Changes in BMI associated with antiretroviral regimens in treatment-experienced, virologically suppressed individuals living with HIV

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Disclosure

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- Advisory Committee/Board: Epividian

Background

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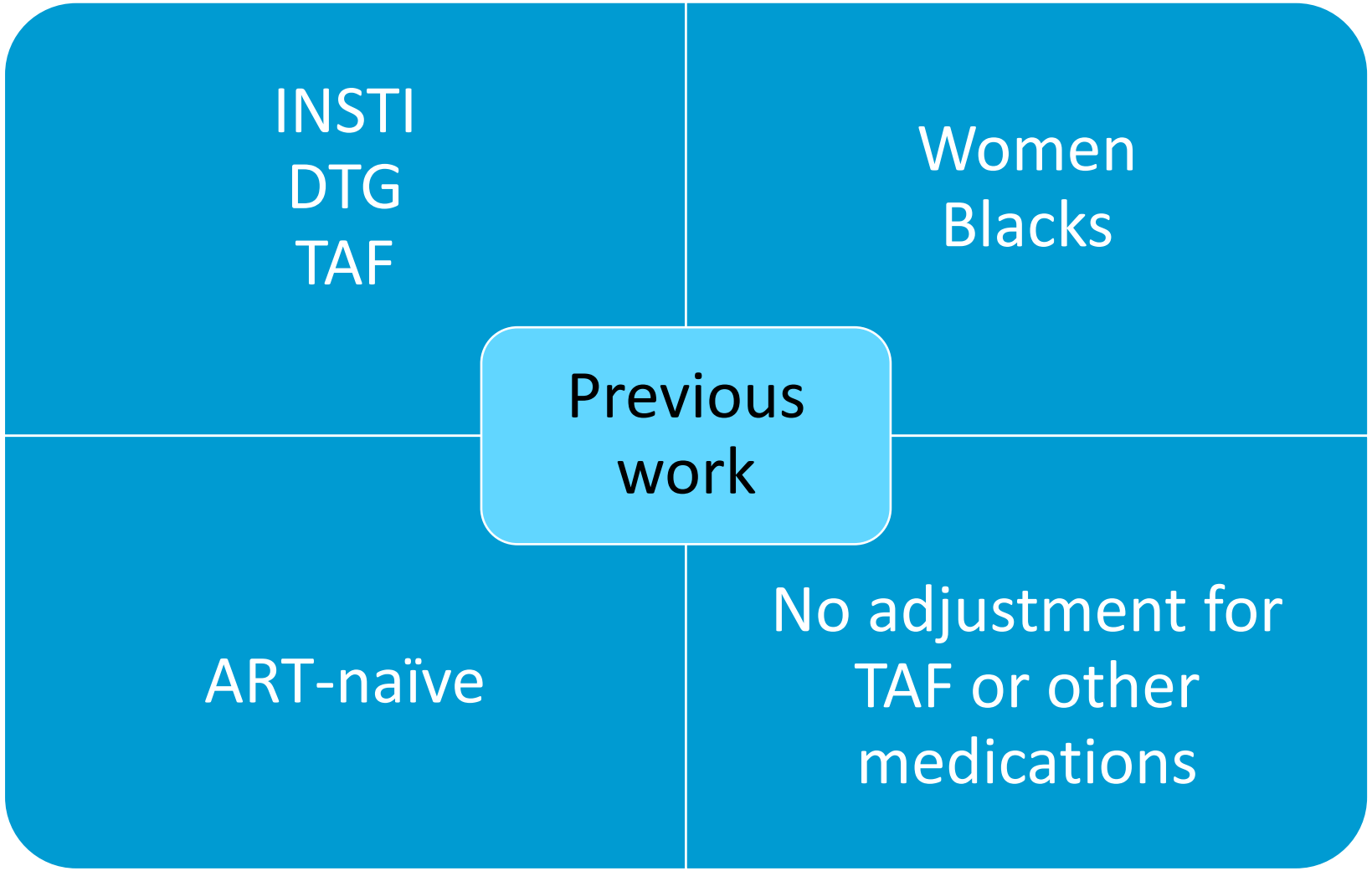

INSTI
DTG
TAF
Women
Blacks
Previous work
ART-naïve
No adjustment for TAF or other medications

