

**HIV/AIDS CLINICAL CARE QUALITY MANAGEMENT CHART REVIEW**

**CHARACTERISTICS OF PATIENTS  
WITH LOW CD4 COUNTS IN 2008**

**AND**

**FACTORS ASSOCIATED WITH IMPROVED IMMUNOLOGIC STATUS  
FROM 2004 THROUGH 2008**



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## BACKGROUND

A primary receptor used by HIV to gain entry into host T cells is termed “cluster of differentiation 4” or CD4. HIV infection leads to a reduction in the number of T cells possessing CD4 receptors, commonly referred to as CD4 cells. The CD4 cell count is a key measure of the health of the immune system. Regardless of HIV status, an optimal CD4 count ranges between 500-1500, but the lower the count, the greater damage HIV has done. Anyone who has less than 200 CD4 cells, or a CD4 percentage less than 14%, is considered to have AIDS according to the US Centers for Disease Control.

Viral load is the measure of the number of virus particles (in this case HIV) present in the bloodstream, expressed as copies per milliliter. In addition to CD4 counts, measures of viral load can indicate whether the HIV disease is controlled and managed appropriately. *HIV suppression* is defined as a viral load less than 400 ( $VL \leq 400$ ) and *immunosuppression* is defined as CD4 count less than 200 ( $CD4 < 200$ ). A goal is for patients to have a high CD4 count ( $> 200$ ) and a low viral load ( $\leq 400$ ). Antiretroviral therapy (ART) is medications for the treatment of infection by retroviruses, primarily HIV.

To understand how the CD4 counts and viral loads are used to monitor patients with HIV, the analogy of a car has been used. The CD4 count represents the distance from *immunosuppression* (how far someone is from AIDS) and the viral load measures the speed of movement. The higher the viral load, the faster CD4 cells are killed by HIV. Slowing the speed of disease progression by reducing the viral load with ART is generally effective and results in recovery of CD4 cell counts after a few months on medications.

Data from the HIV/AIDS Clinical Care Quality Management Chart Review project funded by the Boston Public Health Commission and the Massachusetts Department of Public Health have shown overall high quality of care provided by clinics across Massachusetts. Nevertheless, there remain some patients who continue to have *immunosuppression* ( $CD4 < 200$ ) despite advances in ART. Since low CD4 counts increase risk for disease progression and death, it is important to (1) identify populations at higher risk of having low CD4 counts that could benefit from additional attention and (2) understand factors associated with CD4 cell recovery above 200 and improved immunologic status. This report represents an exploration of these questions.

The methods used to address these goals involved a two-step approach. The first step is a descriptive analysis of patients in the clinical chart review sample who had *immunosuppression* with CD4<200 when last checked in the most recent year of data collection, 2008. Taking this year as a snapshot of our study population, the research question answered by this phase is *What patient-level or clinic-level factors increase the risk of CD4<200?* The second step follows patients who had CD4<200 in 2003 for the next five years (from 2004 through 2008) to focus on trends over time for CD4 count recovery, medical hospitalization, loss to follow-up or death. Statistical methods helped to identify the factors that can predict immune system recovery and other outcomes. Taken together, the significant factors that emerge from each step can highlight any potential disparities and help to inform program or policy changes that may be warranted.

## **Step 1: Characteristics of Patients with a Last Measured CD4 $\leq$ 200 in 2008**

### **A1. Objectives**

The objectives of this analysis were (1) to describe the characteristics of patients whose last measured CD4 in 2008 (most recent chart review data available) was  $\leq$ 200 and (2) to identify factors associated with CD4 $\leq$ 200.

### **A2. Methods**

Using primary care chart review data from the Boston Public Health Commission (BPHC)-Massachusetts Department of Public Health Office of HIV/AIDS (MDPH) joint HIV clinical care quality management project, 1,139 of 1,267 patients (90%) reviewed in 2008 with at least one CD4 count and one viral load test measured during the year were identified for inclusion in this cross-sectional analysis. Patients who were newly diagnosed in 2008 (N= 73) were excluded. A total of 17 sites across Massachusetts receiving funds from BPHC and MDPH were represented in this sample. Multivariate logistic regression analyses were used to identify factors associated with having a last CD4 $\leq$ 200, with predictor variables including gender, age, country of birth, race/ethnicity, risk, diagnosis year, antiretroviral therapy (ART) status, history of mental illness, history of substance abuse, and last viral load suppression (VL $\leq$ 400) in 2008.

### **A3. Results**

#### **i. Sample Demographics**

**Table 1** shows that of the 1,139 eligible patients in this cross-sectional analysis, 61% were male, 38% White non-Hispanic, 30% Black non-Hispanic, and 28% Hispanic. About 29% of patients were MSM and 22% had IDU as a risk factor. Sixty-two percent were born in the US and 71% were under age 50. About 22% were diagnosed with HIV prior to 1996, 23% were diagnosed between 1996 and 2000, 30% between 2001 and 2005, and 24% after 2005. The rate of ever having a history of mental illness documented from 2003-2008 was 58% and 40% of patients

had history of any substance abuse during the same time period. About 25% of patients were hepatitis C virus positive (HCV positive).

Thirteen percent of patients had at least one documented hospitalization in 2008. Ninety-six percent of patients who were eligible for ART were ever on ART during the year. ART eligible is defined by Health Resources and Services Administration (HRSA) as having ever been on ART or having any  $CD4 \leq 200$  or any  $VL > 100,000$  in the year. Approximately 30% of patients had their first  $CD4 \leq 200$  when they entered care at the clinic.

A total of 17 sites were included (**Appendix A – Table C**): 9 are located in the metro Boston area, 11 are community health centers, and 4 sites have caseloads of greater than 200. Some sites fall into more than one category.

**Table 1. Sample Characteristics & Characteristics of Patients with Last CD4<200 in 2008**

	Eligible from Chart Review in 2008 % (n)	Last CD4>200 In 2008 % (n)	Last CD4<200 In 2008 % (n)
<b>Total</b>	N=1,139	N=1011	N= 128
<b>Gender</b>			
Male	61% (691)	61% (614)	60% (77)
Female	39% (441)	39% (391)	39% (50)
Transgender	<1% (7)	<1%(6)	<1% (1)
<b>Race/Ethnicity</b>			
White non-Hispanic	38% (436)	39% (395)	32% (41)
Black non-Hispanic	31% (347)	30%(307)	31% (40)
Hispanic	28% (322)	28% (279)	34% (43)
Other	3% (33)	3% (29)	3% (4)
<b>HIV Risk</b>			
IDU	22% (251)	20% (199)	<b>41% (52)†</b>
MSM	29% (326)	30% (307)	<b>15% (19) **</b>
Heterosexual	62% (700)	62% (623)	60% (77)
<b>Country of Birth</b>			
US born	62% (709)	61% (617)	<b>72% (92)*</b>
Non US born	38% (407)	39% (391)	28% (36)
<b>Age</b>			
<50	70% (802)	71% (713)	70% (89)
≥50	30% (336)	29% (297)	30% (39)
<b>HIV Diagnosis Year</b>			
<1996	22% (246)	20% (200)	<b>38% (46)†</b>
1996-2000	23% (249)	23% (226)	19% (23)
2001-2005	31% (335)	32% (317)	15% (18)
2006 onwards	24% (268)	24% (234)	28% (34)
<b>Hepatitis C Positive</b>			
Yes	25% (284)	23% (227)	<b>45% (57)†</b>
<b>Anti-retroviral Therapy</b>			
Ever on ART in 2008	84% (956)	83% (843)	88% (113)
On ART at last visit	82% (937)	82% (832)	82% (105)
On ART	84% (956)	83% (843)	<b>88% (113)†</b>
Not eligible	12% (139)	14% (139)	-
Eligible but not on ART	4% (44)	3% (29)	12% (15)
<b>Mental Illness</b>			
Any history between 2003 & 2008	58% (660)	58% (585)	59% (75)
<b>Substance Abuse</b>			
Any history between 2003 & 2008	40% (451)	38% (387)	<b>50% (64)*</b>

\*p<0.05, \*\*p<0.01, †p<0.0001

<b>Table 1 (continued). Sample Characteristics &amp; Characteristics of Patients with Last CD4<math>\leq</math>200 in 2008</b>			
	Eligible from Chart review in 2008 % (n)	Last CD4 $>$ 200 In 2008 % (n)	<b>Last CD4<math>\leq</math>200 In 2008 % (n)</b>
<b>Hospitalization in 2008</b>			
Any (including non-HIV/AIDS related, substance use, and mental health)	13% (146)	11% (110)	<b>28% (36)†</b>
Any Medical Only (including non-HIV/AIDS related but excluding substance use and mental health)	12% (135)	10% (100)	<b>27% (35)†</b>
<b>Number of Primary Care Visits in 2008</b>			
$\geq 2$ visits	93% (1063)	94% (946)	91% (117)
1 visit	5% (62)	5% (55)	5% (7)
0 visits	1% (14)	1% (10)	3% (4)
<b>Initial CD4 at Entry to Care at the Current Site of Care</b>			
$\leq 50$	11% (127)	9% (95)	<b>25% (32)†</b>
51-200	19% (218)	18% (181)	29% (37)
201-500	40% (451)	40% (405)	36% (46)
$> 500$	29% (332)	32% (320)	9% (12)
Not available	1% (11)	1% (10)	$< 1\%$ (1)
<b>Last VL<math>\leq 400</math> in 2008</b>			
$\leq 400$	78% (889)	81% (816)	57% (73)
<b>Site Characteristics</b>			
Metro-Boston	55% (627)	56% (564)	49% (63)
Community Health Center	53% (606)	54% (542)	50% (64)
Caseload $> 200$	47% (535)	47% (478)	45% (57)

\*p $<$ 0.05, \*\*p $<$ 0.01, †p $<$ 0.0001

## ii. CD4 Count Results

Of the 1,139 patients, 18% (199) had any CD4 $\leq$ 200 during the year, with 11% (128) having a last CD4  $\leq$ 200 in 2008. Of those with any CD4 $\leq$ 200, about half remained with a CD4 $\leq$ 200 throughout the year (**Table 2**).

