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## Late Presentation for HIV Care in the United States and Canada

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### Abstract

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**Background:** Initiatives to improve early detection and access to HIV services have increased over time. We assessed the immune status of patients at initial presentation for HIV care from 1997-2007 in 13 US and Canadian clinical cohorts.

**Methods:** We analyzed data from 44,491 HIV-infected patients enrolled in the North American – AIDS Cohort Collaboration on Research and Design. We identified first presentation for HIV care as the time of first CD4+ T-lymphocyte (CD4) measurement and excluded patients who prior to this date had HIV RNA measurements, evidence of antiretroviral exposure, or a history of AIDS-defining illness. Trends in mean CD4 count (measured as cells/mm<sup>3</sup>) and 95% confidence intervals ([,]) were determined using linear regression adjusted for age, gender, race/ethnicity, HIV transmission risk and cohort.

**Results:** Median age at first presentation for HIV care increased over time (range 40-43 years,  $p<0.01$ ), while the proportion of patients with injection drug use HIV transmission risk decreased (26% to 14%,  $p<0.01$ ) and heterosexual transmission risk increased (16% to 23%,  $p<0.01$ ). Median CD4 at presentation increased from 256 (IQR: 96-455) to 317 (IQR: 135-517) in 1997 to 2007 ( $p<0.01$ ). The proportion with a CD4 count  $\geq 350$  at first presentation also increased from 1997 to 2007 (38% to 46%,  $p<0.01$ ). The estimated adjusted mean CD4 count increased at a rate of 6 [5, 7] per year.

**Conclusion:** CD4 count at first presentation for HIV care has increased annually over the past 11 years, but has remained  $<350$  cells/mm<sup>3</sup>, suggesting the urgent need for earlier HIV diagnosis and treatment.

## Keywords

CD4 Lymphocyte Count; Delivery of Health Care / statistics & numerical data; HIV Infections / therapy; United States; Canada

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## BACKGROUND

Approximately 25% of the estimated 1.1 million Americans and 58,000 Canadians living with HIV infection are unaware they are infected [1,2]. Among the estimated 56,000 new infections occurring each year in the US [3], over half are estimated to be transmitted by persons who are unaware of their HIV infection [4]. In the US from 2000 to 2006, rates for a history of ever being tested for HIV infection have remained stable at less than 40%; among persons with established risk factors for HIV during 2006 only 23% were tested [5]. In Canada in 2003, a general population survey found that 29% of women and 24% of men reported ever being tested for HIV [6]; in 1996, 71% of men who have sex with men (MSM), 62% of injection drug users (IDUs) and 51% of high-risk heterosexuals reported ever being tested, although these higher proportions may be due to testing for research participation [2]. Even among pregnant women in the US in 2006, only 61% had been tested despite long-standing recommendations and extensive efforts to incorporate routine opt-out testing into pregnancy care [5]. Similar guidelines for testing during pregnancy exist in Canada; however, prenatal HIV screening programs vary. Data from 2002 to 2006 show the proportion of pregnant women screened for HIV ranges from 60% in Manitoba to  $\geq 95\%$  in Alberta, Newfoundland and Labrador, and the Northwest Territories [2]. Persons who are unaware of their HIV status are unable to benefit from the advances made in HIV treatment, and late presentation for HIV care is associated with higher mortality even after receipt of antiretroviral therapy [7,8], and a diminished recovery of CD4+ T-lymphocytes (CD4) [9]. Late presenters also have a prolonged opportunity to transmit HIV while unaware of their HIV infection.

To assess when individuals are entering HIV care, we analyzed the immune status in patients who newly presented for care over the past 11 years in the US and Canada. Given the improvements that have occurred in HIV therapy, and efforts to improve early diagnosis and

treatment of HIV [10-12], our objective was to assess whether patients presented for HIV care earlier in the course of their HIV infection over time and to determine factors associated with a later presentation to HIV care.

## METHODS

### Study design and population

All patients were part of the North American Cohort Collaboration on Research and Design (NA-ACCORD), a regional group of the International Epidemiological Databases to Evaluate AIDS (IeDEA) project. The NA-ACCORD is a multisite collaboration of 8 interval and 14 clinical cohort studies with sites in the US and Canada [13]. Each cohort's participation in NA-ACCORD was approved by the respective local institutional review boards. Contributing cohorts have used standardized methods of data collection and have submitted demographic, treatment, clinical, laboratory, and vital status data on enrolled participants.

