

Growth of infants with perinatal exposure to maternal DTG vs EFV and TDF vs TAF: the randomized IMPAACT 2010 trial

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<https://www.impaactnetwork.org/studies/impaact2010>

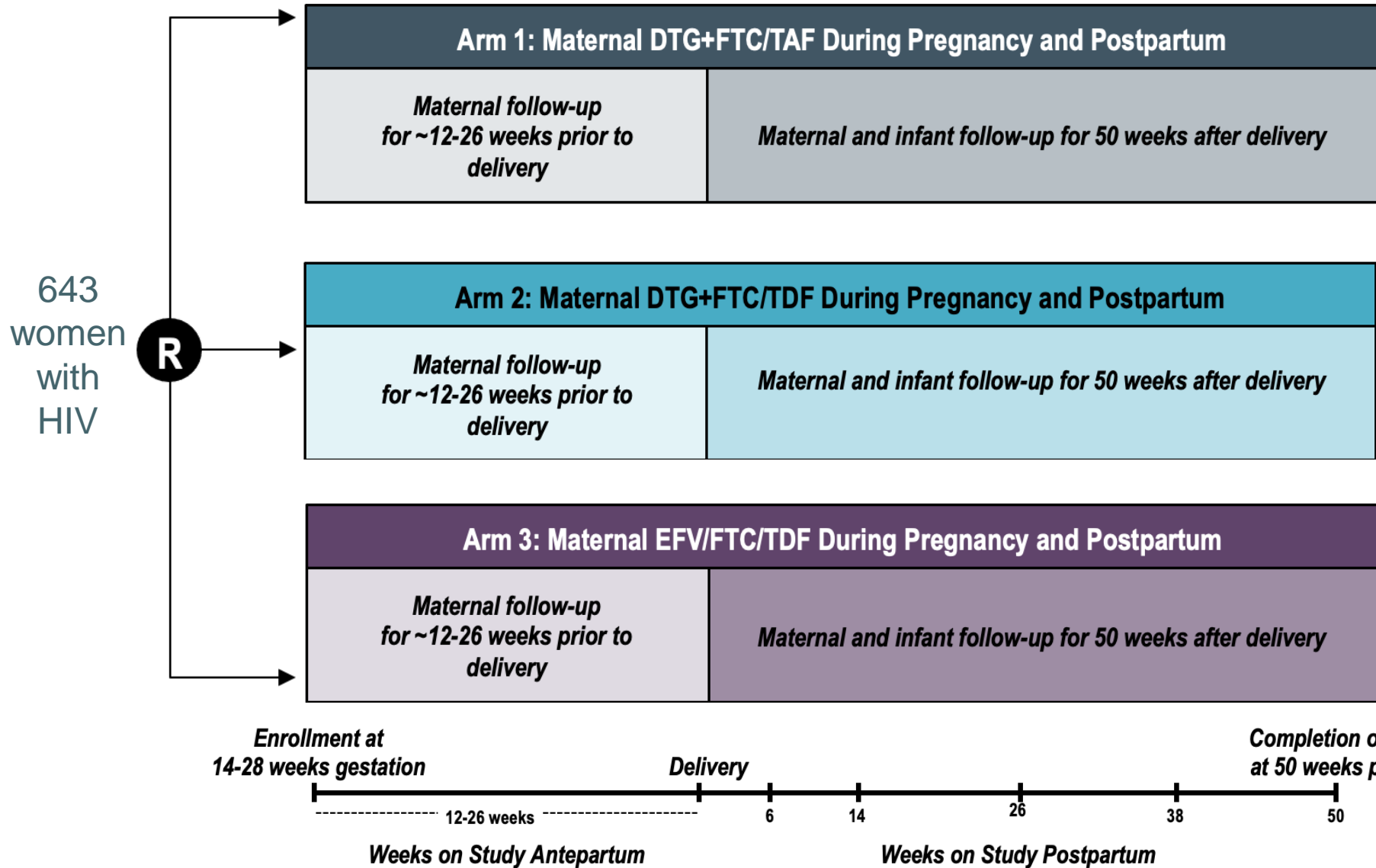
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Background



