMI, CD4 count, endocrine disorders, concurrent Rx that could modify weight

Weight changes on TDF and TAF

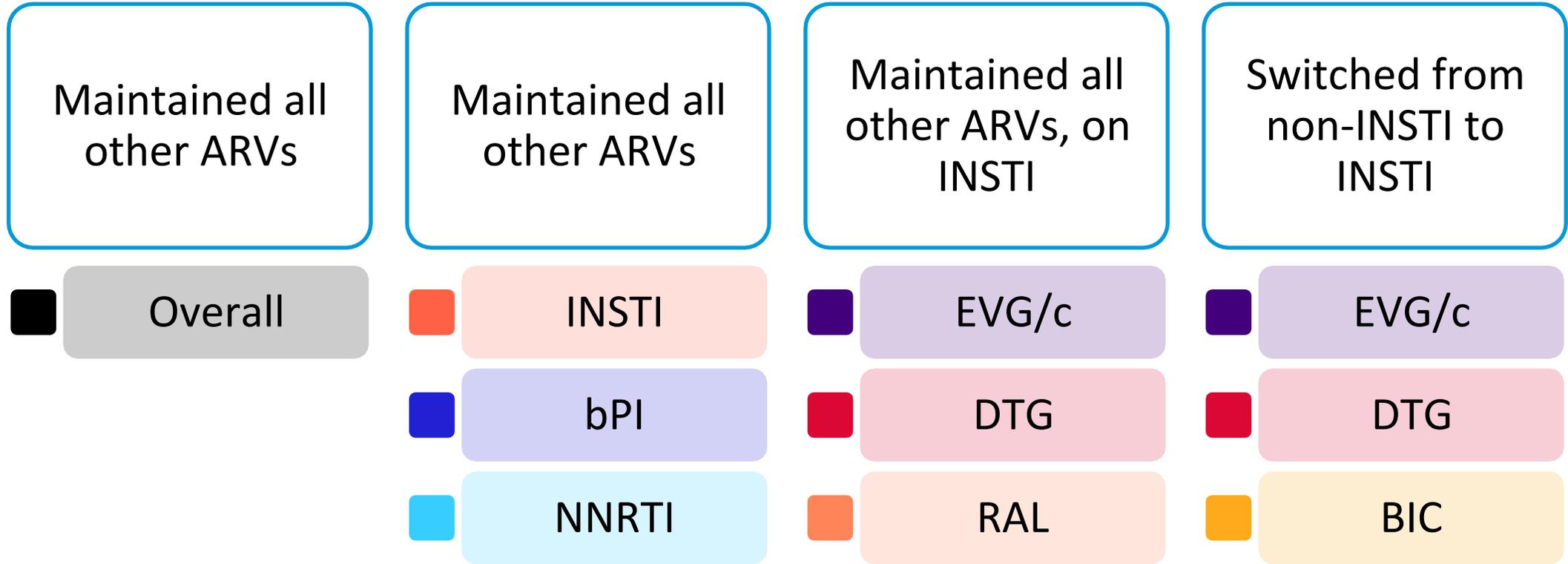
Restricted cubic splines on time
(knots at -48, -12, 0, 3, 6, 12, 24, 36 months, based on data distribution)

Rates of weight changes over time

Linear splines on time
(knots at 0 and 9 months, based on shape of the curves)



Groups of Analysis



RESULTS



Population characteristics at switch

	Maintained NNRTI n=1,454	Maintained bPI n=747	Maintained INSTI n=3,288	Switched to INSTI n=1,430
Age [†]	45 (34, 54)	51 (42, 57)	44 (33, 52)	49 (39, 56)
Women	19%	21%	15%	18%
Black	41%	39%	37%	38%
Hispanic	24%	25%	26%	26%
BMI (kg/m ²) [†]	27 (24, 31)	27 (24, 31)	26 (24, 30)	27 (24, 30)
CD4 cell count [†]	717 (542, 939)	608 (441, 826)	654 (475, 868)	668 (493, 875)
Endocrine disorders	19%	25%	21%	23%
Rx weight gain [‡]	28%	37%	30%	34%
Rx weight loss [§]	18%	23%	20%	19%

[†] Median (IQR)

[‡] Antipsychotics and mood stabilizers, antidepressants, antihyperglycemics, antihypertensives, oral corticosteroids, hormones, anticonvulsants, antihistamines, or appetite stimulants

[§] Anti-infectives, antineoplastics, bronchodilators, cardiovascular drugs, stimulants, antidepressants, antipsychotics, anticonvulsants, antihyperglycemics, anti-inflammatories, weight loss drugs, dementia treatment

