Changes In Demographics and Risk Factors Among Persons Living With HIV In an Academic Medical Center From 2003-2007

Fizza S. Gillani, PhD, Nickolas D. Zaller PhD, Kimberly Zeller, MD; Josiah D. Rich, MD, Susan Cu-Uvin, MD, Timothy P. Flanigan, MD, Charles CJ Carpenter, MD

National epidemiological data indicate that the HIV epidemic in the United States has been continually changing since its initial recognition in 1981. There has been no decrease in the incidence of HIV infection in the US for over a decade, and over 55,400 individuals were newly infected with HIV in the US in 2007.[1] Of these new infections, 62% contracted their infection through **sex with other men (MSM)** compared with 44% a decade ago.[2-3] Gradual annual increases in the proportion of incident infections in women in the US have been observed for the past 15 years, with the great majority acquired via heterosexual contact.[2] During this period, the number of HIV infections attributable to **injection drug use (IDU)** for both men and women dramatically declined, with estimates of a 42% overall reduction between 1994 and 2000 [4] and continued decreases in many areas through 2007.[5] There has been no significant improvement in the early diagnosis of HIV among newly infected individuals, either nationally or in Rhode Island, since the 1990s.[6]

The Samuel and Esther Chester Immunology Center at The Miriam Hospital track changes in demographics, risk factors, and clinical markers in order to evaluate the changing environment, and accessibility and adherence to care in the Rhode Island community. The Immunology Center, located on the campus of **The Miriam Hospital (TMH)**, is the largest HIV care provider in Rhode Island, with roughly 1,200 active HIV/AIDS patients in 2007, greater than 75% of the total known HIV/AIDS cases in the state. The proportion of Rhode Islanders known to be living with HIV who receive care at the Immunology Center has been consistently between 75 and 80% from 2003 through 2008.

Created in 1987, the Center was originally designed to fill a gap in care for HIV-positive women; but the composition of the clinic has gradually shifted to reflect the statewide epidemic. The Center now offers comprehensive health care for all Rhode Islanders living with HIV. Since 1994, a federal Ryan White Part C (Title III) grant has supported primary care and early intervention services. The Center provides multiple supportive services onsite including free HIV counseling and testing (rapid blood and oral antibody testing), social services, laboratory testing, antiretroviral adherence training, limited psychiatric care, viral hepatitis testing and treatment, and a substance use treatment referral system. It has served as the base site for past and current controlled clinical trials through the NIH AIDS Clinical Trials Group, and the USPHS Centers for Disease Control and Prevention.

Materials and Methods

Study Design

This evaluation examines data from the **Immunology Center database (ICDB)** for patients actively receiving care at the Immunology Center between January 1, 2003, and December 31, 2007. The ICDB system was created with funding from the NIH-supported **Lifespan/Tufts/Brown Center for AIDS Research (LTB-CFAR).** This system was designed after visiting several other CFARs, which had created electronic database systems that facilitated clinical research and enhanced the medical management of HIV/AIDS patients. This database, updated daily. assists physicians in patient management and enables researchers to access clinical data. At each visit, clinicians use the data base, allowing them to make corrections promptly.

The 18 physicians who provide HIV care for patients in the Immunology Center provide the patients' histories of treatment, laboratory results, and antiretroviral regimens, as well as other clinical and risk factor information.

Target Population

The Immunology Center provides care to any Rhode Island adult with HIV, and has targeted women, minorities, ex-offenders, and substance users for its services. For detailed analyses, we organized patients into four groups: **Baseline group:** all active patients who were enrolled and active in care on January 1, 2003 are included in the Baseline group. **Exiting group:** patients who died, moved away, transferred care or were lost-to-follow-up during each year (2003 to 2007). **Entering group**: all newly diagnosed patients registering to receive care from the Immunology Center, patients transferring care from another provider, and patients who were reactivated into care. Patients newly diagnosed for a specific year are defined as patients who were registered at the Immunology Center within that calendar year and who had been diagnosed with HIV within the previous twelve months. The "newly registered but not newly diagnosed" patients have transferred their care to the Center from any other medical facility and were diagnosed more than twelve months before registration date at the Immunology Center. Reactivated patients were discharged from the Immunology Center before 2003 and were reactivated during the time of the study. The **End Group** includes all patients alive, active, and in-care at the end of 2007.

