Changes in Bone Turnover Markers after Delivery in Breastfeeding Mothers with and without ART

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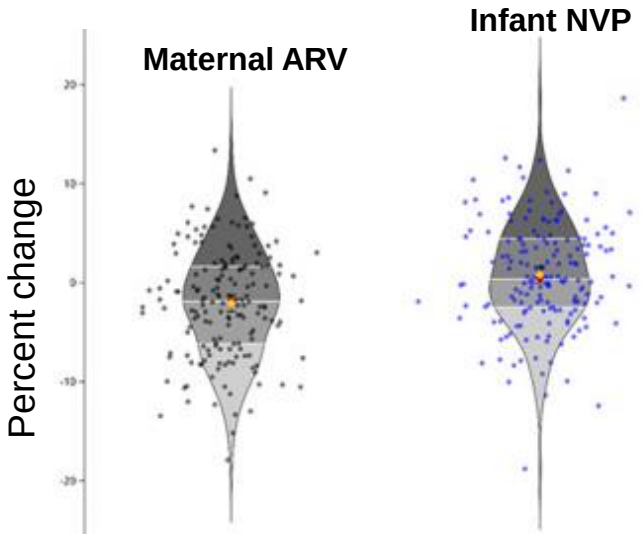
The IMPAACT PROMISE* trial randomized breastfeeding mothers with HIV and their infants to either a maternal TDF-based ART regimen (Maternal ARV) or infant nevirapine prophylaxis without maternal ART (Infant NVP) to prevent HIV transmission through breastmilk.



Women in the Maternal ARV arm experienced greater decline in bone mineral density (BMD) from postpartum Week 1 to Week 74 than women in the Infant NVP arm**

Figure 1. Percent Change in Lumbar Spine BMD**

*NCT01061151: https://www.impaactnetwork.org/studies/1077bf

**Stranix-Chibanda *et al*. Impact of postpartum tenofovir-based antiretroviral therapy on bone mineral density in breastfeeding women with HIV enrolled in a randomized clinical trial. PLoS One. 2021 Feb

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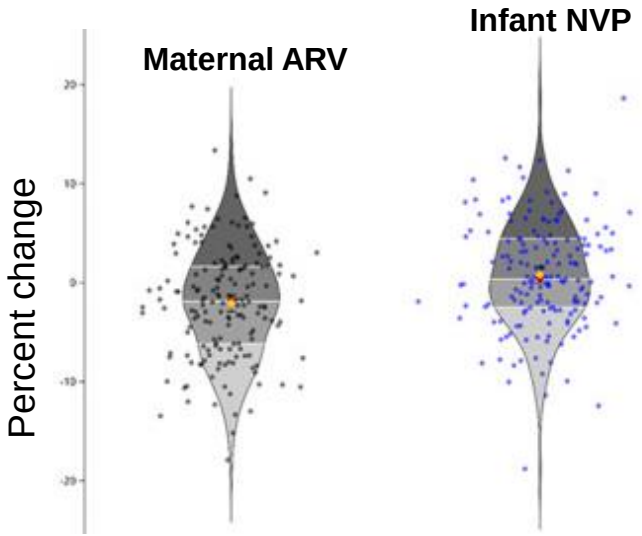
Underlying mechanism of observed differences in percent change in BMD not fully established



We compared the trajectory of bone turnover biomarkers between arms and evaluated their association with change in BMD

Figure 1. Percent Change in Lumbar Spine BMD*

*Stranix-Chibanda *et al*. Impact of postpartum tenofovir-based antiretroviral therapy on bone mineral density in breastfeeding women with HIV enrolled in a randomized clinical trial. PLoS One. 2021 Feb