- Last CD4  $\leq$ 200 in 2008: 11% (128/1139)
- Any (Ever) CD4  $\leq$ 200: 18% (199/1139)
  - Always CD4 $\leq$ 200: 8% (90);
  - Sometimes  $\leq$ 200: 10% (109);
- Never  $\leq$ 200: 83% (940)

<b>Table 2. Frequency of CD4<math>\leq</math>200 and viral suppression (VL<math>\leq</math>400) throughout the year</b>		
	CD4 $\leq$ 200 (N=1,139)	VL $\leq$ 400 (N=1,000)*
<b>Ever (includes Always and Sometimes)</b>	<b>18%</b>	<b>90%</b>
Always	8%	73%
Sometimes	10%	16%
<b>Never</b>	<b>83%</b>	<b>10%</b>

\*Not including patients who are not eligible for ART in viral load analysis.

As discussed, in addition to CD4 counts, measures of viral load can indicate whether HIV disease is controlled and managed appropriately. In this sample, approximately 90% of patients who were eligible for ART were ever viral suppressed in 2008 (73% always suppressed, 16% sometimes suppressed). Ten percent of patients were never suppressed or had all viral loads  $>$ 400 during the year.

Focusing on the last CD4 and last viral load measured during the year and excluding patients ineligible for ART, patients were categorized into four groups (**Table 3**). About 79% of patients were suppressed with a last CD4 $>$ 200, 9% had last CD4 $>$ 200 but were not viral suppressed, 7% had a last CD4 $\leq$ 200 but were viral suppressed, and 6% were not suppressed and had a CD4 $\leq$ 200. The median last CD4 count among those **suppressed** with a last CD4 $\leq$ 200 was somewhat higher (median = 157 cells/mm<sup>3</sup>) than those who were *not suppressed* (median = 105 cells/mm<sup>3</sup>) (p $<$ 0.05). Results of this show as expected **that there is less viral suppression among patients with CD4 $\leq$ 200.**

<b>Table 3. Last CD4 and last viral load (suppression is VL<math>\leq</math>400) (N=1,000)*</b>		
	Total	%
Last CD4 $>$ 200 and VL $\leq$ 400	785	79%
<b>Last CD4<math>\leq</math>200 and VL<math>\leq</math>400</b>	<b>73</b>	<b>7%</b>
Last CD4 $>$ 200 and VL $>$ 400	87	9%
<b>Last CD4<math>\leq</math>200 and VL<math>&gt;</math>400</b>	<b>55</b>	<b>6%</b>

\*Excluding patients not eligible for ART in viral load analysis.

Viral suppression rates were lower among patients with last CD4 $\leq$ 200 versus those with CD4 $>$ 200 (**Figure 1** and **Table 4**). Among patients with a last CD4 $\leq$ 200, 41% were always suppressed throughout the year and 35% were never suppressed. This compares to 78% of patients with last CD4 $>$ 200 who were always suppressed and 7% never suppressed.

**Figure 1. Viral suppression rates among patients with last CD4 $\leq$ 200 versus CD4 $>$ 200 (N=1000, ART eligible)**

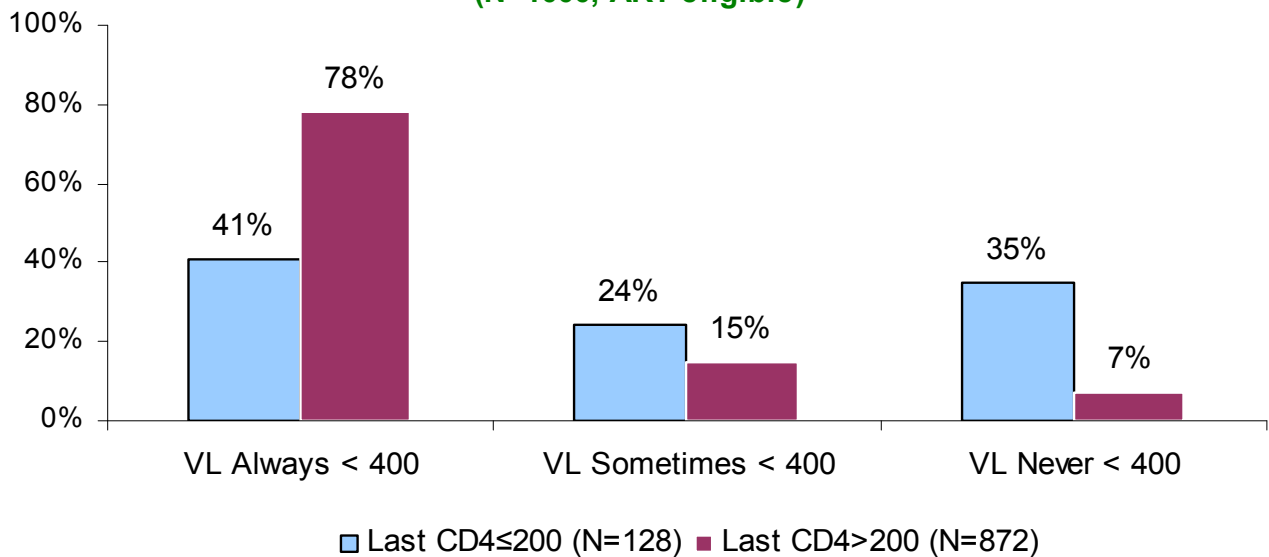


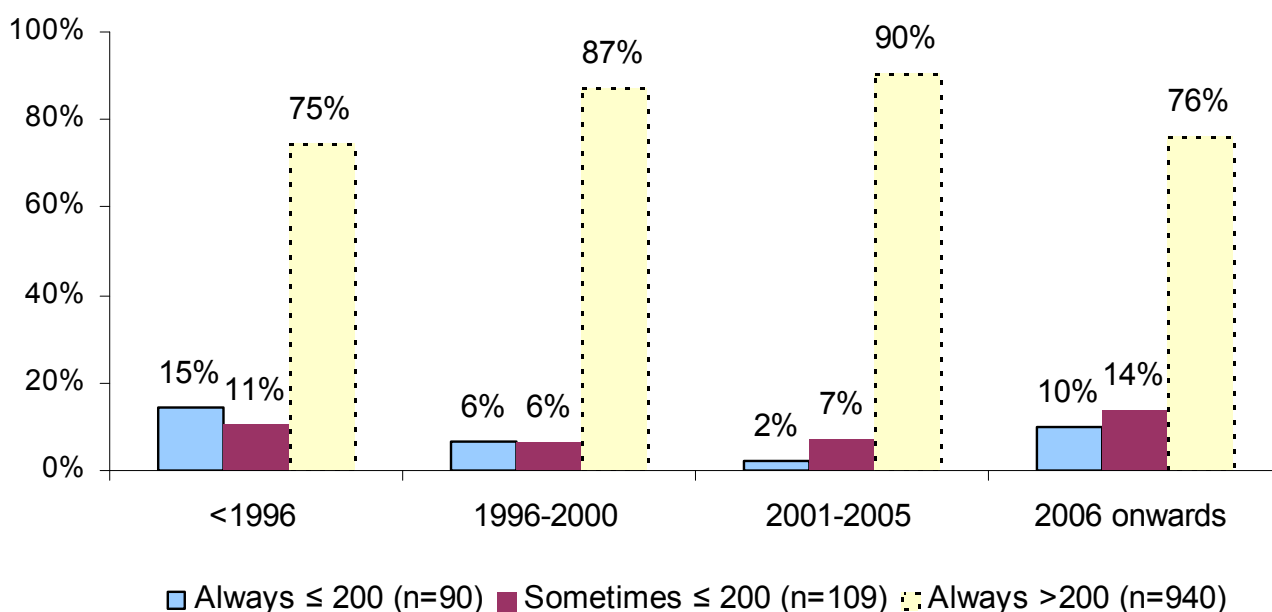
Table 4. Viral suppression rates overall among patients with last CD4 $\leq$ 200 versus CD4 $>$ 200 (N=1,000)*		
	Last CD4 $\leq$ 200 (N=128)	Last CD4 $>$ 200 (N=872)
VL Always $\leq$ 400	41%	78%
VL Sometimes $\leq$ 400	24%	15%
VL Never $\leq$ 400	35%	7%

\*Excluding patients not eligible for ART in viral load analysis.

