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# **HIV viral load levels and CD4+ cell counts of youth in 14 cities**

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# **Abstract**

**Objectives—To describe the HIV viral load and CD4<sup>+</sup> cell counts of youth (12–24 years) in 14** cities from March 2010 through November 2011.

**Methods—**Baseline HIV viral load and CD4<sup>+</sup> cell count data were electronically abstracted in a central location and in an anonymous manner through a random computer-generated coding system without any ability to link codes to individual cases.

**Results—**Among 1409 HIV reported cases, 852 participants had data on both viral load and  $CD4^+$  cell counts. Of these youth, 34% had  $CD4^+$  cell counts of 350 or less, 27% had cell counts from 351 to 500, and 39% had CD4<sup>+</sup> cell counts greater than 500. Youth whose transmission risk was male-to-male sexual contact had higher viral loads compared with youth whose transmission risk was perinatal or heterosexual contact. Greater than 30% of those who reported male-to-male sexual contact had viral loads greater than 50 000 copies, whereas less than 20% of heterosexual contact youth had viral loads greater than 50 000 copies. There were no differences noted in viral load by type of testing site.

**Conclusion—**Most HIV-infected youth have CD4<sup>+</sup> cell counts and viral load levels associated with high rates of sexual transmission. Untreated, these youth may directly contribute to high rates

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of ongoing transmission. It is essential that any public health test and treat strategy place a strong emphasis on youth, particularly young MSM.

#### **Keywords**

CD4+ cell count; HIV; linkage to care; viral load; youth

## **Introduction**

The National HIV/AIDS Strategy emphasizes the importance of linkage to care (LTC) for persons with newly diagnosed HIV infection [1]. Timely diagnosis and initiation of care has been associated with a reduction in patients diagnosed with late-stage clinical disease and improvements of temporal mortality trends [2]. Furthermore, in a large prospective cohort of HIV-infected adults, temporal increases in HAART utilization were associated with increases in viral load suppression rates and higher median CD4+ T-cell counts [3]. Early linkage to and retention in care also may lead to earlier viral load suppression and may lower the cumulative individual viral load burden. Moreover, on an epidemiologic scale, improved viral load suppression is associated with reductions in community viral loads and with reductions in new cases of HIV infection [4–8]. However, this landscape is vastly unexplored and not characterized in adolescents and young adults, who represent a growing concern domestically.

In the United States, HIV disproportionately impacts vulnerable youth and minority MSM populations. Youth ages 13–24 years accounted for 26% of incident HIV infections in 2010 [9]. About 87% of all new youth infections among men occurred in young MSM (YMSM) [9]. About 60% of youth with HIV do not know they are infected and cannot receive treatment [9]. Among black YMSM, new HIV infections increased 48% from 2006 to 2009 [10].

Strategic Multisite Initiative for the Identification, Linkage and Engagement in Care of Youth with Undiagnosed HIV Infection (SMILE in Caring for Youth) is a National Institutes of Health, Centers for Disease Control and Prevention, and Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN) collaboration designed to improve the identification of youth with undiagnosed HIV infection, link them to care at a clinical site with adolescent HIV medicine expertise, and to ultimately inform best practices for the continuum of care for youth with HIV in the United States. The objective of this article is to describe the HIV viral load and CD4+ cell counts of youth reported to the SMILE program.

#### **Methods**

# **Strategic Multisite Initiative for the Identification, Linkage and Engagement in Care of Youth with Undiagnosed HIV Infection program**

The SMILE program was established at 15 ATN sites located in 14 cities in the United States and Puerto Rico. An ATN adolescent-expert outreach worker was provided as a clinical resource to testing facilities and health departments to help facilitate the linkage service process between the testing and treatment sites. This was accomplished by creation

of memoranda of understanding between local collaborating ATN sites and testing and health department sites, which delineated roles and responsibilities and included aspects on communication and bidirectional data sharing. The study was conducted between March 2010 and November 2011.

An administrative database was created to collect the records of HIV-positive youth, ages 12–24, who were referred as a new case, linked to care within 42 days of referral, and engaged in care within 16 weeks of linkage. Additionally, demographics, case dispositions, and reasons for failure in care linkage/engagement were recorded by the outreach worker and included for both ATN sites and their affiliates.

