Statewide Trends of Acquired HIV-1 Drug Resistance in Rhode Island over 2004-2021

CROI 2023
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BACKGROUND

- HIV-1 acquired drug resistance (ADR) may compromise sustainable antiretroviral therapy (ART) effectiveness and efforts toward ending the HIV epidemic.
- Comprehensive and longitudinal data on ADR, and its current extent and impact on ART options and newer medications are limited and can inform care.

METHODS

- We aggregated *all* available HIV-1 protease-reverse-transcriptase-integrase sequences from persons who have been on ART ≥90 days, and who are or have been in care in Rhode Island (RI). One sequence per person per year was used (last sequence when >1).
- Detailed ART histories were reviewed for all persons with available sequences.
- Statewide ADR extent and impact were evaluated using Stanford Database tools and trends were measured with Mann-Kendall statistic.
- Multivariable regression analyses were used to evaluate predictors of impactful resistance and treatment options.

In a unique statewide analysis of longitudinal ADR trends within a densely-sampled HIV epidemic over 2004-2021, we found **extensive but decreasing ADR among persons failing ART**.

Lower observed ADR to high-resistance-barrier medications is reassuring, however **~25% of persons who would benefit most from OPOD options for improved adherence are not eligible for them**.

Continued ADR monitoring is important to maintain ART success, particularly with rising use of INSTIs in all lines of therapy and 2-drug regimens.

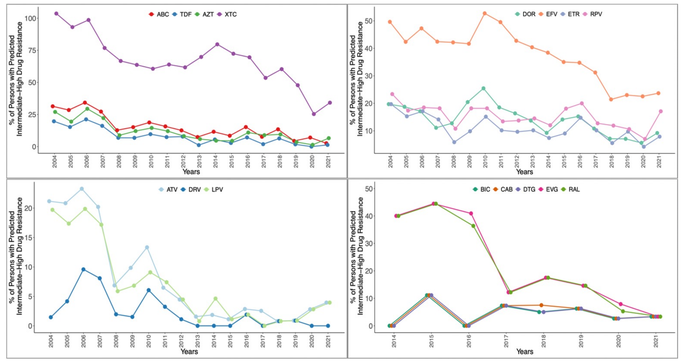

Figure 3: Acquired drug resistance from 2004 – 2021 by class (upper left: NRTI, upper right: NNRTI, lower left: PI, lower right, INSTI) and commonly-used drugs within each respective ART class



Figure 4: Longitudinal multiclass drug resistance trends in RI (Based on PRRT sequence data)

Table 1: Demographic and Clinical Information

Variables	Total (%, range)
Gender	
Female	310 (34%)
Male	564 (62%)
Transgender	<5 (<1%)
Unknown	37 (4%)
Age (years)	
< 18	55 (6%)
18-24	148 (16%)
25-34	361 (40%)
35-44	231 (25%)
> 45	118 (13%)
Unknown	1 (<1%)
Race	
White	507 (56%)
African American or Black	329 (36%)
Asians	10 (1%)
Other	13 (1%)
Unknown	55 (6%)
Ethnicity	
Hispanic	242 (27%)
Non-Hispanic	672 (74%)
Men who have sex with men (MSM)	
Yes	312 (34%)
No	602 (66%)
History of substance use	
Yes	412 (45%)
No	429 (47%)
Unknown	73 (8%)
History of mental illness	
Yes	319 (35%)
No	497 (54%)
Unknown	98 (11%)
History of treatment failure	
Yes	836 (92%)
No	38 (4%)
Unknown	40 (4%)
Number of ART regimens per person	4 (1-16)
Number of sequences per person	3 (1-34)
Mean years on ART	11
Most recent CD4 count (cells/mm³)	474 (0-1956)
HIV-1 subtype	
B	771 (84%)
Non-B	143 (16%)