- ▶ Impact of contemporary antiretrovirals taken in pregnancy/breastfeeding on infant growth is not fully established
- ▶ Stunting in infancy impacts cognitive development and adult height
- ▶ We compared growth through 1 year of age in infants randomized to one of 3 maternal ART regimens started in pregnancy in the IMPAACT 2010 trial

Randomized Open-label Trial of the Virologic Efficacy and Safety of Three ART Regimens Started in Pregnancy



Participants enrolled at 22 sites in 9 countries

DTG = dolutegravir
 FTC = emtricitabine
 TAF = tenofovir alafenamide
 TDF = tenofovir disoproxil fumarate
 EFV = efavirenz

Key Eligibility Criteria

- Pregnant WLHIV 14-28 weeks gestation
- ART-naïve (up to 14 days ART in current pregnancy allowed)

Key Outcomes at Delivery/Birth

▶ Maternal **DTG-containing ART** vs **EFV/FTC/TDF**:

- ▶ Superior virologic efficacy at delivery
- ▶ Closer to expected weight gain in pregnancy

Insufficient weight gain in pregnancy: **DTG+FTC/TAF 15%** vs **DTG+FTC/TDF 24%** vs **EFV/FTC/TDF 30%**

▶ Maternal **DTG+FTC/TAF** lowest composite frequency of adverse pregnancy outcome**

Low weight gain in pregnancy associated with the composite adverse pregnancy outcome

▶ Liveborn infants—similar except for weight

- ▶ Higher proportion low birth weight <2500g **EFV/FTC/TDF**

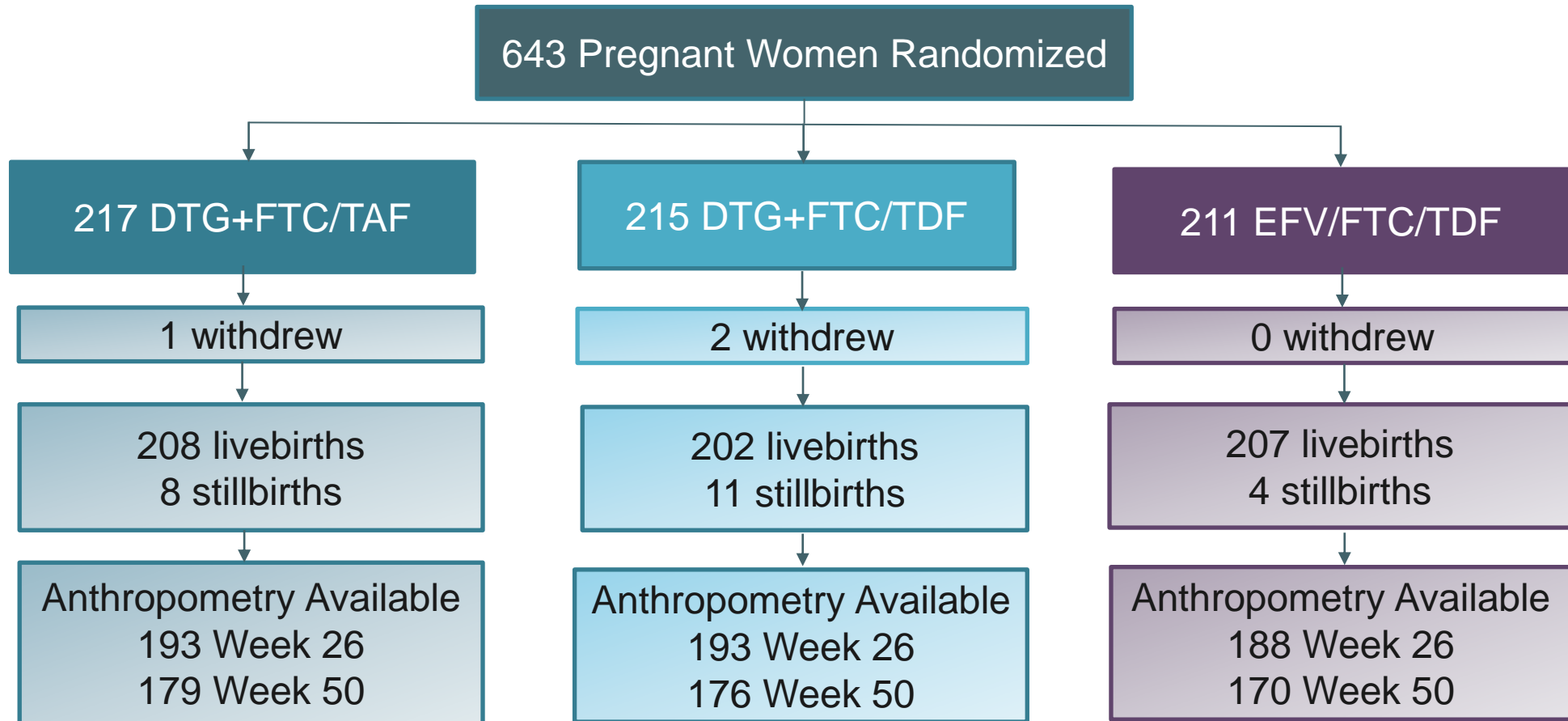
Low Birth Weight: **DTG+FTC/TAF 6.4%** vs **DTG+FTC/TDF 9.5%** vs **EFV/FTC/TDF 12.0%**