### **ATN 093**

ATN 093 was a research protocol designed to evaluate the effectiveness of the SMILE program using de-identified data abstracted electronically. Data were electronically abstracted in a central location and in an anonymous manner through a random computergenerated coding system without any ability to link codes to individual cases. This anonymized research database provided HIV viral load and CD4+ cell count data that were compared by demographics, socioeconomics, risk behaviors, and ATN site using Kruskal– Wallis tests. Both univariate and multivariable linear regression analyses were performed to assess the relationship of viral load with potentially associated factors. Because of skewed data, raw viral load was transformed using ranks for the regression analysis. Covariates with an unadjusted *P* value <0.05 were entered into the initial full multivariable model and retained in the final model if the overall *P* value was less than 0.05 after the model selection. Data included in this analysis were abstracted for cases reported to SMILE that had both CD4+ cell count and viral load levels from 2010 to 2011. To evaluate the possible effect of excluding these cases, the overall mean viral load was recalculated including the excluded cases and assuming that patients of the same sexual orientation and HIV acquisition mode would have about the same viral load as those who were included. Each ATN site's local Institutional Review Board approved or exempted the protocol prior to implementation.

# **Results**

There were 1409 cases reported to SMILE [median age 21 (12–24 years), 78.1% men, 18.0% women, and 3.5% transgendered; 18.3% Hispanic/Latino ethnicity, 67.1% black, 5.7% white]. Among all 1409 cases, 852 (60%) participants had data on both CD4+ cell counts and viral load for this analysis. The remaining 557 (40%) did not have both data points and were not included in this analysis. Table 1 shows a comparison of demographics and risk characteristics of these two groups. Of the 852 with sufficient data, 671 (78.8%) were linked to care during the study period, 119 (14%) had been linked to care prior to the study, and 62 (7.3%) that could not be located or were not linked to care for other reasons. The mean viral load and  $CD4^+$  cell counts were 94 398 copies/ml and 456 cells/ $\mu$ l, respectively.

Table 2 shows the mean viral load and its distribution over a range of categories (<400 to >100 000 RNA copies/ml) by demographic and clinical variables. Young men had significantly higher viral loads than young women. Whereas there were variations by site,

with median viral load ranging from 4427 to 30 363, there were no significant differences by geographic region. Youth who self-reported their sexual orientation as homosexual or bisexual had higher viral loads compared with those reporting to be heterosexual. More than 30% of homosexual or bisexual youth had viral loads greater than 50 000 copies, whereas 21.5% of heterosexual youth had viral loads greater than 50 000 copies. In addition, youth whose transmission risk was male-to-male sexual contact had higher viral loads compared with youth whose transmission risk was perinatal or heterosexual contact. Greater than 30% of those who report male-to-male sexual contact had viral loads greater than 50 000 copies, whereas less than 20% of heterosexual contact youth had viral loads greater than 50 000 copies. In an adjusted, multivariable model, only CD4+ cell count and transmission risk were significantly associated with viral load. Sensitivity analyses based on sexual orientation and mode of HIV acquisition indicated that the overall mean viral load may be overestimated by about 4.6% due to excluding cases for which viral load and  $CD4<sup>+</sup>$  cell data were not available.

# **Discussion**

These data show that almost 30% of infected youth have HIV viral load levels of 50 000 copies or more and that the majority of youth have CD4<sup>+</sup> cell counts below 500. These viral load levels are associated with high rates of transmission, both in person-years and per coital act [11,12]. YMSM are well represented in these data, which is consistent with testing frequency [13], and they have the highest viral loads, which is consistent with the high rates of ongoing transmission in this population in the United States [14,15].

