

Bone mineral density changes in young African women initiating tenofovir disoproxil fumarate based antiretroviral therapy and non-hormonal contraception



Flavia Matovu Kiweewa, Noah Kiwanuka, Martin Nabwana, Esther Isingel, Juliet Allen Babirye, Monica Nolan, Philippa Musoke, Mary Glenn Fowler, Mags Beksinska, John M. Pettifor, Todd T. Brown

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Introduction

- Sub Saharan Africa bears greatest burden of the HIV epidemic globally;
 - Women account for about 57% of 38million PLWH
 - Women more likely to acquire HIV at an earlier age
- Roll out of HAART in RLS has resulted in increased survival
- Current Rx options like TDF promise even further increases in survival
- Antiretroviral therapy is associated with accelerated BMD loss, higher rates of osteopenia, osteoporosis, and subsequent fractures
- Potential effect of TDF on bone is concerning

Introduction

- Rapid acceleration of bone turnover with ART-initiation; bone resorption outstrips bone formation → reduced BMD
- Majority of previous studies involved mainly men (>85%), and had no country based BMD reference data
- It is unclear, how BMD changes in young HIV-infected women initiating TDF-containing ART compare to demographically similar HIV-uninfected controls

Aim

To compare BMD changes over 2 years in young HIV-infected women in Uganda initiating TDF-containing ART to age and sex matched HIV uninfected controls from the same country

Methods

- Study based at MU-JHU Research Collaboration, Kampala - Uganda
- Women recruited from 11 HIV clinics and general health care facilities

HIV infected and uninfected

- aged 18 to 35 years
- able and willing to provide written informed consent
- having a documented HIV and pregnancy test result

HIV+, TDF ART, non-hormonal
contraception

- Eligible but naïve for ART at screening (CD4 \leq 500 cells/ μ l, or \geq WHO stage 3)
- Using non-hormonal contraception (IUCD, condoms)
- No h/o use of hormonal contraception including DMPA in last 2yrs

