

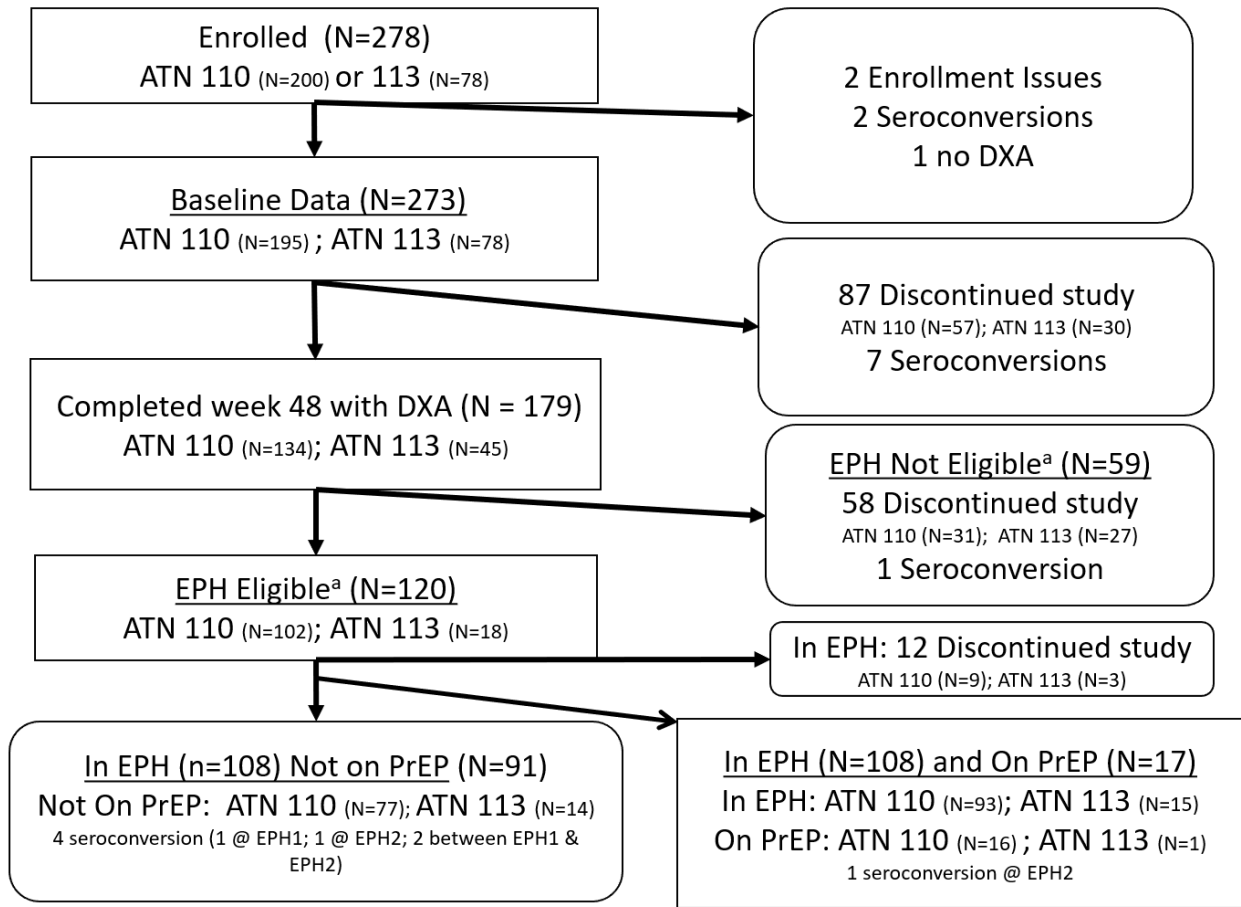
## Supplemental Figures and Tables

### Changes in Bone Mass After Discontinuation of Pre-Exposure Prophylaxis (PrEP) with Tenofovir Disoproxil Fumarate/Emtricitabine in Young Men Who Have Sex With Men: Extension Phase Results of Adolescent Trials Network Protocols 110 and 113

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Figure 1. Participant Flow Diagram.



Abbreviations: ATN, Adolescent Trials Network for HIV/AIDS Intervention; DXA, dual-energy X-ray absorptiometry; EPH, extension phase; PrEP, Pre-exposure prophylaxis

a. See text for eligibility criteria.

