

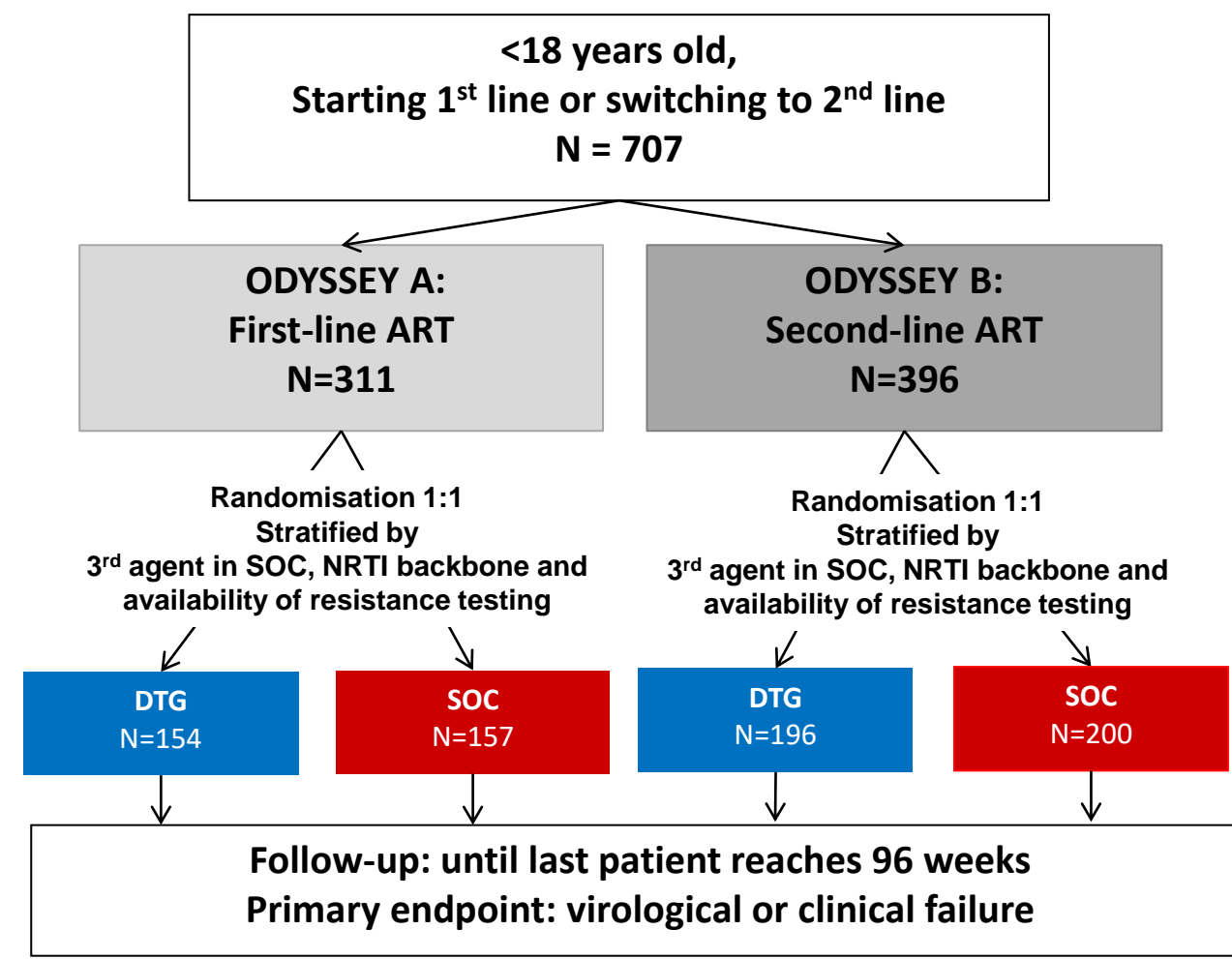
Background

- Dolutegravir is associated with excessive weight gain in adults.
- ADVANCE trial reported 10kg weight gain on DTG+TAF/FTC and 6kg on DTG+TDF/FTC over 144 weeks.[1]
- There are limited and conflicting data on DTG-associated weight gain in observational studies in children.
- A study in the UK CHIPS cohort (n=300) showed no difference in change of BMI-for-age at 12 months after switch to DTG vs PI-based ART in virologically suppressed children.[2]
- A retrospective study in Eswatini (n=460) showed that switch to DTG in virologically suppressed adolescents was associated with an increase in the rate of BMI gain. [3]
- A small study in the US adolescents (n=51) has also shown a greater rate of BMI and BMI-for-age increase following switch to INSTI [4]
- We present the first randomised data in children and adolescents.