Patient data for each year of the study period were aggregated and contingency table analyses were performed to compare demographics and HIV related risk behaviors. Contingency table analyses were also used to assess potential differences in important demographic characteristics. All 95% **confidence intervals (CI)** and associated *p*-values for the observed categorical, dichotomous outcomes were calculated using **Cochrane-Mantel-Haenszel (CMH)** chi-square tests. For variables that are not dichotomous (have more than two outcome levels and values in each cell are not large), Fisher Exact tests were used to examine statistical significance. Continuous variables were tested using Cochrane and Cox (1950) approximations examining whether the mean or median values of any two groups differ significantly. All tests are two-sided and p-values <= 0.05 were con-

sidered statistically significant. To investigate trends/association between the specific years and different covariates, normal chi-square tests were performed and score tables were used to analyze the trend/associations. All statistical analyses were performed using SAS version 9.1. The Miriam Hospital **Institutional Review Board (IRB)** approved all aspects of this study.

Results

Table 1a presents overall demographic data for the total number of active patients for 2003 to 2007. The clinic population has not changed significantly over the five-year period with respect to gender, race/ethnicity or age. However, important differences have occurred in the modes of transmission. (Table 1b). The proportion of transmissions via IVDU decreased significantly in both men and women from 2003 to 2007, while the proportion of sexual transmissions (including both MSM and heterosexual transmission in men) increased in both men and women. The risk factor data reported here are based on self-reports by the patients during their intake interviews with social workers.

Table 2a presents the demographic data for all newly diagnosed patients. The proportion of newly diagnosed non-Hispanic white patients increased significantly during that time period. The observed sharp increase in total HIV cases in 2004 may have been influenced by the introduction of rapid testing to the community by the largest **AIDS Service Organizations (ASOs)** in the greater Providence area. The proportion of AIDS diagnoses at entry into care at The Immunology Center rose from 28% to 37% during 2002-2007.

Table 2b presents transmission modes by gender of all newly diagnosed patients. A significant change has occurred in the mode of transmission for newly diagnosed women from 2003 to 2007. Prior to 2003, one third of Rhode Island women living with HIV had acquired the infection via IV drug use. Since 2003, women have seldom acquired HIV by this route. Since 2005, no newly diagnosed woman has had history of exposure by any route other than heterosexual sex.

Tables 3a and 3b provide CD4 categories (CD4 < 200, CD4 between 200 and 350, and CD4 > 350) and median CD4 values for existing and newly diagnosed patients each year of the study period. A CD4 count of <200 meets the CDC criteria for the diagnosis of AIDS. The median CD4 of the total clinic population gradually increased between 2005 and 2007. As anticipated because of the effectiveness of antiretroviral therapy, median CD4 counts among newly diagnosed patients were generally lower than CD4 counts among patients already in care at the Immunology Center, with the largest difference (110 cells/μL) observed in 2007 (p= 0.001).

Table 3b shows the CD4 counts of newly diagnosed patients by gender. In 2007, nearly 40% of both women and men entering into care met the CDC criteria for the diagnosis of AIDS, indicating an increasing delay in diagnosis and entry into care of Rhode Islanders living with HIV infection.

Overall, there were remarkably few differences between the Baseline and the End groups in relation to age, partnership status, primary language spoken and age at diagnosis. With respect to insurance status, more clinic patients had private insurance at the end of 2007 than in 2003 (22% vs. 32%). The proportion of patients receiving Ryan White Part C funded free care more than doubled during this period.

