HIV-1 Antiretroviral (ARV) Drug Resistance and Health Outcomes in Florida, 2015–2017

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Objectives

To understand the current state of HIV ARV drug resistance across Florida so treatment regimens can be adjusted and optimized prior to, and following treatment failures, and reduce the incidence and transmission HIV in Florida’s population.

Objectives of the study include;

▪ Recognize geographic and temporal patterns and emergence of HIV ARV drug resistance across the state

▪ Understand the burden of transmitted resistance (newly infected acute cases) versus acquired resistance (those on long term ARVs without prior resistance)

▪ Measure whether current ARV practices and genotypic testing timeframes are successful across the state by assessing viral load suppression following ARV initiation and monitoring for virologic failure
HIV In Florida
HIV Diagnoses by Year of Diagnosis, 2008–2017, Florida
Percentage of Adult (Age 13+) HIV and AIDS Diagnoses and Population\(^1\), by Race/Ethnicity, 2017, Florida

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Population</th>
<th>AIDS</th>
<th>HIV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black</td>
<td>15%</td>
<td>26%</td>
<td>50%</td>
</tr>
<tr>
<td>White</td>
<td>24%</td>
<td>24%</td>
<td>57%</td>
</tr>
<tr>
<td>Hispanic</td>
<td>24%</td>
<td>24%</td>
<td>31%</td>
</tr>
<tr>
<td>Other</td>
<td>4%</td>
<td>3%</td>
<td>2%</td>
</tr>
</tbody>
</table>

HIV
N=4,933

Flaoda Adult Population Estimates
N=17,600,236

AIDS
N=2,039

\(^1\)Source: Population data are provided by Florida CHARTS
Other includes American Indian/Alaska Native, Asian/Pacific Islander, and multi-racial.
Persons Living with HIV (PLWH) in Florida along the HIV Care Continuum in 2017

- **PLWH**: 116,944 (100%)
- **Ever in Care**: 108,461 (93%)
- **In Care**: 87,184 (75%)
- **Retained in Care**: 79,831 (68%)
- **Suppressed Viral Load**: 71,955 (62%)
Florida’s Plan to Eliminate HIV Transmission and Reduce HIV-related Deaths

- Implement routine HIV and Sexually Transmitted Infections (STIs) screening in health care settings and priority testing in non-health care settings

- Provide rapid access to treatment and ensure retention in care (Test and Treat)

- Improve and promote access to antiretroviral pre-exposure prophylaxis (PrEP) and non-occupational post-exposure prophylaxis (nPEP)

- Increase HIV awareness and community response through outreach, engagement, and messaging
HIV-1 Antiretroviral Therapies
HIV Antiretroviral Therapy Timeline

- AIDS Epidemic officially begins, with cases in New York, California and Florida
- 1981
- HIV develops resistance to AZT
- 1987
- AZT a nucleoside reverse transcriptase inhibitor (NRTI) approved by FDA
- Congress approved $30 million in emergency drug assistance funding
- 1989
- First Protease Inhibitor approved
- 1995
- Highly Active Antiretroviral Treatment (HAART) triple combination therapy shown to be effective
- 1996
- Protease Inhibitor drug resistance becomes a concern
- 1997
- ARV resistance testing becomes a standard part of HIV care
- 2000
- First Integrase Inhibitor approved by FDA
- 2007
# HIV-1 ARV Drug Classes

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nucleoside Reverse Transcriptase Inhibitor (NRTI)</strong></td>
<td>Prevent HIV reverse transcription of HIV RNA to viral DNA</td>
</tr>
<tr>
<td><strong>Non-nucleoside Reverse Transcriptase Inhibitor (NNRTI)</strong></td>
<td>Prevent HIV reverse transcription of HIV RNA to viral DNA</td>
</tr>
<tr>
<td><strong>Protease Inhibitor (PI)</strong></td>
<td>Prevent maturation of HIV proteins by protease enzyme</td>
</tr>
<tr>
<td><strong>Integrase Inhibitor (IN)</strong></td>
<td>Prevent and block the integration of viral DNA into the genome of host cells with CD4 receptors</td>
</tr>
</tbody>
</table>

![Diagram of HIV-1](image)

**HIV-1**
HIV-1 Antiretroviral Resistance

Key
- HIV Genetic Sequence
- Antiretroviral drug
- Gene Mutation

Wild type HIV
- Antiretroviral drug blocks virus replication and leads to viral suppression

Mutated HIV
- Drug resistance occurs following mutation and viral replication continues
- Viral replication can lead to more mutations which can lead to multiple drug resistance
# ARV Treatment Guidelines

