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Bone Density in HIV- and ART treated HIV+ subjects in follow-up; HIV UPBEAT results

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Introduction

- Decreases in bone mineral density (BMD) in people with HIV (PWH) have been associated with initiation of antiretroviral therapy (ART) containing tenofovir disproxil fumarate (TDF)[1]
- With recent introduction of new ART strategies we aimed to explore the effect of switching to non-TDF regimes on BMD

Methods

- HIV UPBEAT (*Understanding the Pathology of Bone Disease in HIV-infected Subjects*) is a prospective cohort study enrolling HIV+ and HIV- subjects from similar demographic backgrounds[2]
- Demographic, clinical, medication history and BMD measured by dual Xray absorptiometry (DXA) at lumbar spine (LS) and femoral neck (FN) were recorded at four visits spanning at least five years
- Subjects with ≥2 DXA were included in the analysis
- We used mixed-effects regression models to determine predictors of rate of absolute change in BMD adjusting for HIV status, age gender, ethnicity and smoking status
- To assess effect of switching-off TDF in PWH the effect of time was allowed to change during TDF and non-TDF exposure, thereby allowing estimation of on-TDF and off-TDF BMD slopes in the mixed effects model

Results

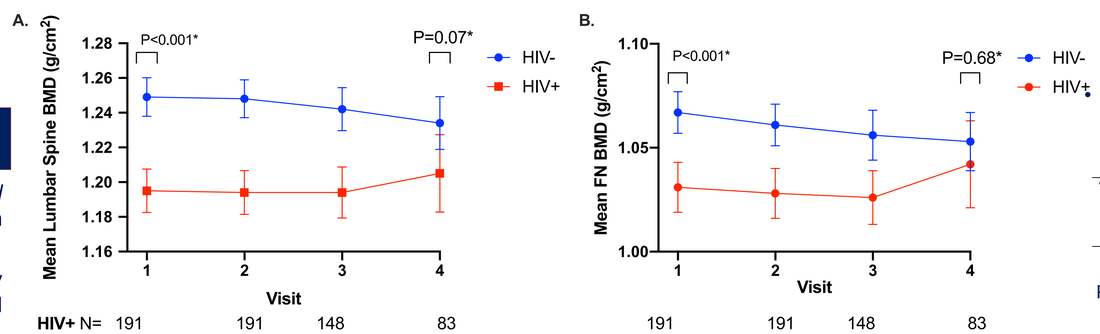
- Baseline characteristics of the cohort are presented in table 1:

Table 1. Baseline characteristics of the cohort

	HIV- N=218	HIV+ N=191	P
Age (years)	42 [35, 49]	39 [34, 47]	0.02
Male n (%)	97 (45%)	117 (62%)	<0.001
Caucasian n(%)	169 (77%)	101 (61%)	0.003
BMI (kg/m^2)	27.1 [23.4, 30.3]	26 [23.1, 29.9]	0.06
Current Smoker n(%)	33 (15%)	62 (32%)	<0.001
Alcohol drinker n(%)	170 (78%)	97 (51%)	<0.001
Baseline BMD LS (g/cm^2)	1.24 [1.13, 1.35]	1.17 [1.07, 1.31]	0.002
Visit 4 BMD LS (g/cm^2)	1.233 [1.126, 1.351]	1.197 [1.070, 1.359]	0.35
Baseline BMD FN (g/cm^2)	1.05 [0.96, 1.16]	1.02 [0.93, 1.13]	0.02
Visit 4 BMD FN (g/cm^2)	1.055 [0.935, 1.143]	1.043 [0.935, 1.152]	0.86
HIV Specific Factors			
Years since HIV diagnosis (years)		11 [8, 14]	
Current ART *n* (%)		166 (87%)	
Cumulative ART exposure (years)		7.9 [6.0, 10.3]	
On TDF *n* (%)		136 (76%)	
Never on TDF		28 (16%)	
Switch-off TDF		48 (28%)	
Switch-to TDF		10 (6%)	
Follow up time for those switching from TDF (years)		1.01 [0.4, 1.5]	