**Poster 679 Brummel; Other IMPAACT 2010 posters—Fairlie; Chinula; Boyce

Additional Infant Characteristics

	DTG+FTC/TAF (N = 208)	DTG+FTC/TDF (N = 202)	EFV/FTC/TDF (N = 207)	Total (N = 617)
Initiated breastfeeding, n (%)	161 (77)	158 (78)	160 (77)	479 (78)
Median (Q1, Q3) breastfeeding duration (weeks)	50 (44, 51)	50 (44, 51)	50 (41, 51)	50 (43, 51)
ARV prophylaxis, n (%)	203 (98)	200 (99)	196 (95)	599 (97)
Cotrimoxazole prophylaxis, n (%)	179 (86)	174 (86)	169 (82)	522 (85)
Acquired HIV, n (%)	2 (1)	1 (0.5)	1 (0.5)	4 (0.6)

Inclusion Flow Chart

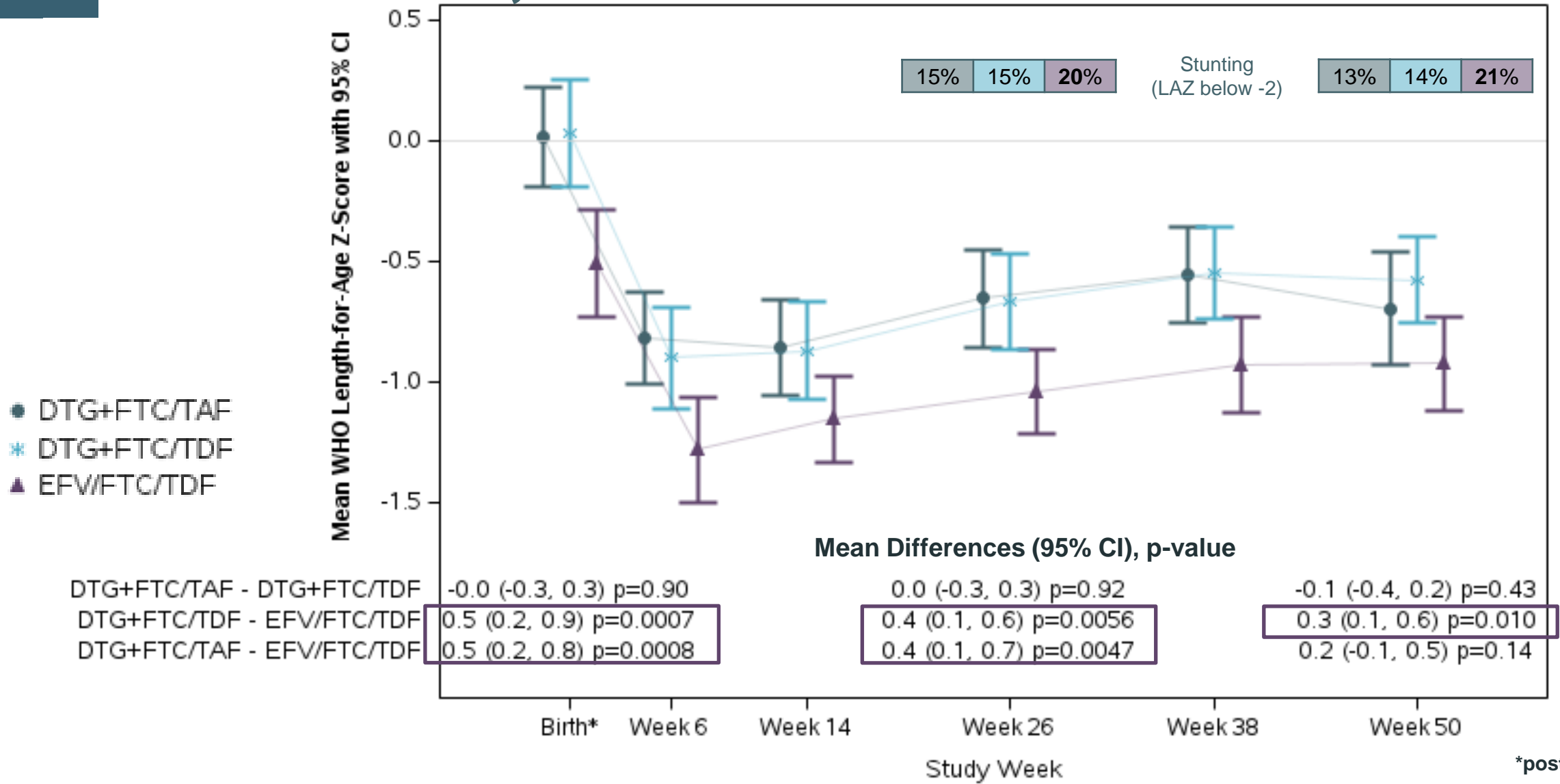


20 infants died: DTG+FTC/TAF— 2 (1%); DTG+FTC/TDF—4 (2%); EFV/FTC/TDF—14 (7%)