Table 1-a: Demographics of total active patients from 2003 to 2007*

	2003	2004	2005	2006	2007
Total	**N=925**	**N=954**	**N=991**	**N=1073**	**N=1144**
New patients	116	187	127	164	127
Deceased	27	27	17	23	20
Gender %					
Male	65	64	63	65	67
Female	35	37	37	35	33
Race/Ethnicity %					
Non-Hispanic Black	31	31	31	31	30
Non-Hispanic White	46	48	47	47	47
Hispanic	20	19	20	20	21
Others	3	2	2	2	2
Age at Diagnosis %					
< 25 Years	18	16	17	17	18
26-35 Years	44	43	40	40	39
36-45 Years	29	31	32	32	31
>45 Years	9	10	11	11	12

Table 1b: Transmission Mode by Gender, Total Active Patients from 2003-2007

	2003	2004	2005	2006	2007
Female	**N=326**	**N=350**	**N=363**	**N-374**	**N=380**
% Heterosexual*	63	69	73	74	75
% IDU	37	31	27	26	25
Male	**N=599**	**N=604**	**N=628**	**N=699**	**N=764**
% MSM	43	46	46	50	50
% IDU	31	26	25	23	21
% MSM/IDU	3	3	3	2	2
% Heterosexual/uncertain**	23	25	26	25	27

*Defined as no risk factors other than heterosexual intercourse.
**This category is not precise, as a large proportion of men who initially reported heterosexual transmission subsequently indicated that their major relationship had been MSM.

Discussion

The changes observed in the HIV epidemic in Rhode Island are generally similar to nationwide changes. Among new infections, African Americans and Hispanics accounted for 46% of all new HIV cases in Rhode Island despite the fact that these two groups comprise only 14% of the state's total population.[7] Nationally, the CDC estimates that 67% of all new HIV infections in 2006 were among African Americans and Hispanics.[2] With respect to new registrations in the Immunology Center at The Miriam Hospital, the proportion of African American patients remained relatively stable, while the

Table 2a: Demographics of Newly Diagnosed patients from 2003 to 2007

	2003	2004	2005	2006	2007
TOTAL	**N=47**	**N=110**	**N=64**	**N=84**	**N=76**
Gender %					
Male	72	62	68	72	76
Female	28	38	33	29	24
Race/Ethnicity %					
Non-Hispanic Black	36	36	28	32	21
Non-Hispanic White	32	44	42	46	57
Hispanic and Others	32	20	30	22	22
Age at Diagnosis %					
< 25 Years	19	13	11	8	17
26-35 Years	43	34	24	25	24
36-45 Years	26	35	38	47	31
>45 Years	13	19	28	19	29

Table 2b: Transmission Mode by Gender of Newly Diagnosed Patients from 2003 to 2007

	2003	2004	2005	2006	2007
TOTAL	**N=47**	**N=110**	**N=64**	**N=84**	**N=76**
Gender					
Female	**N=13**	**N=42**	**N=21**	**N=24**	**N=18**
Heterosexual %*	92	91	100	100	100
IDU %	8	9	0	0	0
Male	**N=34**	**N=68**	**N=43**	**N=60**	**N=58**
MSM + MSM/IDU %	50	65	65	61	68
IDU %	0	0	0	5	1
Heterosexual/uncertain**	50	35	35	33	33

*Includes all women who reported no risk factors other than heterosexual contact.
**Sexual category for men includes both MSM and heterosexual transmission as a large proportion of men who initially reported heterosexual transmission subsequently indicated that transmission had been via MSM.

proportion of Hispanic patients increased steadily between 2003 and 2007.

The risk factors are self-reported at clinic Intake. Some patients changed, or added to, the list of risk factors they initially reported. A number of men initially reported only heterosexual contact as their risk factor at the first interview, but later indicated that they were engaged primarily in MSM sexual contact. Initial reluctance to report MSM behavior may be attributed to cultural stigma. We observed a substantial increase in the numbers of new MSM clinic patients, with a greater than 30% increase in the proportion of MSM clinic patients in 2007 compared to 2003. Over the years, MSM as the primary risk factor has been largely reported by non-Hispanic white males. In 2007, of 34 newly diagnosed MSMs, only 9% were Hispanic, 12% percent were non-Hispanic blacks, and 79% were Non-Hispanic white.