Methods

- ODYSSEY is a randomised multi-country trial evaluating dolutegravir + 2NRTIs (DTG) versus standard-of-care (SOC) in children starting first-line or second-line ART
- The main trial enrolled children ≥ 14 kg between September 2016 and June 2018
- We compared weight, height, BMI and BMI-for-age Z-scores (BAZ) between treatment arms using normal regression models adjusting for first-/second-line, randomisation stratification factors and baseline measurements
- The difference in treatment effect on BAZ in the DTG and SOC arms was assessed by first- and second treatment lines, sex, age and NRTI backbone (non-TDF vs TDF)
- Proportions becoming newly overweight (BAZ > 1- ≤ 2) or newly obese (BAZ > 2) are described

ODYSSEY trial schema



Results

- 707 children were randomised (sub Saharan Africa 88%, Thailand 9%, Europe 4%)
- 311 started first-line (92% efavirenz-based in SOC); 396 second-line (72% lopinavir/ritonavir, 25% atazanavir/ritonavir in SOC)
- 65% initiated ABC+3TC, 23% TDF+XTC, 11% ZDV+3TC
- At baseline, median age was 12.2 years (IQR 9.1, 14.9; range 2.9-18.0)
- 49% were female
- Median follow-up 142 weeks (IQR 124, 159)

Population at baseline (n=707)

Weight, Height and BMI at baseline

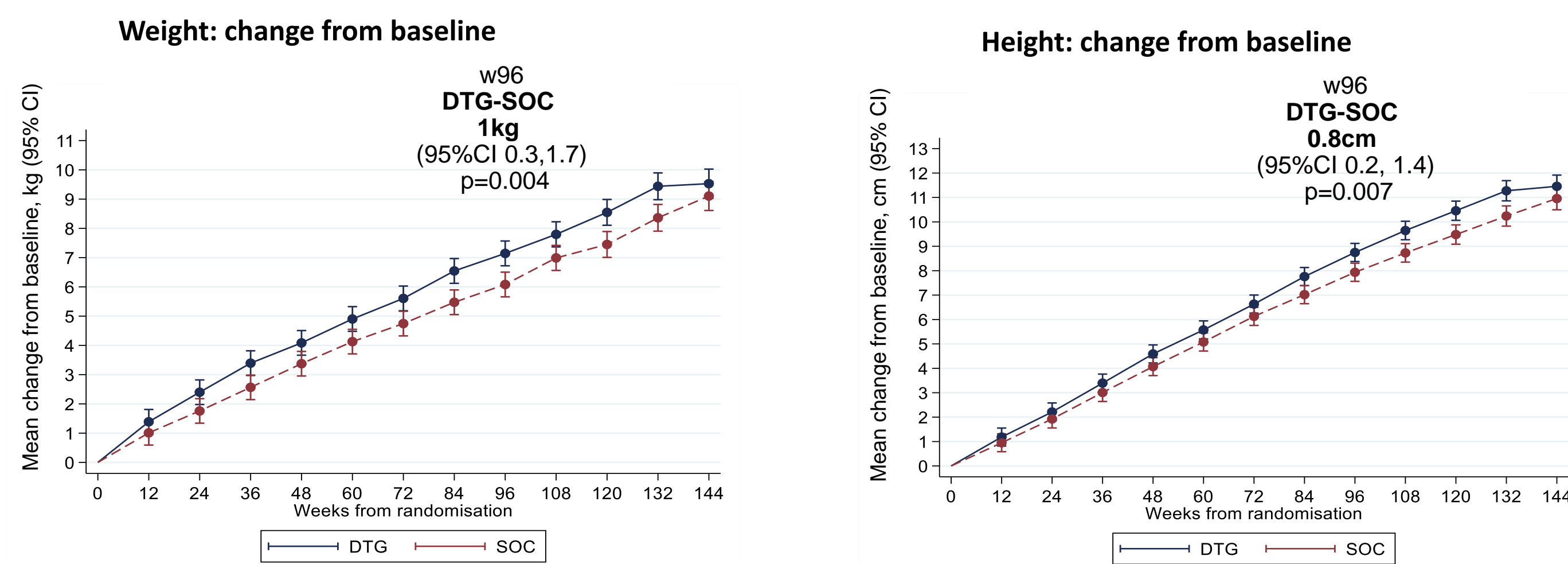
	Median	IQR	Range
Weight, kg	31	(24, 43)	[14 to 85]
Height, cm	138	(125, 153)	[89 to 182]
BMI, kg/m ²	16.3	(14.9, 18.5)	[9.8, 34.5]
BMI-for-age, Z-score*	-0.6	(-1.4, 0.0)	[-7.8, 2.8]