### iii. CD4 counts throughout 2008 by HIV diagnosis year

Figure 2 shows the frequency of CD4 $\leq$ 200 throughout 2008 by the categories of year of diagnosis or first entry to care at the clinic. Patients who were diagnosed *prior to 1996* or *in 2006 or later* had a higher risk of always having a CD4 $\leq$ 200 than patients who were diagnosed during 1996-2005 ( $p<0.0001$ ).

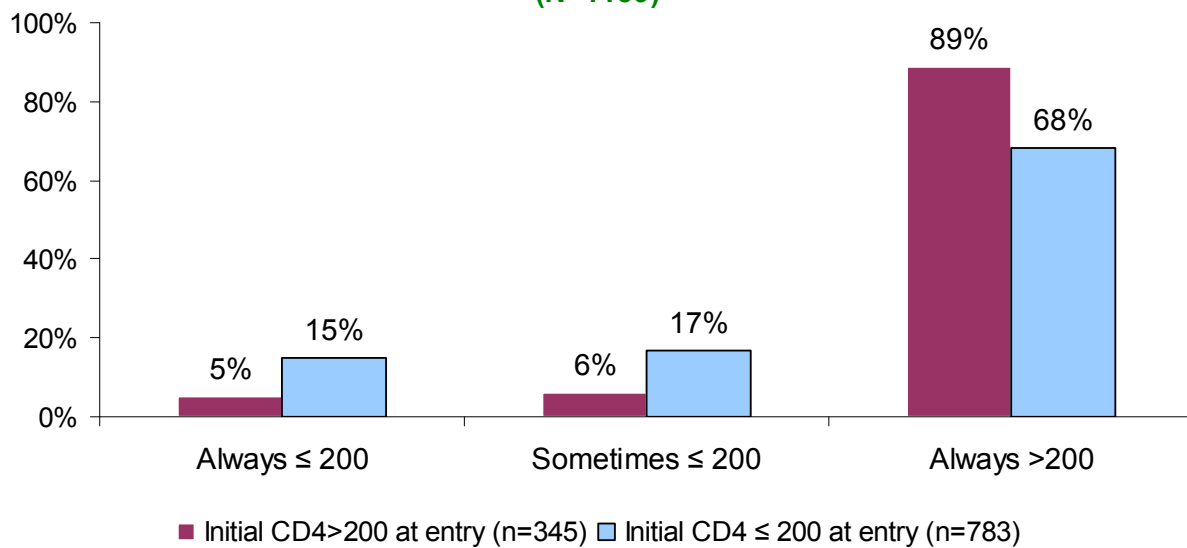
Figure 2. CD4 counts throughout 2008 by year of diagnosis (N=1139)



#### iv. CD4 counts throughout 2008 by initial CD4 count at entry to care

Not surprisingly, patients who first entered care with  $CD4 \leq 200$  were much more likely to remain with  $CD4 \leq 200$  in 2008 (15%) compared to patients who entered care with a  $CD4 > 200$  (5%) (Figure 3). Likewise, patients who entered care with a  $CD4 > 200$  were more likely to always have a  $CD4 > 200$  in 2008 than patients who entered with an initial  $CD4 \leq 200$  (89% versus 68%).

**Figure 3. CD4 counts throughout 2008 by initial CD4 count at entry to care**  
(N=1139)



## v. Characteristics of Patients with Last Measured CD4≤200 in 2008

Looking at the last CD4 count and viral load results in 2008, it is evident that (Table 5):

- (1) Low CD4 ≤200, rather than viral load status, is associated with higher rates of hospitalizations: 26%-31% with CD4 ≤200 were hospitalized versus 11%-12% among patients with higher last CD4 count were hospitalized.
- (2) IDU risk or being hepatitis C positive (which are highly correlated) is more associated with CD4 than viral load status: a greater percentage of patients with CD4≤200 (~40%) had IDU risk or were hepatitis C positive versus patients with last CD4>200 (~20%).

Older patients had higher rates of viral suppression, regardless of CD4 count; this may represent better adherence to medications or more consistent time on treatment, both of which could improve suppression. However, the degree of CD4 count “rebound” decreases with age (a biological factor). Also as expected, being on ART at last visit was more associated with higher rates of viral suppression than with CD4 counts. US born patients also appeared to have the highest risk of having both CD4≤200 and VL>400 (84%). **There were no differences by gender, race, or history of mental illness.**

Table 5. Characteristics of patients with last CD4≤200, with viral suppression or not									
	Male	Age ≥50 **	US Born **	White non- Hispanic	MSM Risk **	IDU Risk†	ART last visit†	HCV+ †	Any Medical Hospitalization †
Last CD4 >200 and VL≤400 (n=816)	61%	32%	61%	40%	29%	20%	95%	23%	10%
Last CD4 ≤200 and VL≤400 (n=73)	59%	34%	63%	30%	10%	40%	96%	49%	26%
Last CD4 >200 and VL>400 (n=195)	61%	18%	63%	36%	37%	18%	28%	22%	9%
Last CD4 ≤200 and VL>400 (n=55)	62%	26%	84%	35%	22%	42%	64%	41%	29%

\*p<0.05, \*\*p<0.01, †p<0.0001

Comparing the characteristics of patients with last CD4>200 versus those with last CD4≤200 in 2008 regardless of viral load status showed some similar findings (**Table 6**). Non-US born patients and patients with MSM risk were *less likely* to have a last CD4≤200. Patients with documented IDU risk at entry and those who were hepatitis C positive were *more likely* to have a last CD4≤200 in 2008.

<b>Table 6. Characteristics of patients with last CD4≤200 versus last CD4&gt;200</b>									
	Male	Age ≥50	US Born*	White non-Hispanic	MSM Risk **	IDU Risk †	ART last visit	HCV+ †	Any Medical Hospitalization †
Last CD4 ≤200 (n=128)	60%	30%	<b>72%</b>	32%	<b>15%</b>	<b>41%</b>	82%	<b>45%</b>	<b>27%</b>
Last CD4 >200 (n=1011)	61%	29%	<b>61%</b>	39%	<b>30%</b>	<b>20%</b>	82%	<b>23%</b>	<b>10%</b>

\*p<0.05, \*\*p<0.01, †p<0.0001

Furthermore, 54% of patients with last CD4≤200 in 2008 had an initial CD4≤200 compared to 27% of patients with last CD4>200. Patients with last CD4≤200 were also more likely to have any history of substance abuse than patients with last CD4>200. Patients diagnosed *prior to 1996 or in 2006 or after* were also more likely to have a last CD4≤200, potentially indicating long-term resistance or exposure to less effective medications among those diagnosed earlier and not yet sufficient time in care since diagnosis for immune recovery among those more recently diagnosed. (See **Table A – Appendix A**).

## **vi. Factors Associated with Last CD4≤200 – Multivariate Analysis**

We used multivariate regression modeling to identify factors associated with a last CD4≤200 in 2008. Independent variables included in the final model were gender, age, country of birth, race/ethnicity, risk, diagnosis year, history of mental illness, history of substance abuse, appropriate ART management (defined as being on ART or not ART eligible; inappropriate defined as eligible but not on ART), last viral load in 2008, and initial CD4 at entry to site. Site factors such as caseload (greater than 200 versus less than 200), facility type (community health center versus other), and location (metro-Boston versus not) were also controlled for in the model.

Factors presented at entry to care, including first CD4 count at the site  $\leq 200$  and entering care prior to 1996 were associated with higher risk of having a CD4  $\leq 200$  in 2008. Entering care prior to 1996 may be a marker for resistance due to longer term exposure to less effective ART. This factor remained significant after controlling for viral suppression in 2008. Entering care in the last two years (2006 or 2007) was also associated with higher risk of CD  $\leq 200$  in 2008 even after adjusting for CD4 count at entry. Factors associated with lower risk of having a low CD4 count in 2008 included having viral suppression ( $\leq 400$ ) by the end of the year and being on ART. Among patient demographic factors, having IDU as a risk (but not history of substance use while in care at the site) was associated with higher risk of having a CD4 $\leq 200$ . There were no patient demographics (race/ethnicity, age, gender) or site factors associated with low CD4 counts. **Table 7** shows those factors which were significantly associated with a last CD4 $\leq 200$  (See **Table B-Appendix A**, which shows all factors included in the model, including those non-significant).

