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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23 June 2021

IMPAACT Annual **Meeting** 2021

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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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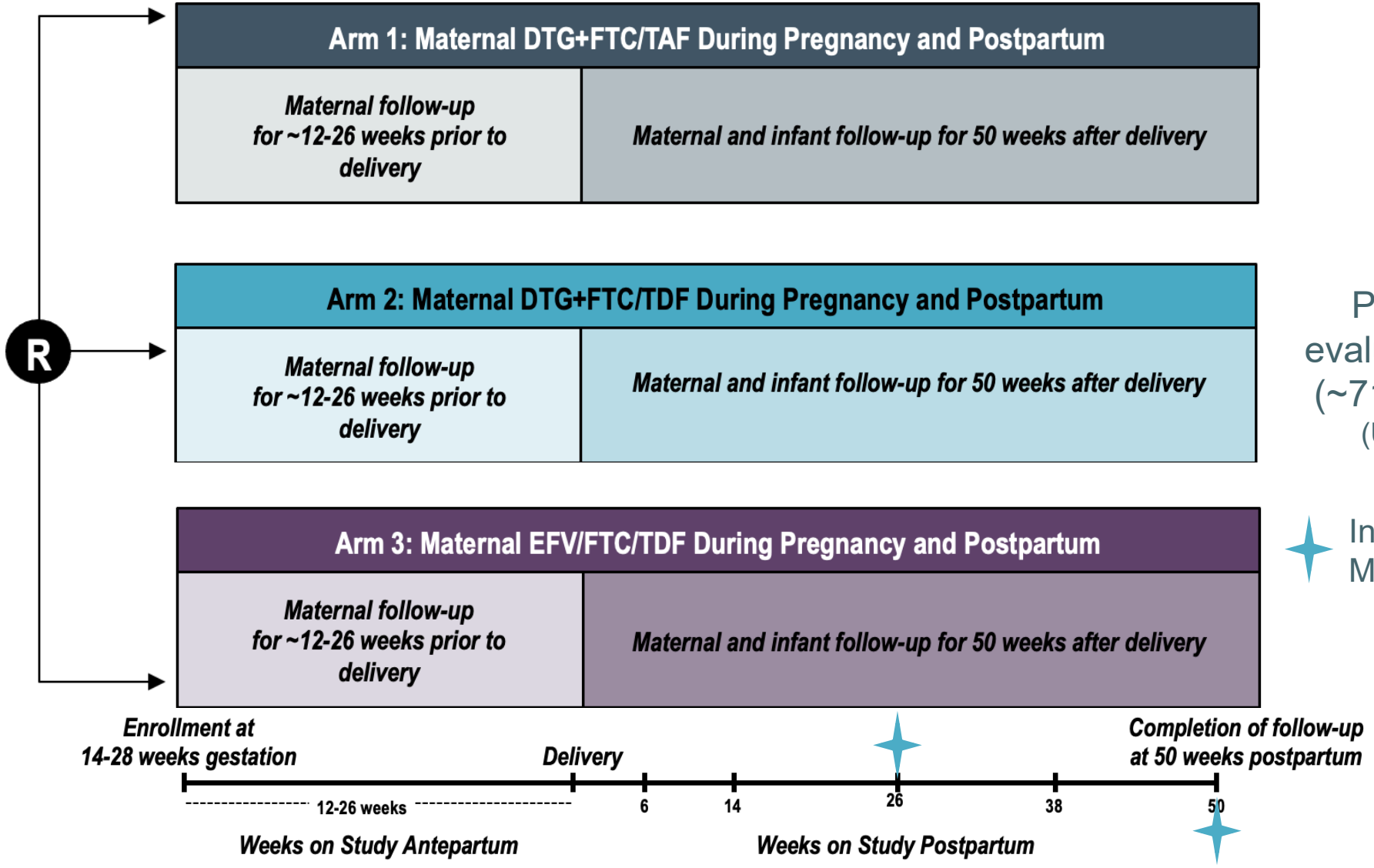
Study Design

