

## Background

- Persons living with HIV (PLWH) and diabetes mellitus (DM) have increased levels of pro-inflammatory cytokines<sup>1</sup>
- The increased inflammation damages CD4 cells<sup>2,4</sup>, and can result in greater deleterious effects when one or both diseases are uncontrolled<sup>5</sup>
- However, PLWH with DM have faster CD4 count recovery<sup>6</sup> and higher CD4 counts<sup>5,7</sup> compared to PLWH without DM
- Despite PLWH and DM having higher CD4 counts than PLWH without DM, there has been no research on whether different glycosylated hemoglobin (HbA1c) levels are associated with CD4 count trends

## Objectives

- To examine the association between different levels of HbA1c control on the patterns of change in CD4 count among PLWH receiving care in Washington, DC

## Methods

- Study population:** DC Cohort, an observational clinical cohort of PLWH followed from Jan 2011-Mar 2018 at 14 sites in Washington, DC
- Inclusion criteria:** diagnosis of DM; ≥18 years old; ≥1 year of follow-up with ≥2 HbA1c results and ≥2 CD4 count results; and prescribed an ongoing antiretroviral (ART) regimen
- Glycemic control groups:** based on the most recent HbA1c result categorized into one of three control levels
  - Strict, HbA1c <7.5%;
  - Moderate, HbA1c between 7.5-9.0%;
  - Uncontrolled, HbA1c >9.0%
- CD4 cell count:** defined as a continuous, time-dependent variable based on repeated laboratory measurements
- Additional independent variables including: age, sex at birth, most recent BMI, use of oral DM medications, use of insulin, nadir CD4, sustained viral suppression (VS) (viral load <200 copies/mL throughout study period), AIDS diagnosis status, and ever having a cancer diagnosis were collected from the participant's medical record
- Statistical analysis:** linear mixed effects (LME) model using an unstructured variance-covariance form in the repeated CD4 count measurements

**Table 1. Baseline characteristics and co-morbidities of PLWH and DM, DC Cohort, 2011-2018. (n=554)**

Characteristic	N	%
Age at enrollment (median, IQR)	54	(48, 60)
Sex (male)	391	70.6%
Race/ethnicity		
NH Black	458	82.7%
Other/unknown	96	17.3%
Duration of infection at time of enrollment (median, IQR)	14.4	(8.0, 19.8)
Sustained VS (VL<200 copies/mL)	374	67.50%
AIDS diagnosis at enrollment	273	49.3%
Nadir CD4 at enrollment (cells/μl) (median, IQR)	281.5	(122,425)
Co-morbidities		
Cancer	52	9.4%
Dyslipidemia	431	77.8%
Hypertension	432	78.0%

## Summary of Results:

- Among 554 participants, there were 5,122 total CD4 count measurements with a median of nine measurements (IQR 6,12) per participant
- All three HbA1c groups had a similar increase over time in CD4 count (p=0.49); however, participants with moderate HbA1c had higher mean CD4 counts over the follow-up period than strict HbA1c control (strict: 687 cells/μL, moderate: 726 cells/μL; p=0.0463)
- PLWH with DM who were female, of younger age, overweight or obese, had a higher nadir CD4 count, were continually virally suppressed, had no history of cancer or an AIDS diagnosis had higher mean CD4 counts over the follow-up period
- CD4 count change was not affected by duration of HIV diagnosis, being newly diagnosed with diabetes, or use of diabetic medications
- In multivariate analysis, participants with moderate HbA1c control showed a significant difference in CD4 count compared to those with strict control (mean difference=18.6; p=0.026)

## Conclusions

- The rate of increase in CD4 count over the study period was similar between the three HbA1c groups
- PLWH and DM with moderate HbA1c control had higher CD4 counts than those with strict HbA1c control and similar CD4 counts compared to those with uncontrolled HbA1c levels
- Strict HbA1c control may improve other outcomes, such as cardiovascular disease; however, there was no observed effect on maintaining strict control to benefit CD4 count
- Additional research may help clarify which groups of PLWH benefit most from strict versus moderate glucose control for improving overall outcomes

## Results

**Table 2. Univariate and multivariate models of average mean difference in CD4 cell count among PLWH with DM, DC Cohort, 2011-2018**

Category	Univariate Analysis		Multivariate Analysis**		
	Average mean difference in CD4 count cells/μL (SE)	p-value*	Average mean difference in CD4 count cells/μL (SE)	p-value*	
HbA1c group	Uncontrolled (>9.0%)	20.9 (11.9)	0.185	15.4( 11.6)	0.184
	Moderate Control (7.5-9.0%)	21.5 (8.6)	0.032	18.1(8.3)	0.029
	Strict Control (<7.5%)	reference		reference	
Age at enrollment (per 10 year interval)		-38.7 (13.1)	0.003	-2.2 (1.1)	0.043
Sex	Females	167.1 (28.1)	<0.0001	96.7 (23.3)	<0.0001
	Males	reference		reference	
Race/ethnicity	Non-Hispanic black	reference		-----	
	All other race/ethnicities	-28.9 (32.0)	0.366	-----	
Most recent BMI category	>30 kg/m2	83.5 (14.2)	<0.0001	65.1 (13.7)	<0.0001
	25-30 kg/m2	37.3 (12.1)	0.002	31.0 (11.7)	0.083
	<25 kg/m2	reference		reference	
Diabetes diagnosis at enrollment	No	56.5 (30.1)	0.061	-----	
	Yes	reference		-----	
On a non-insulin medication	No	-16.8 (10.5)	0.110	-----	
	Yes	reference		-----	
On insulin	No	-5.8(14.3)	0.685	-----	
	Yes	reference		-----	
Duration of HIV diagnosis (median 14.3 years )	<Median	4.9 (26.6)	0.852	-----	
	≥ Median	reference		-----	
Nadir CD4 (median 281.5 cells/μL )	<Median	-287.3 (23.6)	<0.0001	0.71 (0.05)	<0.0001
	≥ Median	reference		reference	
Sustained VS (VL <200 copies/ML)	Yes	101.9 (29.1)	0.0005	80.7 (22.6)	0.0004
	No	reference		reference	
Duration of ARV use in database (median 4.4 years )	<Median	-36.2 (26.5)	0.172	-----	
	≥ Median	reference		-----	
Has a cancer diagnosis	Yes	-118.9 (29.7)	<0.0001	-101.5 (27.3)	0.0002
	No	reference		reference	
Has an AIDS defining diagnosis	Yes	-188.2 (32.8)	<0.0001	-----	
	No	reference		-----	
Hypertension	Yes	35.1 (19.3)	0.068	-----	
	No	reference		-----	
Dyslipidemia	Yes	20.0 (15.2)	0.188	-----	
	No	reference		-----	

All statistical tests performed within the framework of the linear mixed effects model.

\*p values in bold represent variables significant a p value of <0.05; p values for variables with more than two groups are adjusted for multiple comparisons with the Tukey method.

\*\*Multivariate model was first fit with all variables found to be significant in univariate analysis. Having an AIDS diagnosis was no longer significant in the multivariate model. Final multivariate model reported was adjusted for sex, age at enrollment, most recent BMI category, continuous nadir CD4, sustained viral suppression, and ever having cancer diagnosis.