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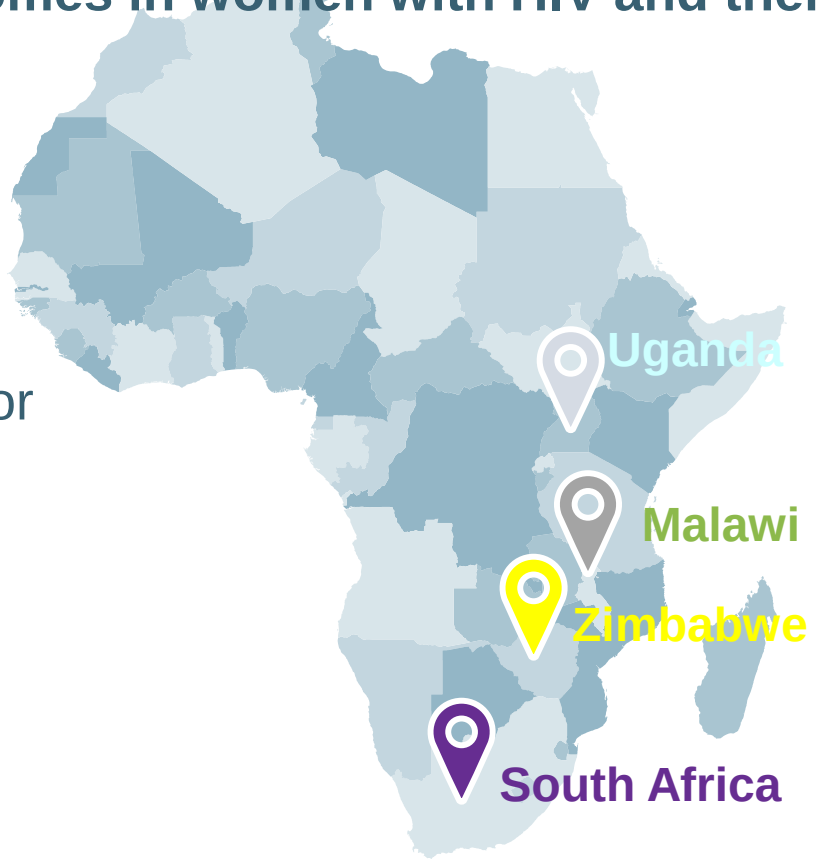
P1084s* substudy was a nested, comparative study of bone, renal, and growth outcomes in women with HIV and their infants

400 women from 8 sites in 4 African countries with capacity for BMD evaluation and no prior exposure to TDF ART



*NCT01066858: https://www.impaactnetwork.org/studies/p1084s

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Methods - Trial Procedures

Urine and Serum Collection:

- Entry (within 2 weeks of Delivery)
- Week 6 (postpartum)
- Week 26 (postpartum)
- Week 74 (postpartum)

Bone Resorption Markers:

- urinary deoxypyridinoline to creatinine (**uDPD**)
- serum C-terminal telopeptides (**CTX**)

Bone Formation Marker:

- **osteocalcin**

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Methods – Statistical Analysis

- **Compared** uDPD between arms at Week 74 using two-sided Student's t-tests (primary)
- **Described** the postpartum trajectories of biomarkers using spaghetti plots and LOESS regression
- **Compared** biomarkers longitudinally using generalized estimating equation (GEE) models that accounted for repeated measures
- **Evaluated** the association between biomarkers at Entry and percent change in lumbar spine and hip BMD from Entry to Week 74 using adjusted linear regression models

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Baseline characteristics were similar across arms

Characteristic	Maternal ARV (N=200)	Infant NVP (N=198)	Overall (N=398)
Age (years) Median (Q1, Q3)	26.3 (23.4, 29.5)	26.7 (23.2, 31.3)	26.5 (23.3, 30.2)
WHO Clinical Stage I	187 (94%)	185 (93%)	372 (93%)
CD4 Cell Count (cells/mm^3) Median (Q1, Q3)	737.0 (571.0, 935.0)	695.0 (581.0, 896.0)	714.0 (575.0, 911.0)
HIV RNA level <400 copies/mL	110 (55%)	104 (53%)	214 (54%)
Calculated CrCl (mL/min) Median (Q1, Q3)	133.6 (117.3, 158.4)	135.7 (115.9, 151.1)	134.4 (116.6, 155.8)