<b>Table 7. Multivariate logistic regression: Significant factors associated with last CD4<math>\leq 200</math> in 2008</b>		
	Adjusted Odds Ratio	95% Confidence Interval
IDU risk	<b>2.82**</b>	1.56-5.09
Diagnosed prior to 1996	<b>3.35†</b>	1.98-5.66
Diagnosed 2006 or later	<b>1.80*</b>	1.08-3.02
Last VL $\leq 400$ in 2008	<b>0.23†</b>	0.14-0.37
Initial CD4 $\leq 200$ at entry to care	<b>7.69†</b>	4.72-12.5
Appropriate ART management (On ART or not ART eligible)	<b>0.29**</b>	0.13-0.63

\*p<0.05, \*\*p<0.01, †p<0.0001. Referent categories: no IDU risk, diagnosed between 1996 and 2005, last viral load>400 in 2008, initial CD4>200, eligible but not on ART

#### **A4. Conclusions**

Overall, there is high quality of care provided at Massachusetts clinics serving people living with HIV/AIDS as indicated in previous work. In this analysis, most patients eligible for antiretroviral therapy were on treatment. A risk factor associated with having a low CD4 count is being more recently diagnosed (2006 and later), potentially representing not enough time in

care to achieve immunologic recovery. Being a long term HIV patient diagnosed prior to the ART era (1996) is another risk factor for having a low CD4 count, potentially representing long standing resistance.

Among patient demographics, only IDU risk was associated with higher risk of advanced immunosuppression ( $CD4 \leq 200$ ) even after adjusting for age, race/ethnicity and substance abuse while in care at the site. While this association may be due to HCV co-infection, the two factors were highly correlated and therefore not distinguishable. Further work to understand this association will be important. ART and viral suppression ( $\leq 400$ ) were both associated with lower risk of  $CD4 \leq 200$ . **No other demographic subpopulations were identified as having higher risk for low CD4 counts.**

To continue delivering high quality of HIV care and to ensure optimal health outcomes, it is important that patients enter into care soon after an HIV diagnosis. This will minimize further compromise to the immune system. Aggressive ART treatment should also be initiated for patients presenting with advanced immune suppression. Given the medical advances in ART for HIV, the majority of patients can be successfully treated.

## **A5. Limitations**

While ART and viral suppression were both associated with lower risk of  $CD4 \leq 200$ , the appropriateness of the regimen was not assessed in this study; as resistance testing information was not always available. Factors such as active substance use were based on available documentation in the primary care chart and therefore may be incomplete if this information were recorded elsewhere, such as in case management charts.

## **Step 2: Five-Year Follow-Up of Patients with Last CD4 $\leq$ 200 in 2003**

### **B1. Objectives**

The objectives of this analysis were to describe the characteristics of patients with a last CD4 cell count (CD4)  $\leq$ 200 in 2003 and to identify factors associated with improved immunologic status during follow-up specifically: (1) achieving a CD4 $>$ 200 and (2) achieving two consecutive CD4 $>$ 200. Additionally, since low CD4 counts can indicate disease progression and poorer health status, factors associated with (3) becoming lost to care at the site or dying and (4) having a documented medical hospitalization during the follow-up period were also examined.

### **B2. Methods**

Using primary care chart review data from the Boston Public Health Commission (BPHC)-Massachusetts Department of Public Health Office of HIV/AIDS (MDPH) joint HIV clinical care quality management project, 189 of 1,358 patients (14%) who were reviewed in 2003 whose last CD4 in 2003 was  $\leq$ 200 were identified and were alive and in care by the end of the year. A total of 22 sites across the Massachusetts receiving funds from BPHC and MDPH were represented (**Appendix B – Table E**).

To identify factors associated with recovery from immune suppression at the end of the follow up period, a statistical method called “survival analysis” was used. Survival analysis is a set of techniques for studying the occurrence and timing of events. In this analysis, we modeled the amount of time patients remained with CD4 $\leq$ 200 and identified the time at which they achieved improved immunologic status: (1) achieving a CD4 $>$ 200 or (2) two consecutive CD4 $>$ 200. We also modeled (3) time to lost to care at the site or dying and (4) time to first medical hospitalization during follow-up after a last CD4 $\leq$ 200 in 2003. For each of the four analyses, a patient was followed or tracked until he/she either (a) reached the event/outcome of interest or (b) was censored, or in other words, when a competing event occurs prior to the event of interest. In this analysis, the competing events included if a patient were no longer receiving care at the

site, were not reviewed anymore<sup>1</sup>, or when the study follow-up time ended. No longer receiving care at the site refers to any patient who has transferred to another clinic, moved, was incarcerated for the year, was institutionalized, died, or was otherwise lost, since no additional data could be gathered. Patients with known reasons for leaving care at the site (transferred, incarcerated, moved, institutionalized) were not included in the definition of outcome number three: “lost to care at the site or death”. The count of the number of follow-up years ended when the event was reached, patient was no longer receiving care at the clinic, or the end of the study follow-up period was reached (12/31/2008 or the year of the last chart review for patients at some sites<sup>2</sup>). Kaplan-Meier (K-M) analyses were used to describe patient level characteristics associated with having each of the four events or outcomes during the study period. Trends were compared by various levels of patient demographics and statistical significance was assessed using the log-rank test.

Cox proportional hazards regression modeling was then used to determine significant factors associated with each of the four events during follow-up. Variables entered in the models included: age (age $\geq$ 50 or age $<$ 50), place of birth (US born or non-US born), race/ethnicity (non-Hispanic White or not), risk (IDU risk), year of entry to care at site, initial CD4 count at entry to care at site, antiretroviral therapy (ART) status, and last viral load suppression (VL $\leq$ 400) in 2003. These models produce “hazard ratios” which are interpreted like odds ratios and explain the degree to which subgroups differ with regards to rates of having an event or not.

### **B3. Results**

*Sample characteristics (see Appendix B – Table A for complete data table)*

Among the 189 patients with a last CD4 $\leq$ 200 in 2003 who were included in this cohort analysis, 65% were male, 33% White non-Hispanic, 26% Black non-Hispanic, and 37% Hispanic. About 16% of patients were MSM and 41% had IDU as a risk factor. Seventy-five percent were born in

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<sup>1</sup> Chart reviews were not conducted at seven of the 22 sites in the 2007-2008 cycle, thus the maximum study follow-up period for patients at these sites was three years. Also, one of the 22 sites was only reviewed up to the end of 12/31/2004, thus the study follow-up for patients at this site was one year (see italicized sites in Appendix B. Table E.). The maximum follow-up period for patients reviewed at all other sites was five years.

<sup>2</sup> As a result of the end of chart reviews at some sites, 22 patients were censored before achieving a CD4 $>$ 200, 30 patients were censored before achieving two consecutive CD4 $>$ 200, and 38 were censored before the event of a medical hospitalization was observed. Since patients were not observed for the full five year follow-up study period, it is possible that the rates of the events observed may be underestimated.

the US and 76% were under age 50. About 40% were diagnosed with HIV prior to 1996, 25% were diagnosed between 1996 and 2000, 36% between 2001 and 2003. The rate of ever having a history of mental illness documented from 1999-2003 was 58% and 60% of patients had history of any substance abuse during the same time period. Forty-seven percent of patients were hepatitis C positive and 29% had at least one documented hospitalization in 2003.

Approximately 82% of patients were ever on ART during the year, while 68% were on ART at last visit. Of the 16% (31) who were eligible due to a low CD4<200 but were *not* on ART in 2003, ten patients were newly diagnosed in the year (six of which entered care in October or later) leaving a short period of time to initiate ART in 2003. However, 80% (19) of the 31 patients not on ART in 2003 were on ART in 2004.

A total of 22 sites were included: 8 are located in the metro Boston area, 13 are community health centers, and 7 have patient caseloads greater than 200. Some sites fell into one of more categories.

To determine whether these 189 patients with a low CD4 count as of the end of 2003 had improved immunologic status during follow-up, Kaplan-Meier analyses were conducted. The positive outcomes/events of interest included (1) achieving a CD4>200 during follow-up and (2) achieving two consecutive CD4>200, a measure of a stronger immunologic response. Since low CD4 counts may indicate disease progression or poorer health status, two other events were also examined including (3) becoming lost to care at the site or dying and (4) having a documented medical hospitalization during follow-up. The results of these analyses are presented below.

**i. Outcome #1: Achieving CD4>200**

Of the 189 patients with a last CD4 $\leq$ 200 in 2003, 61% (115) achieved a CD4>200 during follow-up, while 39% (74) never achieved a CD4>200 during the observation period. The mean number of years to achieve a CD4 >200 was 1.45 years, indicating on average it took 1.45 years for these patients to improve their immunologic status (**Table 8**).

<b>Table 8. Percentage of patients who achieved a CD4&gt;200 by time to event (1/1/2004 – 12/31/2008<sup>1</sup>)</b>	
Number of Years of Follow-Up until CD4>200 <sup>3</sup>	Percentage of Patients (n)
<1/2 year	14% (16)
1	52% (60)
2	18% (21)
3	8% (9)
4	6% (7)
5	2% (2)
	<b>100% (115)</b>

Of the 74 patients whose CD4 count did not improve, 51% (38) dropped out or became lost to care at the site during the study period: 40% (15) died, 37% (14) were lost, 18% (7) transferred care, and 5% (2) moved. The mean number of years followed among these patients was 1.4 years.