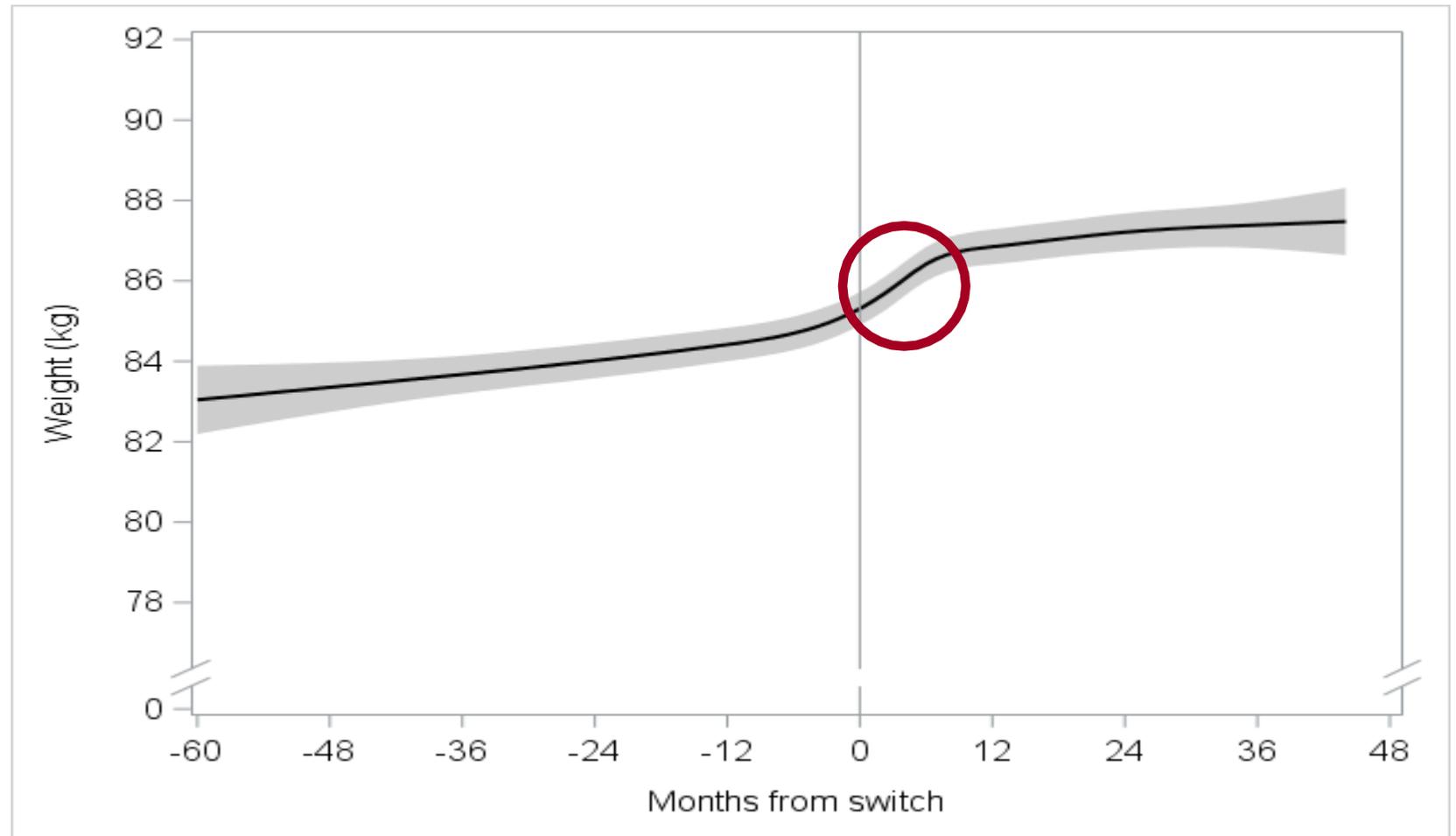


Maintained other ARVs

Referent patient*

45 years old non-Black man, with baseline BMI=27, baseline CD4 cell count: 700, without endocrine disorders and no Rx associated with weight gain/loss