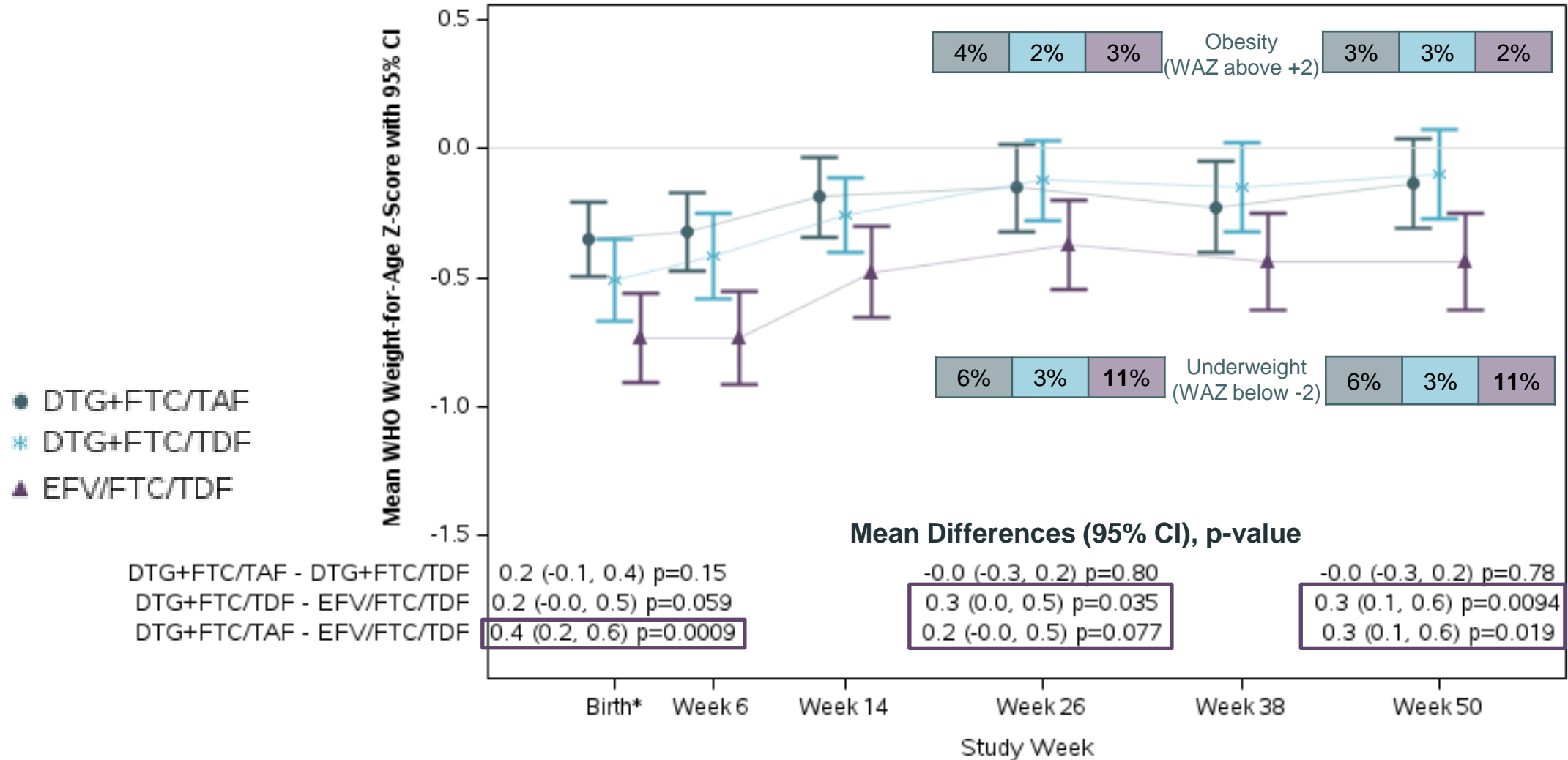
Infant Growth Statistical Approach

- ▶ Infant growth WHO Z-scores computed at Weeks 26 and 50 for liveborn infants retained on-study with length and weight data available:
 - Length-for-age (LAZ)
 - Weight-for-age (WAZ)
 - Weight-for-length (WHZ)
- ▶ WHO standards and software used for Z-score calculations (www.who.int/childgrowth/software/en)
- ▶ Pairwise comparisons of mean z-scores by two-sample t-tests
- ▶ Proportion stunting (LAZ < -2) estimated

