Incident diagnoses of HIV on Oral and Long-Acting Pre-Exposure Prophylaxis in the OPERA Cohort

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Background

- ~1.2 million people in the US could benefit from pre-exposure prophylaxis (PrEP)
  - Only ~36% had received a PrEP prescription in 2022[1]
- Daily oral PrEP
  - TDF/FTC (FDA approval: 16JUL2012) or TAF/FTC (FDA approval: 3OCT2019)
  - When taken as prescribed, lower risk of HIV with TDF/FTC compared to non-PrEP controls (RR: 0.24; 95% CI: 0.11, 0.54)[2]
  - Oral PrEP adherence may be a challenge in key populations due to stigma and risk of disclosure
- Long-acting PrEP
  - Cabotegravir long-acting (CAB-LA) injectable PrEP (FDA approval: 20DEC2021)
  - CAB-LA was superior to TDF/FTC for HIV prevention: (HR: 0.22, 95% CI: 0.08, 0.59)[3]

Objective

- To characterize real-world oral and CAB-LA PrEP users in the US
- To assess the risk of HIV infection during oral and CAB-LA PrEP

Methods

Study population

- OPERA cohort: prospectively captured, routine clinical data from electronic health records in the US (90 clinics, 23 US states/territories)
- Inclusion criteria
  - HIV-negative
  - ≥18 years old
  - Start or switch to a new PrEP formulation (TDF/FTC or TAF/FTC prescription, CAB-LA injection) between 21DEC2021 and 30JUN2023
- Censoring criteria
  - Study end: 30JUN2024
  - Death
  - Lost to follow-up: 12 months after last clinical contact

PrEP episodes

- Continuous use of a specific PrEP type (oral PrEP or CAB-LA PrEP)
- The same person could contribute to multiple PrEP episodes (switch from oral to CAB-LA or from CAB-LA to oral PrEP)

Analyses

- Demographic and clinical characteristics described at the start of each PrEP episode
- HIV acquisition
  - HIV cases attributed to the PrEP type in use at the time of diagnosis
  - Each HIV case was confirmed through a chart review
  - Incidence rates: univariate Poisson regression