### Inclusion criteria and variables of interest

Only participants from clinical cohorts were included in this study because our interest was in the degree of immunosuppression at first presentation for HIV clinical care; the interval research cohorts in the NA-ACCORD do not administer clinical care. *All of the 14 clinical cohorts* agreed to participate in this study although one was excluded because their study population enrollment criteria restricted to those in later stages of HIV disease. These 13 clinical cohorts have clinical sites in the following US states and territories and Canadian provinces: *Alberta*, Alabama, California, Colorado, Florida, *Georgia*, Illinois, Maryland, Michigan, Missouri, New York, North Carolina, Ohio, Ontario, Oregon, Pennsylvania, *Quebec*, Tennessee, Texas, Washington and Washington DC. Due to the geographic dispersion of these clinical cohorts where individuals are receiving their HIV care, the possibility that an individual is participating in more than one of the clinical cohorts is low.

We analyzed data from HIV-infected adults ( $\geq 18$  years of age) who first presented for clinical care between January 1997 through December 2007, where first presentation for HIV clinical care was defined as the date (month and year) at which the first CD4 count was reported. The clinical cohorts of the NA-ACCORD are well-established, and have procedures to determine medical histories at first presentation for care. HIV-related treatments, laboratory results and diagnoses prior to enrollment are routinely recorded.

Several methods were used to eliminate patients who might have been receiving HIV care prior to their first recorded CD4 count. First, we excluded patients who were taking antiretroviral therapy or had an HIV RNA measurement recorded prior to the date of the first CD4 measurement. Second, we also excluded those patients who had an AIDS-defining diagnosis recorded more than 3 months prior to the first CD4 measurement. A period of 3 months prior to the first CD4 measurement was utilized to include those who may have had an AIDS-defining diagnosis at the time of HIV diagnosis and to exclude those who may have been seeking care elsewhere. Third, for each cohort, we excluded all individuals contributing data during the first year that the cohort contributed data to the NA-ACCORD who may have been patients previously in care but contributing data to a new cohort data capture system. Although these criteria might not completely exclude earlier presentation for HIV care (particularly presentation at clinical sites outside of the participating cohort) we believe that these criteria minimize the possibility that the patients in this study had presented for HIV care at an earlier time.

The first measured CD4 was our outcome of interest. The month and year in which the CD4 was measured were recorded. If there was more than one CD4 measurement in the first month

at presentation for HIV care, we calculated the mean CD4 count for the month. Other information obtained at first presentation for care included self-reported date of birth, gender, race/ethnicity and HIV transmission risk group. Race/ethnicity was categorized as black, white, Latino and other/unknown. HIV transmission risk group was categorized as MSM, IDU, heterosexual, and other/unknown. Participants with both sexual and IDU transmission risk were categorized as IDU.

### Statistical Analysis

Statistical comparisons of demographic and clinical characteristics across calendar dates were made using the Cochran-Armitage trend test for categorical variables (e.g. country of care, gender, race/ethnicity and HIV transmission risk group) or using the Cuzick trend test for continuous variables (e.g. age, CD4 count). We determined the median absolute CD4 count at first presentation for HIV clinical care annually from 1997 through 2007. Multivariate linear regression models were used to describe the annual trends in estimated mean CD4 count using a linear variable for year and adjusting for cohort demographic and risk characteristics; 95% confidence intervals ([,]) were also estimated using these models. Two-way interactions between calendar year and age, gender, race/ethnicity and HIV transmission group were considered. Nonlinearity of the relationship between calendar time and CD4 count at first presentation for HIV care was assessed by including a quadratic term for calendar year. Results with a two-sided  $p$ -value of  $<0.05$  were considered statistically significant. Analyses were conducted using SAS, version 9.

## RESULTS

A total of 67,961 patients receiving clinical care at one of the participating NA-ACCORD sites between 1997 and 2007 had complete date and CD4 measurement information. Of these, 21,983 (32%) had a prior history of antiretroviral therapy or HIV RNA results and 1,487 (2%) had an AIDS-defining diagnosis recorded more than 3 months prior to the first recorded CD4 count. Thus, our study population consisted of 44,491 HIV-infected individuals.