The observed steady increase in the number of new MSM clinic patients during the past three years reflects a substantial change in the HIV epidemic in Rhode Island. From the 1980s through the early 1990s, 50% of all new HIV infections in the state were attributable to IDU.[7] Since 2000, with the development of clean needle exchange laws, **injection drug use (IDU)** as a primary risk factor for HIV transmission in Rhode Island has decreased markedly. The decline in incident HIV cases attributable to IDU has been well documented in other states as well.[5,8,9] MSM has become the major risk factor among men for acquiring HIV infection in Rhode Island. While evidence suggests that MSM sexual risk behavior has decreased in certain regions in the US in recent years,[10] this has not been the case in Rhode Island. In a recent population based, cross sectional community health survey in conducted in New York City, 60% of MSM reported not using a condom during the last sexual encounter.[11] Marks et al report that among a total sample of 2,205 MSM of color recruited from three urban areas in the US between 2005 and 2006, nearly one in four HIV positive MSM had engaged in risky sexual behavior with at least one partner.[12]

While many individuals living with HIV infection in the US have greatly benefited from advances in **highly active antiretroviral therapy (HAART)**, data from Baltimore indicate that many persons initially presenting with HIV infection have a greater severity of immunocompromise in recent years of the epidemic.[13] In Rhode Island, a greater severity of HIV disease was observed in newly diagnosed women over the past five years, but not in men.

Limitations

While our data are from the Immunology Center, which provides care to over 75% of Rhode Islanders living with HIV, the data may not be generalizable to all HIV clinical settings in the state. Our database records only those risk factors which are self-reported at the time of clinic intake. Data from patients who later report additional risk factors are not presently captured in our Center database.

Conclusion

The CDC estimates that over 250,000 people living with HIV/AIDS in the US are either: 1) unaware of their status and therefore are not receiving care and/or HIV treatment; 2) are aware of their status but not receiving HIV care. In the Immunology Center in 2007, 26 patients had advanced to AIDS at time of diagnosis: 48% were non-Hispanic white, 38% were non-Hispanic black and 14 % were Hispanic. Among Rhode Island women newly diagnosed in 2007, 39% had progressed to AIDS by the time of diagnosis; reflecting the fact that most women had not been tested earlier, because they were not aware that they had been exposed to a partner living with HIV infection. These data indicate the urgent need for a more effective statewide opt-out HIV screening program, an approach recommended by the CDC.[14]

Table 3a: CD4 levels of Existing versus Newly Diagnosed patients by Year

	2003	2004	2005	2006	2007
CD4 Cell Count Range					
1) Existing patients	**N=742**	**N=774**	**N=880**	**N=915**	**N=982**
% <200	17	17	17	13	12
% 200-350	22	24	25	22	22
% >350	61	59	59	65	66
Median CD4 cell count	423	403	397	432	443
2) Newly diagnosed patients	**N=46**	**N=108**	**N=63**	**N=83**	**N=70**
% <200	28	30	29	28	37
% 201-350	24	19	19	19	19
% >350	48	52	52	53	44
Median CD4 cell count	345	382	396	386	333

Table 3b: CD4 Levels of Newly Diagnosed Patients by Gender

	2003	2004	2005	2006	2007
Female	**N=13**	**N=41**	**N=21**	**N=24**	**N=13**
% <200	23	29	19	29	39
% 201-350	23	22	19	21	23
> 350	54	49	62	50	39
Median CD4 cell count	416	374	450	306	369
Male	**N=33**	**N=67**	**N=42**	**N=59**	**N=57**
% <200	30	30	33	27	37
% 201-350	24	16	19	19	18
% >350	46	54	48	54	46
Median CD4 cell count	339	382	385	394	333

Fizza S. Gillani, PhD, is Assistant Professor of Medicine (Research), The Warren Alpert Medical School of Brown University.

Nickolas D. Zaller, MD, is Instructor of Medicine (Research), The Warren Alpert Medical School of Brown University.

Kimberly Zeller, MD, is Clinical Assistant Professor of Family Medicine, The Warren Alpert Medical School of Brown University.