Objective

To compare changes in **BMI**

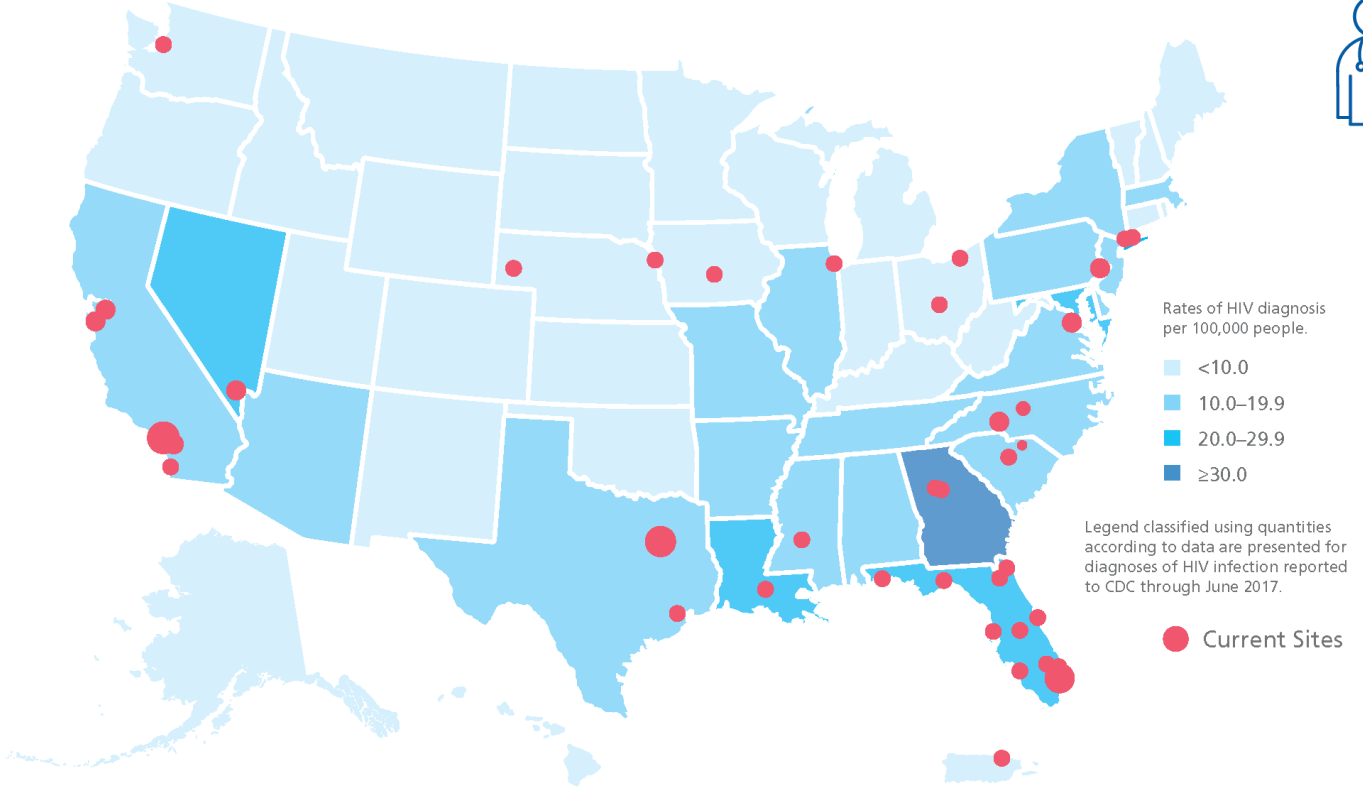
among **ART-experienced, virologically-suppressed** PLWH

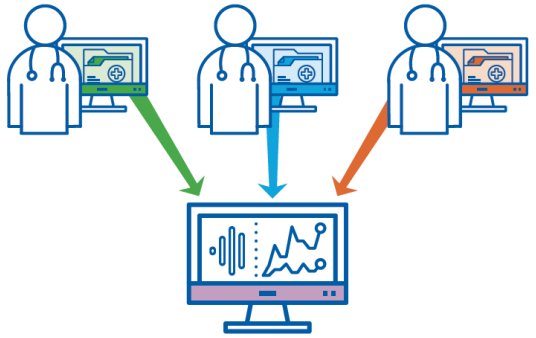
after a switch to DTG, EVG/c, RAL, RPV, or bDRV

Methods

OPERA Cohort

- Prospectively captured, routine clinical data from electronic health records
- 100,000+ PLWH, 65 cities, 19 States, 1 US Territory





~ 8%
of all PLWH receiving care in the US

Study Population

- ART-experienced, suppressed (Baseline viral load <200 copies/mL)
- ≥18 years of age, no pregnancy, not transgender
- Switching to a new 3-drug regimen between 01AUG2013 and 31DEC2017
- First exposure to DTG, EVG/c, RAL, RPV or bDRV
- ≥ 1 plausible BMI ≤ 3 months before or at initiation (plausible BMI ≥10 and ≤50)
- ≥ 1 plausible BMI after switch at 6, 12, or 24 months (±3 months)

Statistical analyses

- Mean BMI changes measured at either 6, 12, or 24 months ± 3 months, by core agent
- Multivariable linear regression adjusted for baseline covariates:
  - BMI
  - Age
  - Sex
  - Race/ethnicity
  - Substance abuse
  - Viral load
  - CD4 count
  - Lipodystrophy
  - Endocrine disorders
  - Hypertension
  - Medications associated with weight gain (≥ 30 days)
  - Medications associated with weight loss (≥ 30 days)
  - TAF use

