Trends in HIV-1 Drug Resistance in the United States: 2019-2024

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Key Takeaways

- **Despite the widespread and increased use of INSTIs in the United States from 2019-2024, resistance to INSTIs among all tested samples was low and stable**
- **Prevalence of INSTI resistance was also similar to previous estimates (2014-2018)**
- **Resistance to NNRTIs and NRTIs declined between the 2 periods; frequency of NRTI resistance also had modest declines across the 2019-2024 period**
- **Multi-class resistance continued to decline and resistance to at least one ARV in ≥3 of the tested classes (MDR HIV) was rare**

Introduction

- Transmitted and acquired HIV-1 drug resistance mutations reduce the effectiveness of antiretrovirals and limit options for both HIV treatment and preexposure prophylaxis (PrEP)[1]
- Shifting patterns in antiretroviral (ARV) use can lead to changes in the frequency of specific drug resistance mutations and associated reduced susceptibility to ARV drug classes[2]
- The availability and use of novel ARV options with high levels of effectiveness and more convenient formulations, particularly within the integrase strand transfer inhibitor (INSTI) class, increased from 2019-2024
- This analysis utilized data from a large, representative commercial testing database to assess trends in ARV class resistance in this period (2019-2024)

Methods

- De-identified HIV-1 samples submitted for drug resistance testing with Monogram Bioscience's GenoSure PRIme® assay were analyzed
  - GenoSure PRIme tests for genotypic resistance to 4 classes of HIV drugs: nucleoside reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), and INSTIs
- Samples collected from adults (age ≥18 years) in the United States or US Territories between January 1, 2019 and December 31, 2024 were included in the analysis
  - All samples were collected and submitted as part of routine clinical care
  - Basic demographic information was reported with each submission (age, gender, region of clinic where collection occurred), but linkage to additional demographic or clinical data was not available
  - For individuals with multiple tested samples, a maximum of one sample per calendar year was included in the analysis (latest test used if more than one submitted within the year)
- Results were assessed using descriptive statistics and 2 denominators for proportions:
  - 1) all submitted samples
  - 2) samples demonstrating genotypic resistance to at least one ARV in one class of ARVs; to minimize bias introduced by changes to resistance testing behaviors and sample submission over time
- Resistance to a class of ARVs was defined as substantial decreased susceptibility to at least one ARV within the class; substantial decreased susceptibility was predicted by Monogram's proprietary HIV-1 genotypic algorithm which is based on >100,000 matched HIV-1 genotype-phenotype results
  - Multi-drug resistance HIV was defined as resistance to at least 3 of the 4 tested ARV classes
- Results from this analysis, reporting data from 2019-2024, were informally compared to a previously published analysis from the authors evaluating similar trends for the period 2012-2018 to evaluate trends over the 2 periods[3]

Results

- A total of 104,074 samples were included in the analysis, of which 32,761 (31.5%) demonstrated reduced susceptibility to at least one ARV

Figure 1. Prevalence of class resistance among samples with resistance, 2012-2018[3]

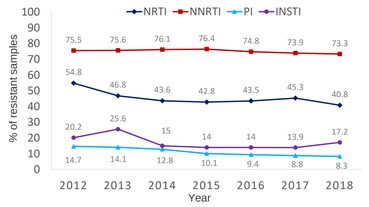


Figure 2. Prevalence of class resistance among samples with resistance, 2019-2024

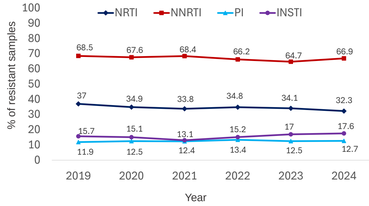
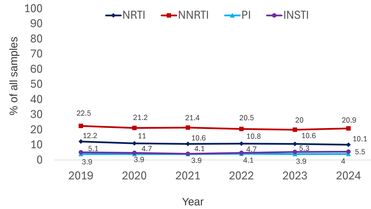


Figure 3. Prevalence of class resistance among all samples, 2019-2024



- Among all samples tested from 2019-2024 (Fig 3), class-level resistance was stable, with <2% change in prevalence across classes
- Among samples showing any resistance (Fig 2), NRTI prevalence decreased by nearly 5% while the change in other classes was smaller (<2%)
- Compared to the 2012-2018 analysis (Fig 1), resistance to NNRTIs (2012-2018: 75.5-73.3%; 2019-2024: 68.5-66.9%) and NRTIs (2012-2018: 54.8-40.8%; 2019-2024: 37.0-32.3%) declined between periods

