Background and Methods

Background

- Weight gain has been associated with the use of the integrase inhibitor dolutegravir (DTG)[1], which is often prescribed in combination with the NRTI[2] tenofovir alafenamide (TAF)
- The independent effects of newer antiretrovirals (ARVs) on weight gain are not fully understood

Objective

- In the RESPOND Cohort Study, to investigate associations between >7%[3] BMI increase and ARV use by comparing pre-ARV BMI to current BMI for each ARV received at each BMI measurement

Statistical Methods

- Logistic regression using generalised estimating equations was used to identify individual ARVs that were associated with first occurrence of >7% BMI increase (and >30% BMI increase [top 5% of weight gainers]), with lamivudine (3TC) as the reference ARV
- Analyses were adjusted for time on specific ARV, pre-ARV BMI, demographics, geographical region, CD4 count and viral load

[1] *Observational studies: Bakal 2018, Bourgi 2020, Kerchberger 2020, Lake 2020, RCTs: ADVANCE 2019, NEAT 2020, NAMSAL 2020.*
[2] *NRTI: nucleotide-analogue reverse transcriptase inhibitor.* [3] *Given lack of consensus on definition of weight gain in the HIV field, >7% increase based on standard definition used in psychiatry (Predictors and Moderators of Antipsychotic-Related Weight Gain in the Treatment of Early-Onset Schizophrenia Spectrum Disorders Study, Taylor et al J Child Adolesc Psychopharmacol. 2018)*
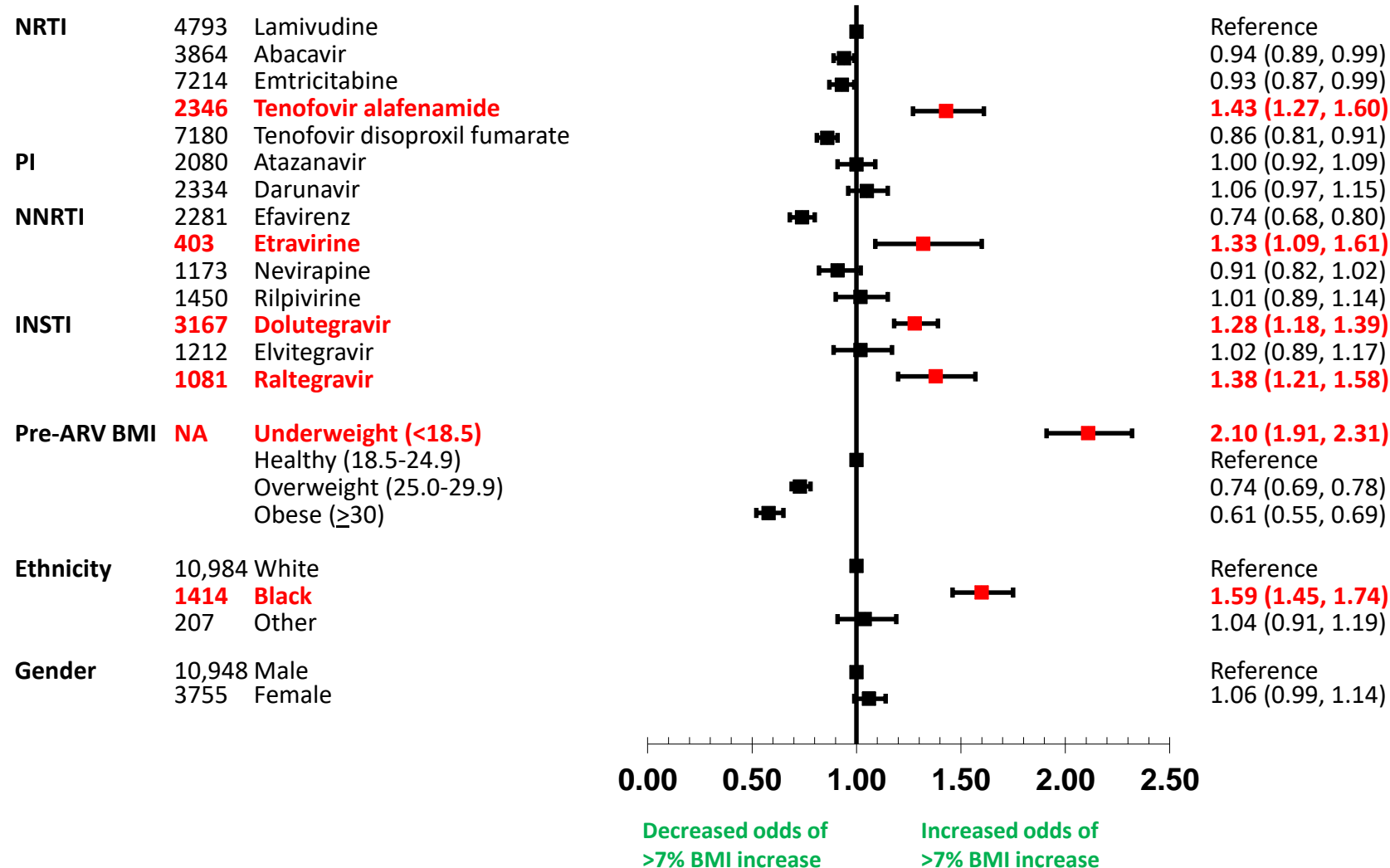
Results

