Bone mineral density/content of postpartum mothers taking treatment including DTG vs EFV, TDF vs TAF in pregnancy and their infants: randomized IMPAACT 2010 trial

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

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Background

- TDF-containing ART regimens are associated with greater bone loss than regimens without TDF
- The impact of the use of DTG, EFV, TDF and TAF in pregnancy and postpartum on maternal and infant bone is unknown

DTG- Dolutegravir

EFV- Efavirenz

TDF- Tenofovir Disoproxil Fumarate

TAF- Tenofovir Alafenamide

Grant, Current Opinion HIV AIDS. 2016

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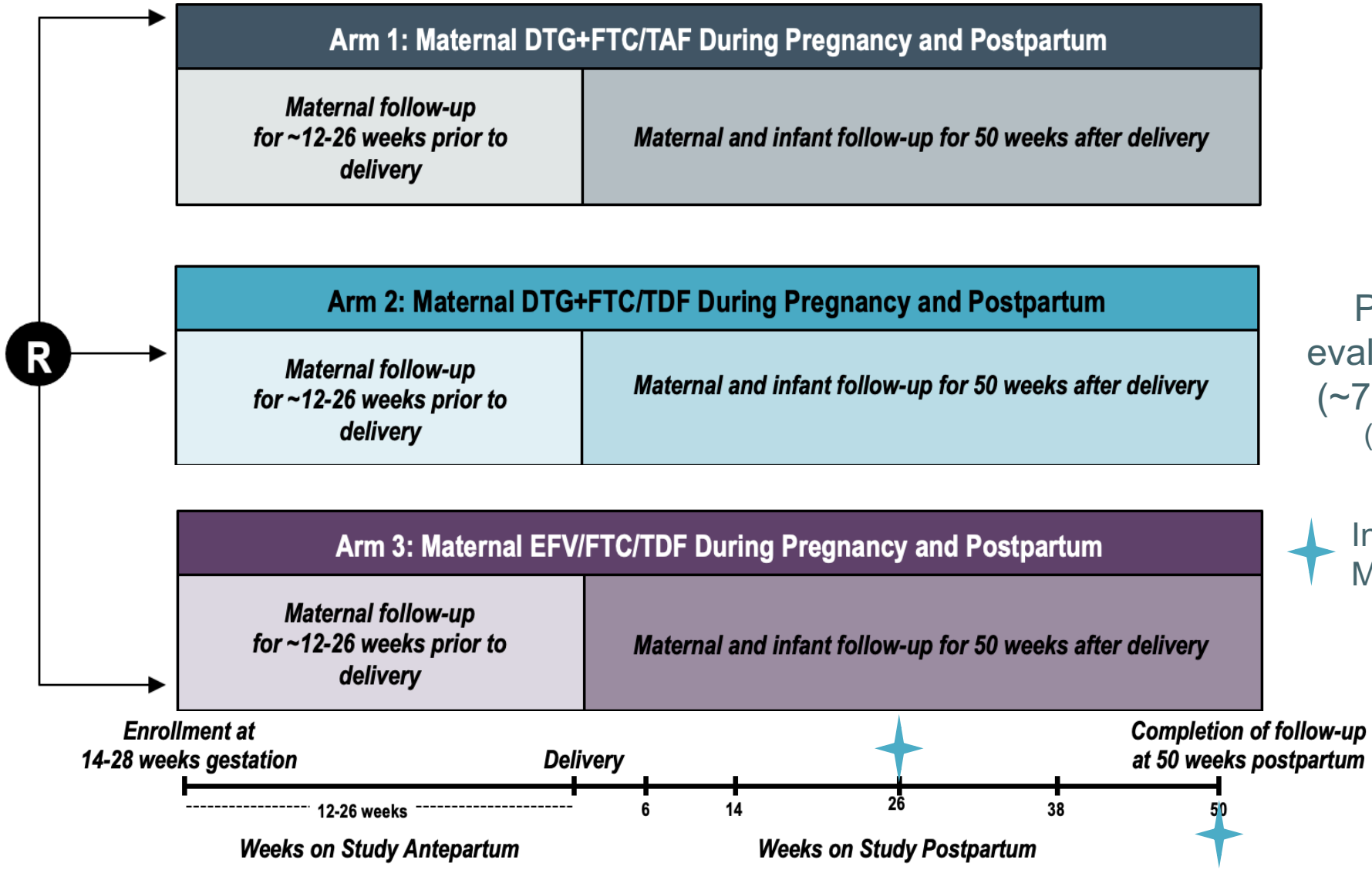
Study Design

