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

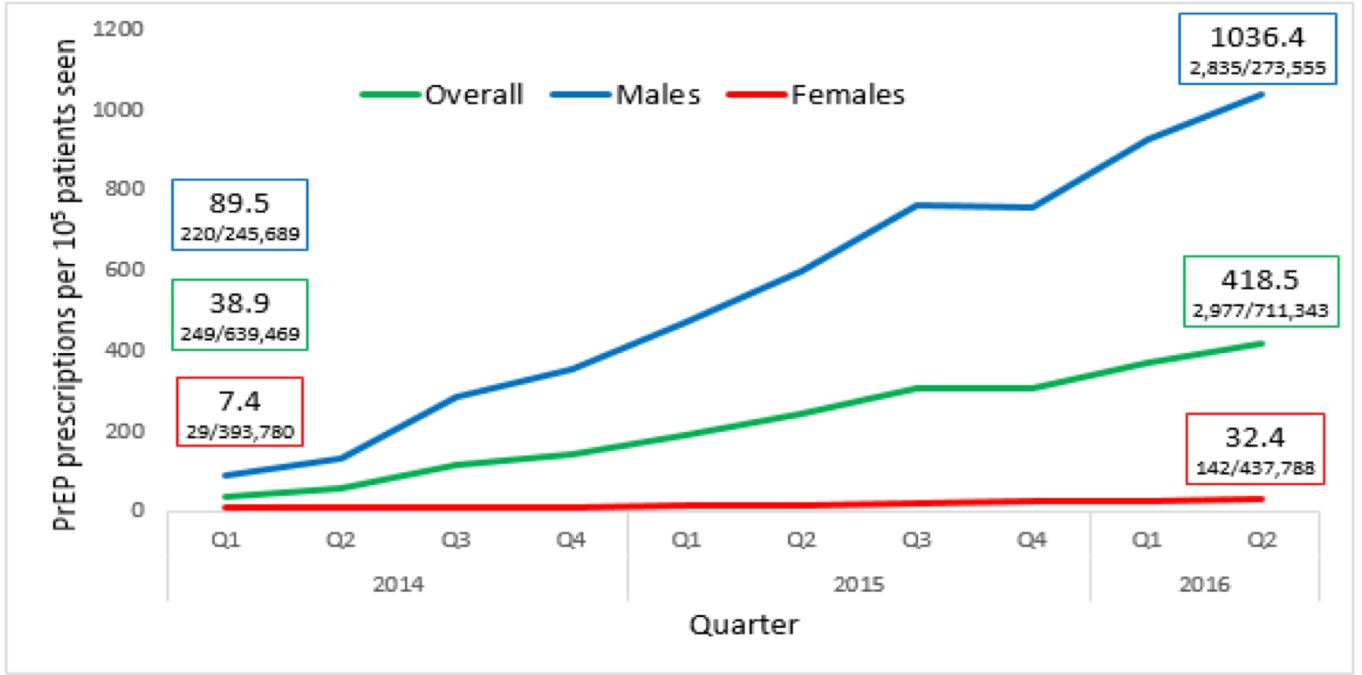
KAVITA MISRA, JAMIE HUANG, DEMETRE DASKALAKIS, CHI-CHI UDEAGU

New York City Department of Health and Mental Hygiene

BACKGROUND

PREP USE INCREASING IN NEW YORK CITY

Figure 1. PrEP prescription rates in 602 ambulatory care practices, overall and by sex, New York City, Q1 2014 – Q2 2016.



- **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/

PREP AND ARV RESISTANCE

- 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 **tenofivir 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 <u>if HIV infections were not averted with PrEP</u>
- Studies using surveillance data on PrEP and resistance not available

Liegler et al. 2014; Grant et al. 2010; Thigpen et al 2012; Van Damme 2012; Marazzo et al. 2015; Parikh et al. 2017; Huang et al. 2018; Supervie et al 2018; van de Vijver et al 2013; Fonner et al 2016