The characteristics of individuals who first presented for HIV care each year are shown in Table 1. Over time, the median age at first presentation increased (range: 40–43 years,  $p<0.01$ ). The proportion of white patients decreased over time (from 30% in 1996 to 24% in 2007,  $p<0.01$ ) while the proportion of black patients fluctuated, but remained higher than the proportion of white and Latino patients ( $p<0.01$ ). The proportion of patients with IDU transmission risk decreased (26% in 1997 to 14% in 2007,  $p<0.01$ ) and heterosexual transmission risk increased (16% in 1997 to 23% in 2007,  $p<0.01$ ). There was a slight increase in the proportion of Canadian patients, however the proportion remained  $<10\%$  over time ( $p<0.01$ ).

The median CD4 count of the study population increased over time but the changes were within a range of 61 cells/mm<sup>3</sup> over all 11 years (Figure 1). The percentage of patients presenting with a CD4 count  $\geq 350$  cells/mm<sup>3</sup> increased from 38% in 1997 to 46% in 2007 ( $p<0.01$ ) (Figure 1). The overall estimated annual change in mean CD4 count was 6 [5,7] cells/mm<sup>3</sup>, adjusting for age, gender, race/ethnicity, transmission risk group and cohort. The quadratic term for calendar year was not significant ( $p=0.27$ ), suggesting the relationship between calendar year and CD4 count at first presentation for HIV care was not U-shaped. However, there were significant interactions between the change in CD4 count per year with race/ethnicity ( $p=0.01$ ) and with transmission risk group ( $p<0.01$ ), but not gender ( $p=0.13$ ).

Table 2 displays the results from the overall and stratified multivariate models. Although females had higher observed mean CD4 counts in 1997, the estimated mean increase in CD4 count per year among females was less than males (females: 5 [3,7] cells/mm<sup>3</sup> per year; males:

6 [5,7] cells/mm<sup>3</sup> per year). Latinos had the greatest annual increase in estimated mean CD4 count since 1997 (9 [7,12] cells/mm<sup>3</sup>) and blacks had the smallest increase (5 [3,7] cells/mm<sup>3</sup>). Latinos showed a lower observed (293 cells/mm<sup>3</sup>) mean CD4 count in 1997 compared with whites (328 cells/mm<sup>3</sup>) and blacks (305 cells/mm<sup>3</sup>). The estimated annual change in mean CD4 count at first presentation was 7 [6,9] cells/mm<sup>3</sup> among MSM, 5 [3,7] cells/mm<sup>3</sup> among IDU and 2 [0, 4] cells/mm<sup>3</sup> among those with heterosexual transmission risk. MSM showed low observed mean CD4 counts in 1997 (303 cells/mm<sup>3</sup>) and those with IDU and heterosexual transmission risk had a slightly higher observed mean CD4 count in 1997 (334 and 328 cells/mm<sup>3</sup>, respectively).

Patients who were older had lower CD4 counts at first presentation for HIV care, with an average decrease of 24 [-27, -21] cells/mm<sup>3</sup> at the time of first presentation for care over 11 years, adjusting for gender, race/ethnicity, transmission risk group and cohort. The interaction of age and calendar time on CD4 count at first presentation for HIV care was borderline statistically significant (p=0.05).

After stratifying by cohort, *n*=6 cohorts showed a significant increase in estimated mean annual change in CD4 count at presentation (range: 5 to 8 cells/mm<sup>3</sup>) and *n*=7 cohorts showed no difference in estimated mean CD4 count over time (Figure 2). Cohort 3 had a borderline significant decrease of 5 cells/mm<sup>3</sup> per year. Participants in cohort 3 had the highest mean CD4 count in 1997, 78% were black and 53% reported heterosexual transmission risk – all factors potentially contributing to this decrease.

## DISCUSSION

Since the mid-1990's, public health efforts have focused on identifying HIV infection at an early stage, which should imply an increase in patients presenting for HIV care earlier in the course of disease. Our data from multiple clinical sites across the US and Canada indicate that although CD4 count at presentation has increased since 1997, most patients continue to first present for HIV care with a CD4 count below 350 cells/mm<sup>3</sup>, the level at which initiation of antiretroviral therapy is currently recommended by multiple major national guideline committees for persons living in developed countries [14-18]. Stratifying out results by cohort demonstrated our findings were not an artifact of the combined data set. Knowing that within-patient variation in CD4 measurements is approximately 25% with increased variation at lower CD4 counts, our estimated mean annual increase in the CD4 count is likely of little clinical relevance [19].