- Baseline = Pre-ARV BMI of each ARV being received on or after RESPOND entry (> 2012).

- 14,703 people from across Europe and Australia were included (median 2.6 (interquartile range [IQR]: 1.2, 5.2) years follow-up, 4 (3, 5) weight measurements), of whom 7863 (54%) experienced >7% increase in BMI

- Baseline demographics (first pre-ARV BMI): 20% ART-naïve, 39% on INSTIs, 74% male, 75% White ethnicity (9% Black ethnicity) and 45% MSM

- Median interquartile range (IQR) age and CD4 count: 43 (36, 51) years and 442 (283, 651) cells/mm^3

Number of people ever exposed to ARV
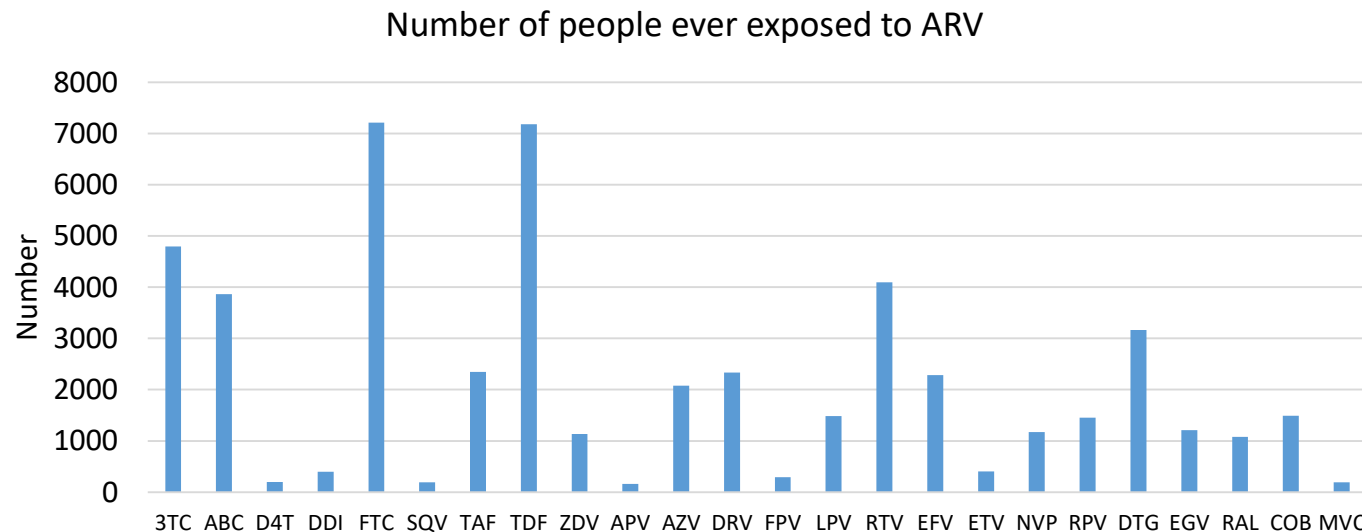
Multivariate odds ratios of >7% BMI increase from pre-ARV BMI