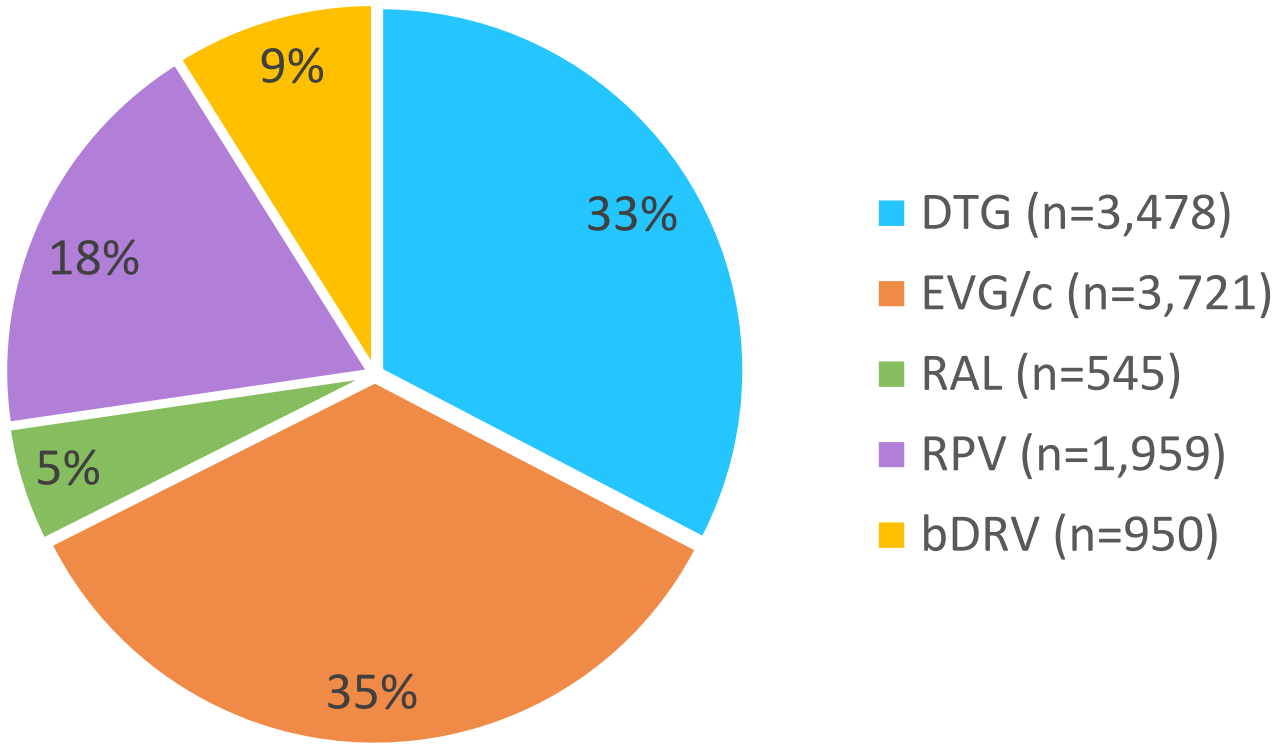
Sensitivity analyses

- Stabilized inverse probability-of-censoring weights (IPCW) to account for censoring
  - Regimen change, Loss to follow-up, Death, Pregnancy, No BMI measured within time window of interest, Study end (31DEC2018)

- Stratification: baseline BMI categories

Results

Overall study population (N=10,653)