* Mean or lower-risk category

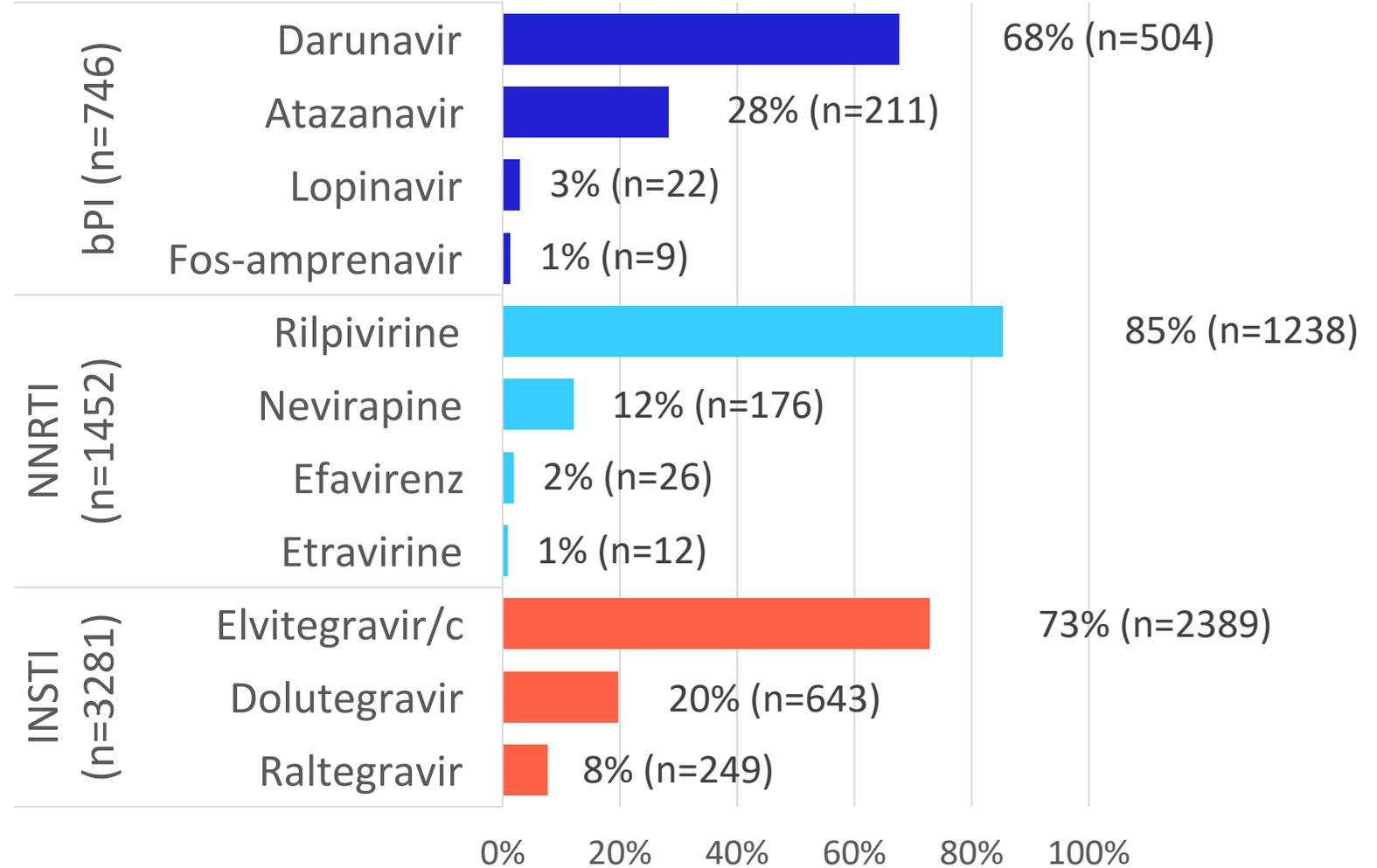


	-60 to 0 months	0 to 9 months	9+ months
Overall (n=5,479), kg/year (95% CI)	0.42 (0.26, 0.59)	2.64 (2.26, 3.01)	0.29 (0.08, 0.51)