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| ARV	N (for ARVs, N refers to ever exposed; N not given for pre-ARV BMI as this is dependant on ARV, not person)		

Category	N	ARV	Odds Ratio (95% CI)
NRTI	4793	Lamivudine	Reference
	3864	Abacavir	0.94 (0.89, 0.99)
	7214	Emtricitabine	0.93 (0.87, 0.99)
	2346	**Tenofovir alafenamide**	**1.43 (1.27, 1.60)**
	7180	Tenofovir disoproxil fumarate	0.86 (0.81, 0.91)
PI	2080	Atazanavir	1.00 (0.92, 1.09)
	2334	Darunavir	1.06 (0.97, 1.15)
NNRTI	2281	Efavirenz	0.74 (0.68, 0.80)
	403	**Etravirine**	**1.33 (1.09, 1.61)**
	1173	Nevirapine	0.91 (0.82, 1.02)
	1450	Rilpivirine	1.01 (0.89, 1.14)
INSTI	**3167**	**Dolutegravir**	**1.28 (1.18, 1.39)**
	1212	Elvitegravir	1.02 (0.89, 1.17)
	1081	**Raltegravir**	**1.38 (1.21, 1.58)**
Pre-ARV BMI	**NA**	**Underweight (<18.5)**	**2.10 (1.91, 2.31)**
		Healthy (18.5-24.9)	Reference
		Overweight (25.0-29.9)	0.74 (0.69, 0.78)
		Obese (≥30)	0.61 (0.55, 0.69)
Ethnicity	10,984	White	Reference
	1414	**Black**	**1.59 (1.45, 1.74)**
	207	Other	1.04 (0.91, 1.19)
Gender	10,948	Male	Reference
	3755	Female	1.06 (0.99, 1.14)

Scale: 0.00 0.50 1.00 1.50 2.00 2.50

Decreased odds of >7% BMI increase ← → **Increased odds of >7% BMI increase**

(Odds ratios for amprenavir, cobicistat, stavudine , didanosine, fosamprenavir, lopinavir, maraviroc, ritonavir, saquinavir and zidovudine, unknown ethnicity not shown).
Model also adjusted for time on ARV, age at baseline, risk group, region, CD4/VL at start of follow up, smoking status, diabetes, dyslipidaemia, hypertension, viral hepatitis, and clinical events at start of follow up.