*using UK WHO Term Reference 2009

At baseline

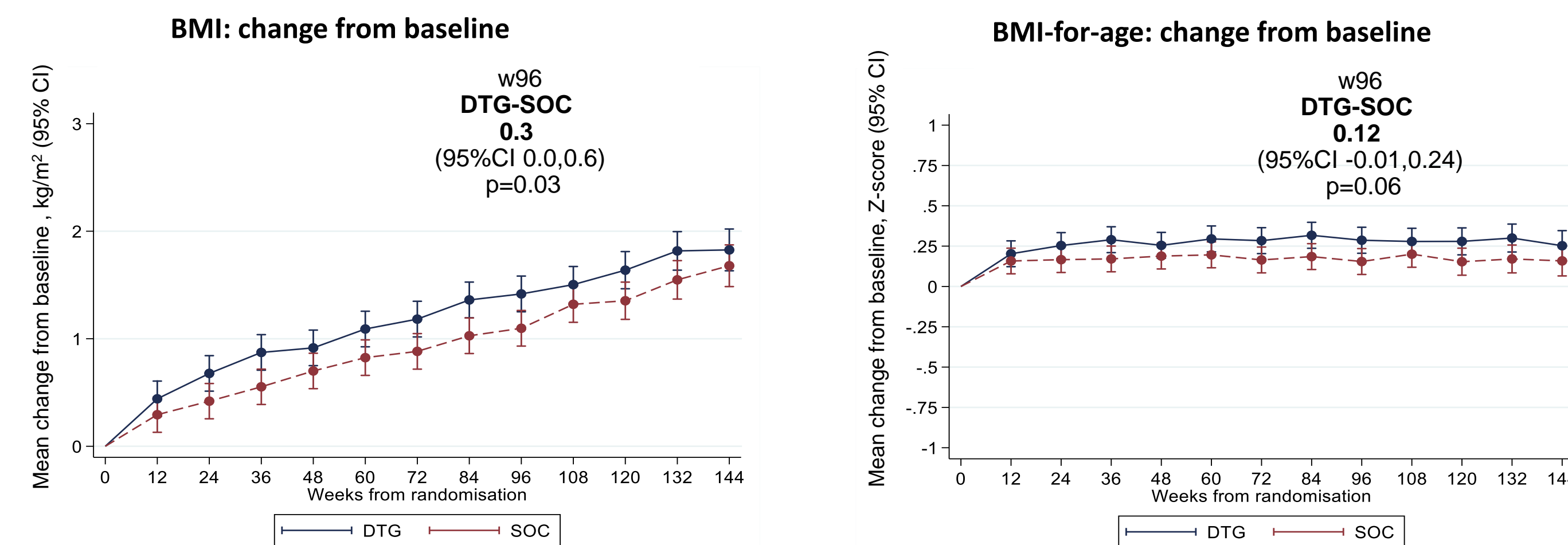
- 11% had severe thinness/thinness (BMI-for-age < -2 SD)
- 5% were overweight (BMI-for-age > 1SD to ≤ 2 SD)
- 1% obese (BMI-for-age > 2SD)

