

Virological suppression and weight gain in children in Europe on dolutegravir compared to protease inhibitors: a propensity score analysis

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Introduction

- Dolutegravir (DTG)-based ART is recommended for treating HIV-1 in children and adolescents living with HIV (CLWHIV).
- Excess weight gain on DTG has been reported in adults but paediatric data are limited.

Aim: to compare viral suppression and changes in BMI and weight in CLWHIV on DTG to a comparator group on protease inhibitors (PI)

Methods

- Inclusion criteria:** CLWHIV aged 6-<18 years receiving 2NRTIs+DTG or 2NRTIs+PI from 2010-2020 in 12 cohorts in the European Pregnancy and Paediatric Infections Cohort Collaboration (EPPICC).
- Outcomes:** Percentage with viral suppression (viral load (VL)<50c/ml), change in BMI-for-age z-score (zBMI), change in weight (kg), at 48 and 96 weeks after DTG or PI start.
- Analysis groups:** defined by treatment experience and VL status at DTG/PI start: ART "Naïve", "ART-experienced/suppressed" (VL<50c/ml), "ART-experienced/unsuppressed" (VL≥50c/ml).
- Randomised controlled trials (RCTs) are the gold standard for assessing the effects of an intervention. **Propensity scores (PS) offer a method to estimate treatment effect in non-randomised data** and can be used to match individuals who are 'treated' to similar 'untreated' individuals.
- Viral suppression, zBMI and weight change on **DTG and PI were compared using PS matching** among those ART-experienced at drug start (insufficient numbers ART naïve).
- PS were based on characteristics at start of DTG/PI: age, sex, ethnicity, time since ART initiation, history of treatment failure, prior AIDS event, CD4 and BMI-for-age z-score.**

Results: Patient characteristics and unadjusted outcomes on DTG and PIs

Table 1: Characteristics of CLWHIV on DTG/PI+2NRTIs

	DTG (N=644)	PI (N=938)
	N (%) Median [IQR]	
Male sex	294 (46%)	433 (46%)
Black ethnicity	360/539 (67%)	464/674 (69%)
Age (years) at ART start	4.4 [0.7, 9.7]	5.6 [1.5, 10.0]
Characteristics at DTG/PI start		
Age (years)	14.0 [11.8, 15.9]	13.7 [10.9, 15.8]
Calendar year	2017 [2016, 2018]	2013 [2011, 2015]
Prior AIDS event	132 (21%)	220 (23%)
CD4 count (cells/mm ³)	719 [500, 973]	591 [366, 844]
Treatment/viral load status		
Naïve	73 (11%)	173 (18%)
ART-experienced/VL<50c/mL	402 (62%)	318 (34%)
ART-experienced/VL≥50c/mL	112 (17%)	304 (32%)
ART-experienced/VL unknown	57 (9%)	143 (15%)
NRTI backbone in DTG/PI regimen		
Includes TAF	60 (9%)	56 (6%)
Includes TDF	54 (8%)	381 (41%)
Previous NRTI backbone (n=571, 765)		
Includes TAF	16 (3%)	8 (1%)
Includes TDF	87 (15%)	206 (27%)
Previous anchor drug/class (n=571, 765)		
NNRTI (efavirenz)	144 (25%)	192 (25%)
NNRTI (other)	91 (16%)	99 (13%)
PI	305 (53%)	467 (61%)
INSTI	34 (6%)	23 (3%)
History of treatment failure	117 (18%)	304 (32%)
Follow-up on DTG/PI (years)	1.7 [0.9, 2.7]	2.6 [1.2, 4.4]

- Overall, **1582 CLWHIV were included; 644 on DTG and 938 on PI** (Tables 1 & 2).
- CLWHIV on PI had lower CD4 counts, were more likely to have failed treatment in the past (table 1) and had lower zBMI (table 2) than those on DTG; these difference disappeared after matching by PS.
- Among those on PI, 51% were on darunavir, 25% atazanavir and 24% lopinavir.
- Overall **suppression was higher on DTG than PI** (Fig 1A/B).
- Among CLWHIV who were **ART-experienced and unsuppressed at DTG/PI start <80% on DTG and <70% on PI, were suppressed at 48/96 weeks** (Fig 1A).
- The **increase in zBMI was highest among those who started DTG ART-experienced with unsuppressed VL** (Fig 1C); this group also had the highest zBMI and weight at start of DTG/PI (Table 2).