The other 49% (36) of patients remained in care at the site and their CD4 count never improved during the entire duration of follow-up. Of these 36 patients, 61% (22) were male, 92% (33) were under the age of 50, 89% (32) were US born, and 25% (9) were White non-Hispanic. The majority had any IDU risk and a history of substance abuse (53%, 19; 75%, 27), while 50% (18) had heterosexual risk. Fifty-six percent (20) were diagnosed prior to 1996 and 56% (20) had a history of mental illness. Most, about three-quarters (72%, 26) were on ART at last visit in 2003, with only 25% (9) having the last VL $\leq$ 400 in 2003.

<sup>3</sup> The count of the number of years followed up ends when the “event” CD4>200 occurs or when patient becomes lost to care whichever comes first. Number of years is rounded to the nearest year. For example, patients who were followed to the end of 2004 or before mid-2005 are considered to have contributed 1 year of follow-up time.

## Analyses

Kaplan-Meier analyses were used to examine rates of achievement of CD4>200 during follow-up for individual patient characteristics. Patients who were born outside of the US, age 50 and over, not HCV positive, and patients with no IDU risk were more likely to ever achieve a CD4>200 during follow-up. Patients on ART at last visit in 2003 and those whose last VL ≤400 in 2003 were also more likely to achieve an improved CD4>200 during follow-up. Patients diagnosed between 2001 and 2003 (versus those diagnosed before 1996 or after 2006) were more likely to have improved immunologic status during follow-up, indicating that newer patients do recover given enough time in care (see **Appendix B – Table B** for complete data table). This supports findings from Step 1 analysis (Characteristics of Patients with a Last Measured CD4≤200).

### *Multivariate analysis – Cox proportional hazards: Achieving a CD4>200*

The multivariate analysis included patient age, race/ethnicity, and factors that were either significantly associated (p<0.05) or had borderline significance (p<0.20) with achieving a CD4>200 from the unadjusted K-M analyses. Only being on ART at the last visit in 2003 remained significantly associated with improved immunologic status, or achieving CD>200, during follow-up (**Table 9**). There were no longer any differences in improved CD4 by country of birth, IDU risk, patient age, year of entry into care at the site, or viral load suppression in 2003.

<b>Table 9. Relative Risk of Achieving a CD4&gt;200 during follow-up, by Patient characteristics</b>			
	<b>Hazard Ratio</b>	<b>95% Confidence Interval</b>	
White non-Hispanic	1.40	0.84	2.34
US Born	0.59	0.33	1.04
Age 50 or over in 2003	1.59	0.91	2.79
IDU risk	0.75	0.46	1.24
Entered care before 1996	0.70	0.34	1.41
Entered care between 1996 and 2000	0.76	0.44	1.30
Initial CD4 ≤200	0.76	0.43	1.32
Last VL≤400 in 2003	1.52	0.92	2.51
<b>On ART at last visit in 2003</b>	<b>1.77*</b>	<b>1.00</b>	<b>3.13</b>

Hazard ratio = relative risk of achieving a CD4>200 during follow-up. Significance levels: \*p<0.05, \*\*p<0.01, †p<0.0001. Referent categories: not White non-Hispanic, non-US born, age<50, no IDU risk, entered care after 2000, initial CD4>200, last viral load>400 in 2003, not on ART at last visit in 2003.

**ii. Outcome #2: Achieving Two Consecutive CD4 > 200**

Achieving two or more consecutive CD4>200 signifies a more robust immunologic response. Of the 189 patients with a last CD4≤200 in 2003, 44% (83) achieved two consecutive CD4>200 during follow-up, while 56% (106) never did (Note: of the 115 patients who achieved at least one CD4>200, 28% (32) of them never achieved two consecutive CD4>200). The mean number of years followed up among patients who had two consecutive CD4>200 was 1.6 years, indicating that on average, it took about 1.6 years for patients who had a last CD4≤200 in 2003 to improve (**Table 10**).

<b>Table 10. Percentage of patients who achieved two consecutive CD4&gt;200 by time to event (1/1/2004 – 12/31/2008<sup>1</sup>)</b>	
Number of Years of Follow-Up until Two Consecutive CD4>200	Percentage of patients (n)
<½ year	17% (14)
1	42% (35)
2	24% (20)
3	6% (5)
4	6% (5)
5	5% (4)
	<b>100% (83)</b>

Of the 106 patients who never had two consecutive CD4 count>200, 43% (46) terminated care at the sites during the study period: 33% (15) died, 35% (16) were lost, 22% (10) transferred care, and 11% (5) moved. The mean number of years followed among these patients was 1.5 years.

Finally, the other 57% (60) of patients remained in care at the sites but never achieved two consecutive CD4>200 and were reviewed each year up to the end of 2008 or the end of their follow-up period. Of these 60 patients, 72% (43) were male, 63% (38) were under the age of 50, 85% (51) were US born, and 23% (14) were White non-Hispanic. Half of the patients had IDU risk and 63% (38) had a history of substance abuse, while 33% (20) had heterosexual risk. Fifty-two percent (31) were diagnosed prior to 1996 and 62% (37) had a history of mental illness. Almost three-quarters (73%, 44) were on ART at last visit in 2003, with only 33% (20) having the last VL≤400 in 2003.

## Analyses

From the unadjusted K-M analyses, patients with a last CD4<200 in 2003 who were born outside of the US were more likely to achieve two consecutive CD4>200 during follow-up. Patients who were HCV positive or had IDU risk were less likely to have improved immunologic status during follow-up. Patients who were more recently diagnosed (2001-2003) were more likely to have improved CD4 count levels during the follow-up period, again supporting the finding that newer patients do recover given adequate time in care. There were no differences by patient gender, race/ethnicity, or age (see **Appendix B - Table C** for complete data table).

### *Multivariate analysis – Cox proportional hazards: Achieving Two Consecutive CD4>200*

The multivariate analysis included patient age, race/ethnicity, and factors that were either significantly associated (p<0.05) or had borderline significance (p<0.20) with achieving two consecutive CD4>200 from the unadjusted K-M analyses. Only having IDU as a risk factor remained significantly associated with *not* attaining immunologic recovery or two consecutive CD4>200 during follow-up (**Table 11**). There were no longer any differences in achieving two consecutive CD4>200 by year of entry into care at the site, initial CD4 count, or last viral load suppression. There were no other demographic factors associated with achieving two or more consecutive CD4>200.

<b>Table 11. Relative Risk of Achieving Two Consecutive CD4&gt;200 during follow-up, by Patient characteristics</b>			
	<b>Hazard Ratio</b>	<b>95% Confidence Interval</b>	
White non-Hispanic	1.74	1.00	3.06
US Born	0.61	0.33	1.12
Age 50 and over in 2003	1.19	0.66	2.17
<b>IDU risk</b>	<b>0.56*</b>	<b>0.32</b>	<b>0.99</b>
Entered care before 1996	0.87	0.40	1.92
Entered care between 1996 and 2000	0.90	0.51	1.60
Initial CD4≤200 at entry to care at site	1.05	0.56	1.97
Last VL≤400 in 2003	1.53	0.89	2.63
On ART at last visit in 2003	1.27	0.68	2.37

Hazard ratio = relative risk of achieving two consecutive CD4>200 during follow-up. Significance levels: \*p<0.05, \*\*p<0.01, †p<0.0001. Referent categories: not White non-Hispanic, non-US born, age<50, no IDU risk, entered care after 2000, initial CD4>200, last viral load>400 in 2003, not on ART at last visit in 2003.

### iii. Outcome #3: Lost to Care at the Site or Death

Twenty percent (37) of the 189 patients with a last CD4 $\leq$ 200 in 2003 became lost to care (21) or died (16) during the study period. Another 24 patients transferred care (16) or moved (8) during the study period; these 24 patients were not included in this outcome. The average number of years followed until becoming lost to care or death among the 37 patients was 1.4 years (**Table 12**).

<b>Table 12. Percentage of patients who became lost to care at the site or died by time to event (1/1/2004 – 12/31/2008<sup>1</sup>)</b>	
Number of Years Followed until Lost to Care or Death	Percentage of Patients (n)
<1/2 year	30% (11)
1	30% (11)
2	16% (6)
3	19% (7)
4	5% (2)
	<b>100% (37)</b>

Of those who became lost to care or died, 54% (20) were male, 46% (17) White non-Hispanic, 22% (8) Black non-Hispanic, 32% (12) Hispanic, and 51% (19) were age 50 or over. Most (81%, 30) were US born. Also, over half of the patients (57%, 21) had IDU risk and 70% (29) had history of substance abuse during time in care at the site. About 49% (18) were on ART at last visit in 2003, 54% (20) had a documented hospitalization in 2003, and only 24% (9) had a last viral load  $\leq$ 400 in the year. The majority (78%, 29) had also entered care at the site with an initial CD4 $\leq$ 200.