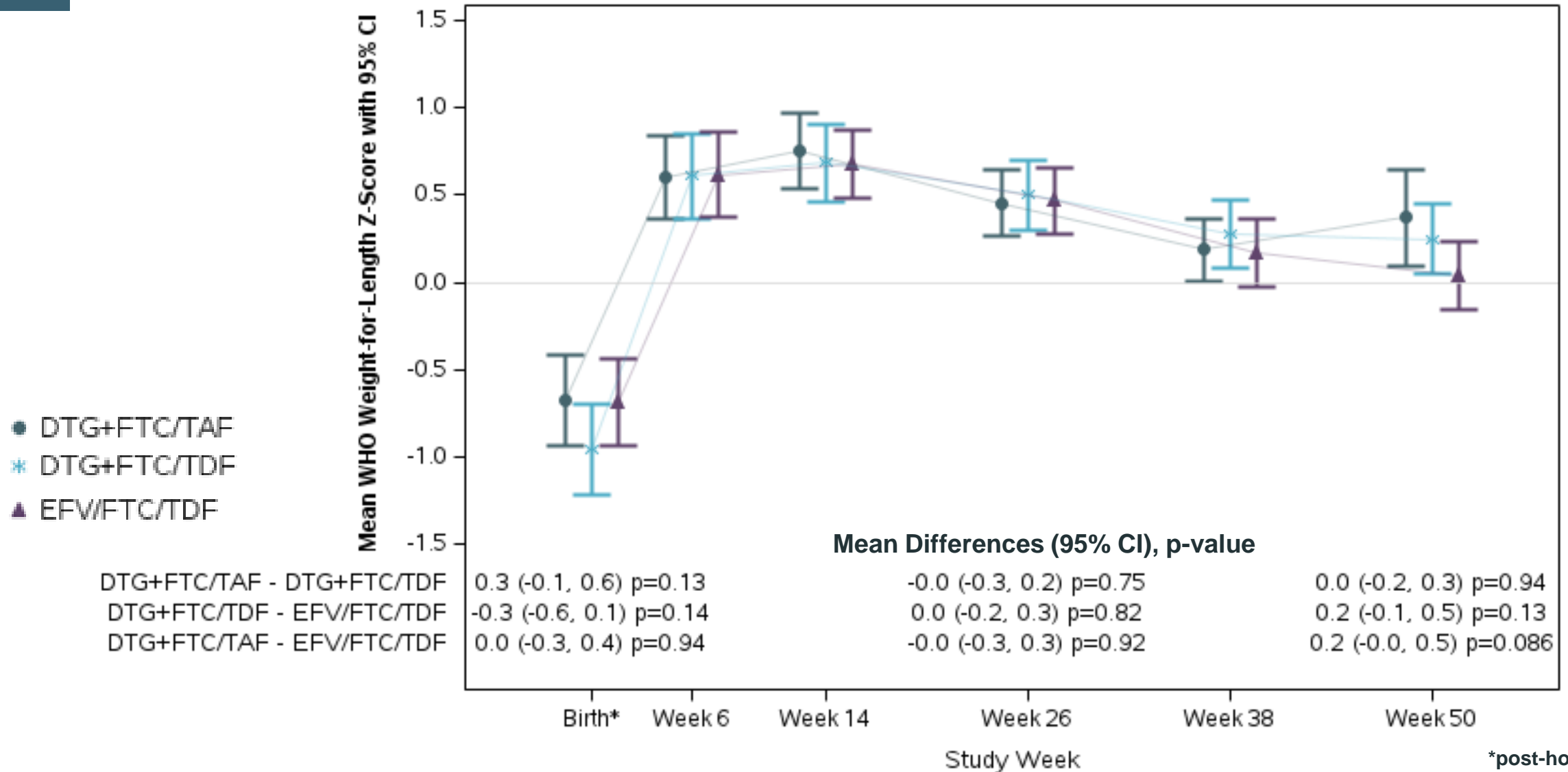
Length-for-Age Z-scores lower in EFV vs DTG arms, similar TDF- vs TAF-DTG



Weight-for-Age Z-scores lower in EFV vs DTG arms, similar TDF- vs TAF-DTG



Weight-for-Length Z-scores, no apparent differences



Limitations

- ▶ Infant follow-up limited to one year of age
- ▶ Included women who started ART in pregnancy (not women conceiving on ART)
- ▶ Predominantly breastfeeding populations studied, primarily in Africa

Conclusions

- ▶ Infants born to mothers who started **EFV/FTC/TDF** in pregnancy were significantly smaller throughout infancy than infants whose mothers started **DTG+FTC/TAF** or **DTG+FTC/TDF**
- ▶ Rates of stunting were high across all arms and higher in **EFV** arm (1 in 5) than the DTG arms (1 in 7)
- ▶ Mechanisms of this difference remain unclear
 - ▶ Potential influence of differential maternal weight gain in pregnancy
- ▶ Infant growth was similar following exposure to maternal TDF vs. **TAF** in combination with DTG+FTC
- ▶ No increase in infant obesity with maternal DTG vs **EFV**

Conclusions

- ▶ **EFV** use in pregnancy associated with concerning [low] growth parameters during first year of life
- ▶ Extended follow-up required to assess persistence of observed differences
- ▶ Infant growth should be factored into the choice of optimal maternal ART regimens during pregnancy and breastfeeding

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