Change in weight and height



- Small additional gains from baseline in weight and height in DTG vs. SOC
- At 96 weeks mean additional gain in DTG vs SOC in weight was 1kg, and in height 0.8cm
- The differences occurred early and stabilised

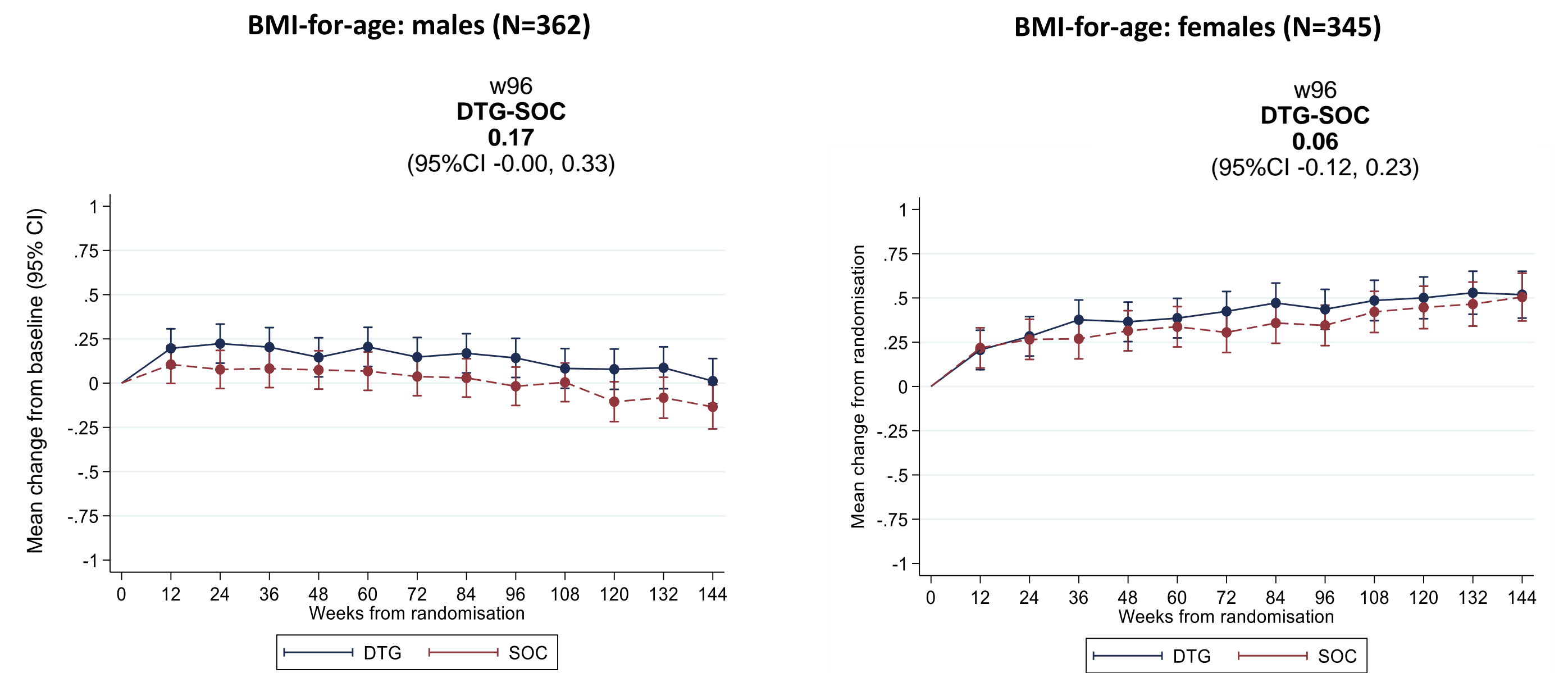
Change in body mass index (BMI) and BMI-for-age



- Small additional gains from baseline in BMI and BMI-for-age in DTG vs. SOC
- Over 96 weeks mean additional gain in BMI in DTG vs SOC was 0.3 kg/m², and in BAZ 0.12 SD
- The gap between arms did not increase with time

