No change in rate of weight gain after switch to integrase inhibitor

Supplemental Digital Content 1

Table: Summary of cohort demographics

	Men	Women*	Overall
Sample (*n*, %)	307 (81.2)	71 (18.8)	378 (100.0)
	[median (IQR)]	[median (IQR)]	[median (IQR)]
Age (years)	49 (43–55)	46 (41–53)	49 (43-55)
ART initiation to INSTI (years)	8.6 (5.2-13.7)	11.6 (8.6-14.7)	9.5 (5.8-14.1)
Time on INSTI (years)	1.26 (0.76-1.64)	1.28 (0.72-1.64)	1.26 (0.76-1.68)
Weight at switch (kg) †	77.0 (70.6–84.6)	73.4 (66.6–84.2)	76.6 (70.1–84.4)
	(*n*=304)	(*n*=68)	(*n*=372)
BMI at switch (kg/m^2)	25.0 (22.8–27.2)	28.0 (24.9–32.4)	25.3 (23.1–27.7)
	(*n*=203)	(*n*=44])	(*n*=247)
CD4+ T-cell count (cells/µL) ‡	610 (490–760)	755 (575–875)	640 (500–790)
	[*n* (%), *n*=307]	[*n* (%), *n*=71]	[*n* (%), *n*=378]
Ethnicity			
White	251 (81.8)	14 (19.7)	265 (70.1)
Black African	20 (6.5)	47 (66.2)	67 (17.7)
Other non-white	36 (11.7)	10 (14.1)	46 (12.2)
INSTI			
RAL	207 (67.4)	41 (57.8)	248 (65.6)
DTG	100 (32.6)	30 (42.3)	130 (34.4)
Pre-switch			
PI	152 (49.5)	41 (57.8)	193 (51.1)
Non-PI	155 (50.5)	30 (42.3)	185 (48.9)
NRTI backbone §			
TDF+FTC+RAL	126 (41.0)	21 (29.6)	147 (38.9)
TDF+FTC+DTG	38 (12.4)	3 (4.2)	41 (10.8)
ABC+3TC+RAL	30 (9.8)	15 (21.1)	45 (11.9)
ABC+3TC+DTG	26 (8.5)	8 (11.3)	34 (9.0)
Variable backbone	87 (28.3)	24 (33.8)	111 (29.4)
Comorbidities ¶			
T2DM	13 (4.2)	6 (8.5)	19 (5.0)
Hypertension	35 (11.1)	17 (23.9)	52 (13.8)
NAFLD	27 (8.8)	3 (4.2)	30 (7.9)
High	49 (16.0)	8 (11.3)	57 (15.1)
IHD/CVD	20 (6.5)	6 (8.5)	26 (6.9)
Renal impairment #	31 (10.1)	6 (8.5)	37 (9.8)
Insomnia	6 (2.0)	3 (4.2)	9 (2.4)
Depression	92 (30.0)	21 (29.6)	113 (29.9)
Hypothyroidism	6 (2.0)	4 (5.6)	10 (2.7)
OSA	1 (0.3)	0	1 (0.3)
Menopause	—	8 (11.3)	8 (2.1)

*Includes one male-to-female transgender, no women were pregnant within two years pre- and post-switch. †Last recorded prior to switch.

‡Last recorded ≤1 year prior to switch. § Individuals had to maintain the same NRTI backbone pre- and post-switch. ¶ Comorbidity data

was collected from reported medical history in patient clinical records. # Includes chronic kidney disease of any cause and proximal renal

tubulopathy.

ABC = abacavir, ART= Antiretroviral therapy, BMI=body mass index, CVD=cerebrovascular disease, DTG=dolutegravir, FTC =

emtricitabine, IQR=interquartile range, IHD=ischaemic heart disease, INSTI = Integrase strand transfer inhibitor, NAFLD=non-alcoholic

fatty liver disease, NRTI = nucleoside reverse transcriptase inhibitor, OSA=obstructive sleep apnoea, PI=Protease Inhibitor,

RAL=raltegravir, TDF = tenofovir disoproxil fumarate, T2DM=type 2 diabetes mellitus, 3TC = lamivudine

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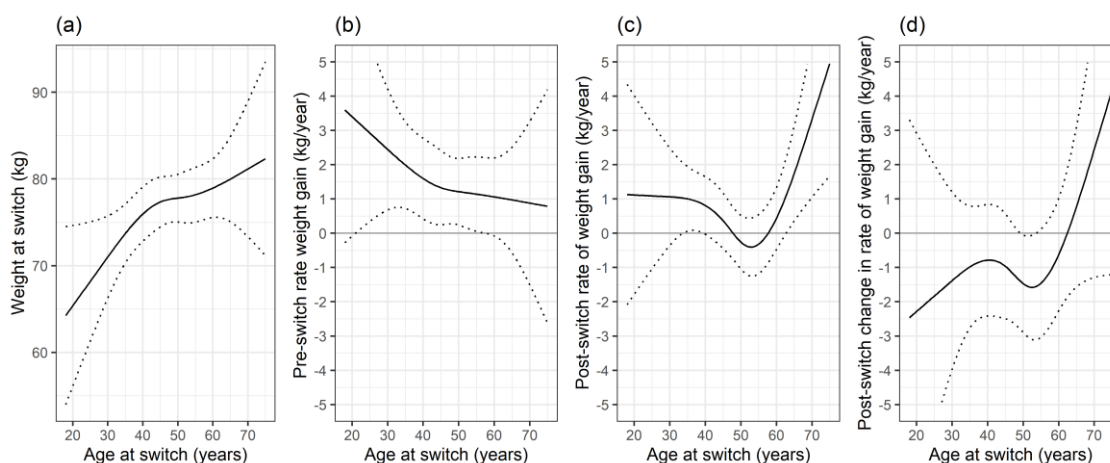**Supplementary Digital Content 2**