Maintained
other ARVs

Anchor agents



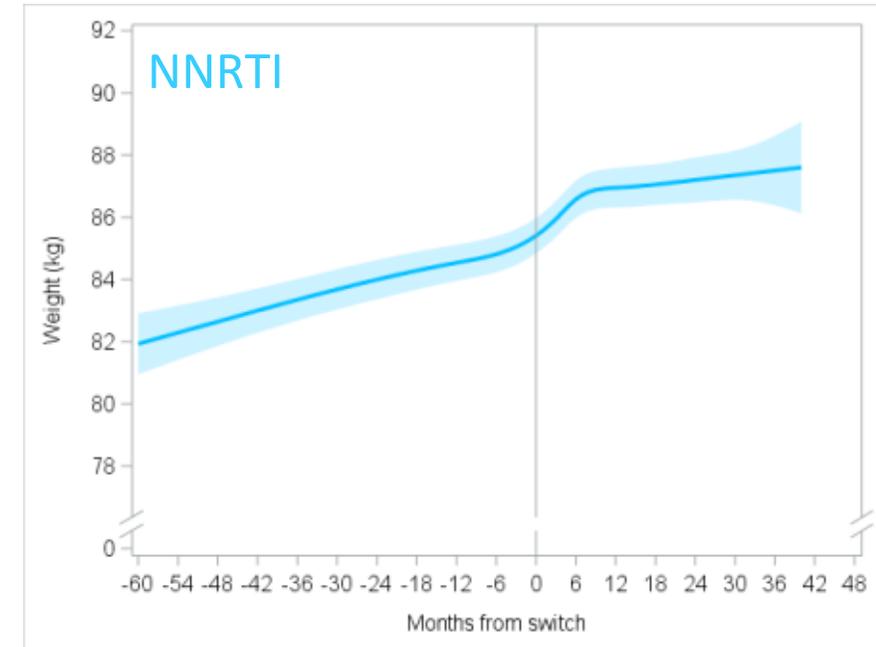
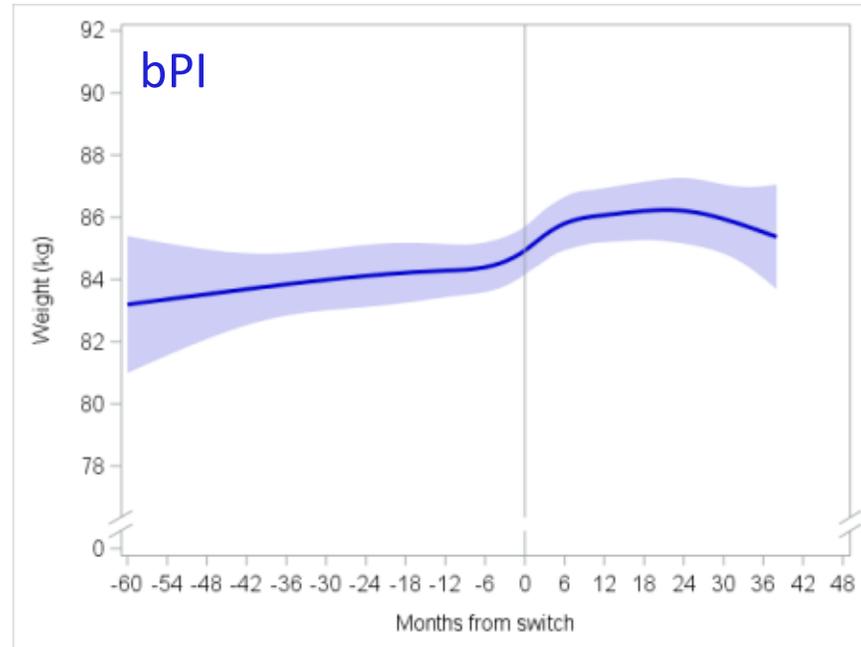
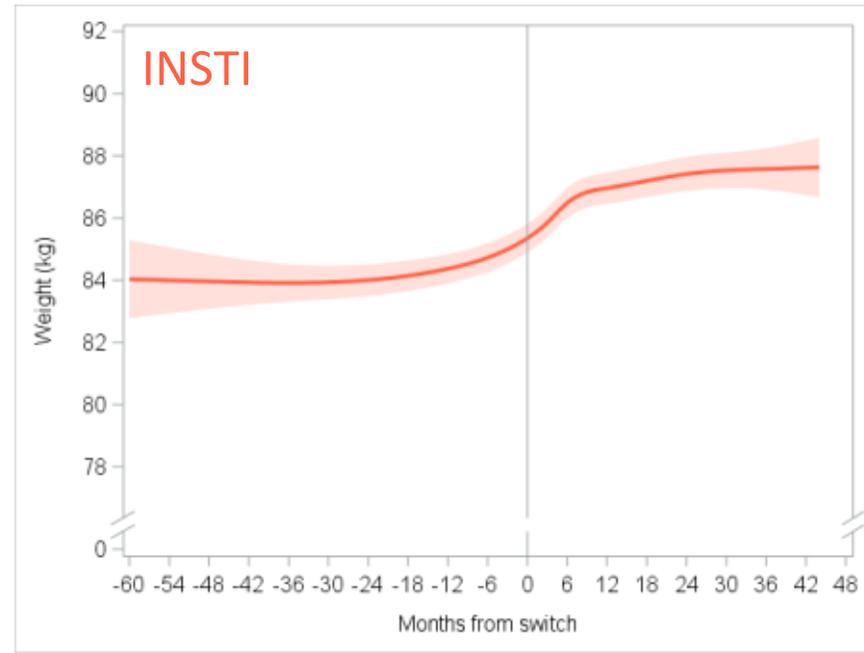