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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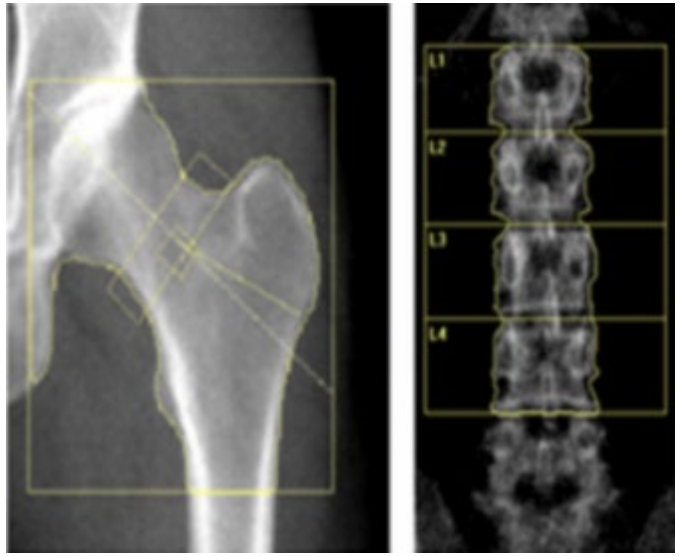
DXA scanning rationale

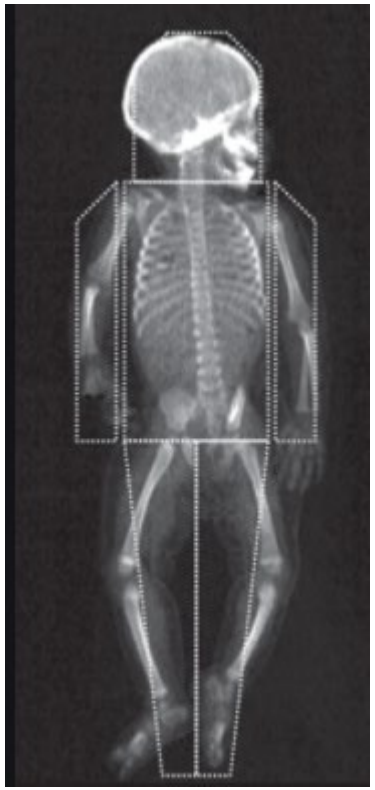
- 213 DXA measurements would provide 80% power to detect at least one half a standard deviation difference which the team assessed as clinically relevant

- 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.

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.

