

## BACKGROUND

Recent studies have increased the awareness of beneficial effects of vitamin D. Besides being essential for bone growth and preservation, antineoplastic and immunomodulatory effects have been described.

Considering the high prevalence of osteopenia (up to 60%) and osteoporosis (up to 15%) as well as the increasing number of neoplasias, adequate vitamin D levels seem particularly important in the HIV-population.

## AIMS

To determine vitamin D levels in HIV-positive patients comparing measurements by season as well as before and after the initiation of cART. To look for predictors for vitamin D deficiency.

## PATIENTS AND METHODS

**25(OH) vitamin D** was measured in 211 HIV-positive patients (Table 1).

Samples were taken **before initiation of cART** from Feb-Apr (**nadir sun exposure**) or from Aug-Oct (**maximal sun exposure**) as well as 12 (same season) and 18 months (alternate season) **after starting cART**.

We defined values **<30 nmol/L** as vitamin D deficiency, while **75 nmol/L 25(OH)D** was set as minimal target.

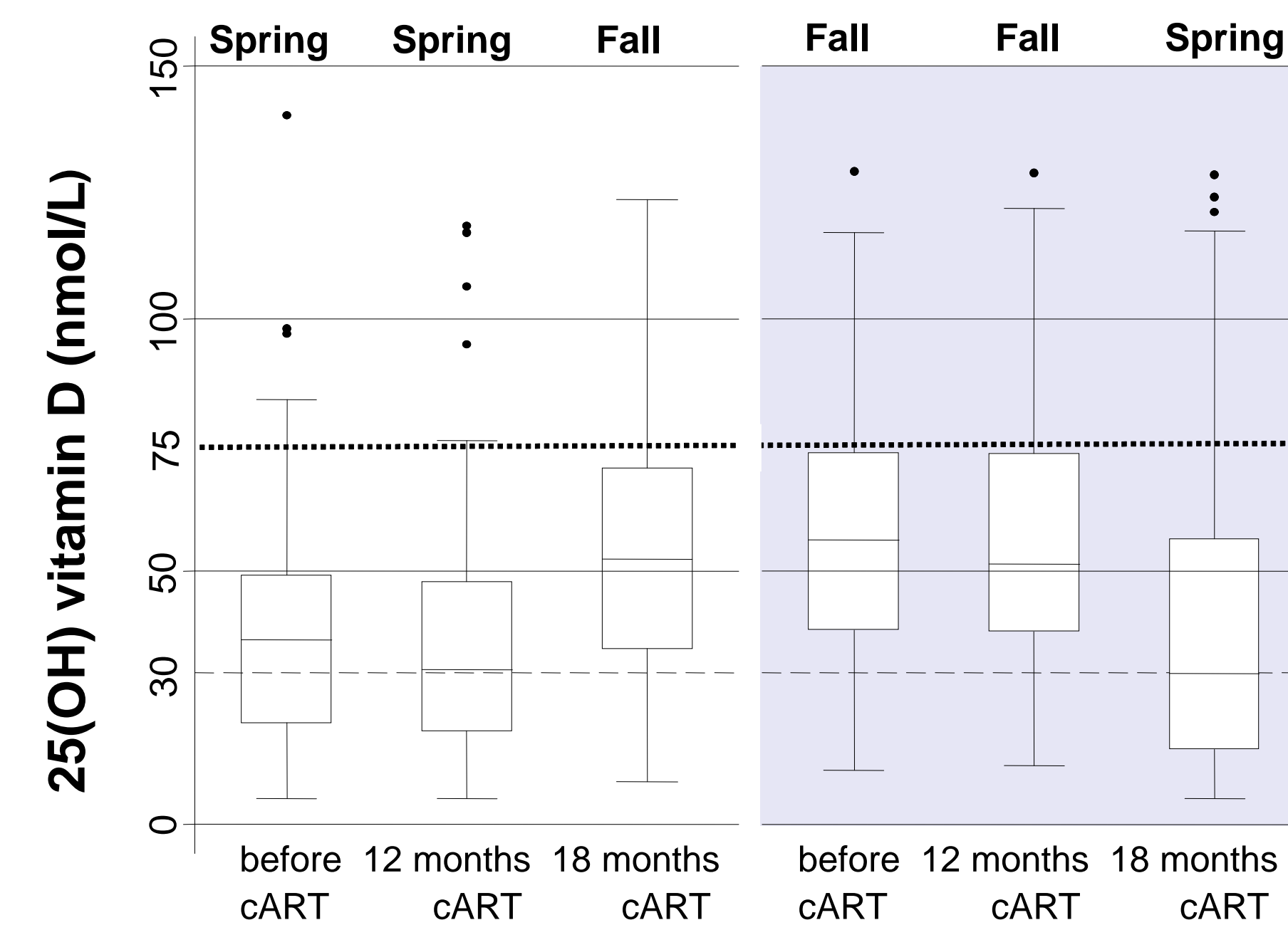
**1,25(OH)<sub>2</sub> vitamin D** was measured in a subset of 74 patients.