Association between DTG, TAF (vs. 3TC) and >7% BMI increase by model
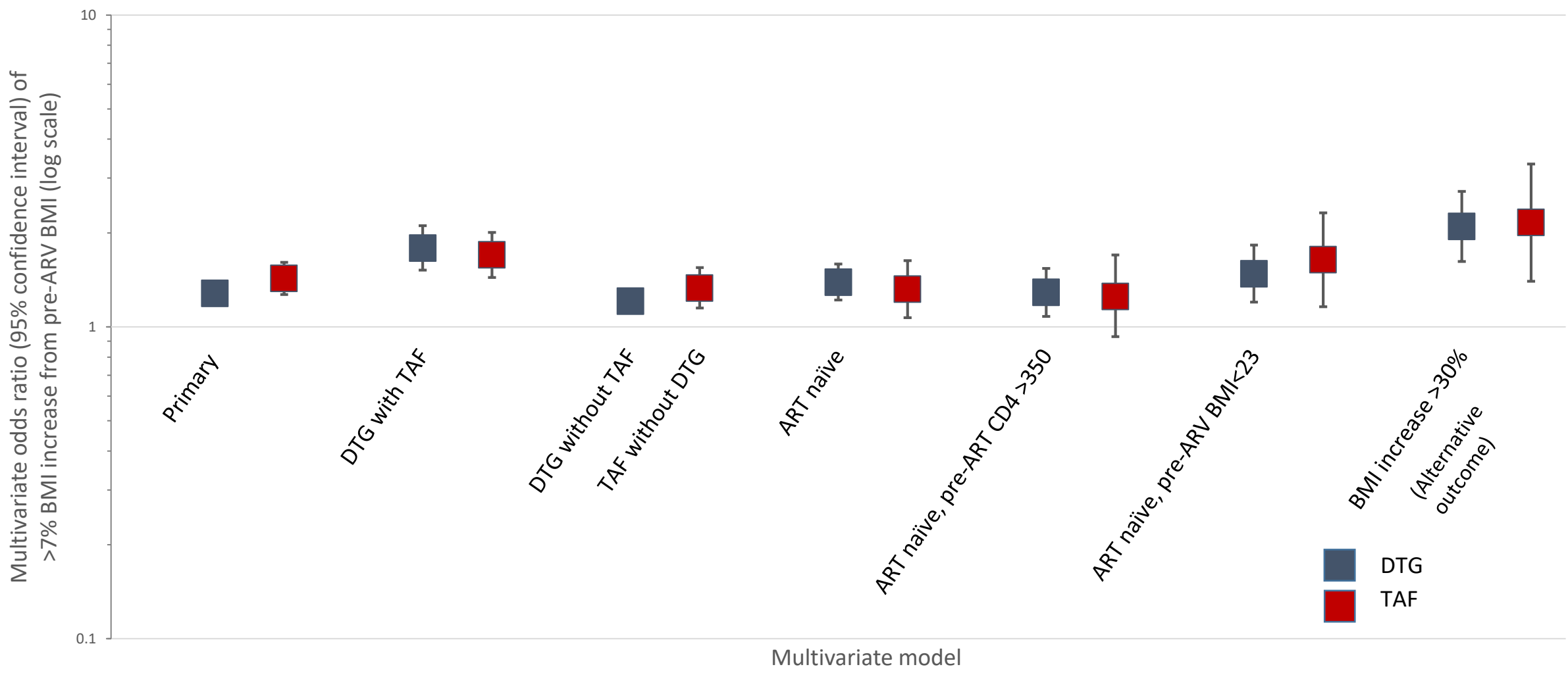
Primary model refers to that seen on the previous slide, adjusted for ARV, pre-ARV BMI, ethnicity, gender, time on ARV, age at baseline, risk group, region, CD4/VL at start of follow up, smoking status and AIDS events at start of follow up.

Limitations and Conclusions

- Data on other factors influencing weight such as diet and exercise, and on BIC not collected

- Use of DTG, etravirine, raltegravir and TAF were independently associated with >7% BMI increase compared to 3TC, as was low pre-ARV BMI and black ethnicity

- Combined use of TAF and DTG was associated with greater risk of >7% BMI increase compared to 3TC. Use of DTG without TAF, and TAF without DTG were also significantly associated with BMI increase

- DTG and TAF were also associated with >7% BMI increase amongst naïve individuals and those naïve with CD4 count >350. Associations also remained significant when the outcome was >30% BMI increase in all individuals.

- Clinicians and people living with HIV should be aware of the effects of the potential weight gain associated with drugs such as DTG and TAF when making the decision to start these ARVs. Further analyses looking at the impact of weight gain on metabolic markers are planned