Maintained other ARVs

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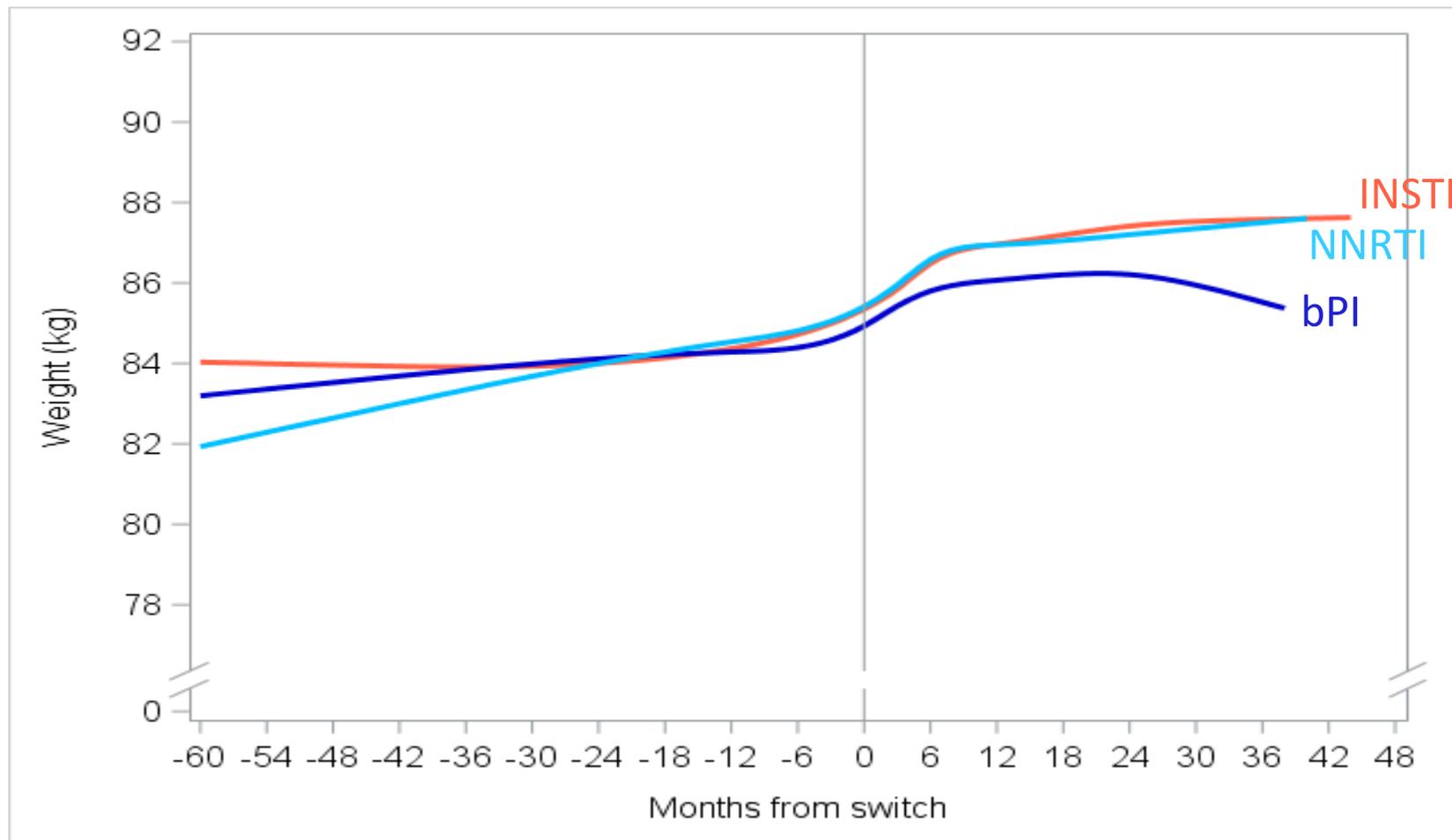


Maintained other ARVs

Referent patient*

45 years old non-Black man, with baseline BMI=27, baseline CD4 cell count: 700, without endocrine disorders and no Rx associated with weight gain/loss

* Mean or lower-risk category



	-60 to 0 months	0 to 9 months	9+ months
INSTI (n=3,281), kg/year (95% CI)	0.42 (0.26, 0.59)	2.64 (2.26, 3.01)	0.29 (0.08, 0.51)
bPI (n=746), kg/year (95% CI)	0.31 (-0.02, 0.64)	1.98 (1.13, 2.83)	-0.11 (-0.57, -0.35)
NNRTI (n=1,452), kg/year (95% CI)	0.66 (0.51, 0.81)	2.25 (1.78, 2.71)	0.20 (-0.14, 0.54)