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

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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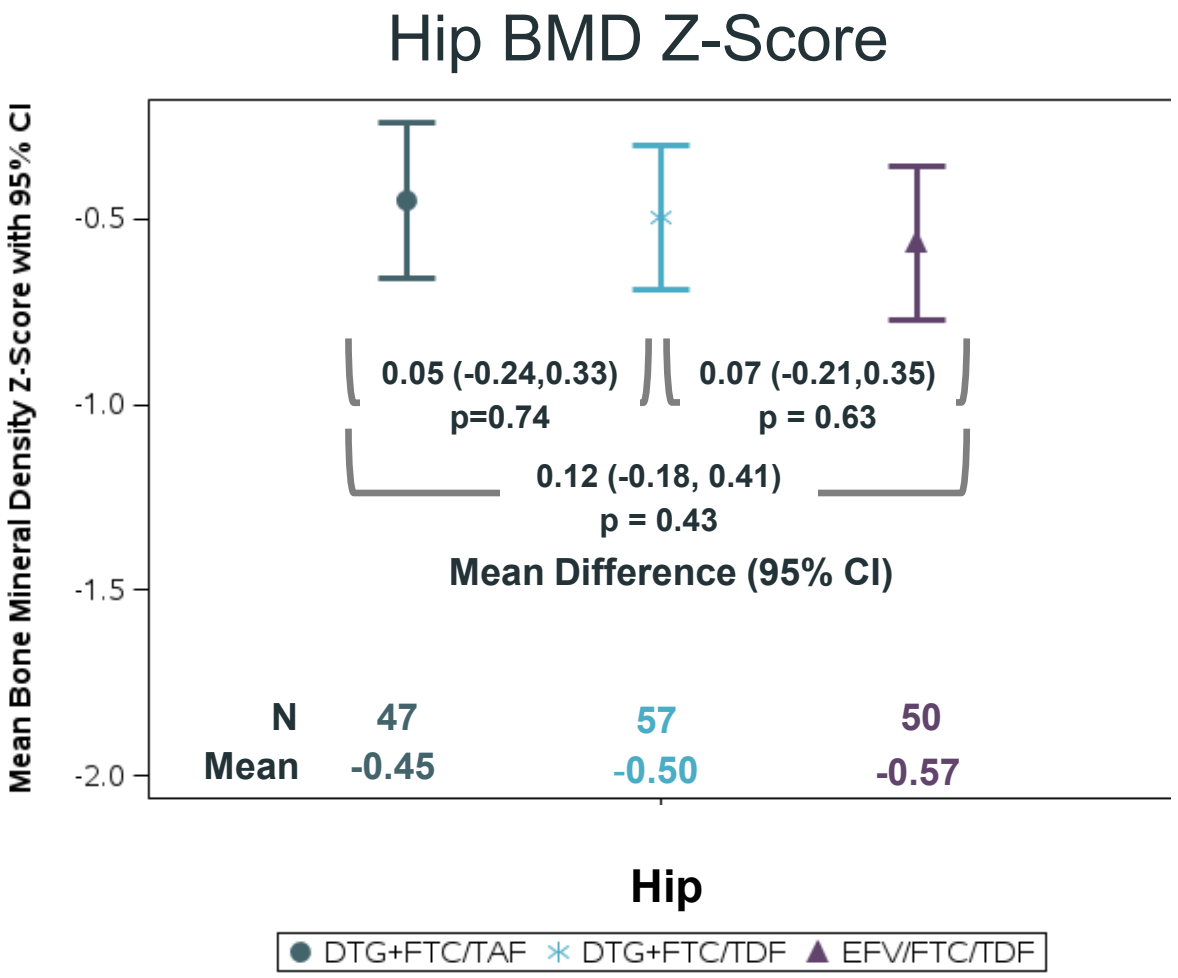
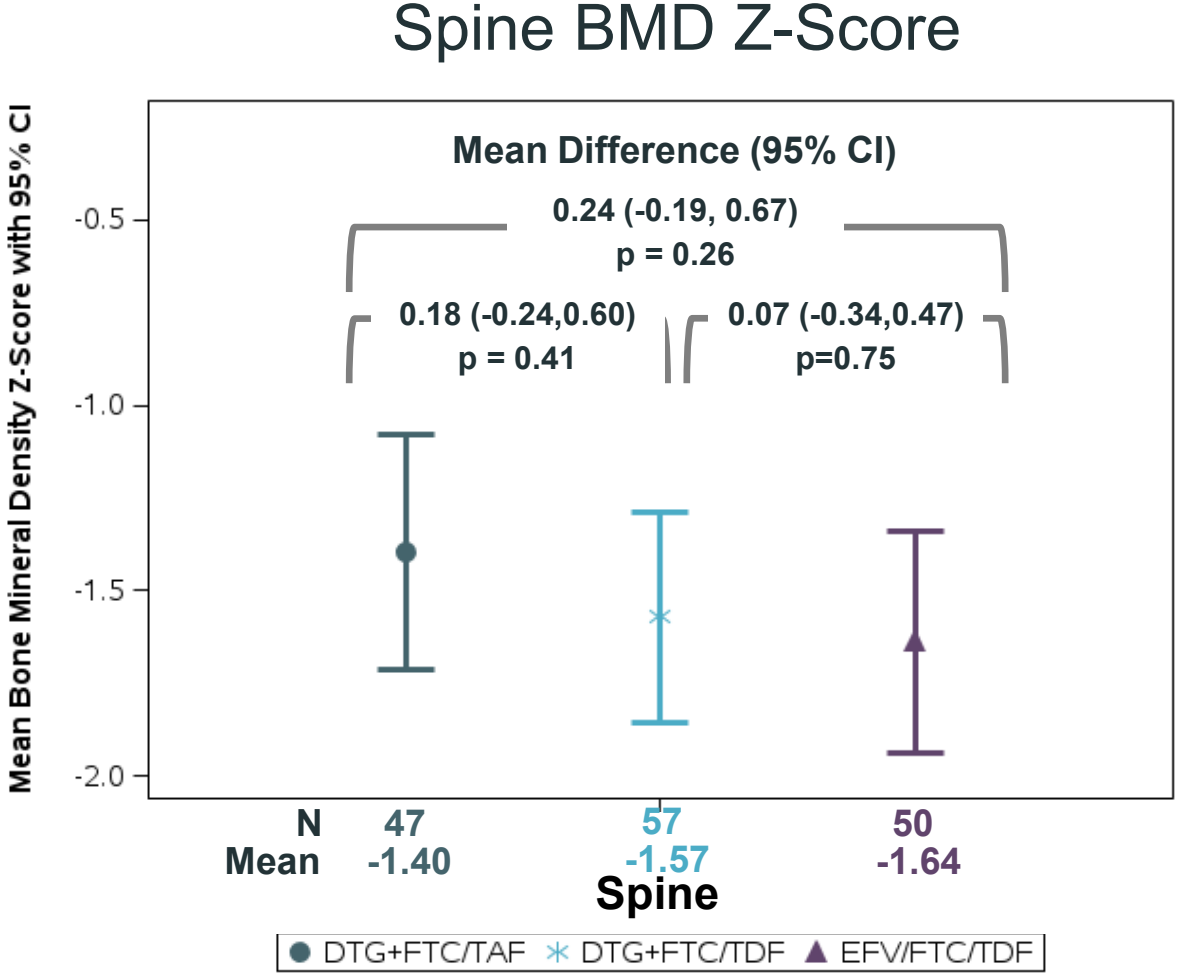
Maternal hip or spine BMD Z-scores between treatment groups