Breastfeeding duration (median 62 weeks) and contraception uptake (64%) were comparable across arms

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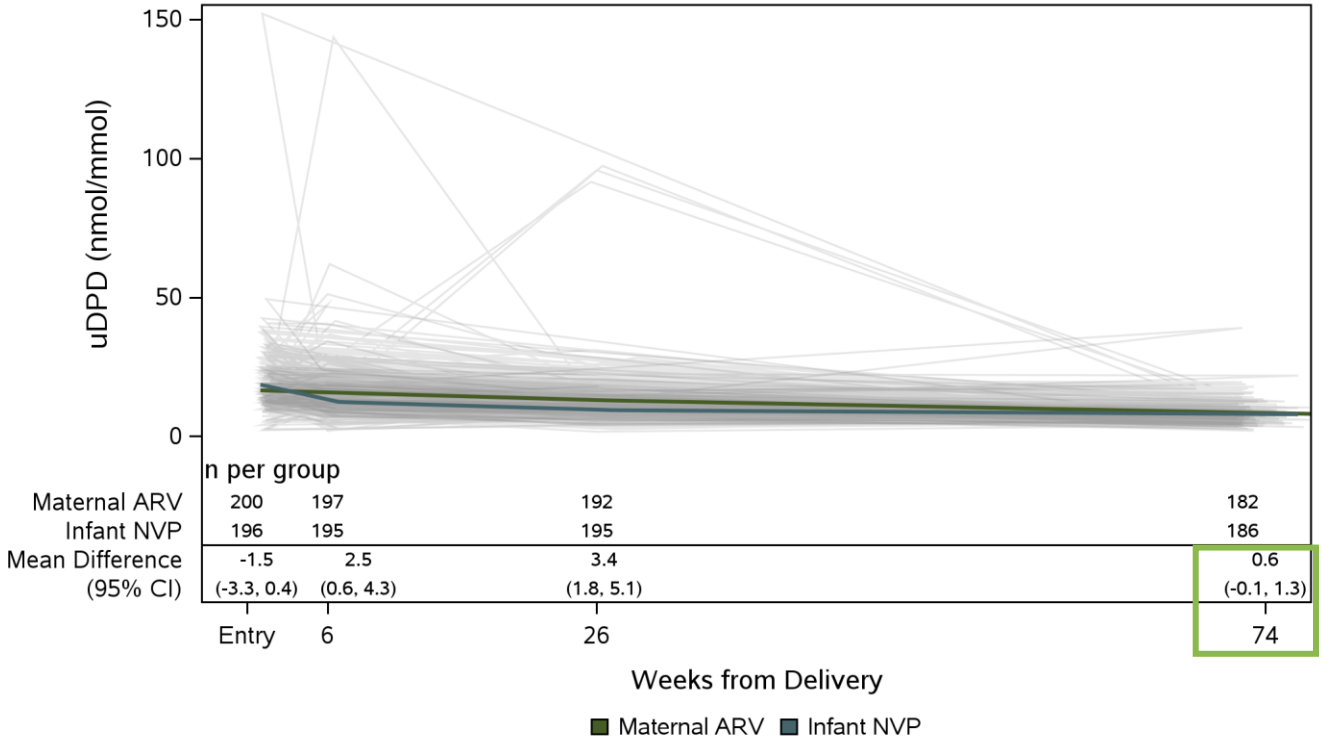
Urinary deoxypyridinoline to creatinine (uDPD)*