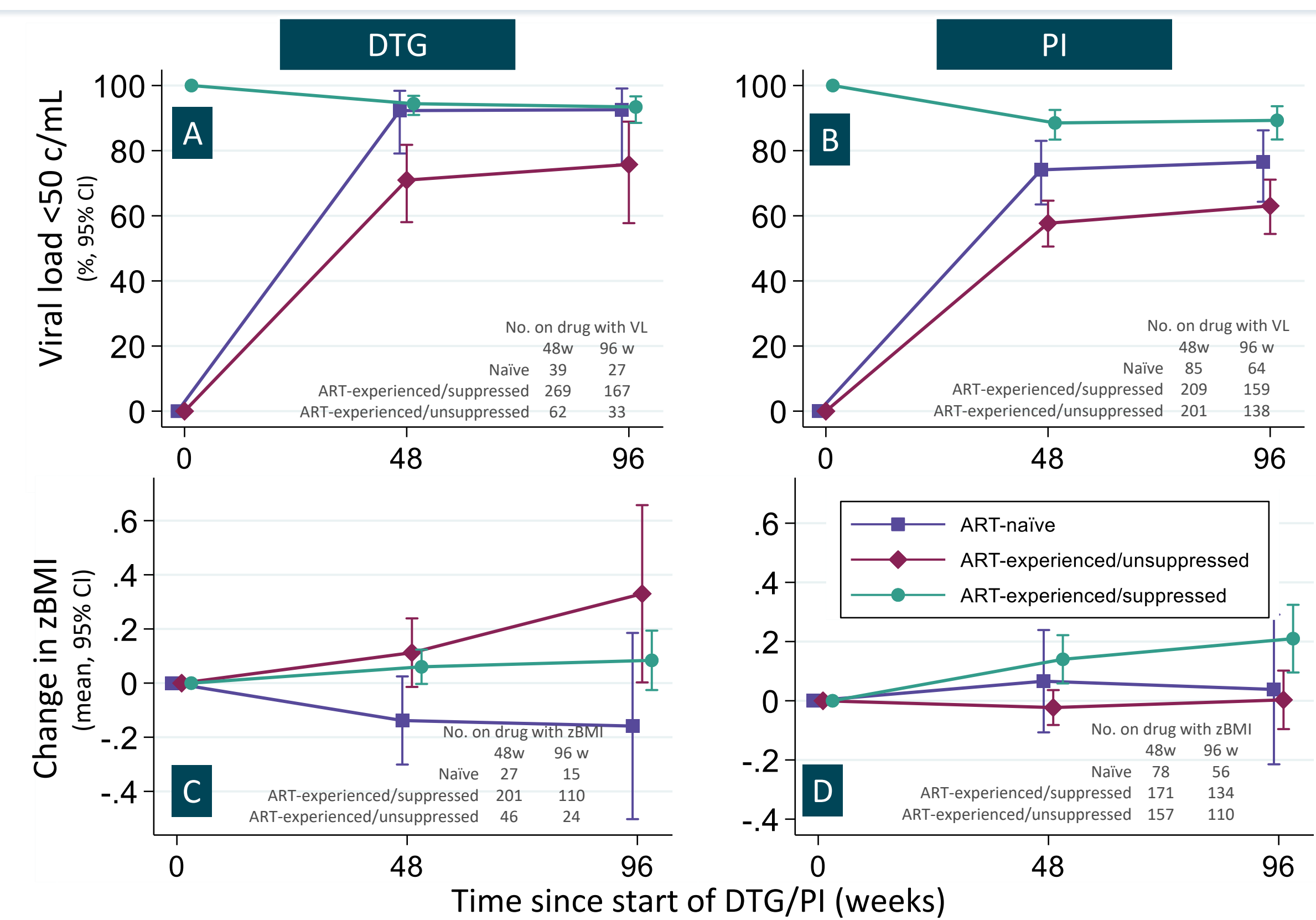


Figure 1: Viral suppression and change in zBMI at 48 and 96 weeks after start of DTG/PI

Table 2: Mean (sd) zBMI and weight at start of DTG/PI by treatment and VL status

Treatment/viral load status	DTG zBMI	PI zBMI	DTG Weight (kg)	PI Weight (kg)
Naïve	0.50 (1.33)	-0.05(1.33)	53 (17)	41 (16)
ART-experienced/VL<50c/mL	0.45 (1.22)	0.22 (1.15)	50 (17)	48 (15)
ART-experienced/VL≥50c/mL	0.62 (1.22)	0.33 (1.17)	55 (16)	51 (16)