## RESULTS

### 25(OH) vitamin D

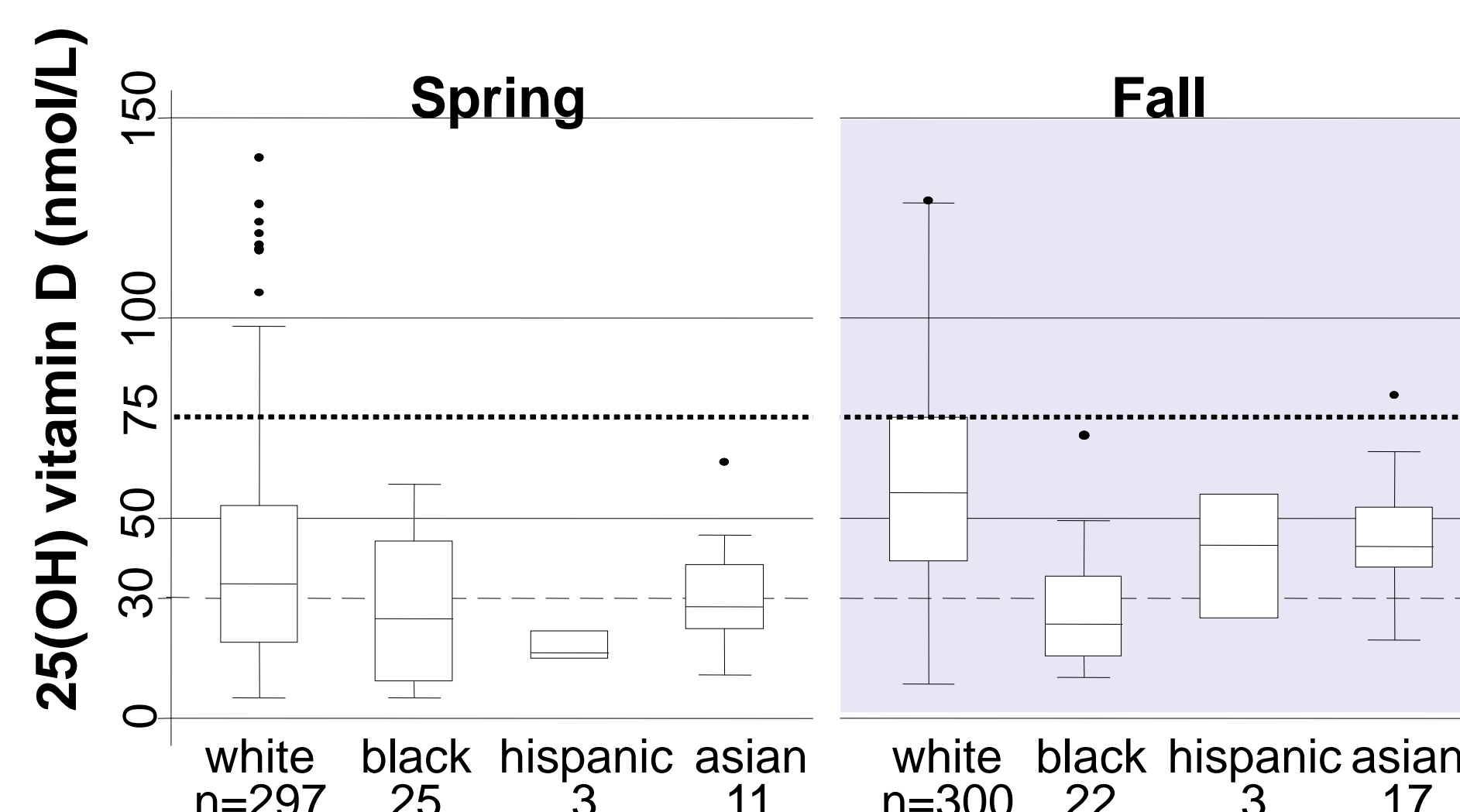
At each timepoint, 25(OH)D levels were significantly higher in fall than in spring (p <0.001), without significant change with respect to cART.

With 42%-52%, vitamin D deficiency was three times more frequent during springtime than in fall.