Text/Figure/Table: Model of change in rate of weight gain when adjusting for TDF+FTC or ABC+3TC

ABC=abacavir, FTC=emtricitabine, TDF=tenofovir disoproxil fumarate, 3TC=lamivudine

Text

Supplementary Digital Content 2, Figure 1 shows the change in rate of weight gain for individuals who remained on either tenofovir disoproxil fumarate + emtricitabine (TDF+FTC) or abacavir + lamivudine (ABC+3TC) [n=267/378, 71%]. The trajectories of rate of weight gain pre- and post-switch are similar to those in figure 1b-d of the main text. Overall, there was no significant change in the rate of weight gain following switch. When looking for any associations with cohort characteristics (see Supplementary Digital Content 2, Table 1 below), only other non-white ethnicity reached significance for post-switch change in rate of weight gain [p=0.01, 3.11 (0.79 to 5.43)]. However, this subgroup is small (n=39) and should be interpreted with caution.

Figure

Supplementary Digital Content 2, Figure 1 Estimates of average (a) weight at switch to INSTI regimen, (b) pre-switch rate of weight gain (c) post-switch rate of weight gain and (d) post-switch change in rate of weight gain in relation to age at switch among those people on a consistent NRTI backbone made up of TDF+FTC or ABC+3TC. These estimates are derived from models with adjustment for the demographic and treatment characteristics listed in Supplementary Digital Content 2, Table 1 (see below). The plots relate to a white male individual switching from a non-PI to a RAL-based regimen with consistent TDF+FTC NRTI backbone. Dotted lines show pointwise 95% CI. Plot (c) represents a summation of the functions in (b) and (d). ABC=abacavir, CI=confidence interval, FTC=emtricitabine, INSTI=Integrase strand transfer inhibitor, NRTI=nucleoside reverse transcriptase inhibitor, PI=Protease Inhibitor, RAL=raltegravir, TDF=tenofovir disoproxil fumarate, 3TC=lamivudine

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Table

Supplementary Digital Content 2, Table 1 Associations between demographic/treatment characteristics and weight trajectories only amongst those people on a consistent TDF+FTC or ABC+3TC NRTI backbone.

		n (%)	Weight at switch		Pre-switch rate of weight gain (per year)		Post-switch change in rate of weight gain (per year)	
			ΔEst. (95%CI)	P-value	ΔEst. (95%CI)	P-value	ΔEst. (95%CI)	P-value
Weight results (kg)								
Gender	Men	217 (83.1)	0 [Reference]		0 [Reference]		0 [Reference]	
	Women	44 (16.9)	-6.16 (-10.89 to -1.43)	<0.01	-0.87 (-2.49 to 0.76)	0.30	0.47 (-1.91 to 2.85)	0.70
Ethnicity	White	179 (68.6)	0 [Reference]		0 [Reference]		0 [Reference]	
	Black African	43 (16.5)	7.08 (2.23 to 11.93)	<0.01	-0.11 (-1.72 to 1.5)	0.90	0.61 (-1.74 to 2.96)	0.61
	Other non-white	39 (14.9)	3.11 (-1.37 to 7.58)	0.17	-1.65 (-3.25 to -0.06)	0.04	3.11 (0.79 to 5.43)	0.01
Pre-switch	Non-PI	143 (54.8)	0 [Reference]		0 [Reference]		0 [Reference]	
	PI	118 (45.2)	1.80 (-1.39 to 5.00)	0.27	-0.73 (-1.86 to 0.4)	0.21	1.18 (-0.42 to 2.78)	0.15
Post-switch	RAL	188 (72.0)	0 [Reference]		0 [Reference]		0 [Reference]	
	DTG	73 (28.0)	-1.00 (-4.60 to 2.60)	0.59	0.02 (-1.27 to 1.3)	0.98	-0.35 (-2.14 to 1.45)	0.71
NRTI backbone	TDF+FTC	184 (70.5)	0 [Reference]		0 [Reference]		0 [Reference]	
	ABC+3TC	77 (29.5)	0.92 (-2.52 to 4.36)	0.60	0.33 (-0.86 to 1.51)	0.59	-0.87 (-2.54 to 0.81)	0.31

Associations between demographic/treatment characteristics and both average weight and BMI trajectories during the two years before and after switch to a RAL or DTG-based INSTI regimen. Adjusted for age at switch and the other variables listed in the table. Estimates are expressed relative (Δ) to the average value at any given age (Figure 1). ABC= abacavir, BMI=Body Mass Index, CI=Confidence Interval, DTG=dolutegravir, FTC=emtricitabine, NRTI=nucleoside reverse transcriptase inhibitor, PI=Protease Inhibitor, RAL=raltegravir, TDF=tenofovir disoproxil fumarate, 3TC=lamivudine.