Due to the small number of patients who became lost to care or died, no additional analyses were conducted for this outcome.

#### iv. Outcome #4: Medical Hospitalization

Of the 189 patients with a last CD4 $\leq$ 200 in 2003, 36% (68) ever had a medical hospitalization documented in the charts during their follow-up period while in care at the site. The average number of years followed until the first medical hospitalization was 2.6 years among patients who were ever hospitalized after 2003 (Table 13).

Table 13. Percentage of patients who had a medical hospitalization by time to event (1/1/2004 – 12/31/2008 <sup>1</sup> )	
Number of Years of Follow-up until first Medical Hospitalization after 2003	Percentage of Patients (n)
1	33.8% (23)
2	19.1% (13)
3	16.2% (11)
4	14.7% (10)
5	16.2% (11)
	<b>100% (68)</b>

Of the 121 patients who did not have a hospitalization, 28% (34) dropped out or became lost to care before the end of the study period: 12% (4) died, 41% (14) were lost, 29% (10) transferred care, and 18% (6) moved. The mean number of years followed among these patients was 1.8 years.

A total of 87 (72%) did not have a documented hospitalization during follow-up and were reviewed up to the end of 2008 or the end of their study period. Of these, 69% (60) were male, 45% (39) were Hispanic, 24% (21) were Black non-Hispanic, 44% (38) were age 50 or over, 72% (63) US born, 38 % (38) had IDU risk, 46% (40) had heterosexual risk, 77% (67) were on ART at last visit in 2003, and 41% (36) had a last VL $\leq$ 400 in 2003.

#### Analyses

Results from unadjusted K-M analyses showed that among patients with a last CD4 $\leq$ 200 in 2003, those not on ART at last visit in 2003 were more likely to have a medical hospitalization during follow-up. Having a hospitalization in 2003 was also associated with having a medical hospitalization sometime again during follow-up. US born patients and patients with any history

of mental illness were also more likely to have a medical hospitalization (see **Appendix B - Table D** for complete data table).

*Multivariate analysis – Cox proportional hazards: Medical Hospitalization*

The multivariate analysis included patient age, race/ethnicity, and factors that were either significantly associated ( $p < 0.05$ ) or had borderline significance ( $p < 0.20$ ) with having a medical hospitalization from the unadjusted K-M analyses. Not surprisingly, being older than age 50 was associated with a higher risk of hospitalization, while achieving a CD4 count  $>200$  reduced the risk of hospitalization (**Table 14**). There were no longer any differences in having a medical hospitalization by country of birth and any history of mental illness. There were no other demographic factors associated with this outcome.

<b>Table 14. Relative Risk of Having a Medical Hospitalization, by Patient characteristics</b>			
	<b>Hazard Ratio</b>	<b>95% Confidence Interval</b>	
White non-Hispanic	1.24	0.66	2.31
US Born	1.44	0.66	3.13
<b>Age 50 and over in 2003</b>	<b>1.89*</b>	<b>1.00</b>	<b>3.58</b>
Any history of mental illness	1.46	0.78	2.72
Entered care before 1996	1.34	0.62	2.87
Entered care between 1996 and 2000	1.29	0.67	2.48
Last VL $\leq 400$ in 2003	0.82	0.44	1.53
On ART at last visit in 2003	0.68	0.38	1.24
Hospitalized in 2003	0.74	0.40	1.35
<b>Any CD4 <math>&gt;200</math> during follow-up</b>	<b>0.40**</b>	<b>0.22</b>	<b>0.73</b>
Community Health Center	1.15	0.64	2.07

Hazard ratio = relative risk of having a medical hospitalization during follow-up. Significance levels: \* $p < 0.05$ , \*\* $p < 0.01$ , † $p < 0.0001$ . Referent categories: not White non-Hispanic, non-US born, age  $< 50$ , no history of mental illness, entered care after 2000, last viral load  $> 400$  in 2003, not hospitalized in 2003, not on ART at last visit in 2003, hospital setting.

### **B3. Conclusions**

Monitoring CD4 counts and maintaining good immune function are critical in HIV patients' care management. A  $CD4 \leq 200$  increases risk for poorer health outcomes, including opportunistic infections and disease progression. Furthermore, according to the Center for Disease Control and Prevention, a person is considered to have AIDS if s/he is infected with HIV and presents with one of the following: a  $CD4 \leq 200$  or one of the defining illnesses. Despite access and provision of quality care, there remained a group of patients reviewed in 2003 who continued to be immunosuppressed and at risk for hospitalization.

The only demographic factor associated with not achieving a higher CD4 count during follow-up was having IDU as an HIV risk. While being on ART by the end of 2003 was associated with decreased risk of remaining with a  $CD4 \leq 200$ , viral suppression was less important. This remained significant even after adjusting for race/ethnicity, though interestingly recent history of substance abuse was not a factor. More work is needed to understand why this group appears to do less well.

The importance of ensuring that patients achieve a CD4 count  $>200$  is highlighted by the increased risk of medical hospitalization for those who remain immunosuppressed. The number of patients who were lost to care or died was insufficient for further exploration of factors associated with this outcome, but this group represents those of most concern in improving the outcomes of all people living with HIV.

## KEY FINDINGS

Despite advances in highly active ART and past evaluation results indicating overall high quality of care delivered across participating chart review clinics in Massachusetts, there remain some patients with immunosuppression and low CD4 $\leq$ 200. Since low CD4 increases risk for disease progression and death, the objectives of this analysis were **(1)** to identify populations at higher risk of having low CD4 counts via a cross sectional snapshot of 2008 primary care chart review data and **(2)** to identify factors associated with a recovery from low CD4 or improved immunological status during 2004-2008 among a group of patients with a last measured CD4 $\leq$ 200 in 2003. The following summarizes the key findings:

### Last CD4 $\leq$ 200 in 2008

- Eleven percent of patients (128/1,139) had a last measured CD4 $\leq$ 200 in 2008.
- Risk factors associated with having a low CD4 count in 2008 include:
  - being more recently diagnosed (in 2006 or later)
  - being long term HIV patients diagnosed prior to the highly active ART era (diagnosed prior to 1996)
  - having an initial low CD4 count at entry to care at the site
  - having IDU history as a risk behavior
- Being on ART and having a viral load less than 400 (VL $\leq$ 400) were both associated with *lower risk* of CD4 $\leq$ 200.
- No disparities based on race/ethnicity, gender or country of birth were found.

Therefore,

- Effective ART treatment should be initiated for patients presenting with advanced immune suppression, because even patients with low CD4 counts at entry to care can be successfully treated given the medical advances in antiretroviral therapy.
  - Efforts to address challenges for those who remain  $\leq$ 200 are important.
- Efforts to ensure that patients are diagnosed and enter into care early in their HIV progression are clearly needed.
- Future work is needed to explore why IDU as an HIV risk increases risk for remaining with CD4 $\leq$ 200 regardless of age, duration of HIV infection, HCV infection, active substance use or mental illness.

### **Five Year Follow-Up of Patients with Last CD4 $\leq$ 200 in 2003**

- Fourteen percent of patients (189/1,358) had a last measured CD4 $\leq$ 200 in 2003.
- Being on ART at the end of 2003 was associated with achieving a CD4 above 200 during follow-up.
- Having IDU history as an HIV risk behavior was the only factor associated with increased risk of *not* achieving CD4 $>$ 200 (remaining immunosuppressed) during follow-up.
- Consistently having a CD4 $\leq$ 200 or not recovering from a low CD4 significantly increased risk for a medical hospitalization during follow-up.

Therefore, it is:

- Important for patients with low CD4 counts to be on ART to help ensure recovery from immunosuppression.
- Important to conduct additional research to understand why IDU as an HIV risk increases patients' risk of remaining with CD4 $\leq$ 200, regardless of age, ART status, and viral suppression.
- Important to ensure that patients achieve and maintain a CD4 $>$ 200 to decrease risk of medical hospitalization and poor clinical outcome.