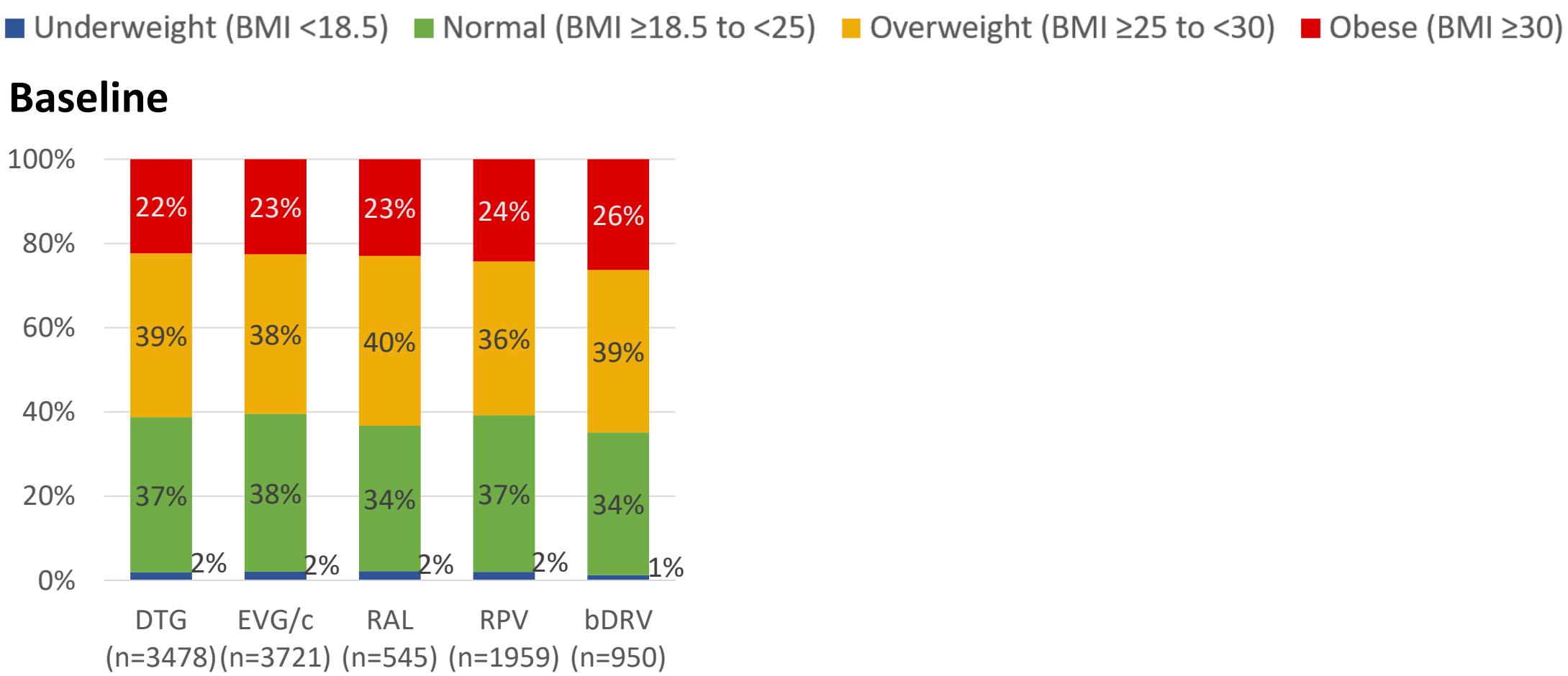
Baseline characteristics

	DTG	EVG/c	RAL	RPV	bDRV
Age ≥50	1446 (42%)	1084 (29%)*	292 (54%)*	615 (31%)*	379 (40%)
Female	491 (14%)	493 (13%)	87 (16%)	373 (19%)*	202 (21%)*
Non-Hispanic Black	1118 (32%)	1240 (33%)	165 (30%)	764 (39%)*	398 (42%)*
Substance abuse	520 (15%)	419 (11%)*	67 (12%)	209 (11%)*	118 (12%)*
Hypertension	1084 (31%)	938 (25%)*	211 (39%)*	489 (25%)*	247 (26%)*
Endocrine disorders†	1462 (42%)	1305 (35%)*	245 (45%)	655 (33%)*	299 (31%)*
Medications associated with weight gain	800 (23%)	621 (17%)*	159 (29%)*	354 (18%)*	203 (21%)
TAF use	362 (10%)	2086 (56%)*	26 (5%)*	770 (39%)*	133 (14%)*

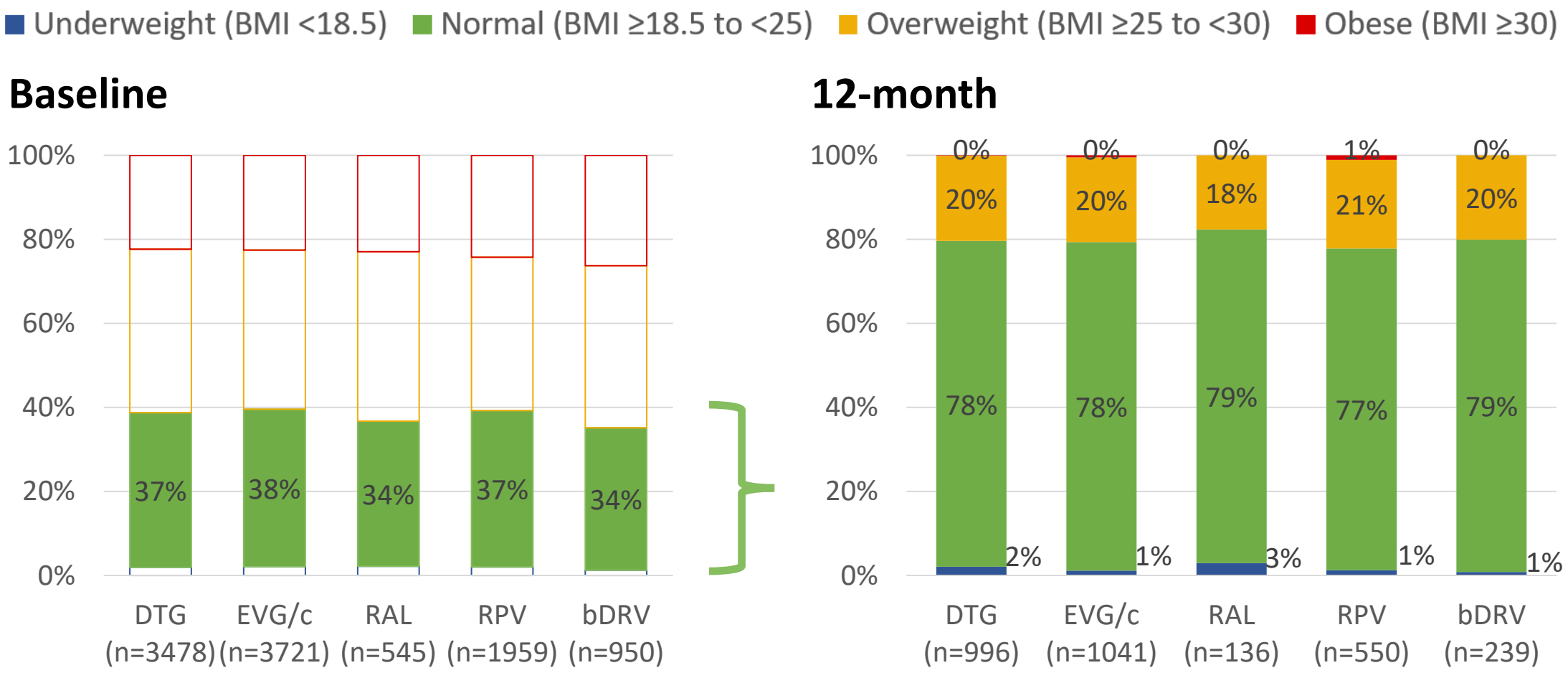
* p-value <0.05 for the comparison with DTG

† Type 1 Diabetes Mellitus, Type 2 Diabetes Mellitus, Hyperlipidemia, Hyperthyroidism, Hypothyroidism, or Thyroiditis