Figure 4. Proportion of samples with 1-, 2-, 3-, and 4-class resistance among samples with resistance, 2012-2018[3]

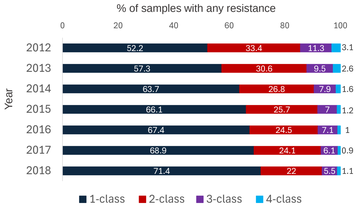
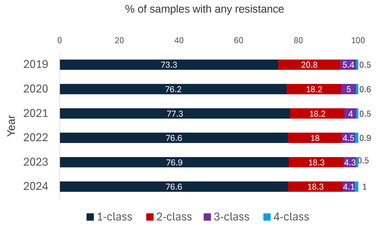


Figure 5. Proportion of samples with 1-, 2-, 3-, and 4-class resistance among samples with resistance, 2019-2024[1]



- In 2012-2018, among samples with resistance, a growing proportion had resistance to a single class (Fig 4); this had stabilized in the 2019-2024 period (Fig 5) with single class resistance accounting for ~77% of resistant samples, primarily driven by NNRTI mutations (Table 1)
- Resistance to 3 or 4 classes of ARV was also stable (Fig 4) and occurred in <1% of all samples (Table 1)

Table 1. Class resistance among samples with 1-, 2-, 3-, and 4-class resistance (2019-2024)

	n samples	% all samples (n=104,074)	% samples with resistance (n=32,761)
1-class resistance			
INSTI only	1770	1.7	5.4
NNRTI only	16128	15.5	49.2
NRTI only	4969	4.8	15.2
PI only	2039	2.0	6.2
2-class resistance			
INSTI + NRTI	1406	1.4	4.3
INSTI + NNRTI	723	0.7	2.2
INSTI + PI	66	0.1	0.2
NRTI + NNRTI	2884	2.8	8.8
NRTI + PI	410	0.4	1.3
NNRTI + PI	650	0.6	2.0
3-class resistance			
INSTI + NRTI + NNRTI	780	0.8	2.4
INSTI + NRTI + PI	92	0.1	0.3
INSTI + NNRTI + PI	47	0.1	0.1
NRTI + NNRTI + PI	582	0.6	1.8
4-class resistance			
INSTI + NRTI + NNRTI + PI	215	0.2	0.7

Figure 6. Prevalence of class resistance by demographic characteristics (age, gender, region), 2019-2024

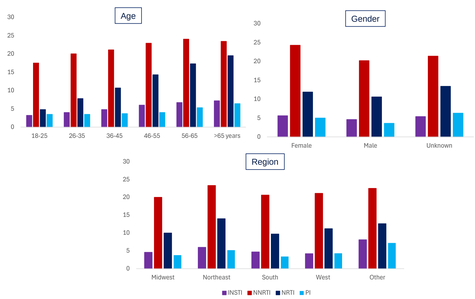
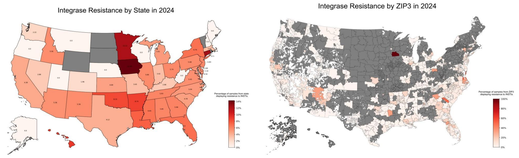


Figure 7. Geographic distribution within the United States of class-level integrase inhibitor resistance (2024) reported at the state and 3-digit zip code levels



- Generally, prevalence of resistance increased with increasing age, although this was most notable for NNRTI and NRTI resistance (Fig 6)
- Regionally, class-level resistance was slightly higher in the Northeast United States (Fig 6), although differences within smaller geographic areas were identified for INSTIs (Fig 7)
- A key limitation of the dataset is the lack of linked clinical data, which means it is not possible to distinguish transmitted and acquired resistance

Conclusions

- The observed trends align with the introduction (2012-2018) and increasing use (2019-2024) of second-generation INSTIs, which have higher resistance barriers, improved adherence, and high clinical effectiveness
- Extensive resistance across multiple ARV classes remained uncommon across the analysis period, and samples with detected resistance most commonly showed reduced susceptibility only to NNRTIs

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References: 1. Poon et al. *PLoS One*. 2011;6:e21189. **2.** Paquet et al. *Antivir Ther*. 2014; DOI: 10.3851/IMP2748. **3.** Henegar et al. CROI 2020; Boston, MA. Poster #0521.

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