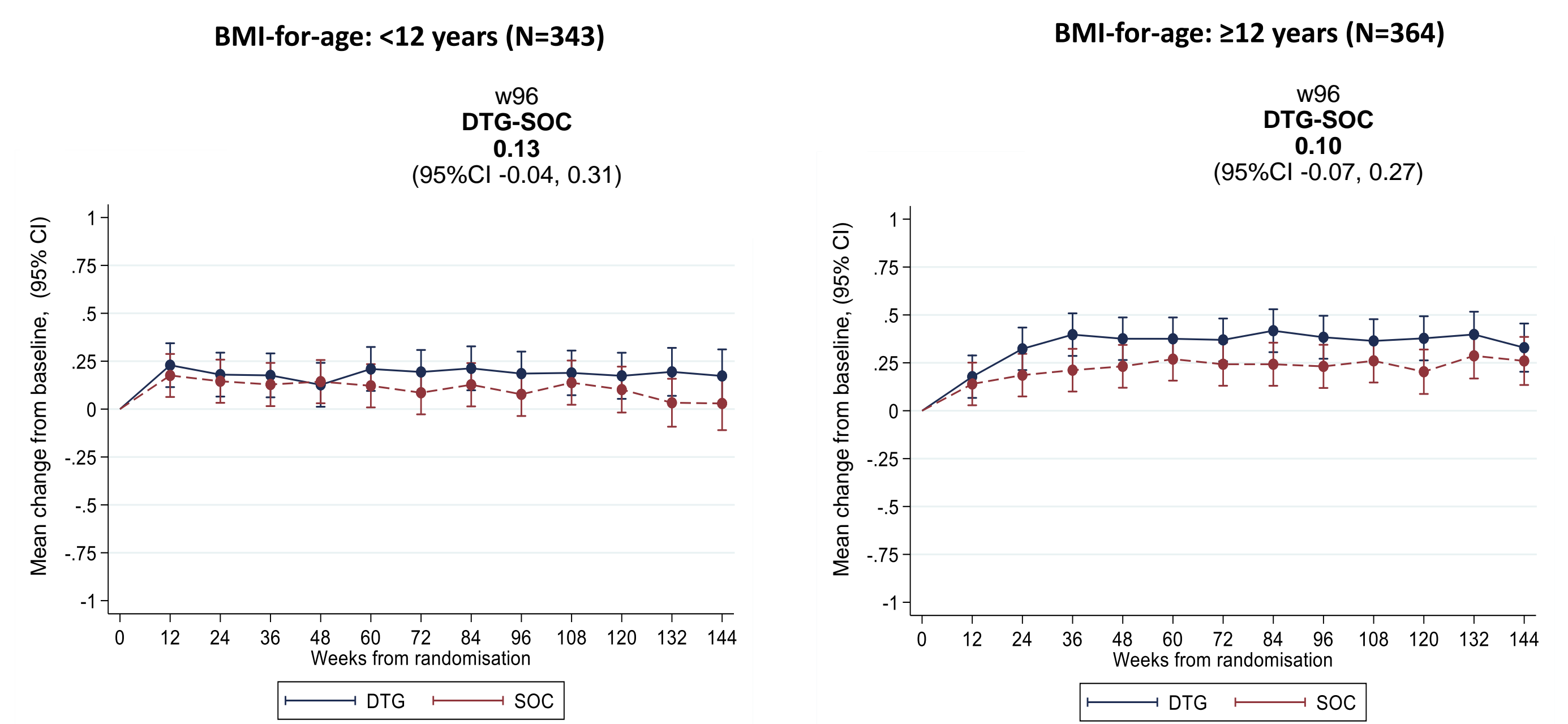
Results

Change in BMI-for-age: by sex



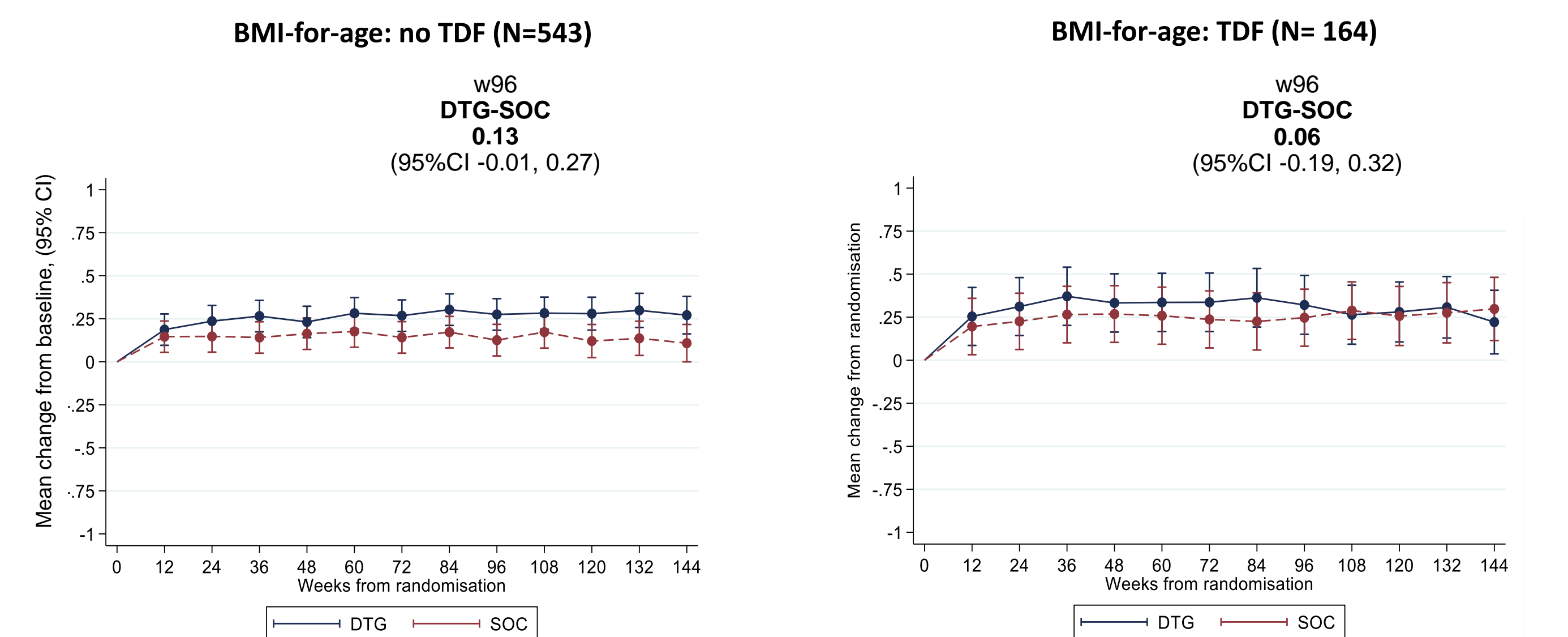
- Treatment effects did not differ significantly between boys and girls (heterogeneity p=0.37)

Change in BMI-for-age: by baseline age group



- There was no difference in treatment effects by age group (heterogeneity p=0.78)

Change in BMI-for-age: by TDF at baseline



- Treatment effects did not differ significantly between children not on TDF and those on TDF (heterogeneity p=0.65)

New overweight and obesity

- Overall, 25 (4%) were newly overweight or obese at 96 weeks: 14 (4%) in the DTG arm & 11 (3%) in SOC (p=0.55)
- Characteristics of those newly overweight or obese:
 - Median age at enrolment: 13.0 years (IQR 10.3, 15.4)
 - 15/311 (5%) on first-line vs 10/396 (3%) on second-line ART
 - 15/345 (4%) females vs 10/362 (3%) males
 - 10/167 (6%) on TDF vs 15/540 (3%) not on TDF

Conclusions

- Children grew better after starting DTG compared to non-DTG ART
- Differences between arms in weight, height and BMI were small and stabilised
- Differences between arms were similar by: first- or second-line, sex, age and NRTI backbone (non-TDF / TDF)
- Few became newly overweight or obese in either arm
- DTG-based ART was not associated with excessive weight gain in children and adolescents**

References

- Hindley. CROI 2021. Abs 117
- Crichton et al. HIV Pediatrics 2019
- Thivalapill et al. CID 2020
- Dirajlal-Fargo et al. CROI 2020