Several smaller regional studies have also found that patients present late in the course of HIV infection. Among 1,209 patients who newly presented for care in an infectious diseases clinic in Alabama, 41% had already progressed to AIDS [20]. In South Carolina from 2001-05, 41% of AIDS cases were diagnosed within 1 year of HIV diagnosis [21], in North Carolina from 2000-03, 50% had a CD4 count <200 cells/mm<sup>3</sup> at first presentation for HIV care [22], in Washington DC from 1997-2006, 66% of AIDS cases were diagnosed within one year of HIV diagnosis [23], and in Maryland the CD4 count at first presentation for HIV care declined from 371 to 276 cells/mm<sup>3</sup> from 1990 to 2006 [24]. A Centers for Disease Control and Prevention (CDC) analysis of data collected in 33 US states from 2001-03 found a median CD4 count within 12 months of diagnosis of HIV-infection of only ~170 cells/mm<sup>3</sup> [25]. In a population of primarily Canadian Aboriginals newly-diagnosed patients with HIV from 1998-2003, the median CD4 count was 330 cells/mm<sup>3</sup>; 28% had a CD4 count <200 cells/mm<sup>3</sup> at diagnosis and median time to care was 27 days [26]. Another study from Calgary, Canada found that 39% of patients first presented with a CD4 count <200 cells/mm<sup>3</sup> and had care costs that were 200% higher than for patients who presented with higher CD4 counts [27]. In addition to age, gender, and race/ethnicity [20,22,24,26], these studies have also shown associations between

CD4 count at first presentation and insurance type [20] and nonmetropolitan residence [26] in multivariate analyses; we were unable to systematically measure these variables in our participating cohorts.

Over time, the demography of the HIV epidemic in the US and Canada has shifted [2,28]. Although the greatest proportion of persons diagnosed with HIV/AIDS remain MSM, the proportions of persons diagnosed with HIV/AIDS who are women, who are of minority race/ethnicity, and who have as their principal HIV transmission risk factor IDU or heterosexual contact, have increased. US national surveillance data from 2000-2003 demonstrated that late testers (persons who had their first positive HIV test within one year before diagnosis of AIDS) were significantly more likely to be younger (aged 18-29 years), black or Latino, and to have been infected through heterosexual contact [29]. In Canada from 1997-2004, various studies report younger individuals (age 25-34 years), and those who are higher-risk for acquiring HIV infection (i.e. MSM, IDUs,  $\geq 2$  partners in the last year among heterosexuals) were more likely to be tested [2]. We did not see this shift to younger patients at time of presentation, nor significantly greater percentages among Latino HIV-infected patients. However, black participants had the smallest mean annual increase in CD4 count at first presentation of any racial group. Similarly, the estimated mean annual increase in CD4 count among those with heterosexual transmission risk was dramatically lower than other risk groups. National surveillance data coupled with our findings suggest the number of blacks and high-risk heterosexuals entering into care at a later stage of disease will grow; however, the impact might be diminished with the expansion of routine HIV testing that would likely result in earlier diagnosis and entry into care.

The public health implications for our findings are clear: 1) delayed diagnosis reduces survival; and 2) individuals entry into HIV care had lower CD4 counts than the guideline for antiretroviral therapy initiation. A study from the Netherlands found that mortality after starting antiretroviral therapy could be reduced by 20% if patients were to present for HIV care with a CD4 count  $\geq 400$  cells/mm<sup>3</sup> [8]. Current guidelines recommend starting antiretroviral therapy before the CD4 count reaches 350 cells/mm<sup>3</sup>, and recent data from across the US and Canada suggests that initiating therapy at even higher CD4 levels improves survival [30]. This underscores the importance of identifying infection and engaging in HIV care at a earlier stage than is occurring currently.

A delay in presentation for treatment not only increases the chance of clinical disease progression for that patient but also increases the risk of ongoing transmission. Early effective antiretroviral treatment can lower circulating HIV-1 RNA levels, thereby decreasing the risk of HIV transmission [31-33]. Patients who learn they are infected with HIV may reduce their HIV-1 RNA with the effective antiretroviral treatment and reduce their risk-taking behavior, consequently resulting in reduced risk of transmitting HIV to others [34].

Our results found no significant differences in CD4 trends over time based by gender. Some women were likely tested as part of pre-natal screening (pregnant women are not excluded from these clinical care cohorts), and it is possible the CD4 count at which they presented for care was higher than the CD4 count at which non-pregnant women were tested and subsequently entered care. As the circumstances under which women were tested and subsequently entered care were unknown, we were unable to determine differences in CD4 counts at first presentation for care for these two groups of women.