Supplemental Table 1. Baseline Characteristics of Participants ATN Studies 110/113

Characteristic	All Enrolled <sup>a</sup>	EPH-Eligible	Not EPH-Eligible	<i>p</i> -value
N	273	120	59	
Age years	19.1 ± 2.0	19.7 ± 1.8	18.4 ± 2.1	<b>&lt;0.001</b>
Hispanic	87 (31.8%)	37 (30.8%)	23 (39.0%)	0.551
Black/African American	141 (51.6%)	67 (55.8%)	28 (47.5%)	0.291
Alcohol	219 (82.0%)	100 (84.0%)	45 (78.9%)	0.407
BMI kg/m <sup>2</sup>	24.9 ± 6.6	25.8 ± 7.3	24.3 ± 6.5	0.184
Tanner Stage	4.82 ± 0.46	4.88 ± 0.37	4.75 ± 0.51	0.069
Whole-body BMD g/cm <sup>2</sup>	1.19 ± 0.11	1.19 ± 0.11	1.15 ± 0.11	<b>0.019</b>
Whole-body Z-score	-0.29 ± 1.08	-0.36 ± 1.07	-0.47 ± 1.02	0.507
Whole-body BMC	2668 ± 454	2702.9 ± 445	2521 ± 452	<b>0.011</b>
Lumbar spine (L1-L4) BMD g/cm <sup>2</sup>	1.08 ± 0.15	1.08 ± 0.14	1.04 ± 0.15	0.105
Lumbar spine z-score	-0.36 ± 1.12	-0.45 ± 1.12	-0.45 ± 1.11	0.974
Total hip BMD g/cm <sup>2</sup>	1.09 ± 0.16	1.09 ± 0.15	1.06 ± 0.17	0.257
Total hip Z-score	-0.20 ± 0.98	-0.25 ± 0.95	-0.32 ± 1.00	0.652
History of fractures	55 (20.2%)	25 (20.8%)	10 (16.9%)	0.538
Week 48 TFV-DP fmol/punch <sup>b</sup>	775 ± 575	864 ± 613	585 ± 412	<b>0.009</b>
Week 48 TFV-DP classification				0.361
>700	52 (32.5%)	40 (37.7%)	12 (23.5%)	
350-700	20 (12.5%)	13 (12.3%)	7 (13.7%)	
Detectable-350	31 (19.4%)	19 (17.9%)	11 (21.6%)	
BLQ	57 (35.6%)	34 (32.1%)	21 (41.2%)	

Abbreviations: BLQ, below the limit of quantitation; BMC, bone mineral content; BMD, bone mineral density; BMI, body mass index; EPH, Extension Phase; TFV-DP, tenofovir diphosphate

a. Data presented as Mean ± SD or N (%)

b. TFV-DP values are not imputed. The sample sizes for TFV-DP measurements are 103, 72, and 30 for all enrolled, EPH-eligible, and not EPH-eligible, respectively.

Supplemental Table 2. Baseline Characteristics of Participants Meeting Criteria for Extension Phase By Age