Lockman & Brummel et al, The Lancet, 2021

643 pregnant women with HIV at 22 sites in 9 countries



Planned DXA scan evaluations for 213 pairs (~71 per arm) at 7 sites (Uganda, South Africa, Zimbabwe)

Infant DXA at Week 26; Maternal DXA at Week 50

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Rationale

- 213 DXA measurements would provide 80% power to detect at least one half a standard deviation difference which the team assessed as clinically relevant

- Infants had a whole body and lumbar spine scan performed at 26 weeks to ensure the latest practicable timepoint for performing high quality infant DXA scans, whilst minimizing infant radiation exposure

- Mothers had hip and lumbar spine scans at 50 weeks postpartum to ensure that they were scanned after the longest possible period of ART exposure.

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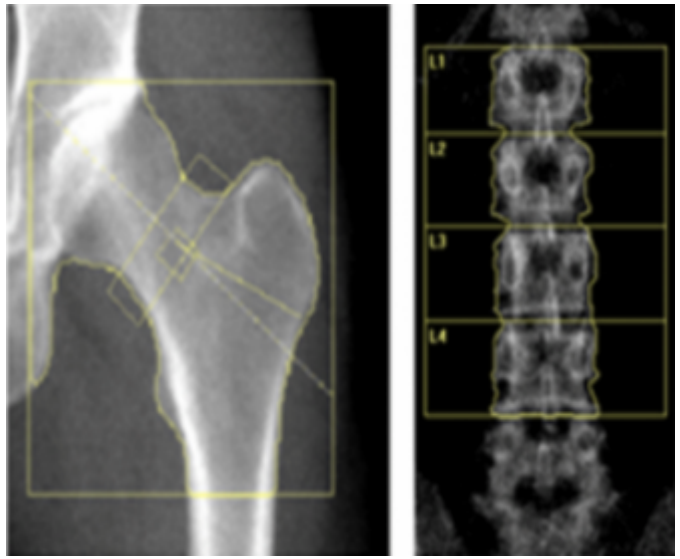
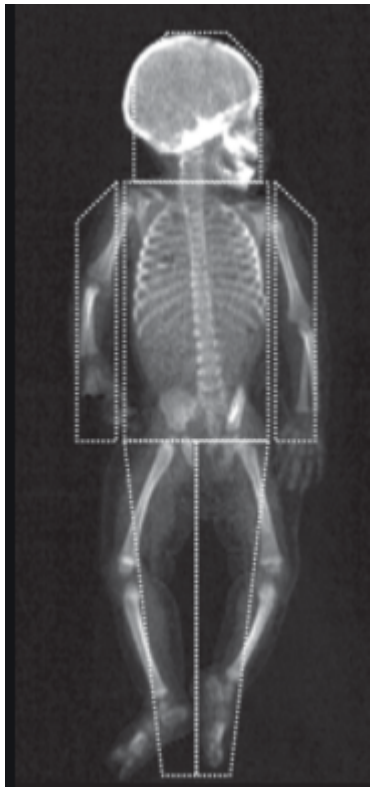
Data Analysis





- DXA scans were read by a central reader
- Pairwise comparisons of mean maternal bone mineral density (BMD) Z-scores and infant bone mineral content (BMC) were performed using two-sample t-tests.

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Maternal Baseline Characteristics

	DTG+FTC/TAF (N = 47)	DTG+FTC/TDF (N = 57)	EFV/FTC/TDF (N = 50)	Total (N = 154)
Age (mean years)	25.9	27.9	29.3	27.7
Black African	47 (100.0%)	57 (100.0%)	50 (100.0%)	154 (100.0%)
Gestational age (mean weeks)	22.9	22.0	22.0	22.3
Gestational age <24 weeks	29 (62%)	37 (65%)	32 (64%)	98 (64%)
BMI (mean g/cm^2)	26.7	26.0	25.9	26.2
Log_{10} HIV-1 RNA (mean copies/mL)	2.9	2.8	2.9	2.9
HIV-1 RNA ≥ 1,000 copies/mL	18 (38.3%)	26 (45.6%)	25 (51.0%)	69 (45.1%)