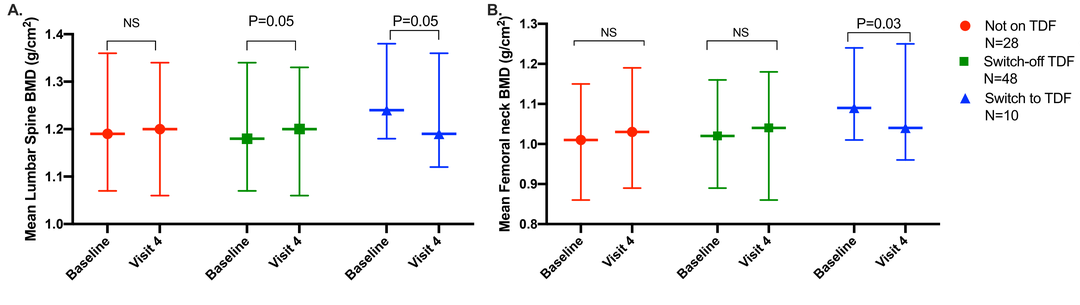
Results

Figure 1: Change in BMD at (A) Lumbar Spine and (B) Femoral Neck in HIV+ and HIV- subjects in the HIV UPBEAT cohort



- Both mean LS and FN BMD were significantly lower in PWH compared to HIV- subjects at baseline visit (Figure 1 (a) and (b))
- We observed no difference in neither absolute nor percentage (%) change in BMD from baseline until last follow-up visit between PWH and HIV- subjects (% change in BMD at LS 0.15 [-3.48, 3.52] vs -0.62 [-3.99, 3.09], P=0.49 and at FN 0.63 [-3.69, 4.69] vs -0.55 [-4.26, 3.97], P=0.31, respectively).
- PWH experienced a small but non-significant gain in FN BMD of 0.0002 [-0.003; 0.003] g/cm^2/year while HIV- subjects had a 0.0004 [-0.003; 0.002] g/cm^2/year non-significant decrease in FN BMD with similar findings at the LS
- As a result, we observed we observed no significant difference in LS or FN BMD between the groups at visit 4 (Figure 1 (a) and (b))

Figure 2: Change in mean BMD at (A) Lumbar spine and (B) Femoral Neck in those never on TDF compared to those switching off or to TDF in HIV UPBEAT over study follow-up



- 48 (28%) of PWH switched off TDF over study follow-up
- In the small (N=10) subgroup of PWH who switched to TDF between baseline and study follow-up, we observed significant declines in both mean FN and LS BMD (Figure 2 (a) and (b))
- In PWH, switching away from TDF was independently associated with a 0.004 g/cm^2/year [0.001, 0.007], P=0.008 gain in LS BMD even after adjustment for sociodemographic factors (Table 2 (a))
- We did not observe any association between switching away from TDF and change in FN BMD (Figure 2(b) and Table 2(b))

Table 2: Effects off switching off TDF on absolute change in (a) LS BMD and (b) FN BMD following adjustment for baseline variables*

	(a) LS BMD			(b) FN BMD		
PWH subgroup	Model estimate	95% C.I	P	Model Estimate	95% C.I	P
Rate of change over follow-up (years)	-0.001	-0.005, 0.002	0.36	-0.002	-0.005, 0.002	0.35
Change in BMD up until time of switch	0.008	-0.008, 0.025	0.33	0.005	-0.013, 0.022	0.61
Change in BMD post switch-off TDF over follow-up	**0.004**	**0.001, 0.007**	**0.008**	0.002	-0.002, 0.006	0.24

** Denotes adjusted for age, gender, ethnicity, smoking status and BMI*

Conclusions

- In this cohort of PWH on contemporary ART regimes and a comparable HIV- control group, change in both LS and FN BMD was similar over time irrespective of HIV status
- Despite baseline differences in BMD between PWH and HIV- subjects, there were no between-group differences in BMD at either site at last study visit
- Switching away from TDF was independently associated with increases in LS BMD, suggesting reversal of previous reductions in BMD in PWH to levels approaching the HIV- population

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References

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