THE IMPACT OF PREP ON DRUG RESISTANCE AND ACUTE HIV INFECTION, NEW YORK CITY 2015-2017

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PREP USE INCREASING IN NEW YORK CITY

- Sexual Health Survey: self-reported PrEP use in NYC MSM increased from 2% in 2013 to 28% in 2016
- HIV Partner Services data: self-reported PrEP use in sex and needle sharing partners of HIV positive persons rose from 11% in 2016 to 21% in 2018

Salcuni, PM et al. 2017; Myers JE et al. 2018; 3. Misra K et al. 2017
PREP SCREENING AND FOLLOW UP

- Concerns about prescribing PrEP to persons with undiagnosed HIV infection leading to induction of resistance
- Factors: inadequate screening/persons screened in window period between HIV exposure and infection
- Reflex NAAT after negative Ab screen can reduce PrEP initiation in undiagnosed phase of HIV infection
- NY State: NAAT for persons with AHI symptoms or with negative Ab test who report condomless sex in past 4 weeks
- PrEP follow up every 3 m facilitates diagnosis in early or acute phase of HIV and timely transition from PrEP to a 3 drug treatment regimen

https://www.hivguidelines.org/prep-for-prevention/
Increased PrEP uptake raises concerns about ARV resistance and virological failure

Most data on PrEP associated resistance come from efficacy trials

Resistance occurs predominantly in individuals who initiated PrEP during undiagnosed HIV infection and rarely from PrEP failure

Emtricitabine (FTC) resistance from M184I/V mutation more commonly reported than tenofovir disoproxil fumarate (TDF) selected K65R mutation

Mathematical models:
- Contribution of PrEP to overall burden of resistance is small (<5%) relative to ART (50-63%) or transmission of resistance (40-50%)
- Levels of resistance from PrEP lower than they would be if HIV infections were not averted with PrEP

Studies using surveillance data on PrEP and resistance not available

OBJECTIVES

- Use routinely collected HIV partner services and surveillance data to determine prevalence of resistance to PrEP drugs in persons with history of pre-diagnosis PrEP use
- Compare a) ARV resistance to PrEP drugs and b) AHI, in PrEP users and never-users
- Determine frequency and timing of pre-PrEP start negative NAAT in PrEP users
METHODS
## DATA SOURCES

<table>
<thead>
<tr>
<th>Variable</th>
<th>Data Source</th>
<th>Method of Collection</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PrEP Use</strong></td>
<td>HIV Partner Services (PS)</td>
<td>• Patient self-report in PS interview</td>
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<tr>
<td></td>
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<td>• Medical chart review</td>
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<td></td>
<td>Medical Provider Report Form</td>
<td>• Provider reported to health department</td>
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<td></td>
<td>NYC Surveillance Field Investigation</td>
<td>• Medical chart review for all new HIV diagnoses</td>
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<tr>
<td>Resistance HIV NAAT AHI</td>
<td>NYC Surveillance Registry and Laboratory Database</td>
<td>• HIV related laboratory results reported to health department</td>
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<td>• Stanford Algorithm: HIV mutations and drug resistance</td>
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STATISTICAL ANALYSIS

- Prevalence of pre-diagnosis PrEP use in persons diagnosed with HIV in past 12 months and assigned for partner services
- Descriptive statistics:
  - Duration of PrEP use and time between PrEP start and HIV diagnosis
  - Characteristics of pre-diagnosis PrEP users and never-users
- Prevalence of M184I/V and K65R mutations associated with FTC and TDF resistance, respectively
- Bivariate analyses comparing prevalence of M184I/V mutation at first genotype and AH1 in pre-diagnosis PrEP users and never users (chi-square/Fisher’s exact test of significance)
RESULTS
PREP USE PREVALENCE IN PERSONS DIAGNOSED WITH HIV IN PAST 12 M AND ASSIGNED FOR PARTNER SERVICES, NYC 2015-2017 (N= 3,685)

Report of any PrEP use prior to HIV diagnosis

- Pre-diagnosis PrEP users (n=91)
- Never-users (n=3,594)

