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# Prevalence and Trends in Transmitted and Acquired Antiretroviral Drug Resistance Washington, DC, 1999-2014


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THE DC COHORT
Advancing HIV Care and Treatment in the District of Columbia

## BACKGROUND

Antiretroviral Drug Resistance

- **Antiretroviral drugs (ARVs)** target HIV genes to prevent viral replication.
- Mutations in the HIV genome can result in drug resistance, leading to fewer treatment options and therefore to poorer health outcomes.
- **Acquired drug resistance (ADR)** results when resistant mutations are selected by drug pressure.
- **Transmitted drug resistance (TDR)** results when a resistant viral strain is transmitted from one person to another.
- Monitoring of resistance can inform treatment and prevention strategies and assess the impact of interventions, guidelines and new ARV regimens.

HIV and ARV Drug Resistance in Washington, DC

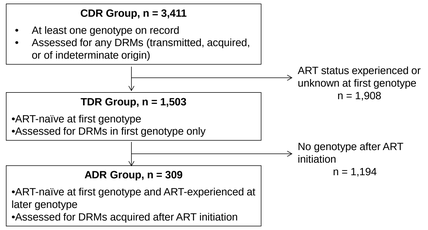
- Washington, DC has a high prevalence of HIV: 2.5%.
- Previous studies have found TDR prevalence up to 17% for Washington, DC[1] compared to 27% for other US locations.[2]
- Few studies have measured prevalence of ADR or of overall **cumulative drug resistance (CDR)**.

## OBJECTIVES

- Estimate the prevalence of TDR, ADR, and CDR in HIV-infected persons in Washington, DC.
- Describe time trends in resistance, by drug class.
- Examine associations between patient characteristics and drug resistance.

## METHODS

- Retrospectively analyzed data from THE DC COHORT:
  - A longitudinal, observational study of HIV-infected persons in care at 13 outpatient clinics in Washington, DC.
  - Enrolled 2011-2014, not perinatally infected.
- Measured prevalence of **drug-resistant mutations (DRMs)** in patient genotype tests from 1999-2014 including:
  - WHO Surveillance Drug Resistance Mutations[3] ; and
  - 2014 **International Antiviral Society-USA (IAS)** HIV-1 drug mutations.[4]
- Interpreted resistance to individual ARVs and to drug classes based on:
  - IAS guidelines; and
  - Stanford HIVDB genotypic resistance interpretation algorithm.[5]
- Assessed resistance by drug class for each year, 2004-2013.
- Conducted bi- and multivariable logistic regression analysis to identify factors associated with development of resistance to any ARV.




## RESULTS

**Table 1. Demographics of Participants Analyzed for CDR**

| Characteristic | n (%) |
|---|---|
| Total | 3,411 (100) |
| Age at consent | |
| 0-29 | 493 (14.45) |
| 30-39 | 619 (18.15) |
| 40-49 | 986 (28.91) |
| 50-59 | 952 (27.91) |
| 60+ | 361 (10.58) |
| Sex | |
| Female | 890 (26.09) |
| Male | 2521 (73.91) |
| Race/ethnicity | |
| Non-Hispanic black | 2748 (80.56) |
| Non-Hispanic white | 376 (11.02) |
| Hispanic | 141 (4.13) |
| Transmission risk group | |
| MSM | 1376 (40.34) |
| Heterosexual contact | 1086 (31.84) |
| IDU | 252 (7.39) |
| Insurance | |
| Public | 2297 (67.34) |
| Private | 835 (24.48) |
| Clinic type | |
| Hospital | 1762 (51.66) |
| Community-based | 1649 (48.34) |
| Clinical status | |
| HIV | 1791 (52.51) |
| AIDS | 1620 (47.49) |
| Median years HIV diagnosis to consent | 7.8 |
| Median Years ARV start to consent | 3.2 |