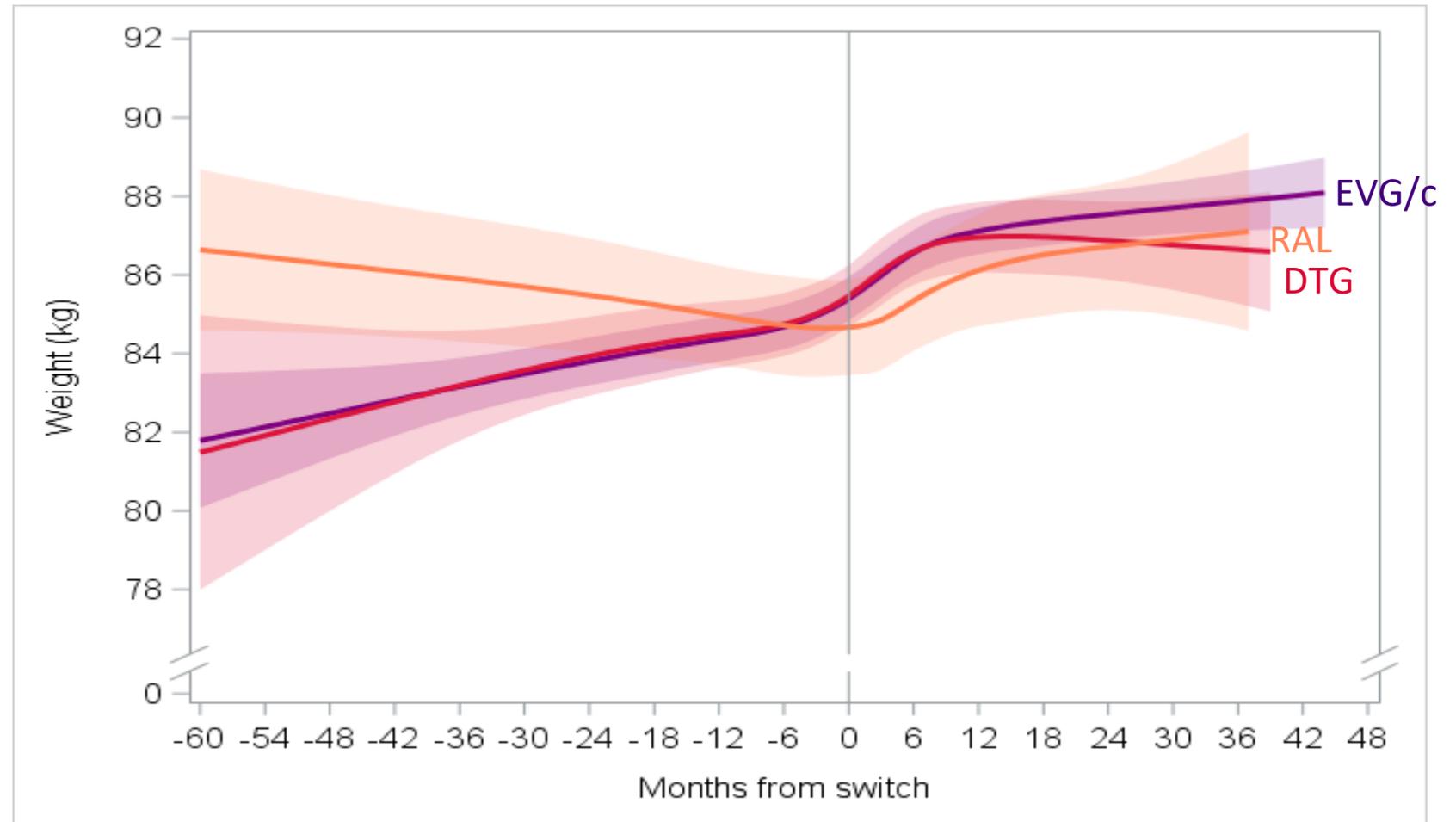


Maintained INSTI

Referent patient*

45 years old non-Black man, with baseline BMI=27, baseline CD4 cell count: 700, without endocrine disorders and no Rx associated with weight gain/loss