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

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

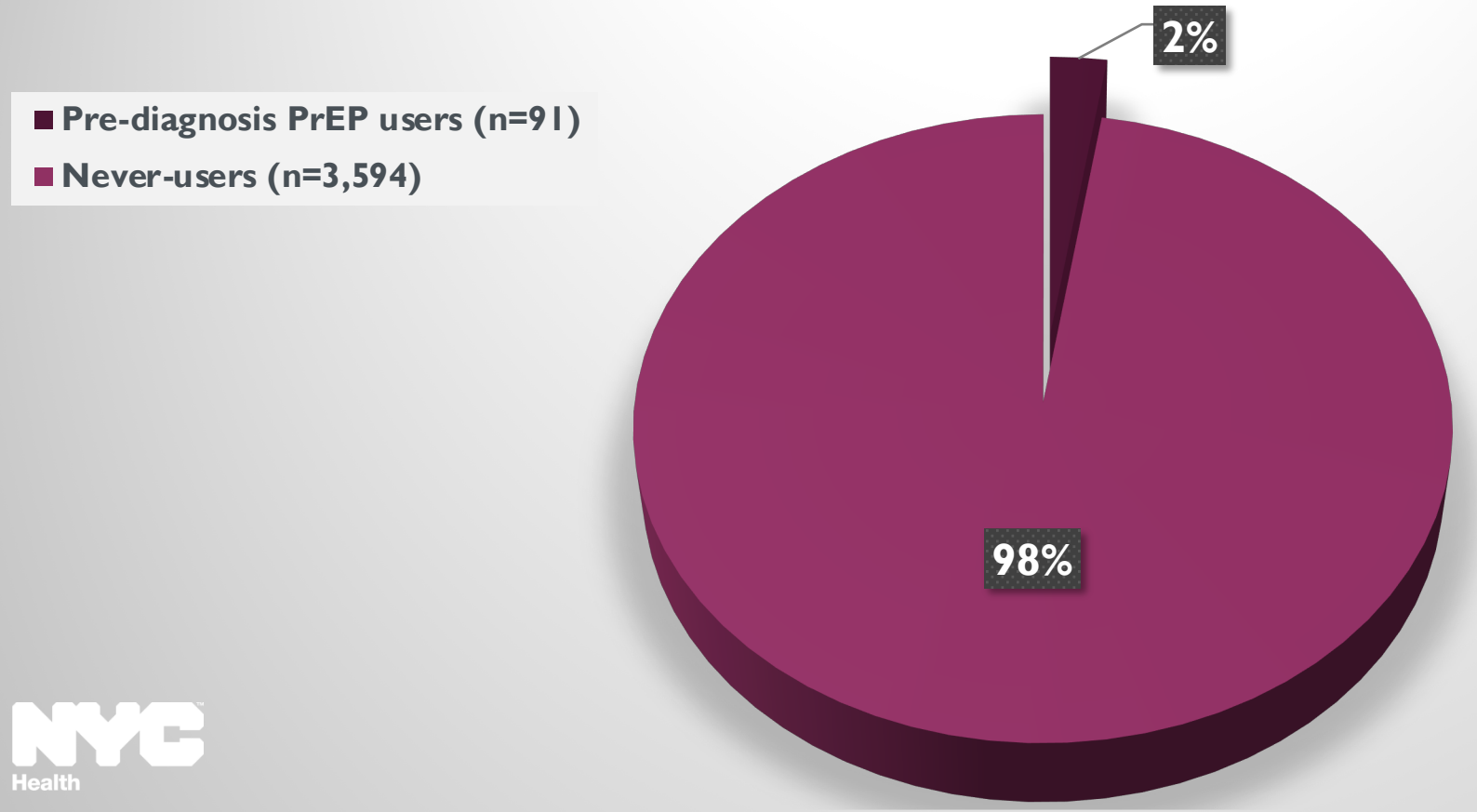
STATISTICAL ANALYSIS

- 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 AHI 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