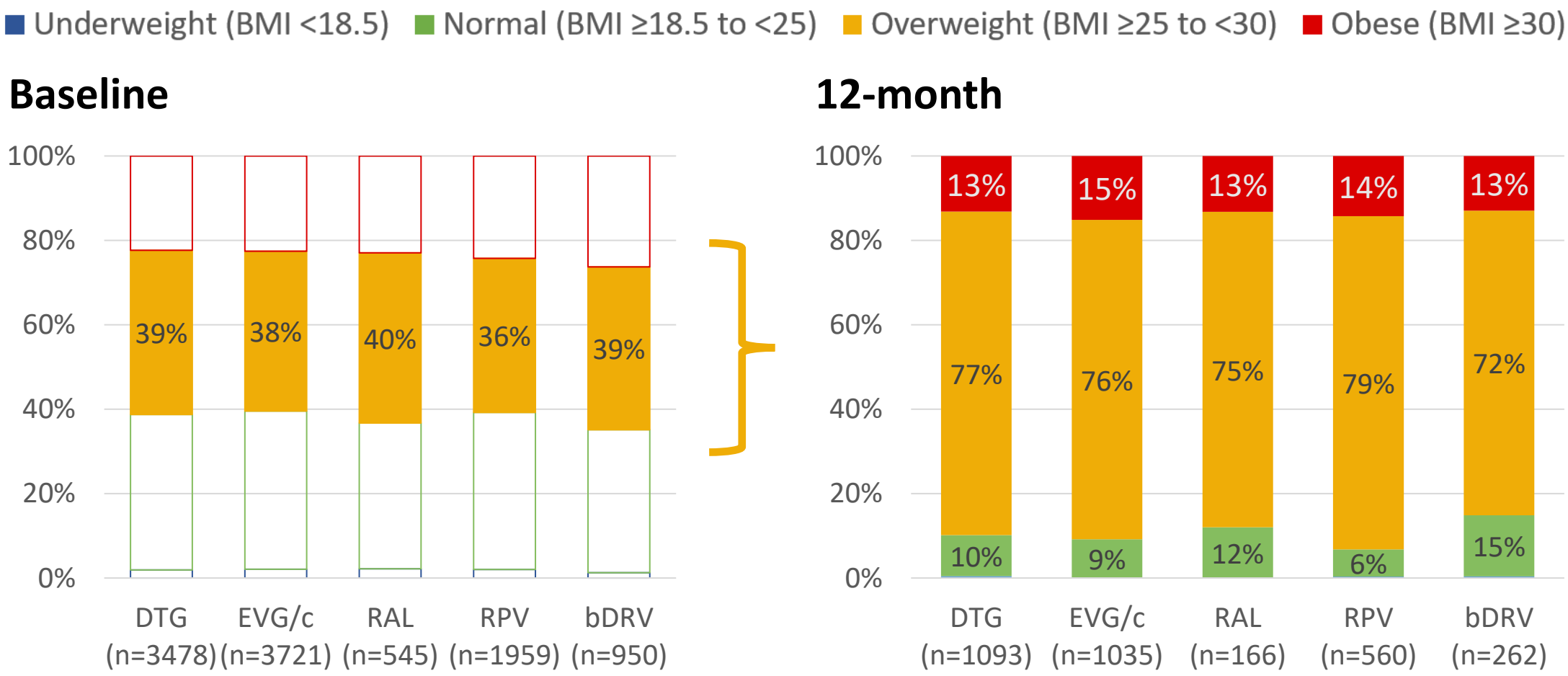
Baseline BMI



12-month BMI among normal weight PLWH at baseline

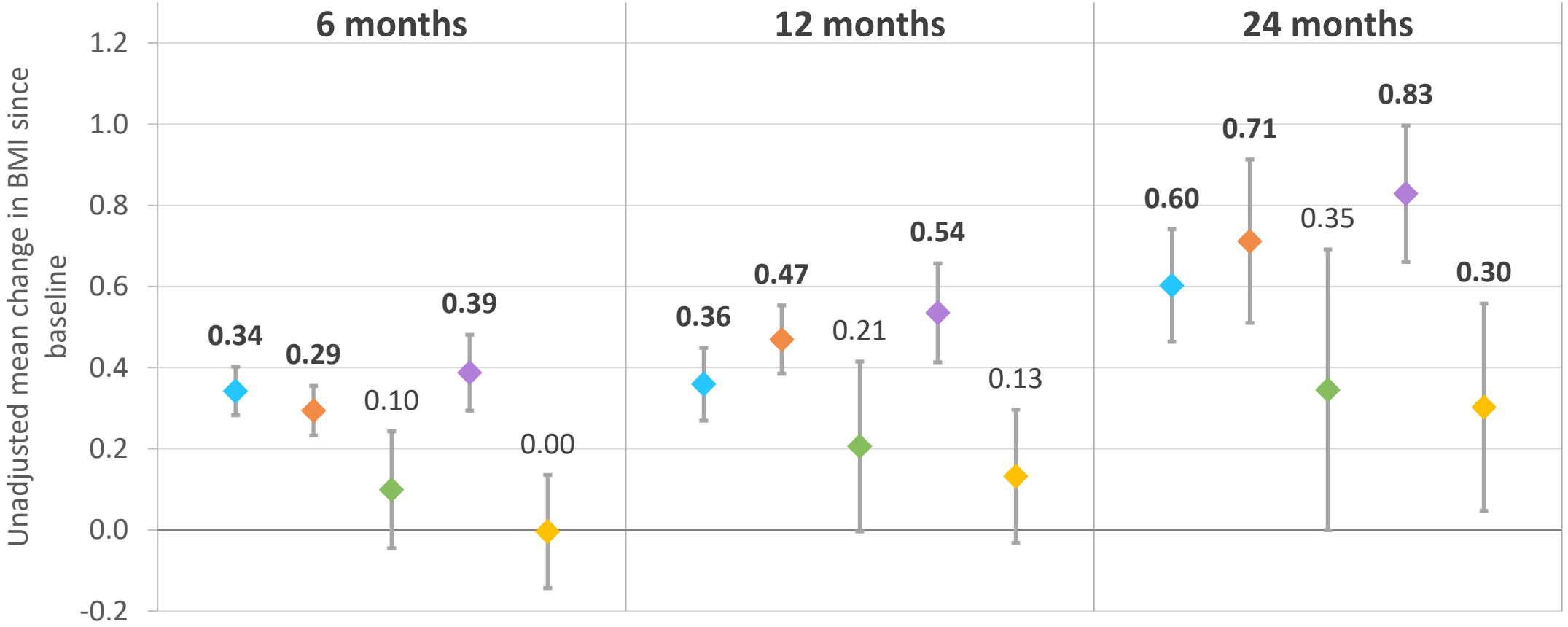


12-month BMI among overweight PLWH at baseline



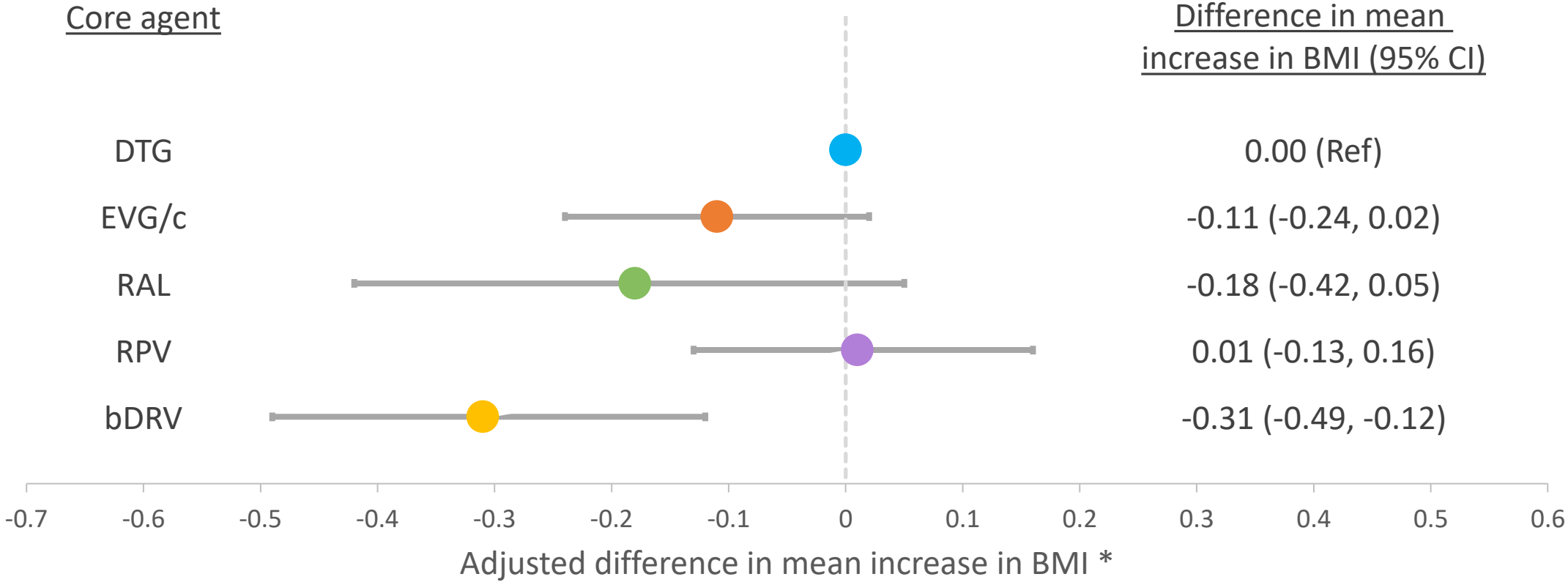
Unadjusted change in BMI (kg/m^2) since core agent initiation

OPERA® The Longitudinal Cohort



12-month adjusted difference in mean increase in BMI from baseline

Core agent	Difference in mean increase in BMI (95% CI)
DTG	0.00 (Ref)
EVG/c	-0.11 (-0.24, 0.02)
RAL	-0.18 (-0.42, 0.05)
RPV	0.01 (-0.13, 0.16)
bDRV	-0.31 (-0.49, -0.12)