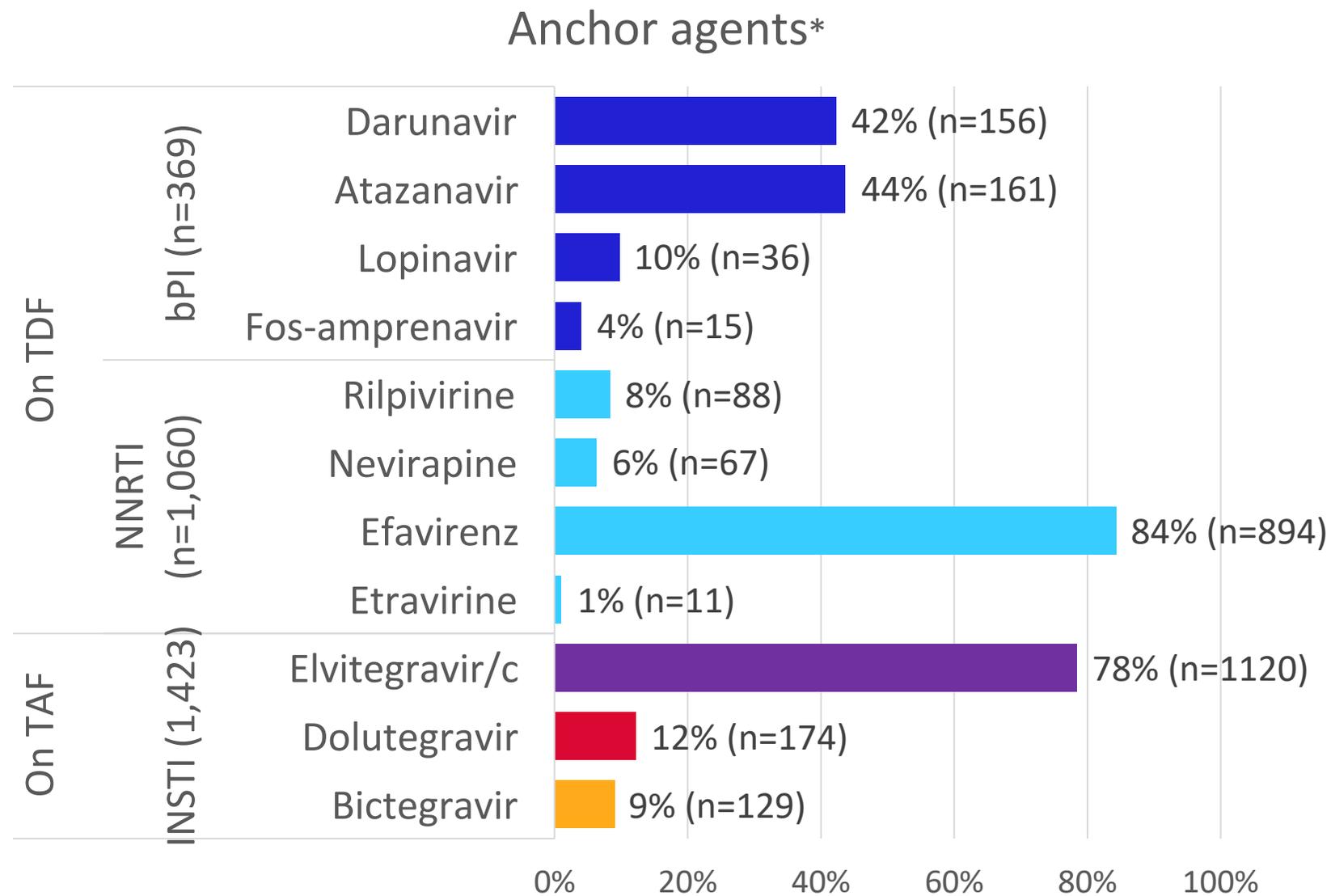
* Mean or lower-risk category



	-60 to 0 months	0 to 9 months	9+ months
EVG/c (n=2,389), kg/year (95% CI)	0.71 (0.53, 0.90)	2.51 (2.05, 2.96)	0.36 (0.12, 0.61)
DTG (n=643), kg/year (95% CI)	0.73 (0.34, 1.11)	2.38 (1.64, 3.13)	-0.18 (-0.64, 0.28)
RAL (n=249), kg/year (95% CI)	-0.44 (-0.79, -0.08)	1.80 (0.57, 3.03)	0.63 (-0.20, 1.46)