**Figure 1. Prevalence of Resistance by Drug Class**

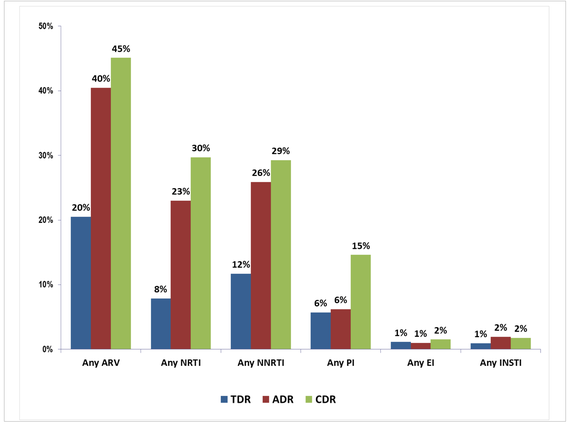



**Figure 2. Time Trends in Resistance by Drug Class**

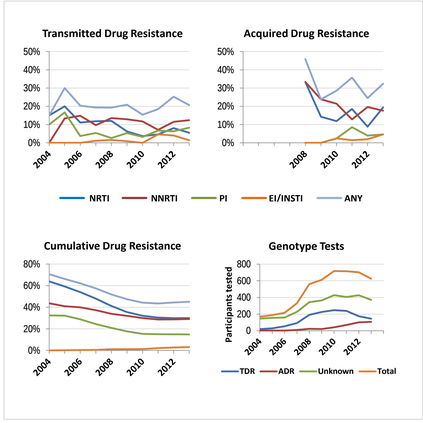
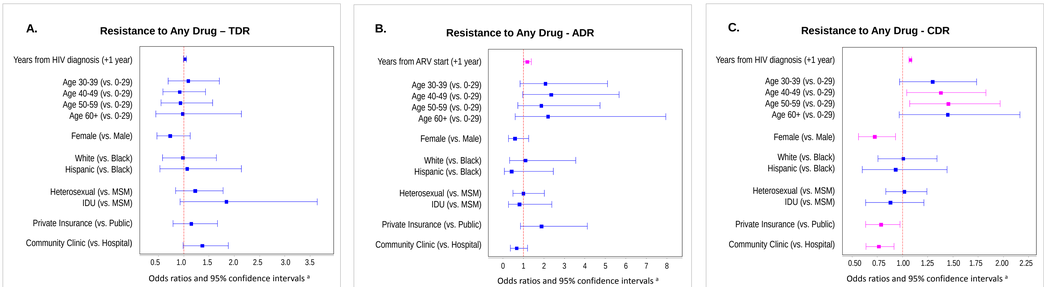



**Table 2. Prevalent Mutations and Resistance to ARVs**

| | ARV Class | TDR % | ADR % | CDR % |
|---|---|---|---|---|
| Mutation | | | | |
| K103N | NNRTI | 7.1 | 18.8 | 20.2 |
| M41L | NRTI | 3.0 | 1.0 | 7.3 |
| M184V | NRTI | 2.8 | 17.8 | 22.9 |
| K70R | NRTI | 1.7 | 1.0 | 5.9 |
| L90M | PI | 1.5 | 0.0 | 5.5 |
| D67N | NRTI | 1.3 | 0.6 | 5.4 |
| M184I | NRTI | 0.1 | 3.9 | 1.8 |
| P225H | NNRTI | 0.7 | 3.2 | 3.7 |
| K101E | NNRTI | 0.7 | 2.9 | 2.1 |
| N88S | PI | 1.3 | 2.6 | 2.6 |
| ARV | | | | |
| Nevirapine | NNRTI | 10.2 | 23.9 | 27.1 |
| Efavirenz | NNRTI | 10.0 | 24.6 | 27.2 |
| Stavudine | NRTI | 5.9 | 7.4 | 17.1 |
| Zidovudine | NRTI | 5.5 | 5.5 | 15.4 |
| Abacavir | NRTI | 3.5 | 19.1 | 24.2 |
| Emtricitabine | NRTI | 3.1 | 20.4 | 24.3 |
| Lamivudine | NRTI | 3.1 | 20.4 | 24.3 |
| Rilpivirine | NNRTI | 2.8 | 7.8 | 9.7 |
| Nelfinavir | PI | 1.9 | 0.0 | 7.2 |
| Atazanavir | PI | 1.8 | 3.2 | 5.3 |

**Figure 3 A-C. Associations between Participant Characteristics and Development of Resistance by Type of Resistance**




[a] Adjusted for days from HIV diagnosis to first genotype (TDR), days from HIV diagnosis to most recent genotype (CDR), days from ARV start to most recent genotype (ADR), age at test, race/ethnicity, HIV risk group, insurance type, and clinic type.

## DISCUSSION

Prevalence of Resistance

- Prevalence of resistance to any drug was TDR: 20%, ADR: 40%, CDR: 45%.
- TDR prevalence was stable overall, but resistance to NRTIs decreased while resistance to PIs, EIs, and INSTIs increased.
- ADR and CDR rates probably overestimate resistance among all HIV-infected due to surveillance bias, (genotype tests prescribed when treatment fails).
- Decrease in CDR reflects increased rate of testing among newly diagnosed individuals following 2007 Department of Health and Human Services revised treatment guidelines.[7]

Predictors of Resistance

- Associations between patient characteristics and resistance were similar for ADR and CDR, but predictors of TDR did not predict ADR and CDR.
- Women had significantly lower odds of CDR than men (and non-significantly lower odds of TDR and ADR).
- Infection through IDU was associated with TDR (borderline significance) but not ADR or CDR, suggesting that in this study population, adherence may have been comparable between IDU and non-IDU.
- Private insurance was associated with lower CDR but higher ADR. One contributing factor may have been changes in private insurance coverage over time.

## CONCLUSIONS

- In this cohort, almost half of participants tested had evidence of resistance to at least one drug, and resistance to newer drug classes appeared to be increasing.
- As new treatment guidelines result in earlier and longer exposure to ARVs, innovations to promote adherence, such as co-formulations and longer-acting regimens, will be more critical than ever.
- Continued surveillance of acquired and transmitted resistance will be essential to evaluating the effect of these changes over time.

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