There is clearly a need for earlier HIV diagnosis and intervention. Relying on clinical indicators for HIV infection to prompt testing is inadequate. A study from a large managed care organization in California indicated that only 22% of patients in medical care had at least one of eight clinical indicators suggested in the literature as reasons to test for HIV within one year

of being diagnosed [35]. A recent study among US veterans suggested that delayed presentation for HIV care is not a result of lack of medical care access for this population [36].

HIV testing is entering a new era as practice guidelines have recently changed to address the need for increased, earlier testing and with linkage to care. In September 2006, the CDC released Revised Recommendations for HIV Testing of Adults, Adolescents, and Pregnant Women in Health-Care Settings [37]. These advised routine HIV screening in health-care settings of adults and adolescents aged 13-64 years and of all pregnant women with prior notification and opt-out allowed. Separate informed consent, a barrier to HIV testing [38,39], is no longer recommended. More recently, the American College of Medicine released recommendations for universal HIV screening [40]. If we are to make any impact on improving the health of HIV-infected persons and reducing the spread of the virus, public health officials, hospital administrators, and clinicians will need to adopt these recommendations into practice and change policies (e.g., legal requirements for informed consent for HIV testing and elimination of the need for HIV pretest counseling in most US states and Canadian provinces) to ensure that more persons are screened and referred for early treatment.

In summary, between 1997 and 2007 in the US and Canada, there was little improvement in the immunologic stage of HIV infection among patients entering HIV care. Patients presented with relatively low CD4 counts, at a stage of disease where the effectiveness of treatment is reduced and providing an extended opportunity to transmit HIV to others. These data provide strong evidence that implementation of new strategies for earlier HIV testing and effective linkage into care are urgently needed.

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## Appendix

### Disclosures:

KNA, MMK, SJG, AGA, ACJ, JTB, SBR, RJB, JNM, LPJ, TRS, GDK, SN, LMC, JGG, SEV, HMC, BL, AMF, and RGM declare they have no conflict of interest.

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#### **NA-ACCORD Participating cohorts (representatives):**

- AIDS Link to the IntraVenous Experience (Gregory Kirk)
- Adult AIDS Clinical Trials Group Longitudinal Linked Randomized Trials (Constance Benson, Ronald Bosch, Ann Collier)
- HAART Observational Medical Evaluation and Research (Robert Hogg, Richard Harrigan, Julio Montaner)
- HIV Outpatient Study (John T. Brooks)
- HIV Research Network (Kelly Gebo)
- Johns Hopkins HIV Clinical Cohort (Richard Moore)
- John T. Carey Special Immunology Unit Patient Care and Research Database, Case Western Reserve University (Benigno Rodriguez)
- Kaiser Permanente Northern California (Michael Horberg, Michael Silverberg)
- Longitudinal Studies of Ocular Complications of AIDS (LSOCA) (Jennifer E. Thorne)
- Multicenter Hemophilia Cohort Study–II (James Goedert)
- Multicenter AIDS Cohort Study (Lisa Jacobson)
- Montreal Chest Institute Immunodeficiency Service Cohort (Marina Klein)
- Ontario HIV Treatment Network Cohort Study (Sean Rourke, Anita Rachlis)
- Southern Alberta Clinic Cohort (John Gill)
- Studies of the Consequences of the Protease Inhibitor Era (Steven Deeks, Jeff Martin)
- University of Alabama at Birmingham 1917 Clinic Cohort (Michael Saag, Michael Mugavero, James Willig)