HIV-, non-hormonal contraception

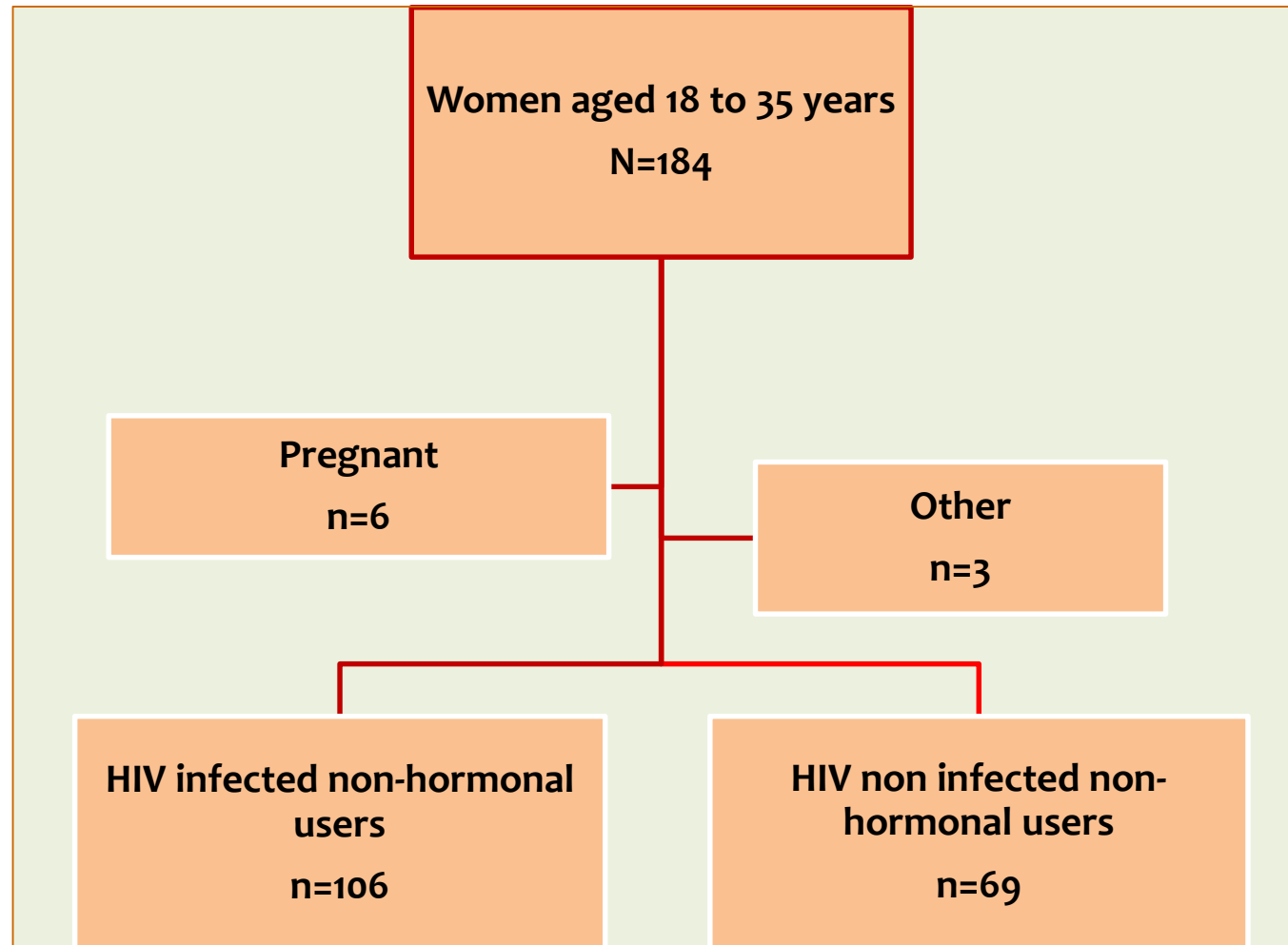
- Using non-hormonal contraception (IUCD, condoms)
- No h/o use of hormonal contraception including DMPA in last 2yrs
- No h/o use of PEP in last 6 months

Methods

- All HIV-infected women were initiated on TDF, 3TC, and EFV (or NVP)
- Visit schedule: enrollment, week 4, month 3, 6, 9, 12, 15, 18, 21, and 24
- Baseline and 6 monthly BMD assessments of lumbar spine, total hip and femoral neck were done on non-pregnant women using hologic explorer dual energy x-ray absorptiometry
- BMD Z-scores were derived using reference data for local age and sex matched HIV negative controls
- We used mixed effects linear modeling to compare the rate of change, calculated as the mean % change in BMD per year between HIV-infected and uninfected women during the initial 2 years of ART initiation
- Adjusted for age, and body mass index

Results

Figure 1: Accrual began March 2015 Completed October 2017



Total enrollment = 175

Table 1: Participant baseline characteristics

Characteristic (Median/ %)	Total (N=175)	HIV infected (n=106)	HIV uninfected (n=69)	P-value
Age (years)	25.9 (4.5)	26.8 (4.6)	24.4(4.0)	<0.001
Education (≥ secondary)	123 (70.3)	66 (62.3)	57 (82.6)	<0.001
Married	56 (32.0)	33 (31.2)	23 (33.0)	0.122
Ever pregnant	117 (66.9)	84 (79.2)	33 (47.8)	<0.001
Parity	1 (0,3)	1 (1,3)	0 (0,2)	<0.001
Alcohol use	34 (19.5)	25 (23.6)	9 (13.2)	0.093
Physical activity (≥150 min/week)	60 (61.9)	32 (58.2)	28 (66.7)	0.394
Income (monthly, USD)	42.1 (27.1,76.0)	40.7 (27.1,71.9)	54.3 (40.7, 81.4)	0.039
Viral Load (log ₁₀ copies/ mL)	4.16 (3.29, 4.60)	4.16 (3.29, 4.60)	N/A	N/A
CD4 count (cells/μL)	442 (309, 641)	442 (309, 641)	N/A	N/A
BMI (g/m ²)	23.5 (21.3, 26.4)	23.7 (21.2, 26.7)	23.3 (21.7, 25.7)	0.183