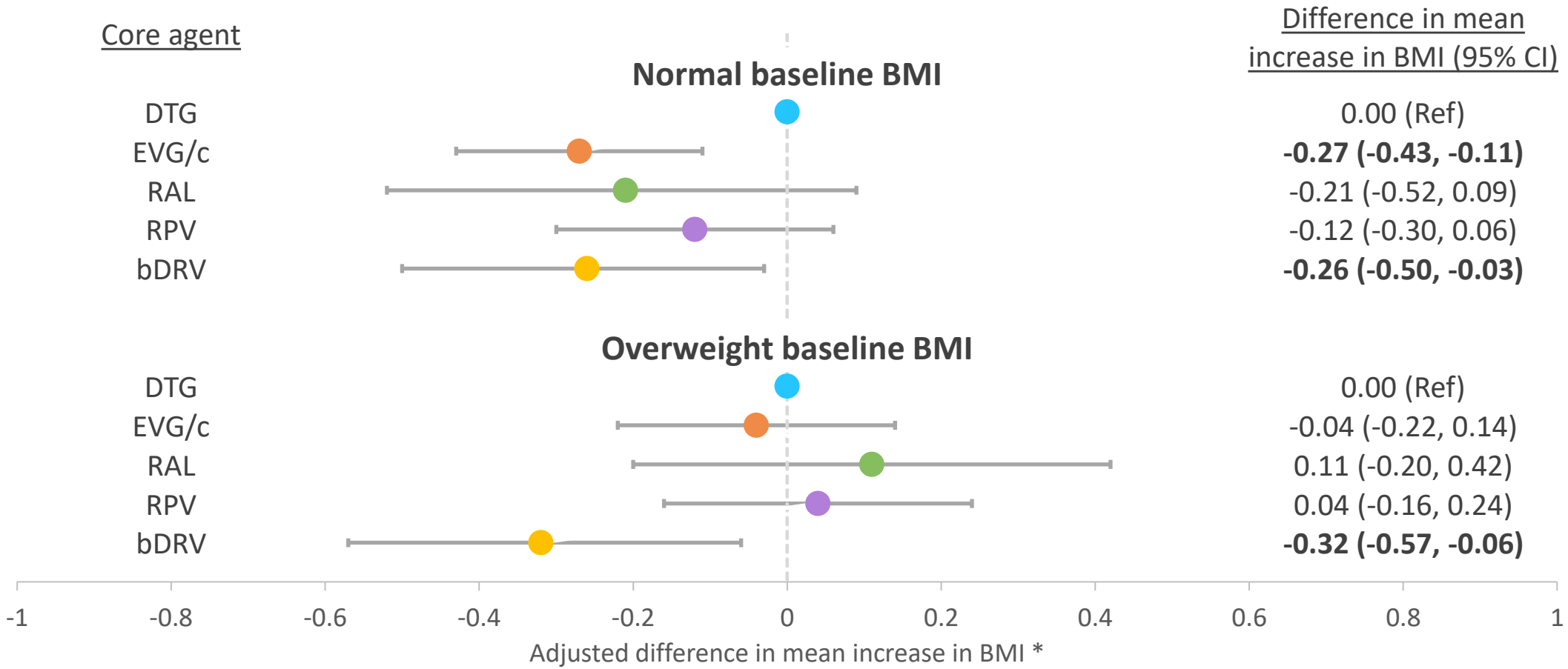
* Adjusted for baseline age, sex, race/ethnicity, BMI, lipodystrophy, endocrine disorders, hypertension, substance abuse, weight-gain associated medication, weight-loss associated medication, CD4 cell count, viral load, and TAF use

6-, 12-, 24-month adjusted difference in mean increase in BMI from baseline

	6-month adjusted difference in mean increase in BMI	12-month adjusted difference in mean increase in BMI	24-month adjusted difference in mean increase in BMI
DTG	0.00 (Ref)	0.00 (Ref)	0.00 (Ref)
EVG/c	**-0.15 (-0.25, -0.06)**	-0.11 (-0.24, 0.02)	-0.06 (-0.26, 0.13)
RAL	**-0.22 (-0.39, -0.06)**	-0.18 (-0.42, 0.05)	-0.25 (-0.60, 0.10)
RPV	0.01 (-0.09, 0.12)	0.01 (-0.13, 0.16)	0.09 (-0.12, 0.31)
bDRV	**-0.30 (-0.44, -0.17)**	**-0.31 (-0.49, -0.12)**	**-0.29 (-0.57, -0.01)**

* Adjusted for baseline age, sex, race/ethnicity, BMI, lipodystrophy, endocrine disorders, hypertension, substance abuse, weight-gain associated medication, weight-loss associated medication, CD4 cell count, viral load, and TAF use

12-month adjusted difference in mean increase in BMI, by baseline BMI



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Summary of findings

Lower increases in mean BMI compared to DTG					
		EVG/c vs. DTG	**RAL vs. DTG**	**RPV vs. DTG**	**bDRV vs. DTG**
Overall	6 -month	↓	↓	≈	↓
	12-month	≈	≈	≈	↓
	24-month	≈	≈	≈	↓
Normal baseline BMI	12-month	↓	≈	≈	↓
Overweight at baseline	12-month	≈	≈	≈	↓

Discussion

Discussion

- Small absolute increases in BMI with all core agents
  - Statistically significant for DTG, EVG/c, RPV
- Increases in BMI persist in treatment-experienced, suppressed patients
  - Return to health does not fully explain weight gain associated with ART
- Both weight gain and weight loss observed across all groups
  - Weight gain may be experienced by a subgroup of PLWH, not by all

Strengths

+ ART experience suppressed PLWH: eliminates impact of return to health

+ Large sample size in each of the treatment groups (545 to 3,721 PLWH), for a total of 10,653 PLWH

+ Adjusted for multiple concurrent medications associated with weight gain, including TAF

+ Electronic medical records
  - Availability of lab results
  - Ability to identify and account for history of disorders

+ Results robust to sensitivity analyses (IPCW, stratification by baseline BMI)

Limitations

- Exclusion of PLWH without BMI measured during specific time windows
  - Different population in each model
- Strong assumption of linearity made by assessing changes in BMI at 3 subsequent time points in different models
- No adjustment for:
  - Marijuana or marinol use
  - Time-updated covariates
- Insufficient number of BIC users at the time of the study