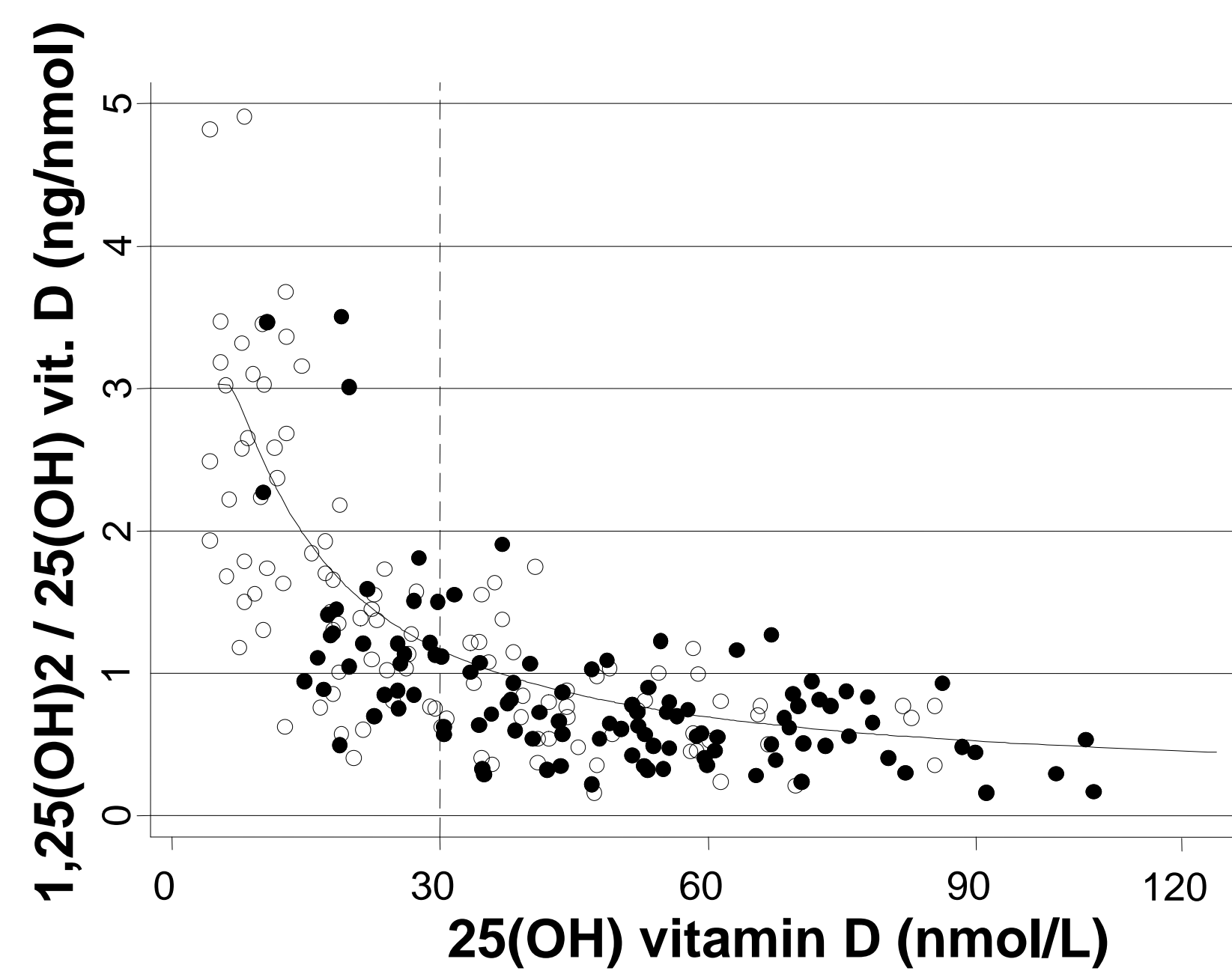
Baseline before cART:	Fall (n=108)	Spring (n=103)
Vitamin D deficiency	14%	42%
insufficiency	62%	53%
target level	24%	5%
12 months after cART start:	Fall	Spring
Vitamin D deficiency	14%	47%
insufficiency	63%	48%
target level	23%	5%
18 months after cART start:	Fall	Spring
Vitamin D deficiency	18%	52%
insufficiency	59%	38%
target level	23%	10%

Ethnicity was a significant predictor for serum 25(OH)D values (p<0.001). In both seasons, Caucasians had a lower prevalence of vitamin D deficiency and insufficiency



### 1,25(OH)<sub>2</sub> vitamin D

Correlating the 1,25(OH)<sub>2</sub>D to 25(OH)D ratio with 25(OH)D levels (below) indicates an exponential increase of 1-hydroxylation (i.e. vitamin D activation) with decreasing 25(OH)D levels. Black circles indicate measurements in fall, white circles in spring. This compensatory increase in renal 1-alpha-hydroxylation with decreasing 25(OH)D levels resulted in a less pronounced seasonal swing for 1,25(OH)<sub>2</sub>D (minus 3-13%) than for 25(OH)D (minus 36-43%).