Median duration of PrEP exposure before HIV dx = 106 days (IQR=214)

Median duration between PrEP start and HIV dx = 250 days (IQR=395)
## Characteristics of PrEP Users and Never Users

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Age-Group</th>
<th>Gender</th>
<th>Transmission Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black</td>
<td>&lt;30 years</td>
<td>Cis-women</td>
<td>Transgender-MTF</td>
</tr>
<tr>
<td>Hispanic</td>
<td>30+ years</td>
<td>Cis-men</td>
<td>Heterosexual</td>
</tr>
<tr>
<td>White</td>
<td></td>
<td></td>
<td>IDU</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td>MSM</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td>Transgender-Sexual Contact</td>
</tr>
</tbody>
</table>

- **Race/ethnicity:** Black (46%), Hispanic (32%), White (27%), Other (9%)
- **Age-group:** <30 years (58%), 30+ years (42%)
- **Gender:** Cis-women (63%), Cis-men (92%)
- **Transmission Risk:** Pre-diagnosis PrEP users, Never users

- **Pre-diagnosis PrEP users:**
  - Race: Black (23%), Hispanic (27%), White (32%), Other (9%)
  - Age: <30 years (37%), 30+ years (42%)
  - Gender: Cis-women (21%), Cis-men (76%)
  - Sexual Contact: Transgender-MTF (5%), Heterosexual (3%), IDU (3%), MSM (28%), Transgender-Sexual Contact (6%)

- **Never users:**
  - Race: Black (23%), Hispanic (27%), White (32%), Other (9%)
  - Age: <30 years (37%), 30+ years (42%)
  - Gender: Cis-women (21%), Cis-men (76%)
  - Sexual Contact: Transgender-MTF (5%), Heterosexual (3%), IDU (3%), MSM (28%), Transgender-Sexual Contact (6%)
K65R mutation associated with TDF resistance was found in 4 persons: none were PrEP users
ACUTE HIV INFECTION IN PREP USERS VS NEVER USERS

<table>
<thead>
<tr>
<th>Category</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-diagnosis PrEP users</td>
<td>33%</td>
</tr>
<tr>
<td>Never-users</td>
<td>9%</td>
</tr>
</tbody>
</table>

AHI
- All
- Pre-diagnosis PrEP users
- Never-users
NEGATIVE NAAT PRIOR TO PREP START

Negative NAAT prevalence and timing relative to PrEP initiation (n=91)

- 5% had a negative NAAT in the 0-2 days window before PrEP start – possible indication of PrEP screening.
- 18% had a negative NAAT in the 15-24 days window before PrEP start.
- 2% had a negative NAAT in the >30 days window before PrEP start.
- 75% had no negative NAAT before PrEP start.

Only 5% of the 91 PrEP users had a negative NAAT in the 0-2 days window before PrEP start – possible indication of PrEP screening.
LIMITATIONS AND STRENGTHS

LIMITATIONS

- Never-users may be misclassified due to incomplete medical chart or interview data
- Genotypes available for only 63% of this population, limiting the measurement of resistance
- Data not sufficient to differentiate between transmitted and acquired drug resistance or to address cause of resistance

STRENGTHS

- Used HIV surveillance data to measure resistance associated with PrEP-use history
- Large sample
- Multiple data sources used to define pre-diagnosis PrEP users
SIGNIFICANT FINDINGS

- Prevalence of resistance mutations to FTC greater in PrEP users than never users (29% versus 2%)
- Signature TDF mutation (K65R) not detected among pre-diagnosis PrEP users
- Higher proportion of PrEP users diagnosed during AHI than never-users (33% versus 9%)
- Proportion of genotyping higher in PrEP users (75% versus 63%)
- No available genotype for 25% of PrEP users
- Infrequent NAAT as part of PrEP screening (5%)
IMPLICATIONS

- Rigorous screening that includes NAAT is critical and can reduce PrEP initiation during undetected HIV infection
- Routine genotype testing at diagnosis is important for persons with recent PrEP history
- PrEP users are more likely to receive regular healthcare and HIV testing, increasing chances of early diagnosis and transition to treatment
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