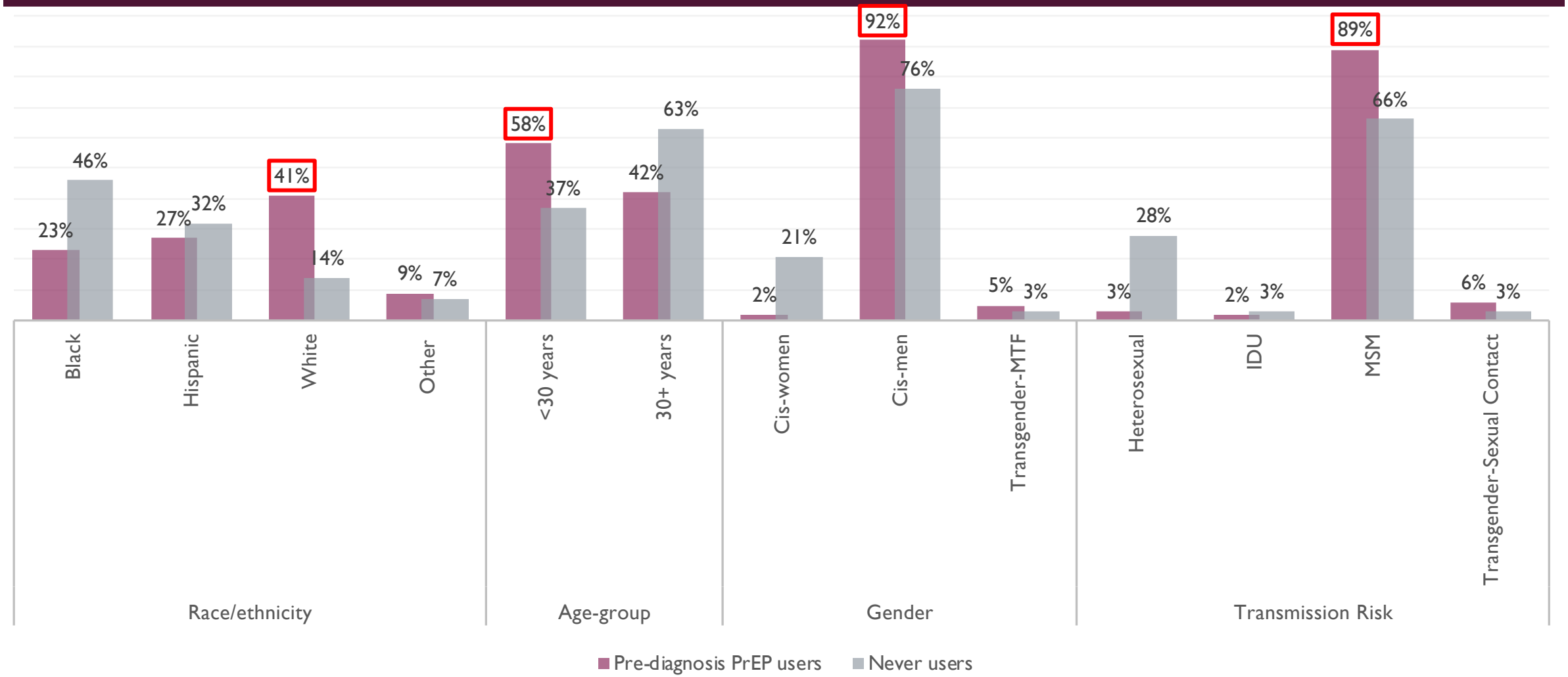


Median duration of PrEP exposure before HIV dx= 106 days (IQR=214)

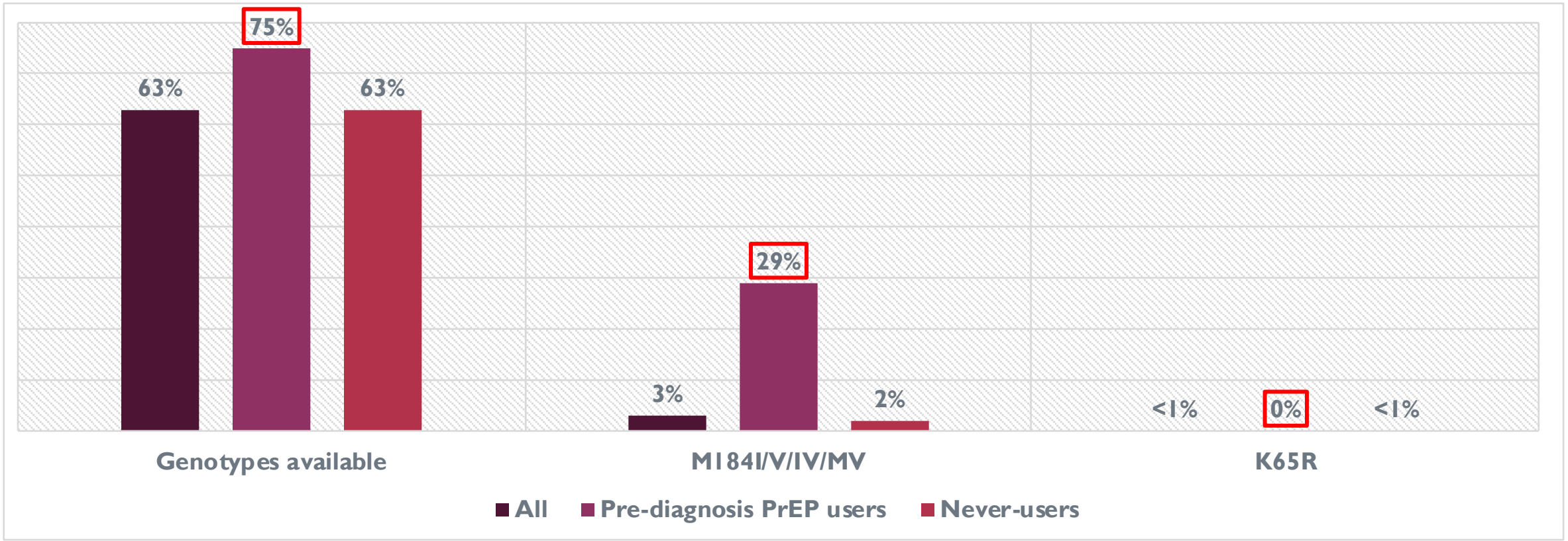
Median duration between PrEP start and HIV dx = 250 days (IQR=395)