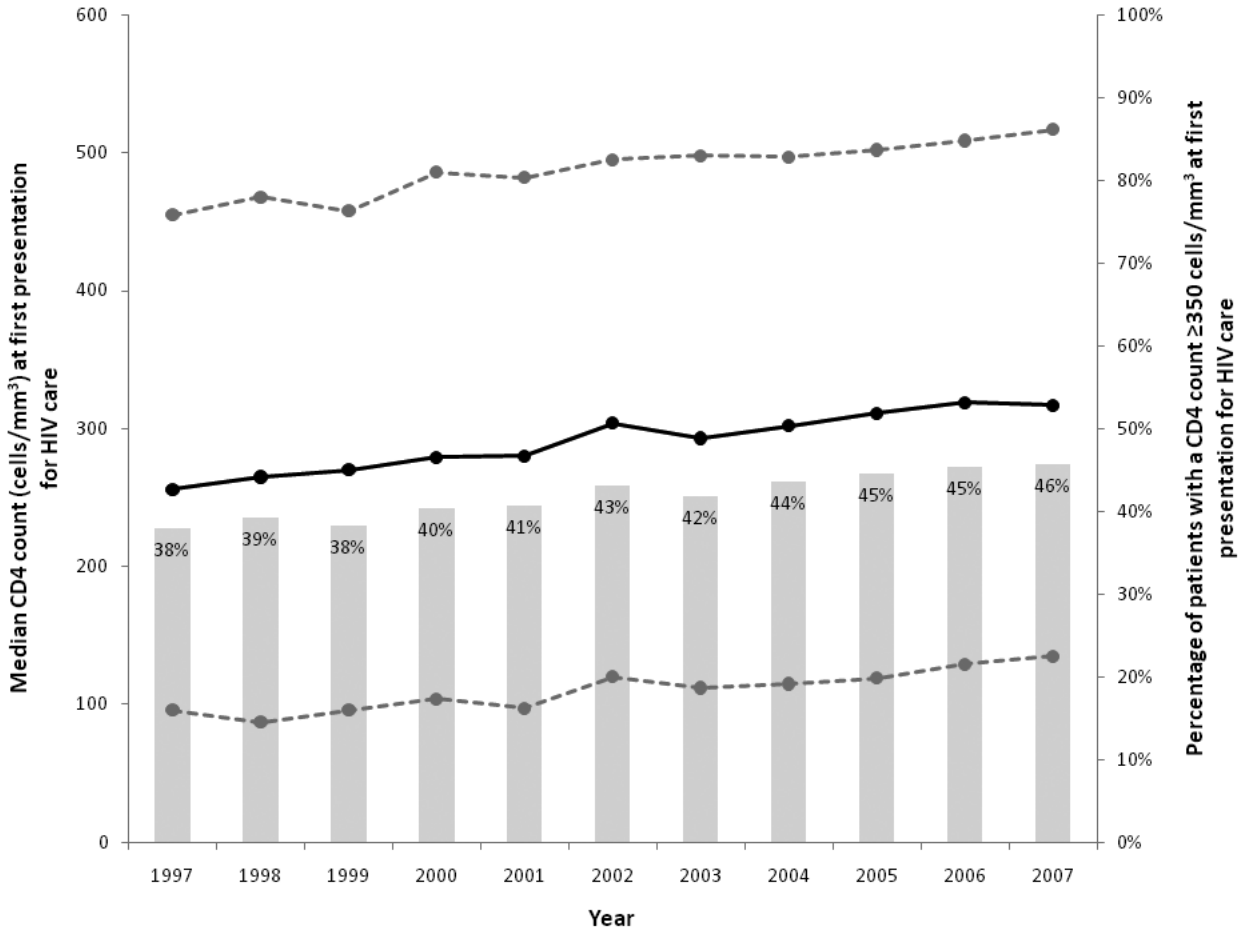
- University of North Carolina, Chapel Hill HIV Clinic Cohort (Joseph Eron, Sonia Napravnik)
- University of Washington HIV Cohort (Mari Kitahata)
- Veterans Aging Cohort Study (Amy Justice, David Fiellin)
- Vanderbilt-Meharry CFAR Cohort (Timothy Sterling, Sam Stinette, Peter Rebeiro, David Haas)
- Women's Interagency HIV Study (Stephen Gange, Kathryn Anastos)