Table 2: Baseline BMD Z-Scores

Z-Score	Total (N=175)	HIV infected (n=106)	HIV uninfected (n=69)	P-value
Lumbar Spine				
Median (IQR)	-0.125 (-0.754, 0.694)	-0.202 (-0.772, 0.606)	-0.031 (-0.658, 0.694)	0.253
Low BMD (≤ -2.0 SD)	6 (3.4)	6 (5.7)	0 (0.0)	0.044
Femoral Neck				
Median (IQR)	-0.137 (0.860, 0.566)	-0.118 (-0.926, 0.503)	-0.137 (-0.643, 0.666)	0.925
Low BMD (≤ -2.0 SD)	10 (5.7)	8 (7.5)	2 (2.9)	0.319
Total Hip				
Median (IQR)	-0.075 (-0.869, 0.725)	-0.131 (-0.985, 0.691)	-0.025 (-0.727, 0.725)	0.404
Low BMD (≤ -2.0 SD)	12 (6.9)	12 (11.3)	0 (0.0)	0.004

Figure 2: Mean percent change in lumbar spine BMD

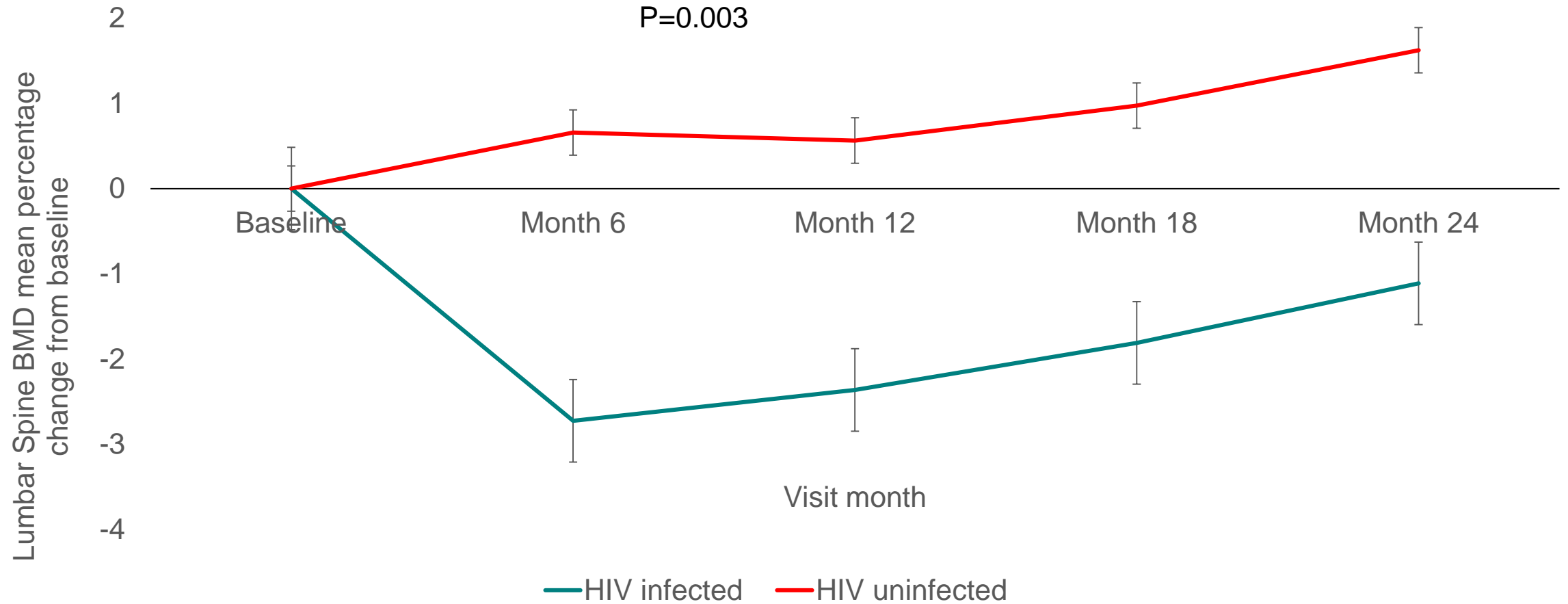


Figure 3: Mean percent change in total hip BMD

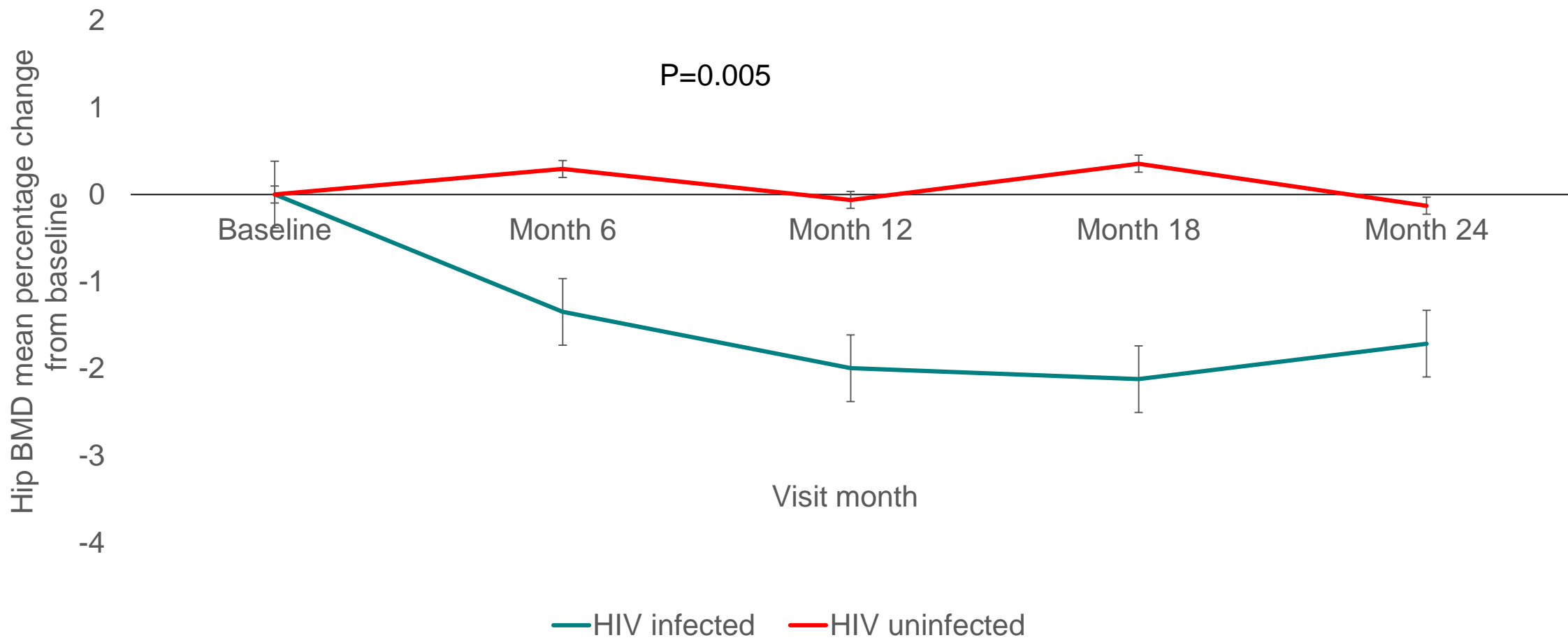


Figure 2: Mean percent change in femoral neck BMD

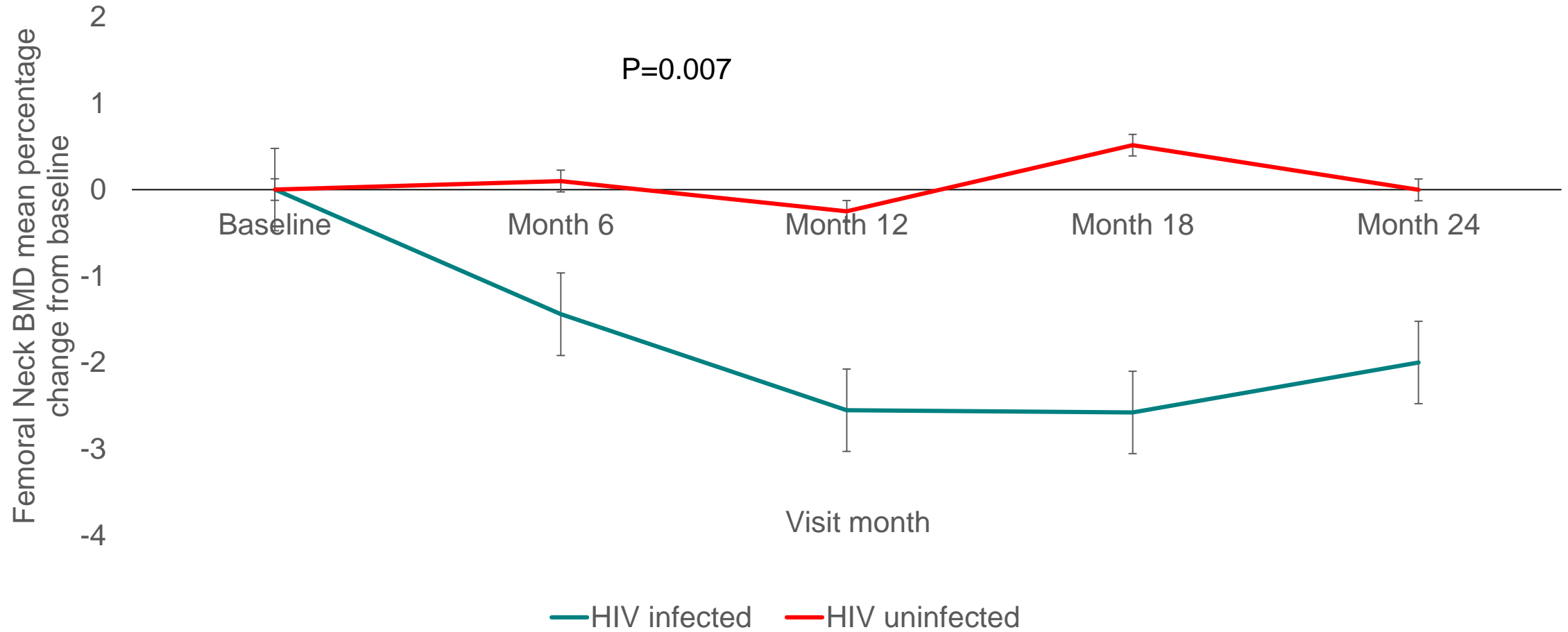


Table 3: Changes in BMD over 24 months

Body site	Crude annualized mean % change in BMD (95% CI)	P-value	Adjusted annualized mean % change in BMD (95% CI)	P-value
Lumbar spine	-1.754 (-2.300, -1.209)	<0.001	-1.752 (-2.290, -1.214)	<0.001
Total hip	-1.103 (-1.674, 0.533)	<0.001	-1.153 (-1.732, -0.574)	<0.001
Femoral Neck	-1.335 (-2.109, -0.562)	0.001	-1.407 (-2.188, -0.626)	<0.001

Adjusted for age and BMI

Conclusion

- Baseline BMD of young HIV infected ART naïve Ugandan women was not significantly different from that of HIV-uninfected age and sex matched controls from the same country
- Young HIV-infected women initiating TDF-based ART subsequently experienced significantly greater BMD loss at the lumbar spine, total hip, and femoral neck over a two year follow-up period compared to population-based controls
- Newer bone sparing treatment regimens like TAF based ART are needed to mitigate BMD loss among HIV infected women in resource limited settings

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