Baseline characteristics were similar between treatment arms

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Additional Maternal Characteristics

By DXA scan at week 50 postpartum:	
Mean (SD) study treatment duration (weeks)	66.0 (8.5)
Mean (SD) breastfeeding duration (weeks)	43.9 (15.0)
Number (%) received medroxyprogesterone acetate contraception	95 (62%)
Bone fractures during follow-up	Zero

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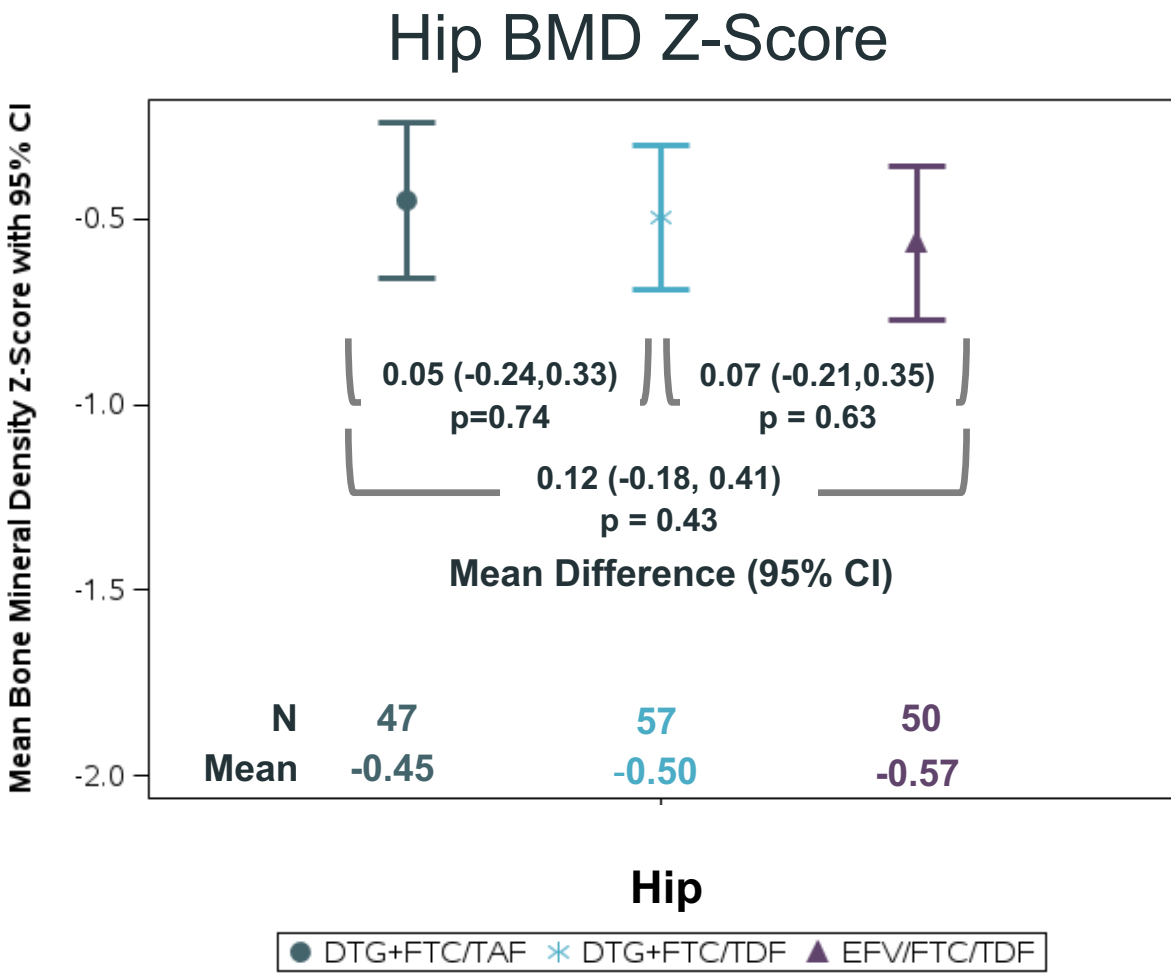
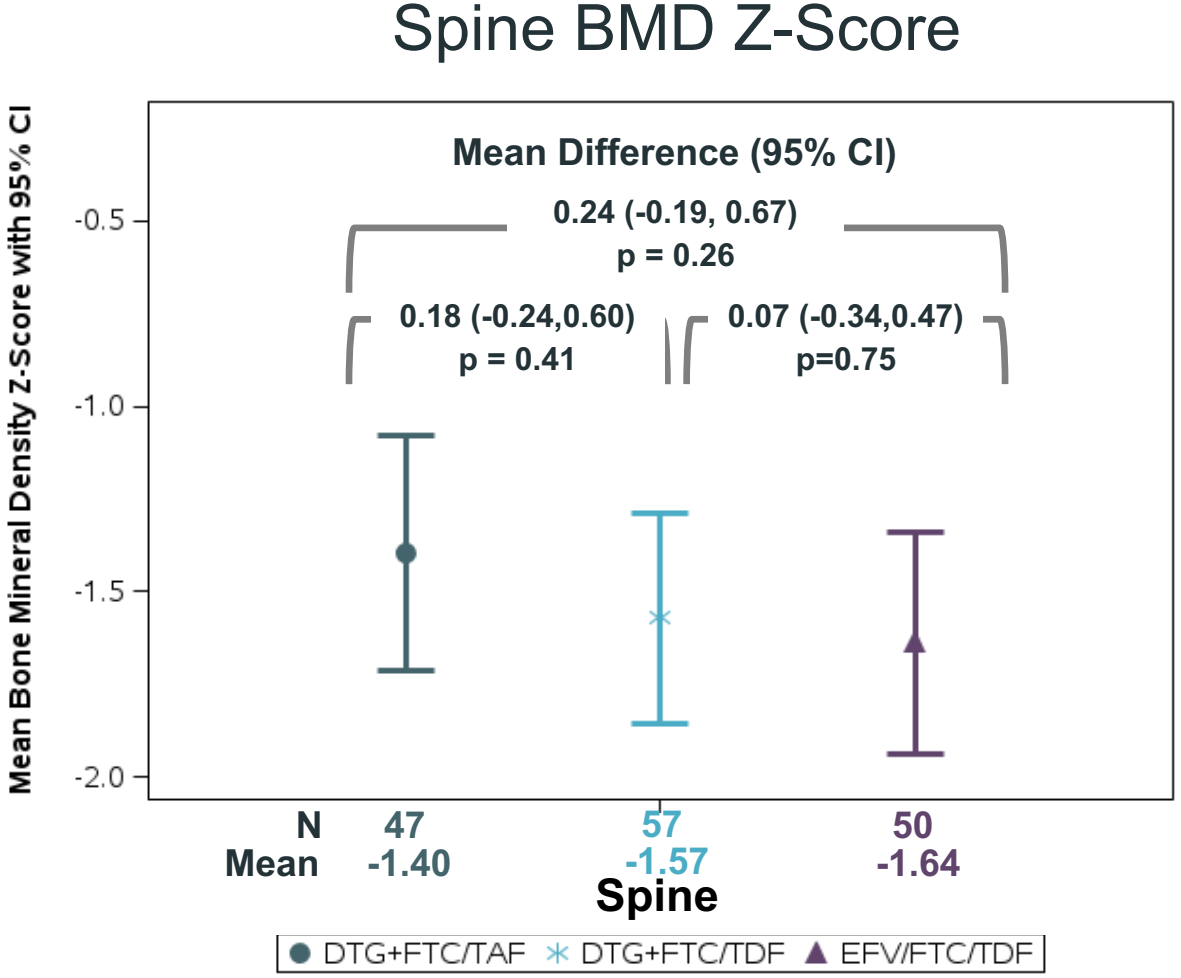
No apparent differences in maternal hip or spine BMD Z-scores between treatment groups