Characteristic	EPH-Eligible <sup>a</sup>	Ages 15-19 years	Ages 20-22 years	p-value
N	120	54	66	
Age years	19.7 ± 1.8	18.0 ± 1.2	21.0 ± 0.8	<b>&lt;0.001</b>
Hispanic	37 (30.8%)	20 (37.0%)	17 (25.8%)	0.206
Black/African American	67 (55.8%)	29 (53.7%)	38 (57.6%)	0.671
Alcohol	100 (84.0%)	40 (75.5%)	60 (90.9%)	<b>0.022</b>
Marijuana	61 (51.3%)	28 (52.8%)	33 (50.0%)	0.759
Height cm	175.0 ± 6.5	174.5 ± 6.3	175.3 ± 6.7	0.518
Weight kg	79.2 ± 22.9	77.4 ± 23.1	80.6 ± 22.9	0.440
BMI kg/m <sup>2</sup>	25.8 ± 7.3	25.5 ± 8.1	26.1 ± 6.6	0.629
Tanner Stage	4.88 ± 0.37	4.83 ± 0.42	4.92 ± 0.32	0.195
Whole-body BMD g/cm <sup>2</sup>	1.19 ± 0.11	1.19 ± 0.12	1.19 ± 0.10	0.729
Whole-body Z-score	-0.36 ± 1.07	-0.22 ± 1.11	-0.48 ± 1.02	0.184
Whole-body BMC	2703 ± 445	2663 ± 470	2735 ± 425	0.383
Lumbar spine (L1-L4) BMD g/cm <sup>2</sup>	1.08 ± 0.14	1.06 ± 0.15	1.08 ± 0.14	0.435
Lumbar spine z-score	-0.45 ± 1.12	-0.22 ± 1.05	-0.64 ± 1.14	<b>0.041</b>
Total hip BMD g/cm <sup>2</sup>	1.09 ± 0.15	1.09 ± 0.15	1.09 ± 0.14	0.798
Total hip Z-score	-0.25 ± 0.95	-0.09 ± 0.88	-0.38 ± 1.00	0.105
History of fractures	25 (20.83%)	10 (18.52%)	15 (22.73%)	0.572
Week 48 TFV-DP fmol/punch <sup>b</sup>	864 ± 613	759 ± 654	943 ± 574	0.208
Week 48 TFV-DP classification				0.216
>700	40 (37.7%)	13 (27.7%)	27 (45.8%)	
350-700	13 (12.3%)	8 (17.0%)	5 (8.5%)	
Detectable-350	19 (17.9%)	10 (21.3%)	9 (15.2%)	
BLQ	34 (32.1%)	16 (34.0%)	18 (30.5%)	

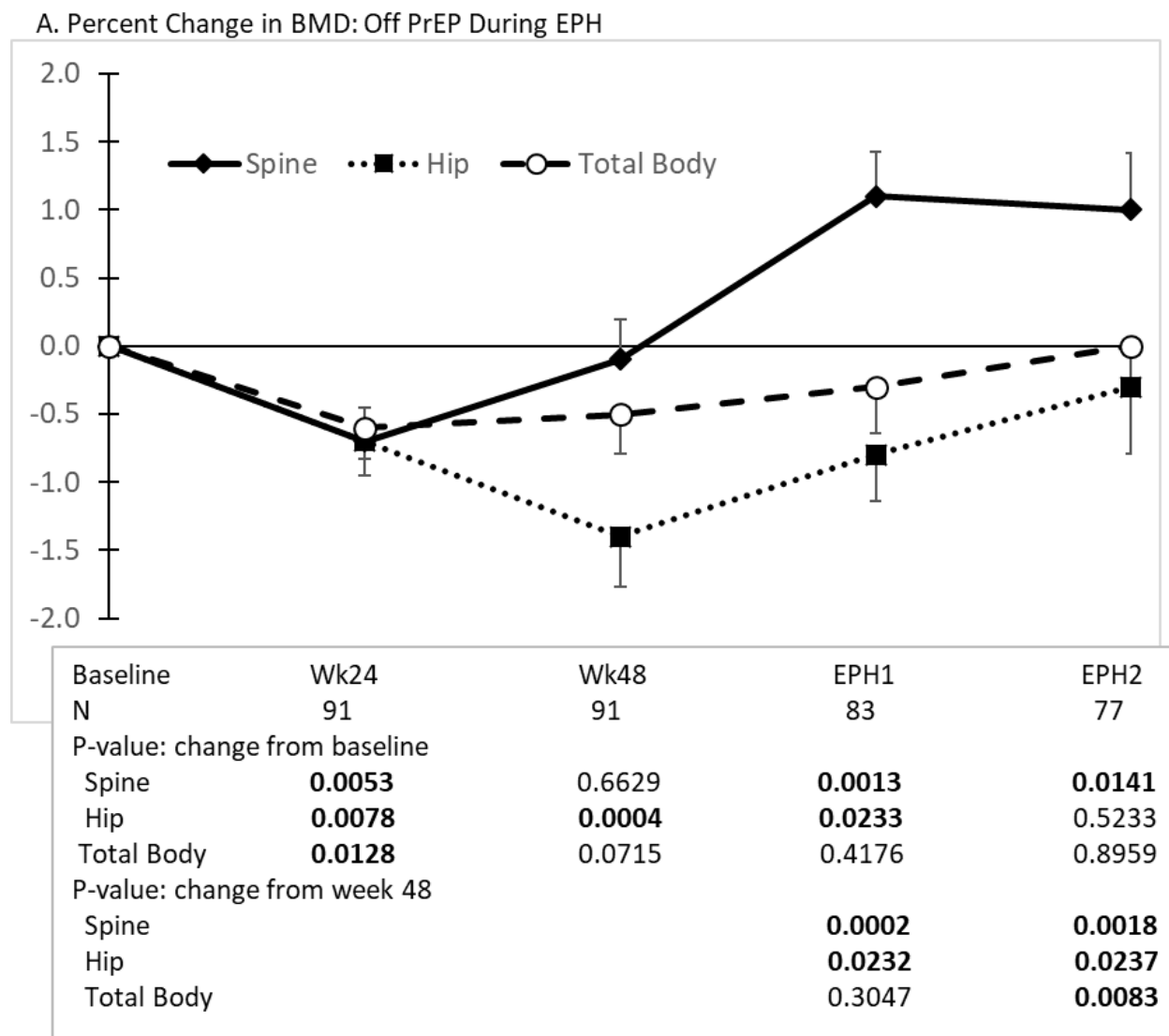
Abbreviations: BLQ, below the limit of quantitation; BMC, bone mineral content; BMD, bone mineral density; BMI, body mass index; EPH, Extension Phase; TFV-DP, tenofovir diphosphate