These data provide important benchmarks for evaluations of 'treatment as prevention' strategies and indicate areas of focus for additional secondary transmission interventions. Few data allow direct comparison of disease status at entry into care among adolescents and young adults. A study using San Francisco HIV surveillance data of 12 512 HIV-positive men and women from 2005 to 2008 found a population mean viral load of 23 348 and that among MSM, the mean viral load was 36 764 (compared with 94 398 and 115 213, respectively in our study) [6]. A study of 676 HIV-infected persons entering care (mean age 36 years) in Birmingham, and Seattle, Washington HIV clinics found that the mean viral load of these individuals to be approximately 39 000 [3]. Finally, a study of 4684 men and women diagnosed with HIV infection in the District of Columbia in 2008 (mean age 45) found a mean viral load of 33 847 [16].

We recognize that the use of mean viral load as an indicator of transmission and incidence at the community or network level has its limitations. As supported by our higher mean CD4<sup>+</sup> cell counts and proportions with  $CD4^+$  cell count more than 350 (over  $2/3$ ) compared with adults (43%) [4], youth are likely diagnosed closer to their time of infection than adults and therefore, viral dynamics in earlier HIV infection may skew viral load data to higher levels characteristic of this stage of infection. Additionally, as Miller *et al.* argue [17], among other things, the mean viral load of a study population may not be representative of ongoing transmission because of selection bias (who was tested and linked to care and from whom viral load information was collected). This is clearly a limitation of our study. Further, they contend that infectivity, as measured by viral load, is only one of several determinants of

transmission. The prevalence of HIV and the mixing patterns within a community are also important factors not captured by the assessment of the mean viral load of a population. Finally, the necessary exclusion of participants missing viral load data may have resulted in an overestimate of the mean viral load by about 4.6%.

Nonetheless, in the context of existing literature, our findings suggest that the population of HIV-infected youth may be a highly infectious population, suggesting they are being identified at an earlier critical window of opportunity for prevention. This concern is most acute in YMSM. If these youth remain untreated, they might support high rates of ongoing transmission at the community level. With new treatment guidelines recommending treatment for all HIV-positive individuals, emphasis needs to be placed on breaking down barriers to care [18]. Furthermore, it is essential that any public health test and treat strategy put a strong emphasis on youth, particularly YMSM.

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## **Table 1**

Selected demographic, sexual risk characteristics, and testing locations by viral loads and CD4<sup>+</sup> cell count availability status among selected 1409 clients from SMILE program as of 30 November 2011.



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LTC, linkage to care, SMILE, Strategic Multisite Initiative for the Identification, Linkage and Engagement in Care of Youth with Undiagnosed HIV Infection; VL, viral load.

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 $\phi^{\dagger}$  *P* value is from  $\chi^2$  test and missing values are not included in the calculation for *P* values.



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**Table 2**

HIV viral load by selected demographic, sexual risk characteristics, and testing locations.

HIV viral load by selected demographic, sexual risk characteristics, and testing locations.

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 $a_{\text{The}\text{~unadjusted}}$  P value tests whether the median differences among categories for a specific characteristic are significant. *a*The unadjusted P value tests whether the median differences among categories for a specific characteristic are significant.

The adjusted P value is from the multivariable linear model with the outcome of viral load ranks. Covariates with an unadjusted P value <0.05 were entered in the initial full multivariable model, including *b*The adjusted P value is from the multivariable linear model with the outcome of viral load ranks. Covariates with an unadjusted P value <0.05 were entered in the initial full multivariable model, including

sex, CD4<sup>+</sup> cell counts, sexual orientation, and mode of HIV acquisition. After model selection, covariates with a type III SS P value <0.05 were retained in the final model. + cell counts, sexual orientation, and mode of HIV acquisition. After model selection, covariates with a type III SS P value <0.05 were retained in the final model. Both continuous and categorical CD4<sup>+</sup> cell counts were examined in separate multivariable models, respectively. After model selection, the results were the similar: CD4<sup>+</sup> cell counts and model of HIV + cell counts and model of HIV + cell counts were examined in separate multivariable models, respectively. After model selection, the results were the similar: CD4 acquisition were retained in the final model. acquisition were retained in the final model.  $c_{\text{Both continuous and categorical CD4}}$ 

 $57(6.7)$  $17(2.0)$  $23(2.7)$   $123(14.4)$ 113 (13.3)

**Total (***N* **= 852)** *n* **(col %)**

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