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Infant Characteristics at birth

	DTG+FTC/TAF (N = 57)	DTG+FTC/TDF (N = 59)	EFV/FTC/TDF (N = 49)	Total (N = 165)
Female	27 (47%)	29 (49%)	27 (55%)	83 (50%)
Gestational age (mean weeks)	40.0	39.5	39.1	39.5
Weight (mean kg)	3.2	3.1	3.0	3.1

Birth characteristics were similar across arms.

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Additional Infant Characteristics

- Of DXA scans taken,104 (54%) whole body and 157 (83%) spine scans were available for analysis at the week 26 visit window.

By DXA scan at week 26 of age:	
Mean (SD) age (months)	5.8 (0.6)
Mean weight (kg)	7.7
Number (%) still breastfeeding	134/165 (81%)
Number (%) received cotrimoxazole prophylaxis	153 (93%)

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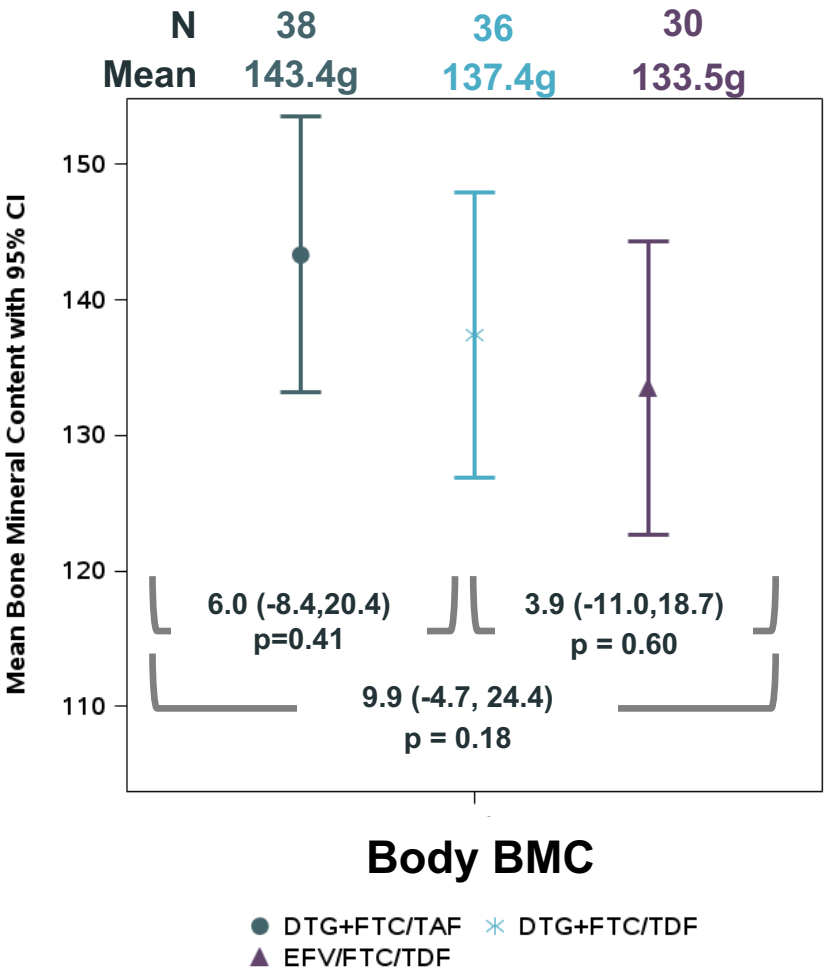