Switched to INSTI



* Groups with n <6 not shown

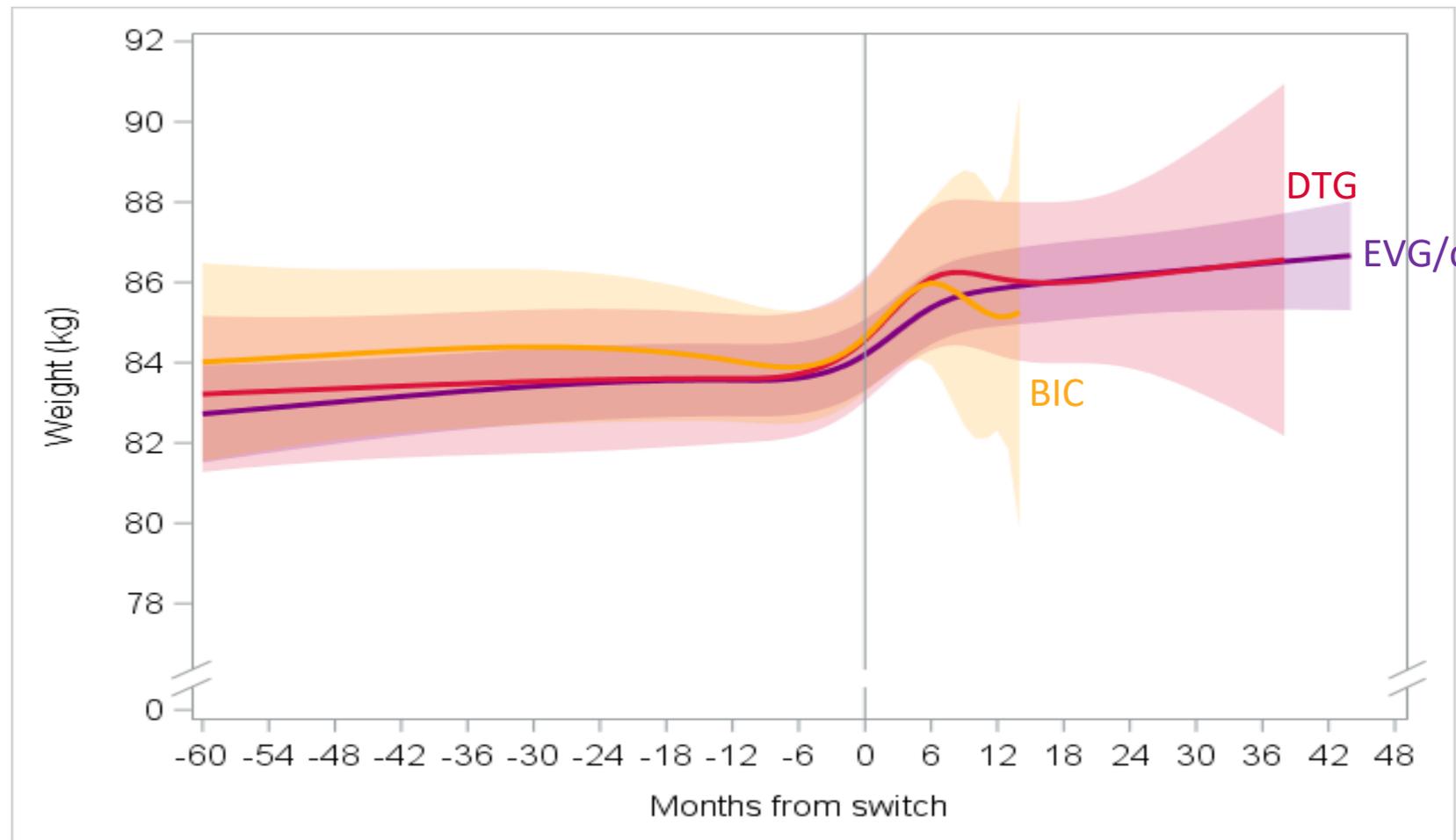


Switched to INSTI

Referent patient*

45 years old non-Black man, with baseline BMI=27, baseline CD4 cell count: 700, without endocrine disorders and no Rx associated with weight gain/loss

* Mean or lower-risk category



	-60 to 0 months	0 to 9 months	9+ months
EVG/c (n=1,120), kg/year (95% CI)	0.24 (0.04, 0.43)	2.55 (1.86, 3.24)	0.26 (-0.10, 0.61)
DTG (n=174), kg/year (95% CI)	0.22 (-0.08, 0.52)	3.09 (1.26, 4.93)	-0.23 (-1.62, 1.16)
BIC (n=129), kg/year (95% CI)	0.01 (-0.38, 0.39)	4.47 (0.81, 8.13)	-9.97 (-23.79, 3.85)

CONCLUSIONS



Large, diverse cohort of virologically suppressed PLWH



Switch to TAF associated with early, pronounced weight increases in all groups over first ~9 months (1.80-4.47 kg/year)



Weight gain slowed down or plateaued ~9 months after switch to TAF (insufficient data for BIC >9 months)



Patterns consistent across regimens



Results suggest an independent effect of TAF on weight



Acknowledgements

This research would not be possible without the participation of people living with HIV and their caregivers

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