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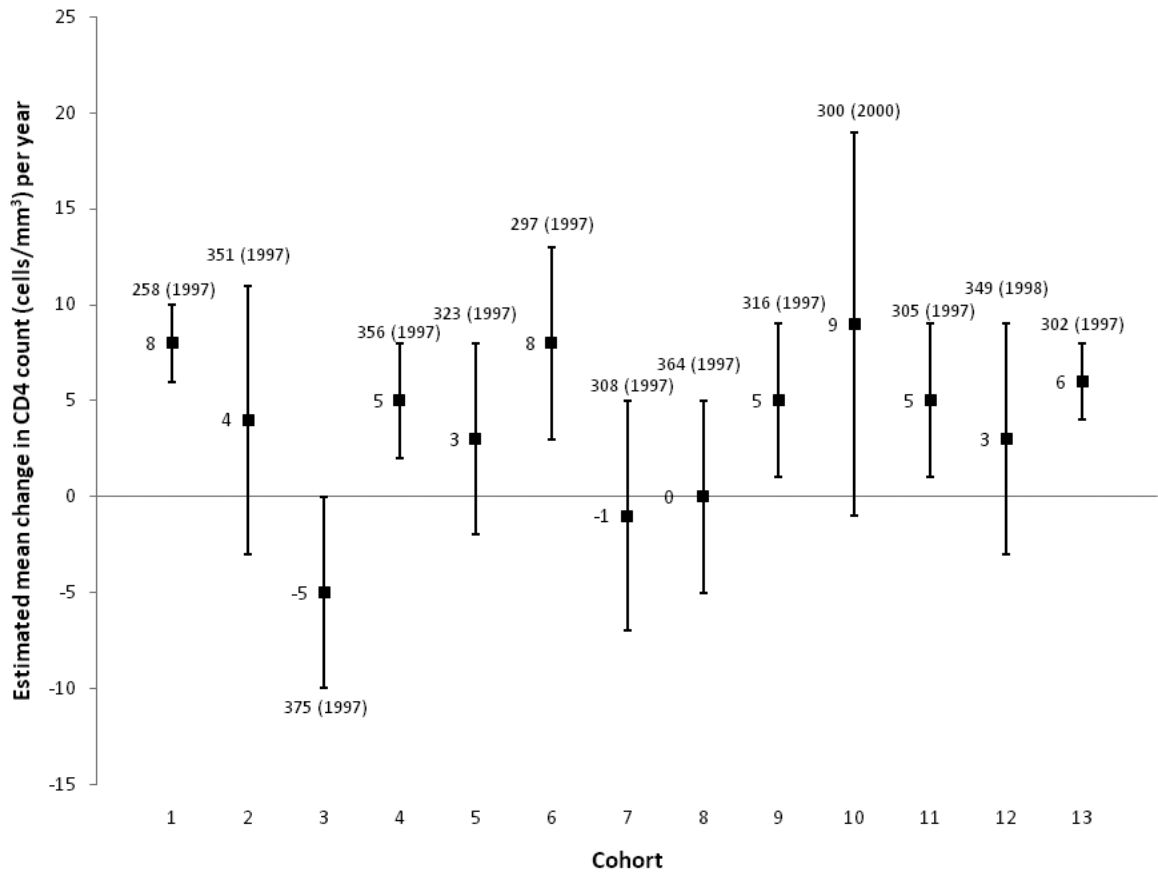
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**Figure 1.** Median CD4 count (and interquartile range), and the percentage of patients with a CD4 count  $\geq 350$  cells/mm<sup>3</sup>, at first presentation for HIV clinical care, NA-ACCORD 1997-2007



**Figure 2.** Observed mean CD4 count (year) and estimated<sup>a</sup> mean annual change in CD4 count and 95% confidence interval at first presentation for HIV clinical care, by cohort, NA-ACCORD, 1997-2007

**Table 1**

Characteristics of N=44,491 participating patients in NA-ACCORD for HIV clinical care, by year at first presentation