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.

Additional Infant Characteristics

- DXA scans done within the allowable week 26 visit window were104 (54%) whole body and 157 (83%) spine scans

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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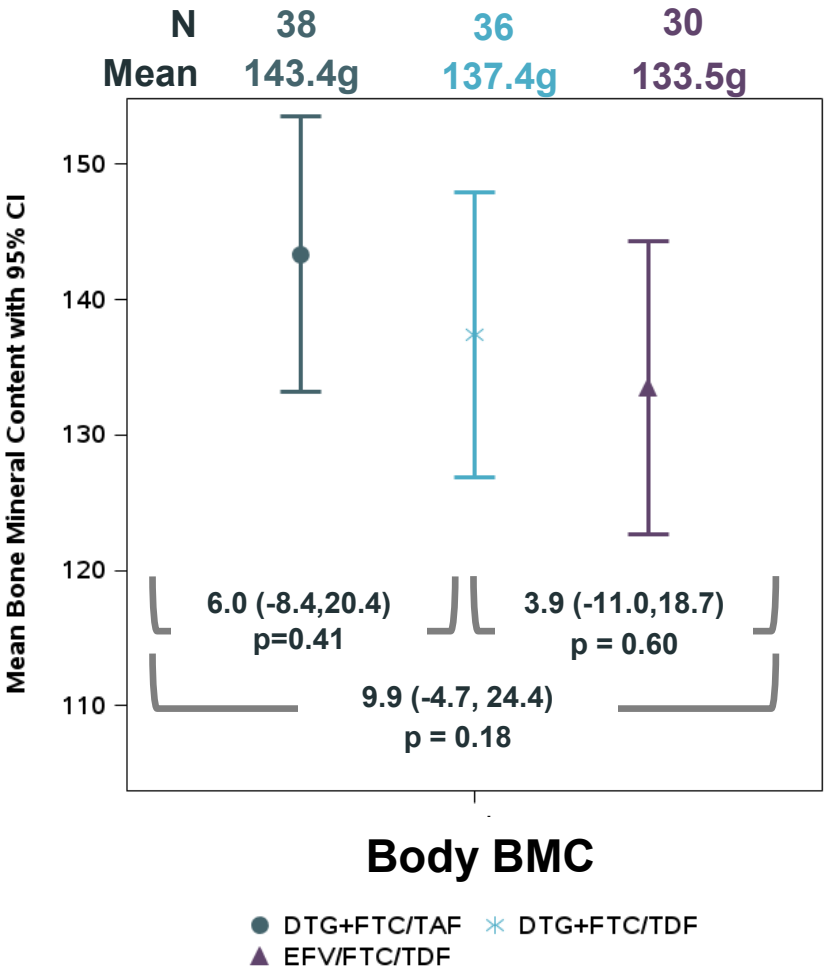
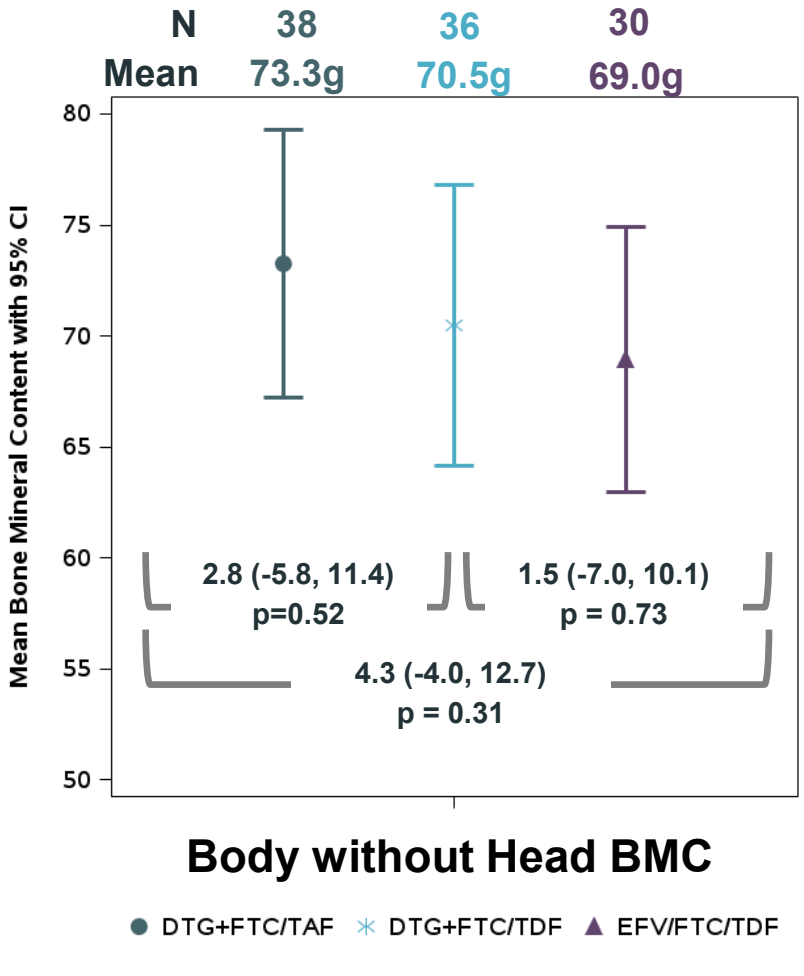
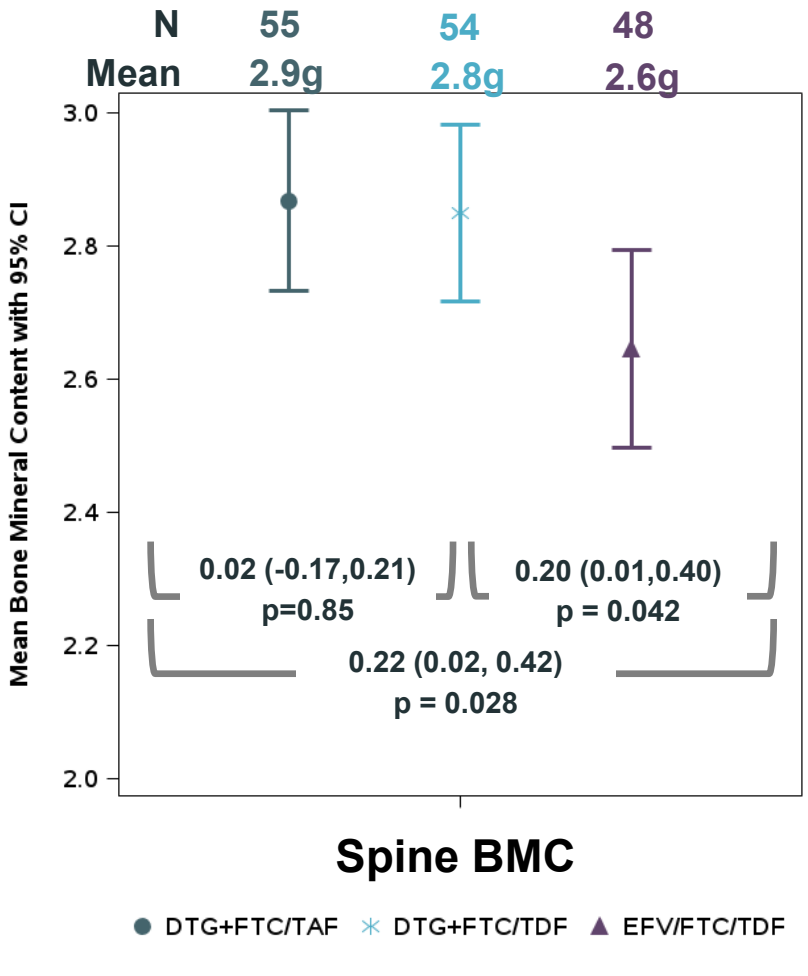
Infant BMC by treatment groups