Josiah D. Rich, MD, is Professor of Medicine and Community Health, The Warren Alpert Medical School of Brown University.

Susan Cu-Uvin, MD, is Professor of Obstetrics and Gynecology and Medicine, The Warren Alpert Medical School of Brown University.

Timothy P. Flanigan, MD, is Professor of Medicine, The Warren Alpert Medical School of Brown University.

Charles CJ Carpenter, MD, is Professor of Medicine, The Warren Alpert Medical School of Brown University.

Disclosure of Financial Interests

Susan Cu-Uvin, MD. Speaker's Bureau: Bohringer Ingelheim

Timothy P. Flanigan, MD. Grant research support: Gilead Pharmaceuticals. Major Stockholder: Gilead Pharmaceuticals, Abbott, Glaxo Smith Kline

Fizza S. Gillani, PhD, Nickolas D. Zaller, PhD, Kimberly Zeller, MD, Josiah D. Rich, MD, and Charles CJ Carpenter, MD, have no financial interests to disclose.

Acknowledgement

This work was supported by NIH CFAR grant P30AI042853.

References

1. Hall HI, Song R, et al. Estimation of HIV incidence in the United States. *JAMA* 2008;300:520-9.
2. CDC. HIV/AIDS Surveillance Report, 2006. Vol. 18. Atlanta: US Department of Health and Human Services, CDC; 2008.
3. Centers for Disease Control and Prevention. HIV/AIDS Surveillance Report, 1997. Vol. 9, No.2. Atlanta, GA: US Department of Health and Human Services, CDC; 2006. http://www.cdc.gov/hiv/topics/surveillance/resources/reports/pdf/hivsur92.pdf.
4. Centers for Disease Control and Prevention. HIV diagnoses among injection-drug users in states with HIV surveillance—25 states, 1994–2000. *MMWR* 2003;52:634–6.
5. Beckwith CG, Moreira CC, et al. *Subst Abuse Treat Pre Policy* 2006;4;1:34
6. Keruly JC, Moore RD. Immune status at presentation to care did not improve among antiretroviral-naive persons from 1990 to 2006. *Clin Infect Dis* 2007;45:1369-74.
7. Rhode Island Department of Health, Division of Community Family Health and Equity, Office of HIV/AIDS & Viral Hepatitis, 2007 Rhode Island HIV/AIDS Epidemiologic Profile with Surrogate Data, 8-2008.
8. Des Jarlais DC, Perlis T, et al. HIV Incidence among injection drug users in New York City, 1990–2002. *Am J Pub Health* 2005, 95:1439-44.
9. Santibanez SS, Garfein RS, et al. Update and overview of practical epidemiologic aspects of HIV/AIDS among injection drug users in the United States. *J Urban Health* 2006; 83:86-100.
10. Brooks RA, Lee SJ, et al. Sexual risk behavior has decreased among men who have sex with men in Los Angeles but remains greater than that among heterosexual men and women. *AIDS Educ Prev* 2008;20:312-24.
11. Manning SE, Thorpe LE, et al. Estimation of HIV prevalence, risk factors, and testing frequency among sexually active men who have sex with men, aged 18–64 years—New York City, 2002. *J Urban Health* 2007;84:212-25.
12. Marks G, Millet GA, et al. Understanding differences in HIV sexual transmission among Latino and Black men who have sex with men. *AIDS Behav.* 2008 Aug 28. [Epub ahead of print]
13. Keruly JC, Moore RD. Immune status at presentation to care did not improve among antiretroviral-naïve persons from 1990-2006. *CID* 2007; 45:1369-74.
14. Mahajan A, Stemple L, et al. Consistency of state statutes with the Centers for Disease Control and Prevention HIV testing recommendations for health care settings. *Ann Int Med* 2009;150:263-9.

Correspondence

Fizza S. Gillani, PhD
The Miriam Hospital
164 Summit Ave
Providence, RI 02906
Phone: (401) 793-4873
e-mail: FGillani@lifespan.org