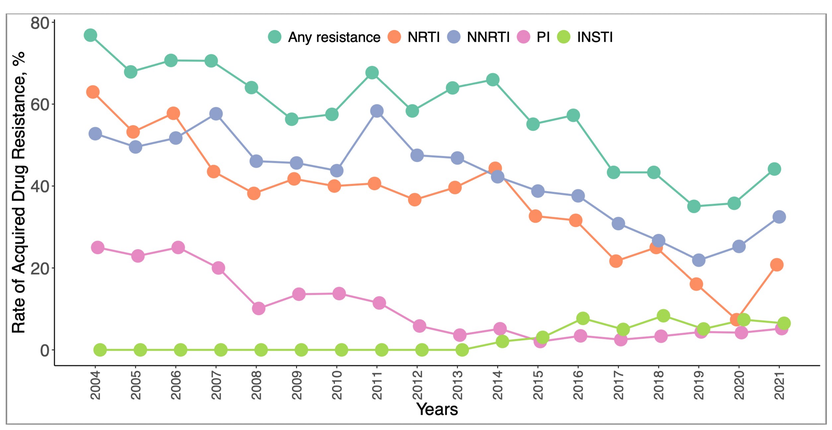

Figure 1. Longitudinal acquired drug resistance trends in RI (Each dot represents an annual value)

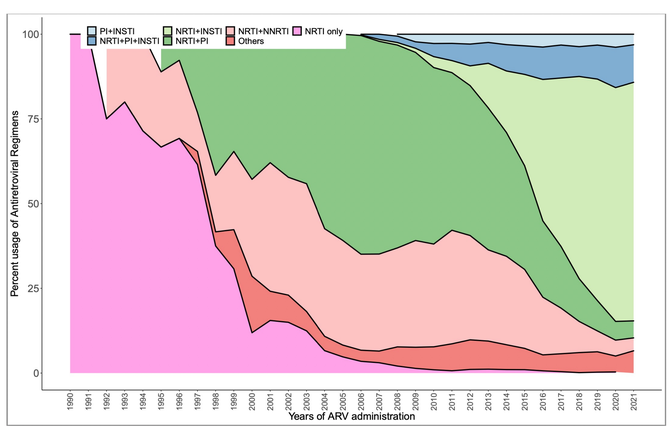

Figure 2. Antiretroviral classes over time in RI

Table 2: Correlates of Multiclass ADR and No OPOD Options (Estimates)

Variables	2-Class	3-Class	≥2-Class	No OPOD options 3-Drug	No OPOD options 2-Drug
HIV Subtype (non-B)	-0.84 *	-15.5	-1.12 *	-0.81 *	-0.89 *
Age	-0.001	-0.02	-0.01	-0.01 *	-0.003
Gender (Male)	0.57 *	-0.08	0.50 *	0.19	0.22
Gender (Transgender)	-12.64	-15.67	-12.97	-13.8	-0.34
MSM	-0.42 *	0.20	-0.34 *	-0.15	-0.27
Number of ART regimens (mean)	0.08 *	0.14 *	0.12 *	0.13 *	0.14 *
Years on ART	0.04 *	0.04	0.05 *	0.01	0.03 *

* P-value < 0.05

RESULTS

- A Total of 2,111 persons with HIV were cared for in RI in 2004-2021. Of those, 914 (43%) eligible ART experienced persons had available sequences in 2004-2021 (Table 1).
- Statewide ADR to any drug decreased from 77% in 2004 to 44% in 2021 (-0.59 Mann-Kendall statistic), with trends mostly driven by NRTI- (63% to 21%) and NNRTI- (53% to 32%), and less by PI- (25% to 5%) associated mutations during those years; and INSTI-associated mutations remaining stable around 5% from 2016 to 2021 (Figure 1);
- ADR trends corresponded to ART used in the examined years (Figure 2) and to drug specific predicted resistance trends (Figure 3).
- Multiclass (2, 3, ≥2) resistance decreased from 44%, 10%, 54% in 2004 to 15%, 3%, 19% in 2021, respectively (Figure 4). Only one person had 4-class resistance (in 2021).
- In 2021, 73% of persons had a three-drug one-pill-once-a-day (OPOD) option and 78% had a 2-drug OPOD option, with increasing availability over time for both.
- Persons who have been exposed to more ART regimens, those with longer time on ART and males were more likely to have ≥2 multiclass resistance. Persons exposed to more ART regimens and with longer time on ART were also less likely to have 3-drug and 2-drug OPOD options (Table 2).

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