## APPENDIX A – CROSS-SECTIONAL ANALYSIS

**Table A.** Characteristics of patients with last CD4 ≤200 versus last CD4 >200, viral suppressed versus not

	Last CD4 ≤200			Last CD4 >200		
	All (N=128) %	Suppressed (N=73) %	Not Suppressed (N=55) %	All (n=1011) %	Suppressed (n=816) %	Not Suppressed (n=195) %
<b>Gender</b>						
Male	60	59	62	61	61	61
Female	39	40	38	39	39	39
Transgender	<1	1	0	<1	<1	1
<b>Race/Ethnicity</b>						
White non-Hispanic	32	30	35	39	40	36
Black non-Hispanic	31	32	31	30	30	30
Hispanic	34	36	31	28	27	30
Other	3	3	4	3	3	4
<b>HIV Risk</b>						
IDU	41†	40	42	20	20	19
MSM	15**	10	22	30	29	37
Heterosexual	60	67	51	62	63	58
<b>Country of Birth</b>						
US born	72*	63	84	61	61	63
Non US born	28	37	16	39	39	37
<b>Age</b>						
<50	70	66	75	71	68	82
≥50	30	34	25	29	32	18
<b>HIV Diagnosis Year</b>						
<1996	38†	39	37	21	22	12
1996-2000	19	13	27	23	25	16
2001-2005	15	7	25	32	33	32
2006 onwards	28	41	12	24	20	40
<b>Hepatitis C Positive</b>						
Yes	45†	49	41	23	23	22
<b>Anti-retroviral Therapy</b>						
On ART ever in 2008	88	97	76	84	96	30
On ART at last visit	82	96	64	83	96	28
On ART or not ART eligible	88†	97	76	97	100	86
<b>Mental Illness</b>						
Any history 2003-2008	59	56	62	58	57	61
<b>Substance Abuse</b>						
Any history 2003-2008	50*	48	52.7	38	38	39
<b>Hospitalization in 2008</b>						
Any <sup>i</sup>	28†	26	31	11	11	12
Any Medical Only <sup>ii</sup>	27†	26	30	10	10	9
<b>Initial CD4 at Entry</b>						
≤50	25†	30	18	9	11	3
51-200	29	30	27	18	21	6
201-500	36	30	44	40	41	36
>500	9	10	9	32	26	55
Not available	<1	0	2	1	1	0

\*p<0.05, \*\*p<0.01, †p<0.0001, showing statistical significant difference between Last CD4 ≤200 versus Last CD4 >200.

<sup>i</sup>Including non-HIV/AIDS related, substance use, or mental health hospitalizations. <sup>ii</sup>Including non-HIV/AIDS related, but excluding substance use and mental health hospitalizations.

**Table B.** Multivariate logistic regression: Factors associated with last CD4 $\leq$ 200 in 2008

	Adjusted Odds Ratio	95% Confidence Interval
Male	0.76	0.48-1.19
Age $\geq$ 50	0.98	0.62-1.56
US born	1.56	0.90-2.74
White non-Hispanic	0.70	0.44-1.11
<b>IDU risk</b>	<b>2.82**</b>	<b>1.56-5.09</b>
<b>Diagnosed prior to 1996</b>	<b>3.35†</b>	<b>1.98-5.66</b>
<b>Diagnosed 2006 or later</b>	<b>1.80*</b>	<b>1.08-3.02</b>
Any history of mental illness	0.83	0.53-1.31
Any history of substance abuse	1.00	0.56-1.79
<b>Last VL<math>\leq</math>400 in 2008</b>	<b>0.23†</b>	<b>0.14-0.37</b>
<b>Initial CD4<math>\leq</math>200 at entry to care</b>	<b>7.69†</b>	<b>4.72-12.5</b>
<b>Appropriate ART management</b>	<b>0.29**</b>	<b>0.13-0.63</b>
Metro-Boston	1.15	0.73-1.82
Caseload > 200	0.92	0.58-1.46
Community health center	0.70	0.45-1.11

\*p<0.05, \*\*p<0.01, †p<0.0001. Referent categories: Female, age<50, non-US born, not White non-Hispanic, no IDU risk, diagnosed between 1996 and 2005, no documented history of mental illness 2003-2008, no documented history of substance abuse 2003-2008, last viral load>400 in 2008, initial CD4>200, eligible but not on ART, site not in Metro-Boston, caseload<200, not CHC.

**Table C.** Sites Included in the 2008 Cross Sectional Analysis

Boston Medical Center
Dimock Community Health Center
Fenway Community Health Center
Great Brook Valley Health Center
Greater Lawrence Family Health Center
Holyoke Health Center
Lowell Community Health Center
Lynn Community Health Center
Martha Eliot
Metrowest Medical Center
MGH Chelsea
Somerville Primary Care, Cambridge Health Alliance
SSTAR Fall River
UMASS Memorial Health Care (UMMHC)-Memorial Campus
UMASS Memorial Health Care-University Campus HIV Clinic
Whittier Street
Zinberg HIV Clinic, Cambridge Health Alliance

## APPENDIX B – FIVE-YEAR FOLLOW-UP COHORT ANALYSIS

**Table A.** Sample Characteristics & Characteristics of Patients with Last CD4 ≤ 200 in 2003

	Eligible sample N=1,358	Last CD4≤ 200 in 2003 N=189
<b>Gender</b>		
Male	60% (814)	65% (122)
Female	40% (544)	35% (67)
<b>Race/Ethnicity</b>		
White non-Hispanic	42% (573)	33% (63)
Black non-Hispanic	26% (358)	26% (49)
Hispanic	29% (389)	37% (70)
Other	3% (35)	4% (7)
<b>Country of Birth</b>		
US born	73% (991)	75% (141)
Non US born	27% (367)	25% (48)
<b>Age</b>		
<50	81% (1099)	76% (144)
≥50	19% (256)	24% (45)
<b>HIV Risk</b>		
IDU risk	32% (432)	41% (78)
MSM risk	25% (341)	16% (31)
Heterosexual risk	56% (759)	56% (106)
<b>HIV Diagnosis Year</b>		
Prior to 1996	39% (498)	40% (69)
1996-2000	32% (412)	25% (43)
2001-2003	30% (380)	36% (62)
<b>Year of Entry to Care at Site</b>		
Prior to 1996	22% (300)	22% (41)
1996-2000	40% (549)	37% (70)
2001-2003	38% (509)	41% (78)
<b>Hepatitis C Positive</b>		
Yes	35% (473)	47% (89)
<b>Anti-retroviral Therapy</b>		
On ART at last visit	66% (894)	68% (129)
On ART ever in the year	72% (976)	82% (155)
Not eligible	23% (305)	-
Eligible but not on ART	6% (77)	16% (31)
<b>Mental Illness</b>		
Any history between 1999 & 2003	64% (872)	58% (109)
<b>Substance Abuse</b>		
Any history between 1999 & 2003	52% (707)	60% (113)
<b>Hospitalization in 2003</b>		
Any	15% (200)	29% (54)
Any Medical Only	12% (167)	27% (50)
<b>Visits in 2003</b>		
≥2 visits	91% (1240)	89% (168)
<b>Initial CD4 at Entry to Care at Site</b>		
≤200	28% (376)	64% (121)
>200	71% (964)	34% (65)
Not available	1% (18)	2% (3)
<b>Last VL≤400 in 2003</b>		
≤400	55% (751)	34% (65)

**Table A (continued).** Sample Characteristics & Characteristics of Patients with Last CD4 ≤ 200 in 2003

	Eligible sample N=1,358	Last CD4 ≤ 200 in 2003 N=189
<b>Site Characteristics</b>		
Metro-Boston	41% (550)	36% (68)
Community health center	52% (706)	46% (87)
Caseload >200	46% (626)	40% (75)

**Table B.** Kaplan Meier Results: Percentage of Patients with CD4>200 during Follow-Up, by Patient Characteristics

	Total # of Patients	Achieved CD4>200 (N=115)	%	Did NOT achieve CD4>200 (N=74)	%	Log-rank p-value
<b>Gender</b>						
Female	67	36	54%	31	46%	0.24
Male	122	79	65%	43	35%	
<b>Race/ethnicity</b>						
White non-Hispanic	63	38	60%	25	40%	0.64
Black non-Hispanic	49	28	57%	21	43%	
Hispanic	70	43	61%	27	39%	
<b>Country of birth</b>						
Outside of US	48	37	77%	11	23%	<b>0.009**</b>
Born in US	141	78	55%	63	45%	
<b>Age group</b>						
Age < 50	105	58	55%	47	45%	<b>0.035*</b>
Age ≥ 50	84	57	68%	27	32%	
<b>Risk Category</b>						
Heterosexual risk	79	53	67%	26	33%	0.061
IDU risk	78	41	53%	37	47%	
MSM risk	24	17	71%	7	29%	
<b>IDU Risk</b>						
No	111	74	67%	37	33%	<b>0.02*</b>
Yes	78	41	53%	37	47%	
<b>Hepatitis C Positive</b>						
No	100	69	69%	31	31%	<b>0.008**</b>
Yes	89	46	52%	43	48%	
<b>Hospitalized in 2003</b>						
No	135	83	62%	52	39%	0.85
Yes	54	32	59%	22	41%	
<b>Last VL ≤ 400 in 2003</b>						
No	124	67	54%	57	46%	<b>0.031*</b>
Yes	65	48	74%	17	26%	
<b>On ART at last visit in 2003</b>						
No	57	26	46%	31	54%	<b>0.037*</b>
Yes	129	87	67%	42	33%	
<b>On ART ever in 2003</b>						
No	31	15	48%	16	52%	
Yes	155	98	63%	57	37%	0.40

Significance levels: \*p<0.05, \*\*p<0.01, †p<0.0001

**Table B (continued).** Kaplan Meier Results: Percentage of Patients with CD4>200 during Follow-Up, by Patient Characteristics