NYC Health

CHARACTERISTICS OF PREP USERS AND NEVER USERS

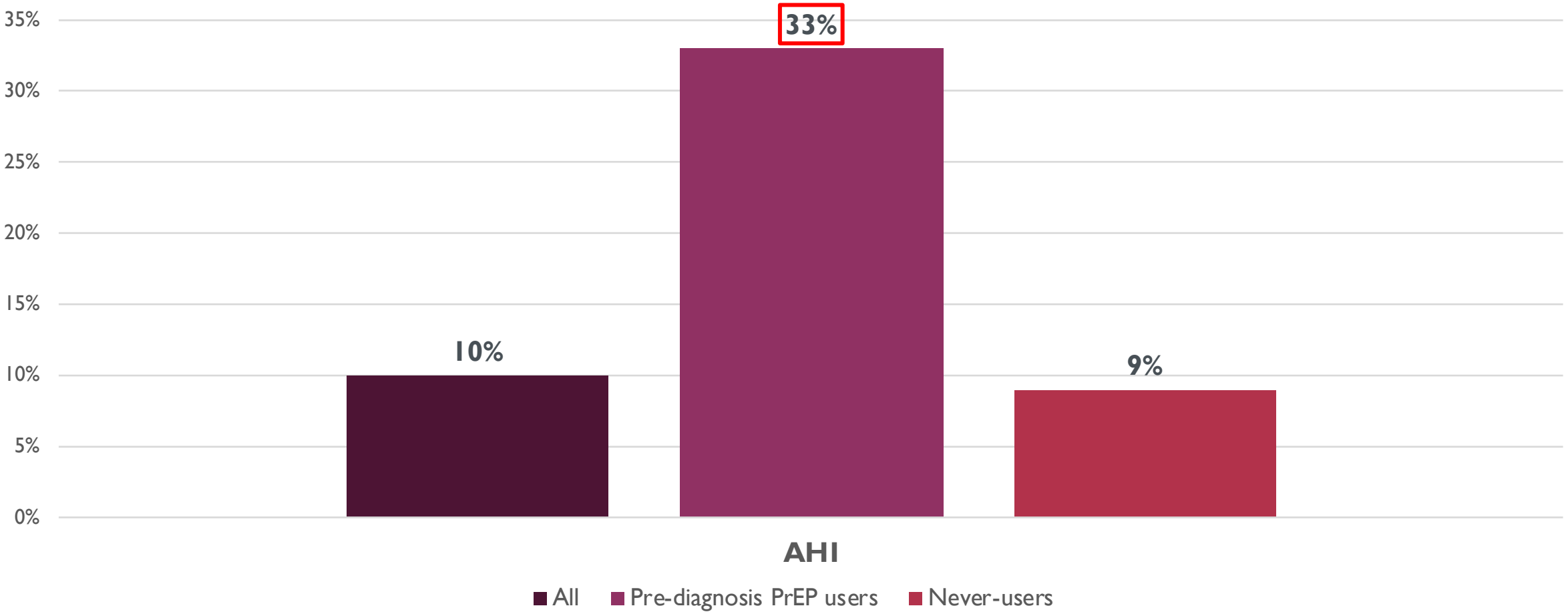


MUTATIONS ASSOCIATED WITH FTC AND TDF RESISTANCE IN GENOTYPED PRE-DIAGNOSIS PREP USERS VERSUS NEVER-USERS

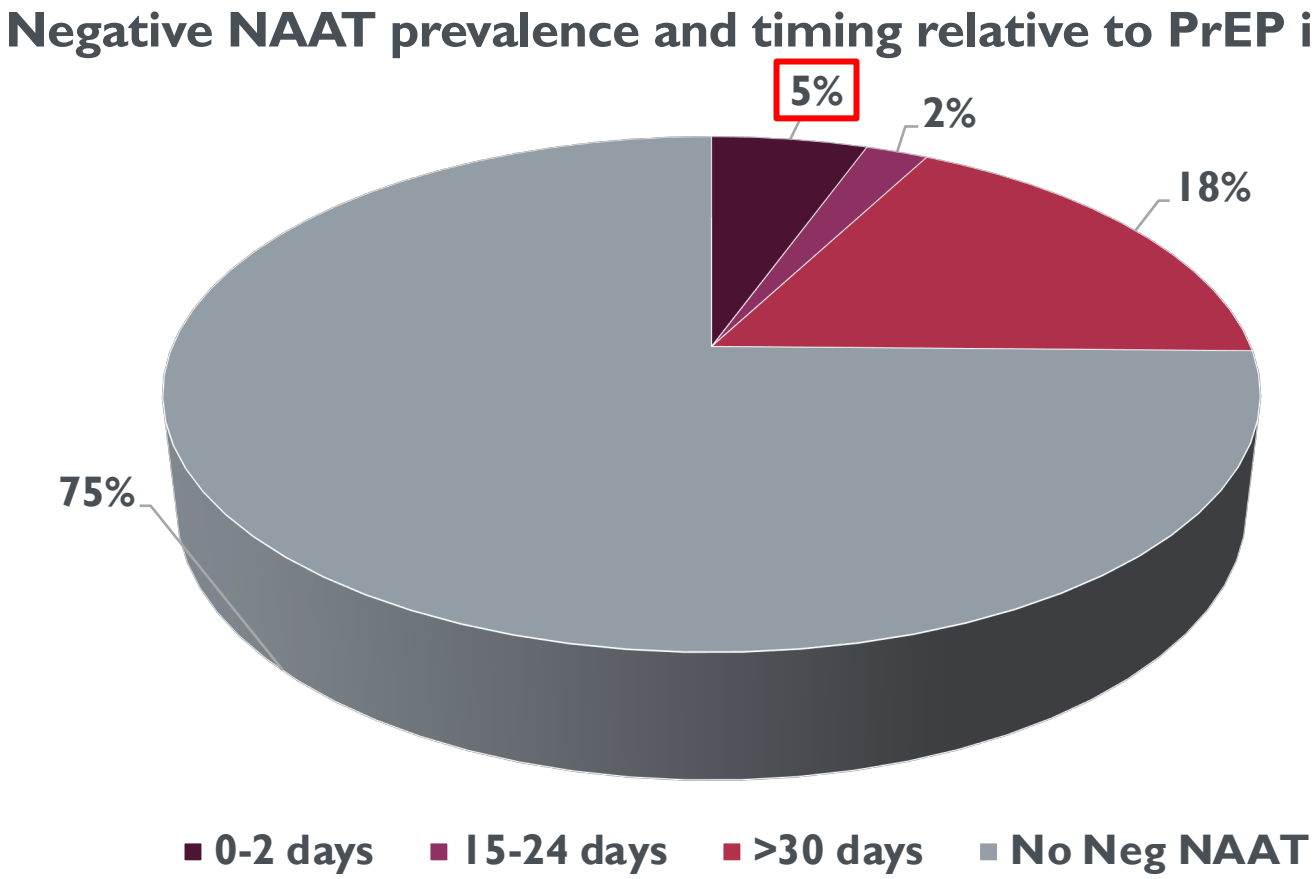


- K65R mutation associated with TDF resistance was found in 4 persons: none were PrEP users

ACUTE HIV INFECTION IN PREP USERS VS NEVER USERS



NEGATIVE NAAT PRIOR TO PREP START



- Only 5 out of the 91 PrEP users (5%) 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

CONCLUSION

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

ACKNOWLEDGMENTS

- Disease Investigation Specialists (Field Services Unit – Bureau of HIV/AIDS Prevention and Control, NYC Department of Health and Mental Hygiene)
- Lucia Torian, Lisa Forgione, Sasinya Scott and Sarah Braunstein (HIV Epidemiology and Field Services - NYC Department of Health and Mental Hygiene)
- Oni Blackstock (Bureau of HIV/AIDS Prevention and Control- NYC Department of Health and Mental Hygiene)
- Kent Sepkowitz (Memorial Sloane Kettering Hospital)

CONTACT

For questions contact:

Kavita Misra, PhD, MPH

Senior Epidemiologist and Program Analyst – Field Services Unit

Bureau of HIV/AIDS Prevention and Control

New York City Department of Health and Mental Hygiene

Email: kmisra@health.nyc.gov