Acknowledgements

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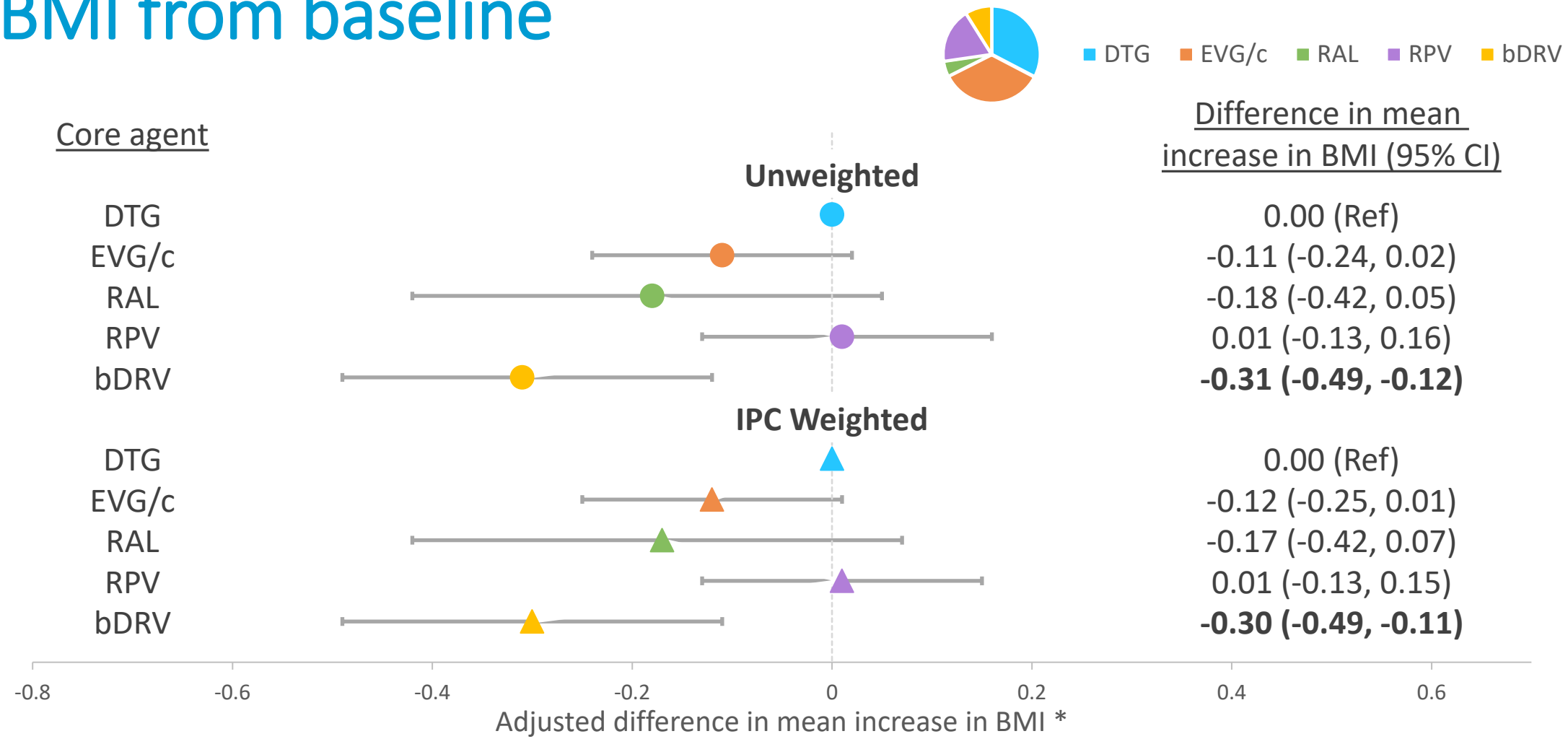
- This research was sponsored by ViiV Healthcare

Additional slides

Extreme weight gain (>10% increase from baseline weight), unadjusted

	>10% weight increase at 6-month	**>10% weight increase at 12-month**	**>10% weight increase at 24-month**
DTG	173/3,273 (5.3%)	239/2,757 (8.7%)	231/1,548 (14.9%)
EVG/c	178/3,484 (5.1%)	280/2,774 (10.1%)	209/1,506 (13.9%)
RAL	16/513 (3.1%)	28/402 (7.0%)	25/217 (11.5%)
RPV	99/1,830 (5.4%)	157/1,513 (10.4%)	121/795 (15.2%)
bDRV	37/880 (4.2%)	53/697 (7.6%)	43/370 (11.6%)

12-month adjusted difference in mean increase in BMI from baseline



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6-, 12-, 24-month IPCW adjusted difference in mean increase in BMI from baseline

	6-month adjusted difference in mean increase in BMI	12-month adjusted difference in mean increase in BMI	24-month adjusted difference in mean increase in BMI
DTG	0.00 (Ref)	0.00 (Ref)	0.00 (Ref)
EVG/c	**-0.15 (-0.24, -0.06)**	-0.12 (-0.25, 0.01)	-0.08 (-0.26, 0.11)
RAL	**-0.18 (-0.33, -0.02)**	-0.17 (-0.42, 0.07)	-0.24 (-0.60, 0.11)
RPV	0.00 (-0.10, 0.11)	0.01 (-0.13, 0.15)	0.09 (-0.12, 0.31)
bDRV	**-0.28 (-0.42, -0.14)**	**-0.30 (-0.49, -0.11)**	**-0.30 (-0.58, -0.01)**

* Adjusted for baseline age, sex, race/ethnicity, BMI, lipodystrophy, endocrine disorders, hypertension, substance abuse, weight-gain associated medication, weight-loss associated medication, CD4 cell count, viral load, and TAF use

12-month adjusted difference in mean increase in BMI, by baseline BMI