P = 0.17

*Bone resorption marker

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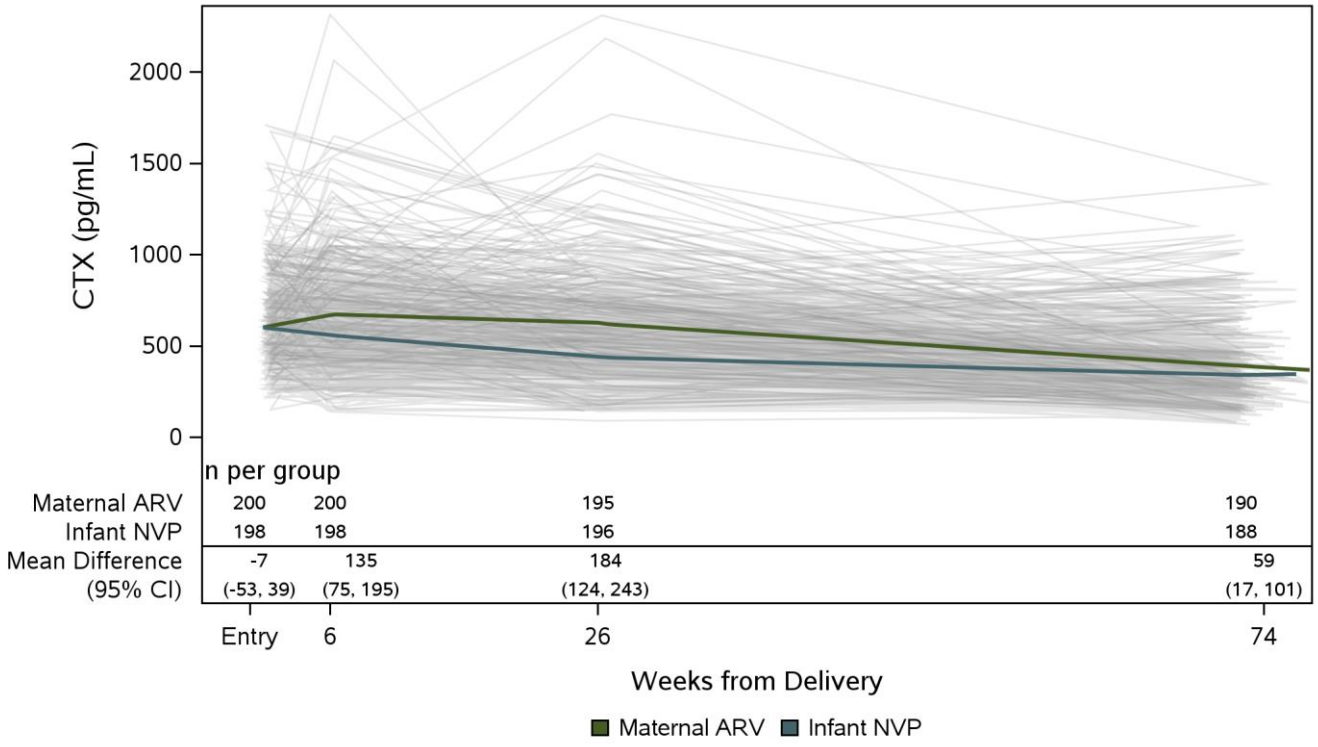
Serum C-terminal telopeptides (CTX)*