	Total N= 44,491	1997 n= 4,479	1998 n= 4,412	1999 n= 4,857	2000 n= 5,262	2001 n= 4,258	2002 n= 4,063	2003 n= 3,688	2004 n= 3,773	2005 n= 3,486	2006 n= 3,354	2007 n= 2,859	p-value <sup>a</sup>
<b>Age (years)</b>													
Median	41	40	41	41	40	41	41	41	41	41	42	43	<0.01
IQR	34-48	34-47	35-47	34-47	34-47	34-48	34-48	34-49	34-49	34-48	34-49	34-50	
<b>Country</b>													
United States, n (%)	42,133 95%	4,229 94%	4,209 95%	4,657 96%	5,083 97%	4,082 96%	3,837 94%	3,488 95%	3,583 95%	3,255 93%	3,101 92%	2,609 91%	
Canada, n (%)	2,358 5%	250 6%	203 5%	200 4%	179 3%	176 4%	226 6%	200 5%	190 5%	231 7%	253 8%	250 9%	<0.01
<b>Sex</b>													
Male, n (%)	36,155 81%	3,843 86%	3,716 84%	3,886 80%	4,013 76%	3,407 80%	3,296 81%	3,027 82%	3,044 81%	2,811 81%	2,724 81%	2,388 84%	
Female, n (%)	8,336 19%	636 14%	696 16%	971 20%	1,249 24%	851 20%	767 19%	661 18%	729 19%	675 19%	630 19%	471 16%	0.31
<b>Race</b>													
White, n (%)	10,255 23%	1,345 30%	1,213 27%	1,064 22%	911 17%	957 22%	899 22%	716 19%	711 19%	903 26%	848 25%	688 24%	<0.01
Black, n (%)	18,745 42%	2,014 45%	2,032 46%	2,202 45%	2,447 47%	1,805 42%	1,651 41%	1,197 32%	1,400 37%	1,484 43%	1,367 41%	1,146 40%	<0.01
Latino, n (%)	6,110 14%	509 11%	532 12%	718 15%	972 18%	653 15%	555 14%	465 13%	505 13%	411 12%	402 12%	388 14%	0.15
Other/Unknown, n (%)	9,381 21%	611 14%	635 14%	873 18%	932 18%	843 20%	958 24%	1,310 36%	1,157 31%	688 20%	737 22%	637 22%	<0.01
<b>HIV Risk Group</b>													
MSM, n (%)	12,931 29%	1,092 24%	1,090 25%	1,333 27%	1,402 27%	1,194 28%	1,212 30%	1,159 31%	1,192 32%	1,140 33%	1,166 35%	951 33%	<0.01
IDU, n (%)	8,615 19%	1,173 26%	1,158 26%	1,121 23%	1,188 23%	844 20%	691 17%	557 15%	529 14%	501 14%	450 13%	403 14%	<0.01
Heterosexual, n (%)	10,272 23%	734 16%	848 19%	1,120 23%	1,451 28%	1,076 25%	960 24%	852 23%	967 26%	813 23%	780 23%	671 23%	<0.01
Other/Unknown, n (%)	12,673 28%	1,480 33%	1,316 30%	1,283 26%	1,221 23%	1,144 27%	1,200 30%	1,120 30%	1,085 29%	1,032 30%	958 29%	834 29%	<0.01
<b>CD4+ T-cell Count (cells/mm<sup>3</sup>)</b>													
Median	288	256	265	270	279	280	304	293	302	311	319	317	<0.01
IQR	107-486	96-455	87-468	96-458	104-486	97-482	120-495	112-498	115-497	119-502	129-509	135-517	

Abbreviations: NA-ACCORD= North American Cohort Collaboration on Research and Design, MSM=men who have sex with men, IDU =injection drug use

<sup>a</sup> P-values calculated using Cochran-Armitage test for categorical variables or Cuzick's test for continuous variables.

**Table 2**

Observed mean CD4 count in 1997 and 2007 and estimated mean annual change in CD4 count at first presentation for HIV clinical care, NA-ACCORD 1997-2007

	Observed mean CD4 count (standard deviation)		Estimated change in CD4 count (95%CI) per year (1997-2007) <sup>a</sup>	
	1997	2007		
<b>Overall<sup>b</sup></b>	307 (259)	360 (283)	6	(5, 7)
<b>Models stratified by sex<sup>c</sup></b>				
Male	300 (255)	353 (278)	6	(5, 7)
Female	349 (281)	395 (303)	5	(3, 7)
<b>Models stratified by race/ethnicity<sup>d</sup></b>				
White	328 (271)	382 (280)	6	(5, 8)
Black	305 (261)	328 (279)	5	(3, 7)
Latino	293 (246)	383 (301)	9	(7, 12)
Other/Unknown	281 (235)	380 (276)	7	(5, 9)
<b>Models stratified by HIV transmission risk group<sup>e</sup></b>				
MSM	303 (255)	374 (263)	7	(6, 9)
IDU	334 (260)	358 (311)	5	(3, 7)
Heterosexual	328 (279)	337 (284)	2	(0, 4)
Other/Unknown	280 (249)	363 (289)	8	(7, 10)

Abbreviations: NA-ACCORD= North American Cohort Collaboration on Research and Design, CI=confidence interval, MSM=men who have sex with men, IDU=injection drug user

<sup>a</sup> Estimated mean CD4 count, estimated change in CD4 count per year from 1996-2007 and 95% confidence intervals from multivariate linear regression models.

<sup>b</sup> Adjusted for age, gender, race/ethnicity, HIV transmission risk group and cohort.

<sup>c</sup> Adjusted for age, race/ethnicity, HIV transmission risk group and cohort.

<sup>d</sup> Adjusted for age, gender, HIV transmission risk group and cohort.

<sup>e</sup> Adjusted for age, gender, race/ethnicity and cohort.