Propensity score matching: comparison of outcomes on DTG and PIs

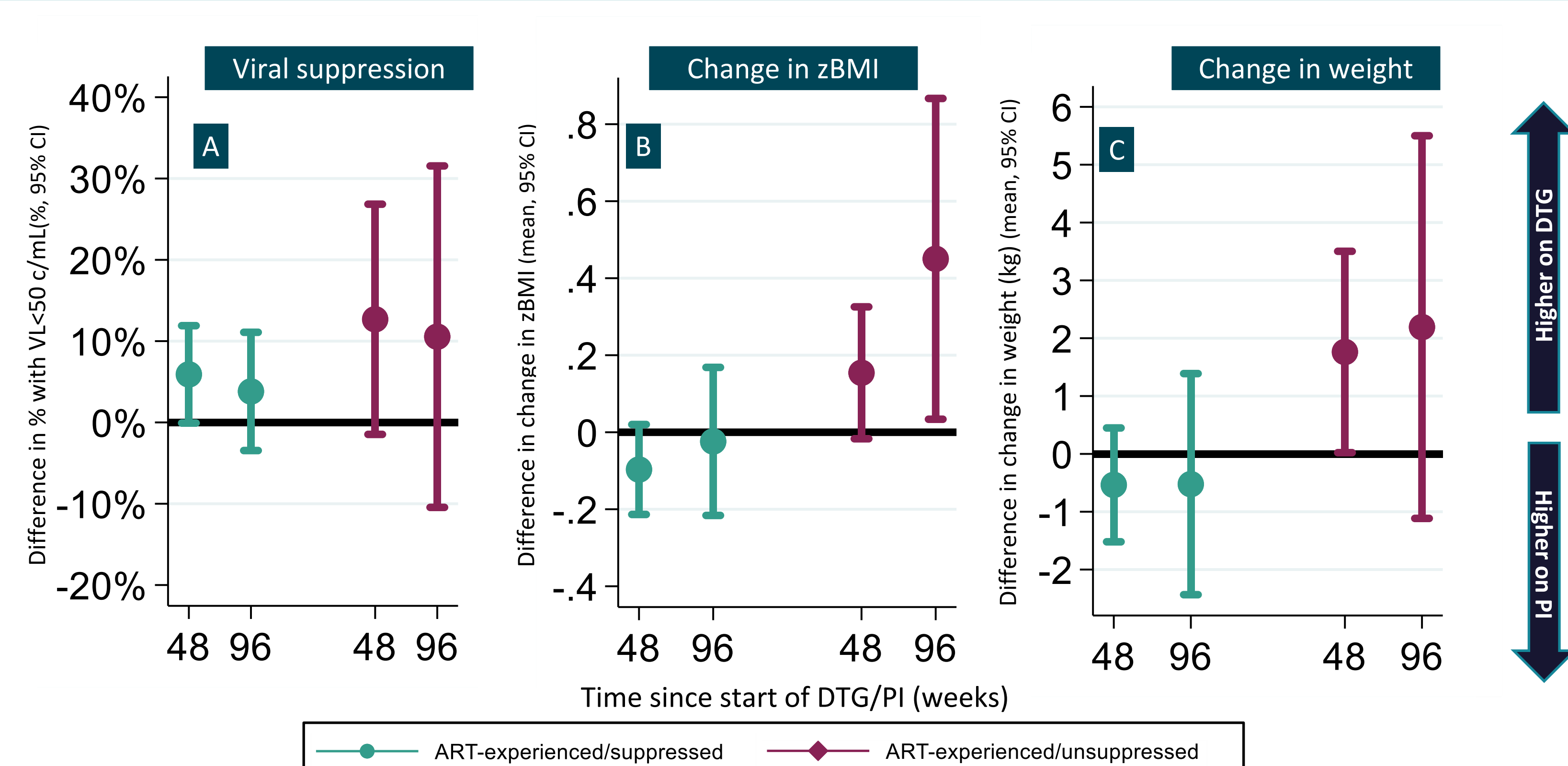


Figure 2: Difference in viral suppression, change in zBMI and change in weight after 48 and 96 weeks on DTG/PI by viral load status at drug start

- After PS matching, **VS was higher on DTG than PI at 48 and 96 weeks though CIs crossed 0** (Fig 2A).
- For children **ART-experienced/unsuppressed, zBMI change was higher on average on DTG than PI though the sample size was small (n=24 had zBMI available at 96 weeks)** (Fig 2B); in this group weight gain was on average **2kg higher on DTG than PI** (Fig 2C).
- For children **ART-experienced/suppressed, changes in zBMI and weight on DTG and PI were not significantly different** (Fig 2B/C).

Summary

- Overall viral suppression was higher on DTG- than PI-based regimens but the differences in the propensity score-matched analysis were not statistically significant.
- Greater gains in zBMI on DTG versus PI were only observed among children ART-experienced and viremic at DTG/PI start. However, numbers were small making it important to corroborate this finding in other datasets.

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