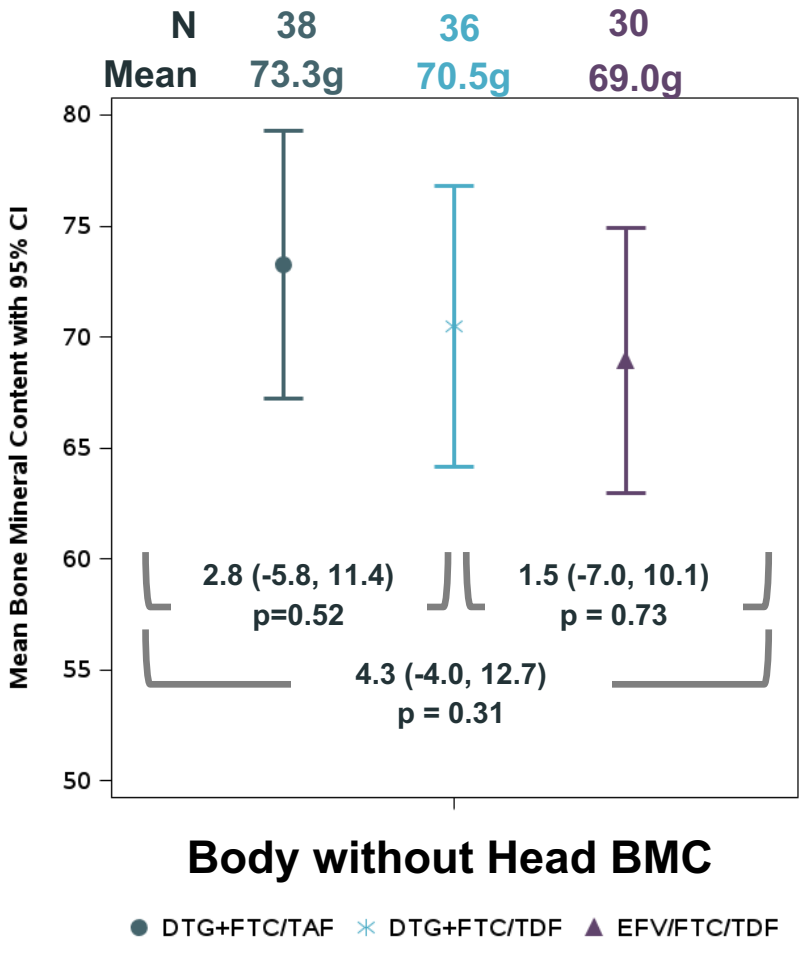
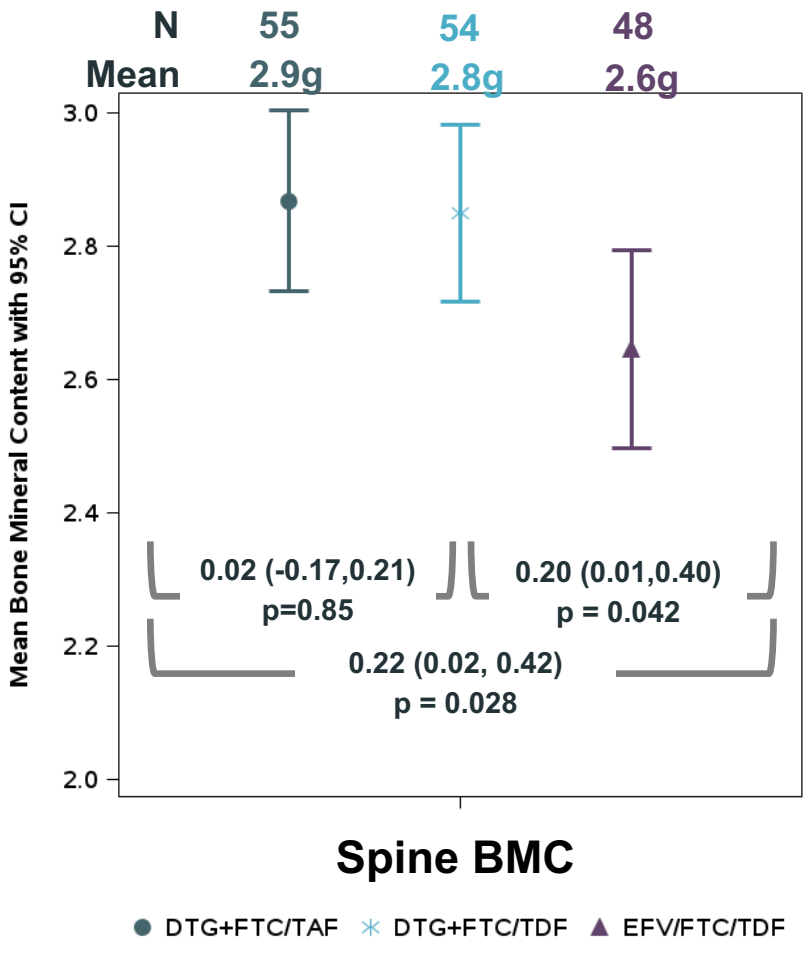
Infant BMC by treatment groups







Limitations

- The sample size for mothers and their infants was smaller than intended
- DXA scans were only done at a single timepoint for both mothers and infants

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Conclusion

- Among women randomized to start DTG vs EFV, TDF vs TAF during pregnancy and their babies:
  - Maternal BMD were similar across study arms at week 50 postpartum however there was a trend to lower BMD in women receiving TDF vs TAF
  - Further analysis is underway to understand the clinically meaningful ½ SD lower lumbar spine BMC in infants randomized to EFV arm compared to either of the DTG arms.

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