Transmitted Drug Resistance and Time of HIV Infection, New York State 2006-2013

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Background

The date of HIV infection cannot be readily established for most HIV cases. Resistance findings for persons newly diagnosed with HIV infection may reflect transmissions that occurred years earlier. This study evaluated the need to classify newly diagnosed cases by recency of infection in order to accurately determine the prevalence of transmitted drug resistance (TDR) and assessed variation in TDR prevalence across demographic and risk groups in New York State (NYS).

Case Selection and Resistance Tests

- Newly diagnosed cases 1/2006 - 9/2013 age ≥13 years in the NYS HIV surveillance registry were included in the study.
- HIV antiretroviral drug resistance test results obtained in clinical care are routinely reported to NYS Department of Health (NYSDOH) as protease (PR), reverse transcriptase (RT), and integrase (IN) *pol* gene nucleotide sequences. The sequences were analyzed using NYSDOH's in-house Resistance Analysis System. Mutations in PR and RT gene sequences were compared to the Transmitted Drug Resistance Mutation (TDRM) list used by CDC to assess presence of TDRMs[1].
- The newly diagnosed cases from the surveillance database were linked to the received genotypic resistance tests. Tests with sample date within 3 months of the HIV diagnosis date were considered "initial" resistance tests and were included in the analyses.

Recency of Infection

Recency of infection - "recent" vs "long"

- "recent" - recent HIV infection: infected up to 6 months before diagnosis
- "long" - long-standing infection: infected > 6 months before diagnosis

Measure of recency of infection:

- Based on BED result, if available, with testing and treatment history data
- For cases without BED result:

1) cases with AIDS diagnosis within 6 months of HIV diagnosis were classified as long-standing infection

2) Cases never diagnosed with AIDS or with AIDS diagnosis > 6 months after HIV diagnosis were classified as "unknown"

Results 1 - Frequency of Initial Resistance Testing and TDR

Among 29,515 newly diagnosed cases 2006-2013, 22,736 had a reported HIV-related lab test and 13,015 (44%) had a reported resistance test within 3 months of diagnosis.

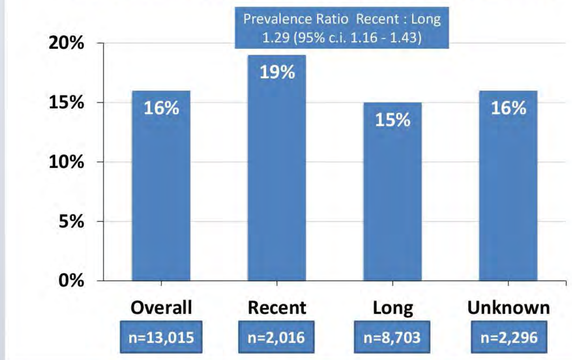
- The proportion of cases with an initial resistance test rose from 31% in 2006 to 62% in 2013.
- Multivariate logistic regression showed that odds of having an initial resistance test were related to year of diagnosis, race/ethnicity, transmission risk group, and residence at diagnosis (p<0.01 for all).

Who Gets Initial Resistance Tests in New York State?
29,515 cases, 2006- 2013

Characteristic		% with initial resistance test
Sex	Male	45%
	Female	41%
Race/ Ethnicity	White	52%
	Black	38%
	Hispanic	46%
	Asian/PI	53%
	Native American	48%
	Multirace	49%
Region	NYC	42%
	Rest of NYS	51%

Characteristic		% with initial resistance test
Risk	MSM	49%
	IDU	37%
	MSM+IDU	45%
	Heterosexual	45%
	FPHC	39%
	Pediatric	70%
	Unknown	37%
Age	13-24	41%
	25-39	45%
	40-59	44%
	60+	44%

Prevalence of ≥ 1 TDR Mutation in Cases with Initial Resistance Tests, by Recency of Infection



Of 13,015 cases with initial resistance tests, 2,016 (15%) were classified as recent, 8,703 (67%) as long-standing and 2,296 (18%) as unknown recency.