a. Data presented as Mean ± SD or N (%)

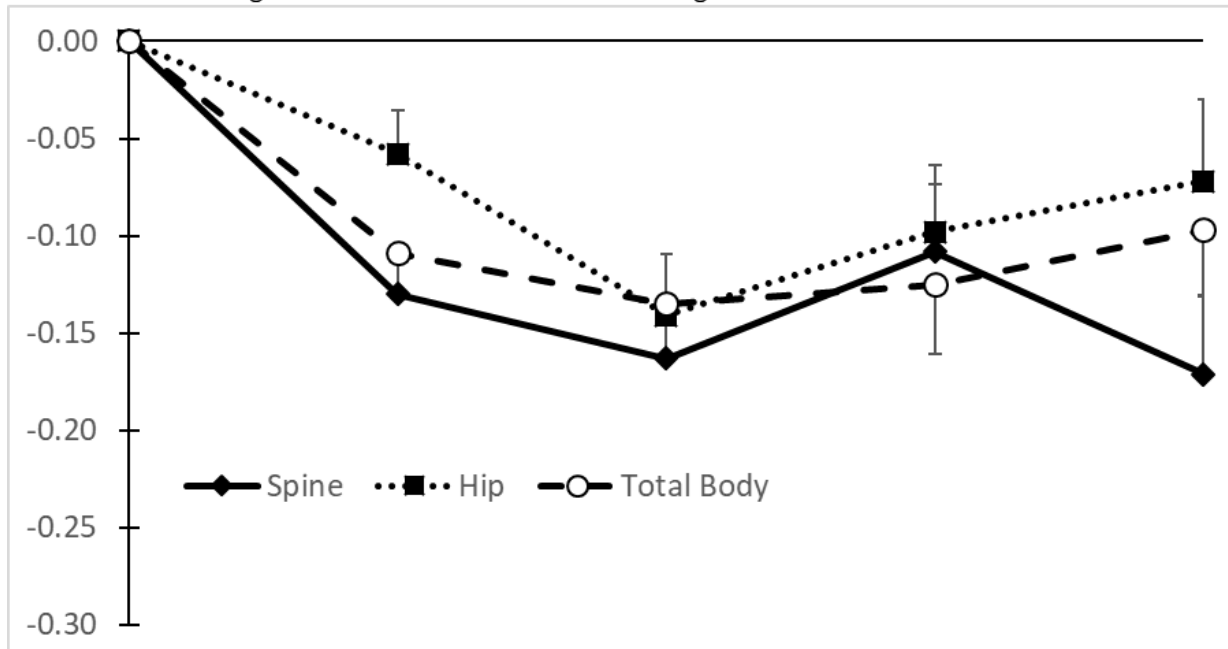
b. TFV-DP values are not imputed. The sample sizes TFV-DP measurements are 72, 31, and 41 for EPH-eligible, Age 15-19, and Age 20-22, respectively.

Figure 2. Changes in bone mass during TDF/FTC PrEP (baseline to week 48) and following PrEP discontinuation (week 48 to the second extension phase visit 48 weeks after stopping PrEP; EPH2) in HIV-seronegative young men who have sex with men (YMSM). Data are presented as percent change in bone mineral density (A) or change in Z-scores from baseline (B) and change in Z-score from baseline by age category for lumbar spine BMD (C) in YMSM who met one or more pre-specified criteria for bone toxicity while receiving PrEP (see text).