	Total # of Patients	Achieved CD4>200 (N=115)	%	Did NOT achieve CD4>200 (N=74)	%	Log-rank p-value
<b>Any adherence problem 2003-2008</b>						
No	79	51	65%	28	35%	0.4305
Yes	110	64	58%	46	42%	
<b>Any history of mental illness 1999-2003</b>						
No	72	44	61%	28	39%	0.69
Yes	117	71	61%	46	39%	
<b>Any history of substance abuse 1999-2003</b>						
No	79	51	65%	28	35%	0.33
Yes	110	64	58%	46	42%	
<b>Diagnosis Year</b>						
Prior to 1996	69	42	61%	27	39%	0.039*
1996-2000	43	21	49%	22	51%	
2001-2003	62	44	71%	18	29%	
<b>Initial CD4≤200</b>						
No	65	39	60%	26	40%	0.27
Yes	121	74	61%	47	39%	
<b>Year of entry to care at the site</b>						
Prior to 1996	70	37	53%	33	47%	0.072
1996-2000	78	53	68%	25	32%	
2001-2003	41	25	61%	16	39%	

Significance levels: \*p&lt;0.05, \*\*p&lt;0.01, †p&lt;0.0001

**Table C.** Kaplan Meier Results: Percentage of Patients with Two Consecutive CD4>200 during Follow-Up, by Patient Characteristics

	Total # of Patients	Achieved Two Consecutive CD4>200 (N=83)	%	Did NOT Achieve Two Consecutive CD4>200 (N=106)	%	Log-rank p-value
<b>Gender</b>						
Female	67	31	46%	36	54%	0.32
Male	122	52	43%	70	57%	
<b>Race/ethnicity</b>						
White non-Hispanic	63	30	48%	33	52%	0.23
Black non-Hispanic	49	18	37%	31	63%	
Hispanic	70	29	41%	41	59%	
<b>Country of birth</b>						
Outside of US	48	30	63%	18	38%	0.006**
US Born	141	53	38%	88	62%	
<b>Age group</b>						
Age<50	105	43	41%	62	59%	0.17
Age≥50	84	40	48%	44	52%	

Significance levels: \*p&lt;0.05, \*\*p&lt;0.01, †p&lt;0.0001

**Table C (continued).** Kaplan Meier Results: Percentage of Patients with Two Consecutive CD4>200 during Follow-Up, by Patient Characteristics

	Total # of Patients	Achieved Two Consecutive CD4>200 (N=83)	%	Did NOT Achieve Two Consecutive CD4>200 (N=106)	%	Log-rank p-value
<b>Risk</b>						
Heterosexual risk	79	42	53%	37	47%	0.02*
IDU risk	78	26	33%	52	67%	
MSM risk	24	11	46%	13	54%	
<b>IDU Risk</b>						
No	111	57	51%	54	49%	0.005**
Yes	78	26	33%	52	67%	
<b>Hepatitis C Positive</b>						
No	100	53	53%	47	47%	0.005**
Yes	89	30	34%	59	66%	
<b>On ART ever in 2003</b>						
No	31	11	36%	20	65%	0.61
Yes	155	70	45%	85	55%	
<b>On ART at last visit in 2003</b>						
No	57	19	33%	38	67%	0.17
Yes	129	62	48%	67	52%	
<b>Any adherence problem 2003-2008</b>						
No	79	37	47%	42	53%	0.2551
Yes	110	46	42%	64	58%	
<b>Hospitalized in 2003</b>						
No	135	63	47%	72	53%	0.36
Yes	54	20	37%	34	63%	
<b>Last VL≤400 in 2003</b>						
No	124	47	38%	77	62%	0.07
Yes	65	36	55%	29	45%	
<b>Any history of mental illness 1999-2003</b>						
No	72	35	49%	37	51%	0.28
Yes	117	48	41%	69	59%	
<b>Any history of substance abuse 1999-2003</b>						
No	79	39	49%	40	51%	0.10
Yes	110	44	40%	66	60%	
<b>Diagnosis Year</b>						
Prior to 1996	69	27	39%	42	61%	0.003**
1996-2000	43	14	33%	29	67%	
2001-2003	62	37	60%	25	40%	
<b>Initial CD4≤200</b>						
No	65	24	37%	41	63%	0.06
Yes	121	58	48%	63	52%	
<b>Year of Entry to Care at Site</b>						
Prior to 1996	70	27	39%	43	61%	0.09
1996-2000	78	40	51%	38	49%	
2001-2003	41	16	39%	25	61%	

Significance levels: \*p<0.05, \*\*p<0.01, †p<0.0001

**Table D.** Kaplan Meier Results: Percentage of Patients who had a Medical Hospitalization during Follow-Up, by Patient Characteristics

	Total # of Patients	Medical Hospitalization (N=68)	%	Did NOT Have a Medical Hospitalization (N=121)	%	Log-rank p-value
<b>Gender</b>						
Female	67	26	39%	41	61%	0.37
Male	122	42	34%	80	66%	
<b>Race/ethnicity</b>						
White non-Hispanic	63	22	35%	41	65%	0.40
Black non-Hispanic	49	20	41%	29	59%	
Hispanic	70	22	31%	48	69%	
<b>Country of birth</b>						
Outside of US	48	12	25%	36	75%	<b>0.049*</b>
US Born	141	56	40%	85	60%	
<b>Age group</b>						
Age <50	105	37	35%	68	65%	0.65
Age ≥50	84	31	37%	53	63%	
<b>Risk</b>						
Heterosexual risk	79	24	30%	55	70%	0.38
IDU risk	78	32	41%	46	59%	
MSM risk	24	8	33%	16	67%	
<b>IDU Risk</b>						
No	111	36	32%	75	68%	0.28
Yes	78	32	41%	46	59%	
<b>Hepatitis C Positive</b>						
No	100	32	32%	68	68%	0.196
Yes	89	36	40%	53	60%	
<b>On ART ever in 2003</b>						
No	31	11	36%	20	65%	0.71
Yes	155	55	36%	100	65%	
<b>On ART at last visit in 2003</b>						
No	57	27	47%	30	53%	<b>0.009**</b>
Yes	129	39	30%	90	70%	
<b>Any adherence problem 2003-2008</b>						
No	79	17	22%	62	78%	<b>0.0005**</b>
Yes	110	51	46%	59	54%	
<b>Hospitalized in 2003</b>						
No	135	43	32%	92	68%	<b>0.040*</b>
Yes	54	25	46%	29	54%	
<b>Last VL ≤400 in 2003</b>						
No	124	48	39%	76	61%	0.11
Yes	65	20	31%	45	69%	
<b>Any history of mental illness 1999-2003</b>						
No	72	20	28%	52	72%	<b>0.0497*</b>
Yes	117	48	41%	69	59%	

Significance levels: \*p<0.05, \*\*p<0.01, †p<0.0001

**Table D (continued).** Kaplan Meier Results: Percentage of Patients who had a Medical Hospitalization during Follow-Up, by Patient Characteristics

	<b>Total # of Patients</b>	<b>Medical Hospitalization (N=68)</b>	<b>%</b>	<b>Did NOT Have a Medical Hospitalization (N=121)</b>	<b>%</b>	<b>Log-rank p-value</b>
<b>Any history of substance abuse 1999-2003</b>						
No	79	23	29%	56	71%	0.16
Yes	110	45	41%	65	59%	
<b>Diagnosis Year</b>						
Prior to 1996	69	26	38%	43	62%	0.15
1996-2000	43	18	42%	25	58%	
2001-2003	62	16	26%	46	74%	
<b>Initial CD4<math>\leq</math>200</b>						
No	65	25	39%	40	62%	0.80
Yes	121	41	34%	80	66%	
<b>Year of Entry to Care at Site</b>						
Prior to 1996	70	27	39%	43	61%	0.15
1996-2000	78	21	27%	57	73%	
2001-2003	41	20	49%	21	51%	

Significance levels: \*p<0.05, \*\*p<0.01, †p<0.0001

**Table E.** Sites Included in the Five-Year Follow-Up Analysis

Boston Medical Center  
 Dimock Community Health Center  
 Fenway Community Health Center  
 Great Brook Valley Health Center  
 Greater Lawrence Family Health Center  
 Holyoke Health Center  
 Lowell Community Health Center  
 Lynn Community Health Center  
 Martha Eliot  
 Metrowest Medical Center  
 MGH Chelsea  
 Somerville Primary Care, Cambridge Health Alliance  
 SSTAR Fall River  
 UMASS Memorial Health Care (UMMHC)-Memorial Campus  
 UMASS Memorial Health Care-University Campus HIV Clinic  
 Whittier Street  
 Zinberg HIV Clinic, Cambridge Health Alliance  
*East Boston*  
*Hyannis IDCS*  
*Taunton Infectious Diseases Associates*  
*Baystate Brightwood Health Center*  
*Outer Cape Health Services*  
*Baystate High Street Health Center*  
*Baystate Mason Square Neighborhood Health Center*  
*Greater New Bedford Community Health Center*