	Baseline before cART		12 months after cART initiation		18 months after cART initiation	
	25(OH)D	1,25(OH) <sub>2</sub> D	25(OH)D	1,25(OH) <sub>2</sub> D	25(OH)D	1,25(OH) <sub>2</sub> D
Fall	57 (39-74)	39 (26-58)	51 (38-73)	36 (27-46)	53 (35-70)	34 (25-49)
Spring	37 (20-49)	34 (24-48)	31 (19-48)	32 (23-44)	30 (15-57)	33 (22-47)
Difference	<b>-36%</b>	-13%	<b>-40%</b>	-11%	<b>-43%</b>	-3%
p-value	<b>&lt;0.001</b>	0.07	<b>&lt;0.001</b>	0.3	<b>&lt;0.001</b>	0.4

Uni- and multivariable regression analyses of parameters influencing serum 25(OH) and 1,25(OH)<sub>2</sub> vitamin D levels

	25(OH)D		1,25(OH) <sub>2</sub> D	
	Univariable Coeff (95% CI)	p-value	Univariable Coeff (95% CI)	p-value
<b>Female sex</b>	-3.5 (-8.4; 1.4)	0.2	-4.2 (-10.2; 1.9)	0.2
<b>Age by 10 yrs</b>	0.8 (-1.2; 2.9)	0.4	0.1 (-2.6; 2.8)	1.0
<b>Caucasian</b>	<b>17.1 (10.7; 23.6)</b>	<b>&lt;0.001</b>	<b>14.1 (6.0; 22.1)</b>	<b>0.001</b>
<b>BMI</b>	-0.4 (-1.0; 0.2)	0.2	-0.7 (-1.5; 0.0)	0.05
<b>Active IDU</b>	-5.0 (-13.2; 3.2)	0.2	<b>-11.2 (-21.0; -1.5)</b>	<b>0.02</b>
<b>HCV positivity</b>	-7.1 (-15.5; 1.2)	0.1	-7.8 (-17.5; 1.9)	0.1
<b>cGFR &lt;60 mL/min</b>	21.3 (-1.4; 44.0)	0.07	8.6 (-17.6; 34.8)	0.5
<b>Duration of HIV by 10 yrs</b>	<b>6.9 (2.9; 11.0)</b>	<b>0.001</b>	<b>6.4 (1.2; 11.7)</b>	<b>0.02</b>
<b>Previous AIDS</b>	2.1 (-3.6; 7.8)	0.5	1.4 (-4.9; 7.7)	0.7
<b>CD4 count by 100 cells/uL</b>	-0.2 (-1.2; 0.7)	0.6	0.2 (-0.9; 1.3)	0.7
<b>Spring vs. Fall</b>	<b>-19.2 (-23.2; -15.2)</b>	<b>&lt;0.001</b>	<b>-17.7 (-22.5; -13.0)</b>	<b>&lt;0.001</b>
<b>TDF use</b>	4.1 (-3.4; 11.6)	0.3	3.8 (-3.8; 11.4)	0.3
<b>NNRTI use</b>	<b>-8.7 (-14.0; -3.5)</b>	<b>0.001</b>	<b>-8.2 (-13.3; -3.0)</b>	<b>0.002</b>

## CONCLUSIONS

- With 42-52% in spring and 14-18% in fall, vitamin D deficiency was highly prevalent
- Black ethnicity was a significant risk factor for vitamin D deficiency
- NNRTI-use was associated with significantly lower 25(OH)D levels
- TDF-use correlated with higher serum 1,25(OH)<sub>2</sub>D and serum alkaline phosphatase levels
- we suggest systematic screening for vitamin D deficiency in all HIV-positive patients

**Table 1:**

Baseline characteristics	Fall (n = 108)	Spring (n = 103)
Male gender	80 (74%)	78 (76%)
Age in years	38 (33-44)	36 (31-45)
Caucasian	93 (86%)	92 (89%)
Previous AIDS	15 (14%)	15 (15%)
HIV transmission		
homosexual	35 (32%)	50 (48%)
heterosexual	54 (50%)	42 (41%)
iv drug use	19 (18%)	11 (11%)
CD4 cells/mL	223 (136-317)	230 (135-352)
BMI (kg/m <sup>2</sup> )	22.6 (20.4-25.4)	23.1 (21.2-25.2)
cGFR (mL/min)	105 (91-124)	109 (98-120)
<b>future cART</b>		
+TDF	20 (19%)	15 (15%)
+NNRTI	53 (49%)	38 (37%)
+PI	55 (51%)	63 (61%)
neither NNRTI nor PI	7 (6%)	8 (8%)