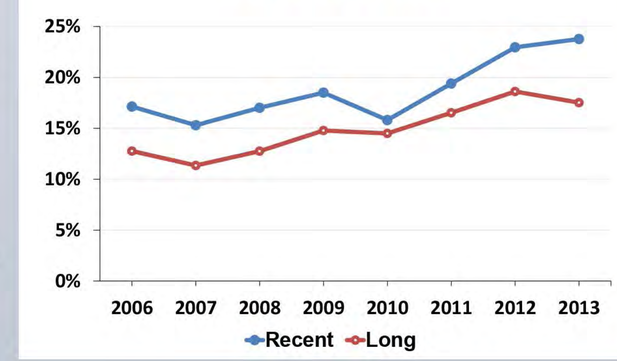
- Demographics and resistance results for the "unknown recency" group were similar to those for the combined recent and long-standing groups.

TDR prevalence was 1.29-fold higher among recently infected (19%) than among longstanding (15%).

TDR prevalence among all cases increased from 13.3% in 2006 to 18.7% in 2013.

- TDR prevalence among recently infected cases rose from 17% in 2006 to 24% in 2013. An increase was also seen in cases with long-standing infection (13% to 18%).
- Multivariate logistic regression showed that odds of having a TDR mutation were related to year of diagnosis and age at diagnosis (p<0.01 for both).

TDR Prevalence by Recency of Infection and Year of Diagnosis



Results 2 - Correlates of TDR in Recent versus Long-standing Infections

For cases with recency data, prevalence of TDR was higher among those with recent infection than those with long-standing infection across all subgroups of sex, age, race/ethnicity, transmission risk (except for injection drug use), and geographic location. Simple prevalence ratios were statistically significant for almost all subgroups.

	TDR Prevalence Rate: Recent Infection	TDR Prevalence Rate: Long-standing Infection	Prevalence Ratio Recent vs Long (95% CI)	
All	19.1%	14.8%	1.29	(1.16, 1.43)
Sex				
Male	18.5%	15.3%	1.21	(1.07, 1.36)
Female	21.4%	13.2%	1.62	(1.31, 2.01)
Race/Ethnicity				
White	15.4%	15.5%	0.99	(0.79, 1.24)
Black	21.0%	14.1%	1.48	(1.25, 1.76)
Hisp	20.6%	15.5%	1.33	(1.12, 1.58)
AsPac	16.9%	13.2%	1.29	(0.67, 2.48)
NatAm	0.0%	20.0%	n/a	n/a
Multirace	17.2%	13.5%	1.27	(0.76, 2.12)
Age at Diagnosis				
13-24	19.6%	18.4%	1.06	(0.87, 1.30)
25-39	19.9%	16.3%	1.22	(1.05, 1.42)
40-59	16.7%	13.0%	1.28	(1.03, 1.60)
60+	18.8%	9.5%	1.98	(0.92, 4.26)
Risk				
MSM	18.8%	16.5%	1.15	(1.0, 1.31)
MSM/IDU	23.4%	11.3%	2.06	(1.14, 3.75)
IDU	9.4%	13.8%	0.68	(0.22, 2.13)
Heterosexual	24.2%	14.5%	1.68	(1.31, 2.15)
FPHC	16.8%	12.1%	1.38	(0.5, 1.05)
Pediatric	0.0%	28.6%	n/a	n/a
No Identified Risk	15.7%	13.6%	1.16	(0.79, 1.69)
Residence at diagnosis				
New York City	19.8%	14.8%	1.34	(1.10, 1.50)
Rest of NYS	16.5%	14.8%	1.12	(0.89, 1.41)

Conclusion

Recency of infection is an important covariate of TDR prevalence among persons newly-diagnosed with HIV. Increasing TDR prevalence among recently infected cases suggests a growing proportion of transmissions from non-ARV-naïve persons with poorly controlled infections.

Lower TDR prevalence seen in long-standing cases in all years supports this, though back-mutation or overgrowth of resistant strains by wild-type virus over time could also contribute to that group's lower TDR rate.

Reference

1. Wheeler W, Ziebell R, Zabina H, et al. Prevalence of transmitted drug resistance associated mutations and HIV-1 subtypes in new HIV-1 diagnoses, U.S.-2006. *AIDS*. 2010; 24(8): 1203-1212.

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