Abbreviations: BMD, bone mineral density; EPH1, extension phase visit 1, 24 weeks after stopping PrEP; EPH2, extension phase visit 2, 48 weeks after stopping PrEP; TDF/FTC, tenofovir disoproxil fumarate / emtricitabine; Wk, week

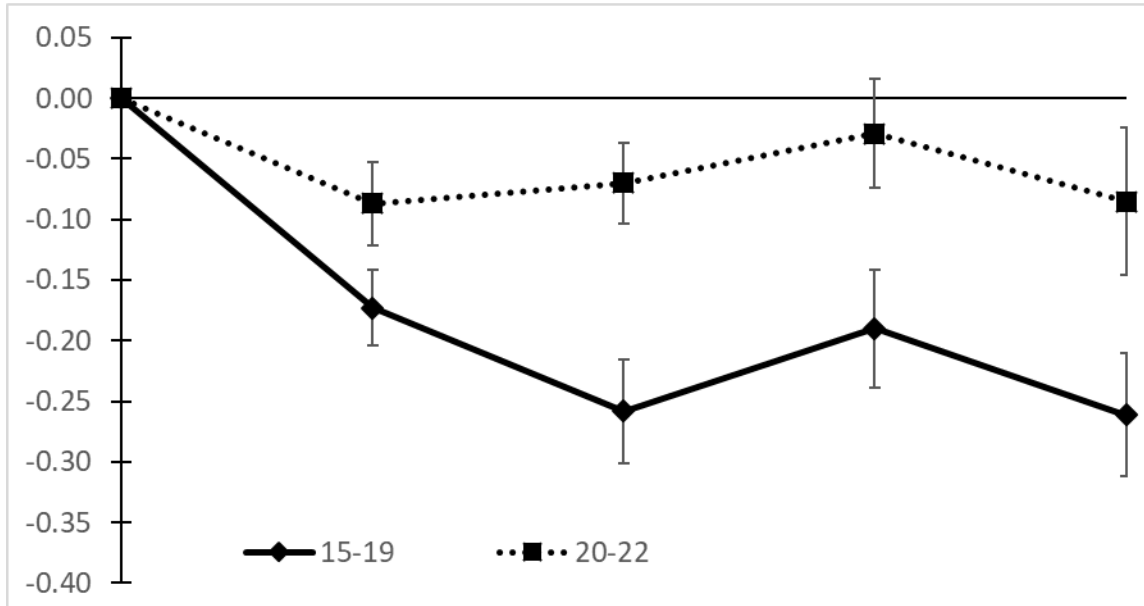


B. Absolute Change in BMD Z-Scores: Off PrEP During EPH



Baseline	Wk24	Wk48	EPH1	EPH2
N	91	91	83	77
P-value: change from baseline				
Spine	<b>&lt;0.0001</b>	<b>&lt;0.0001</b>	<b>0.0022</b>	<b>&lt;0.0001</b>
Hip	<b>0.0113</b>	<b>&lt;0.0001</b>	<b>0.0054</b>	0.0918
Total Body	<b>&lt;0.0001</b>	<b>&lt;0.0001</b>	<b>0.0008</b>	<b>0.0052</b>
P-value: change from week 48:				
Spine			0.1057	0.8834
Hip			0.0673	0.1007
Total Body			0.8555	0.1925

C. Absolute Change in Spine BMD Z-Score by Age: Off PrEP During EPH



	Wk24	Wk48	EPH1	EPH2
Baseline				
N 15-19	45	45	41	38
N 20-22	46	46	42	39
Baseline difference between age groups: p = 0.1200				
P-value for difference between age groups in change from baseline to each timepoint				
15-19 vs 20-22	0.0633	<b>0.0008</b>	<b>0.0175</b>	<b>0.0299</b>
15-19 age group P-values for change:				
From Baseline	<b>&lt;0.001</b>	<b>&lt;0.001</b>	<b>&lt;0.001</b>	<b>&lt;0.001</b>
From wk48			0.141	0.141
20-22 age group P-values for change:				
From Baseline	<b>0.014</b>	<b>0.043</b>	0.531	0.174
From wk48			0.441	0.964