*Bone resorption marker

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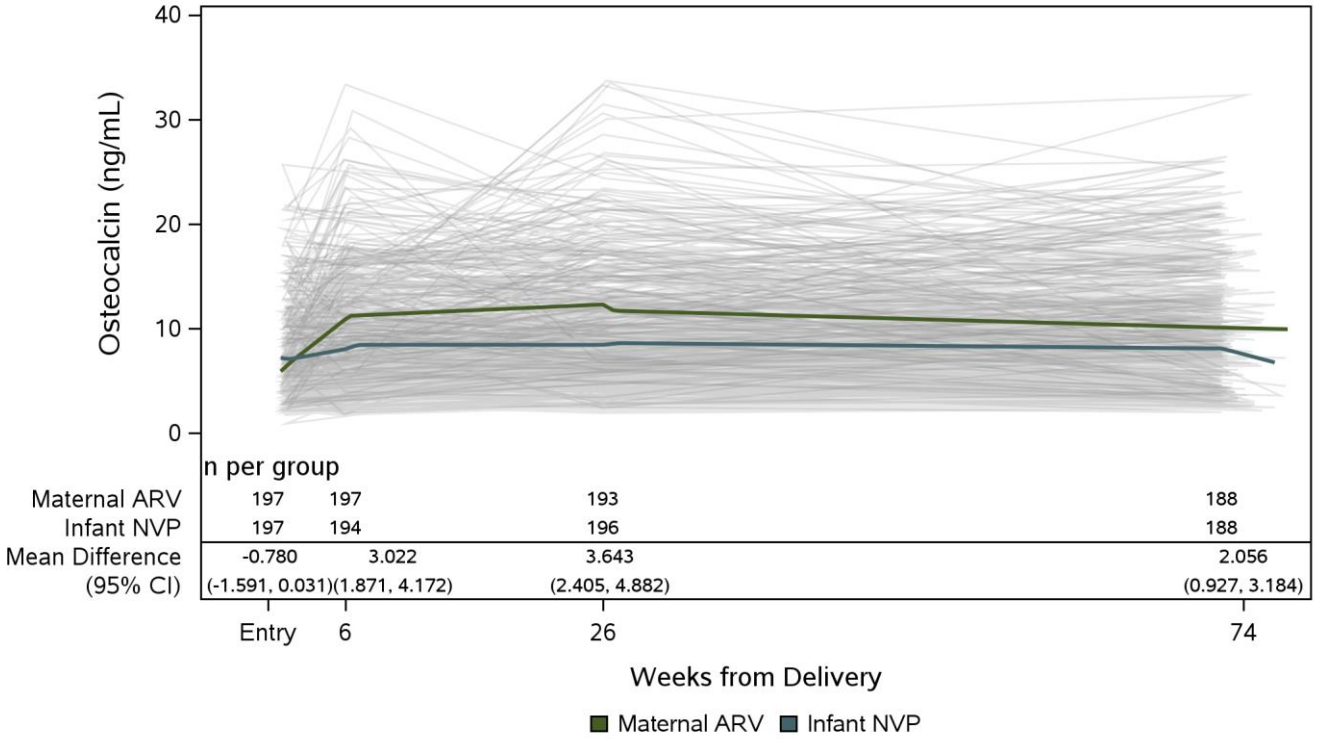
Osteocalcin*



*Bone formation marker

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Percent Change from Entry to Week 74 in Lumbar Spine and Hip BMD

BMD Outcome Measure	Bone Biomarker*	N	Adjusted Coefficient[1] (95% CI)
Lumbar Spine	uDPD (nmol/mmol)	336	0.104% (0.008, 0.200)
	CTX (pg/mL)	337	0.003% (<0, 0.006)
	Osteocalcin (ng/mL)	335	0.255% (0.088, 0.423)
Hip	uDPD (nmol/mmol)	335	0.008% (-0.068, 0.083)
	CTX (pg/mL)	336	0.001% (<0, 0.004)
	Osteocalcin (ng/mL)	334	0.159% (0.028, 0.290)

[1]Models were adjusted for postpartum randomization arm, maternal age at baseline, country, HIV viral load at baseline, maternal weight at baseline, parity, and antepartum ARV exposure at postpartum entry

***Adjusted coefficient represents the mean percent increase in BMD outcome measure per unit increase in bone biomarker at Entry.**

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At postpartum Weeks 6 and 26, the Maternal ART arm had higher mean uDPD, CTX, and osteocalcin compared with the Infant NVP arm.

These results could indicate the underlying mechanism for the greater percent change in BMD observed with postpartum Maternal ART, but the clinical significance of these changes remains to be determined.

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Thank you!

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