<table>
<thead>
<tr>
<th>Test</th>
<th>Drug Resistance Testing (Genotype, Phenotype)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rationale</strong></td>
<td>• To assess whether the patient’s HIV virus is likely to be resistant to specific ARV medications</td>
</tr>
<tr>
<td><strong>Result</strong></td>
<td>• <strong>Genotype:</strong> detects specific mutations to ARV medications</td>
</tr>
<tr>
<td><strong>Frequency and Comments</strong></td>
<td>• Genotype is recommended for all ARV-naïve patients, as early as possible in the course of HIV infection</td>
</tr>
<tr>
<td></td>
<td>• Acute or primary infection</td>
</tr>
<tr>
<td></td>
<td>• Chronic infection and treatment naïve: recommended before initiation of ART</td>
</tr>
<tr>
<td></td>
<td>• Pregnancy: recommended before initiation of ART (repeat if done earlier) or for patients with detectable HIV viral load while taking ART</td>
</tr>
<tr>
<td></td>
<td>• In case of virologic failure</td>
</tr>
<tr>
<td></td>
<td>• Obtain genotype for integrase mutations if integrase inhibitor resistance is a concern</td>
</tr>
</tbody>
</table>

Health Resource and Service Administration (HRSA), 2014
HIV-1 Resistance Data Collection and Analysis
HIV Surveillance Reporting Authority

- Chapter 384.25, Florida Statutes (F.S.) (Sexually Transmissible Diseases)
- Chapter 381.0032, F.S. (Public Health: General Provisions)
- 64D–3.030 Reporting Requirements for Physicians
- 64D–3.031 Reporting Requirements for Laboratories
At least (≥) 60% of newly diagnosed persons should have an initial HIV nucleotide sequence within 3 calendar months following HIV diagnosis.

PLWH may not have sequence data available because:

- They did not enter HIV care
- They entered HIV care but had no drug resistance testing
- They entered care and had drug resistance testing but no sequences were provided for surveillance
Analyzing HIV ARV Resistance

HIV-1 nucleotide genotype sequences in the pol region reported to the Florida Department of Health HIV/AIDS Surveillance System were analyzed for persons whose HIV was diagnosed in Florida with a sequence obtained within 3 months of diagnosis in 2015 (n=2,194), 2016 (n=2,063), and 2017 (n=2,080).

Persons who reported taking ARV drugs before the date of the genotype or with a suppressed viral load within 14 days of the date of the genotype were excluded from the analysis.

ARV drug resistance was determined using the Stanford HIV Drug Resistance Database.

https://hivdb.stanford.edu
High Level HIV ARV Resistance in Florida

Variant, Atypical and Resistance HIV Surveillance

Molecular HIV Surveillance

# Resistant Genotypes

Year


Any Resistance  PI  NRTI  NNRTI  INSTI  Multi-Drug

Data as of 6.30.18
HIV Resistance in Florida Among Persons with HIV Diagnosed in 2015–2017

Data as of 6.30.18

Data as of 6.30.18

*significant at <.0001

**NNRTIs**
- High level resistance
  - EFV = efavirenz
  - NVP = nevirapine

**INSTI**
- Resistance at any level
  - RAL = raltegravir
  - EVG = elvitegravir

Data as of 6.30.18

*significant at <.0001
Continuum of HIV Care by HIV Genotype Status in Florida (2015–2017)

<table>
<thead>
<tr>
<th>Year</th>
<th>No Genotype</th>
<th>Genotype</th>
<th>No Genotype</th>
<th>Genotype</th>
<th>No Genotype</th>
<th>Genotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>2015</td>
<td>Retained in Care</td>
<td>Suppressed VL</td>
<td>Retained in Care with Suppressed VL</td>
<td>Retained in Care</td>
<td>Suppressed VL</td>
<td>Retained in Care with Suppressed VL</td>
</tr>
<tr>
<td>2015</td>
<td>74.6%</td>
<td>63.2%</td>
<td>86.9%</td>
<td>69.4%</td>
<td>75.7%</td>
<td>66.4%</td>
</tr>
<tr>
<td>2016</td>
<td>75.4%</td>
<td>70.8%</td>
<td>86.5%</td>
<td>71%</td>
<td>75.4%</td>
<td>70.8%</td>
</tr>
<tr>
<td>2017</td>
<td>88.7%</td>
<td>84.8%</td>
<td>88.7%</td>
<td>84.8%</td>
<td>88.7%</td>
<td>84.8%</td>
</tr>
</tbody>
</table>

*significant at <.0001
Summary

- HIV-1 resistance is dynamic in nature changing from year to year
- NNRTIs remain the drug class with the highest prevalence in Florida
- Resistance to INSTI is slowly increasing
- Persons without a genotype are less likely to be virally suppressed and retained in care
**ARV Resistance Testing and Reporting**

<table>
<thead>
<tr>
<th>Barriers</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ Missing Labs through Electronic Laboratory Reporting</td>
<td>▪ Priority testing in areas with high incidence and prevalence of TDR</td>
</tr>
<tr>
<td>▪ Labs that report through paper reporting do not provide a full sequence</td>
<td>▪ Single stage HIV testing for new positives</td>
</tr>
<tr>
<td>▪ Provider compliance to order initial genotype at diagnosis not at 100%</td>
<td>▪ Provider and patient education</td>
</tr>
<tr>
<td>▪ Medication adherence issues</td>
<td>▪ Adherence to HRSA performance measures for initial genotyping of newly diagnosed</td>
</tr>
</tbody>
</table>
For more information


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