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

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.

Acknowledgements

The IMPAACT 2010/VESTED Protocol Team gratefully acknowledges the dedication and commitment of the 643 mother-infant pairs, their communities, and CAB representatives, without whom this study would not have been possible.

Sponsors:

US National Institutes of Health (Patrick Jean-Philippe, Renee Browning, Lynette Purdue, Nahida Chakhtoura)

Gilead Sciences, Mylan, ViiV Healthcare Ltd

Protocol Co-Chairs: Shahin Lockman and Lameck Chinula.
Operations Center: Anne Coletti and Katie McCarthy.
Statistical and Data Management Center: Sean Brummel, Lauren Ziemba, Benjamin Johnson, Chelsea Krotje, Kevin Knowles, Kyle Whitson. **Laboratory Center:** Frances Whalen, William Murtaugh, Sikhulile Moyo. **Protocol Team Investigators:** Rivet Amico, Judith Currier, Lee Fairlie, Lisa Frenkel, Risa Hoffman, Lew Holmes, Gaerolwe Masheto, Mark Mirochnick, Jeremiah Momper, Chelsea Morroni, Paul Sax, Roger Shapiro, Lynda Stranix-Chibanda, Jeffrey Stringer. **Community:** Nagawa Jaliaah, Cheryl Blanchette .

Site Investigators of Record: South Africa: *Umlazi*: Sherika Hanley and Vani Chetty; *FAMCRU:* Gerhard Theron and Jeanne de Jager; *Soweto*: Haseena Cassim and Nastassja Ramsagar. **Uganda:** *MUJHU*: Deo Wabwire and Enid Kabugho. **Zimbabwe:** *St. Mary's:* Patricia Mandima and Suzen Maonera; *Seke North:* Lynda Stranix-Chibanda and Teacler Nematadzira; *Harare Family Care*: Tichaona Vhembo and Sukunena Maturure. **Shepherd Research Lab (Centralized DXA Support and Reading):** John Shepherd, Stephanie Rania, Laarni Igawa, Leila Kazemi

IMPAACT 2010/VESTED is funded by the US National Institutes of Health (NIH).

Overall support for the International Maternal Pediatric Adolescent AIDS Clinical Trials Network (IMPAACT) was provided by the National Institute of Allergy and Infectious Diseases (NIAID) with co-funding from the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) and the National Institute of Mental Health (NIMH), all components of the National Institutes of Health (NIH), under Award Numbers UM1AI068632 (IMPAACT LOC), UM1AI068616 (IMPAACT SDMC) and UM1AI106716 (IMPAACT LC), and by NICHD contract number HHSN275201800001I.

The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

The study products were provided by ViiV Healthcare Ltd, Gilead Sciences, Mylan.

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