Results

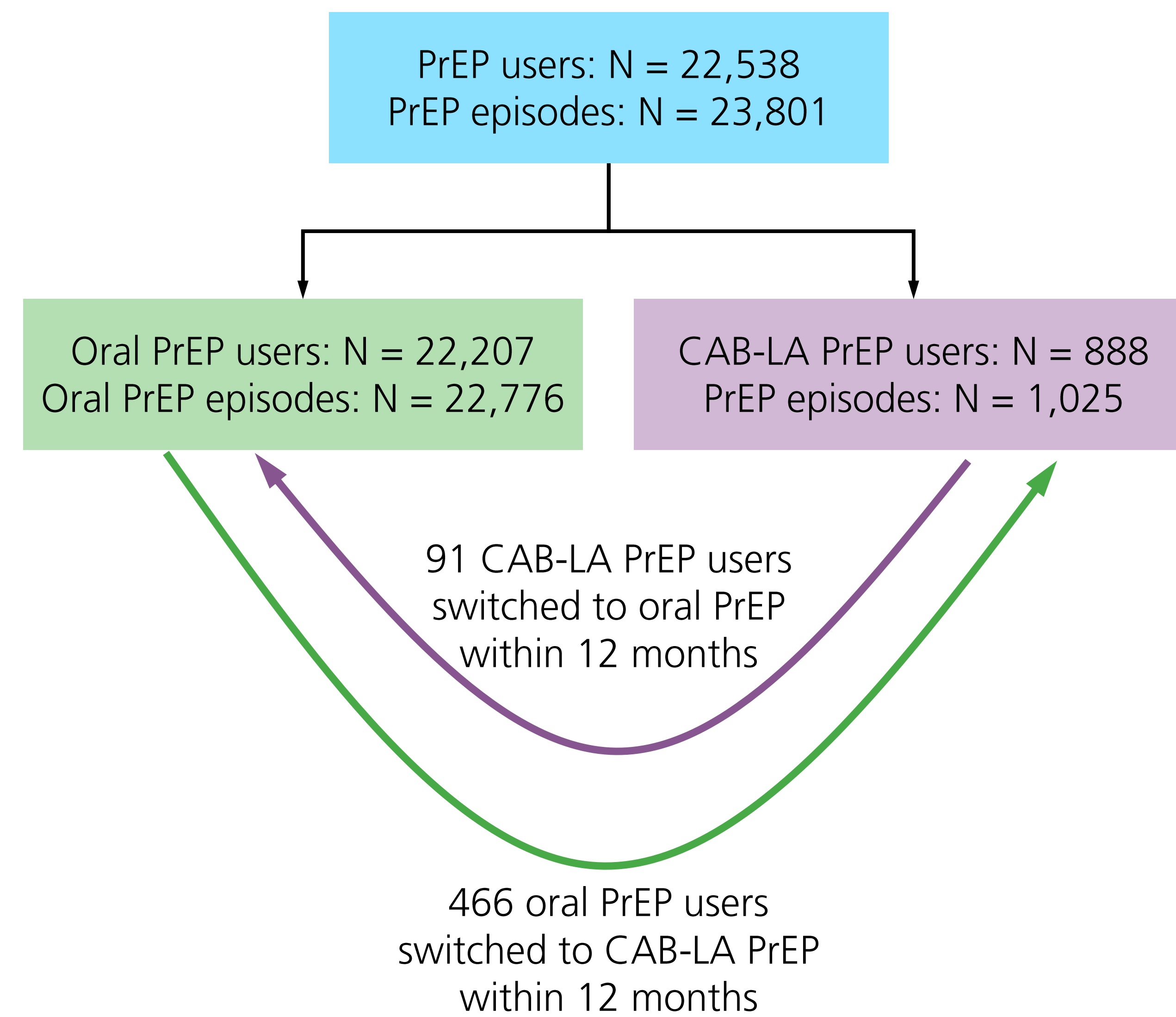### Figure 1. Oral PrEP and CAB-LA PrEP use in OPERA between 21DEC2021 and 30JUN2023

PrEP users: N = 22,538
PrEP episodes: N = 23,801

Oral PrEP users: N = 22,207
Oral PrEP episodes: N = 22,776

CAB-LA PrEP users: N = 888
PrEP episodes: N = 1,025

91 CAB-LA PrEP users switched to oral PrEP within 12 months

466 oral PrEP users switched to CAB-LA PrEP within 12 months

Table 1. Population characteristics at the start of the PrEP episode[a]

	Oral PrEP episodes N = 22,776	CAB-LA PrEP episodes N = 1,025
Age, median (IQR)	31 (26, 38)	32 (26, 40)
Female sex, n (%)	1,778 (8)[b]	128 (12)
Transgender, n (%)	606 (3)	94 (2)
Race, n (%)		
Black	5,357 (24)	309 (30)
White	11,267 (50)	518 (50)
Other	3,208 (14)	119 (12)
Unknown	2,944 (13)	79 (8)
Hispanic	7,462 (33)	283 (28)
Payer, n (%)[c]		
Medicaid	1,515 (7)	330 (32)
Medicare	396 (2)	64 (6)
Commercial Insurance	9,318 (41)	774 (76)
Other[d]	10,474 (46)	270 (26)
History of STI, n (%)		
Ever	8,939 (39)	549 (54)
Past 3 months	5,742 (25)	289 (28)

[a] Individuals who switched PrEP type during follow-up are included in both groups
[b] Unknown sex: n = 10; none switched to CAB-LA PrEP
[c] Payer categories are not mutually exclusive
[d] Any other form of payment (e.g., Veterans Health Administration, pharmacy benefit, state grants worker's comp, other insurance)

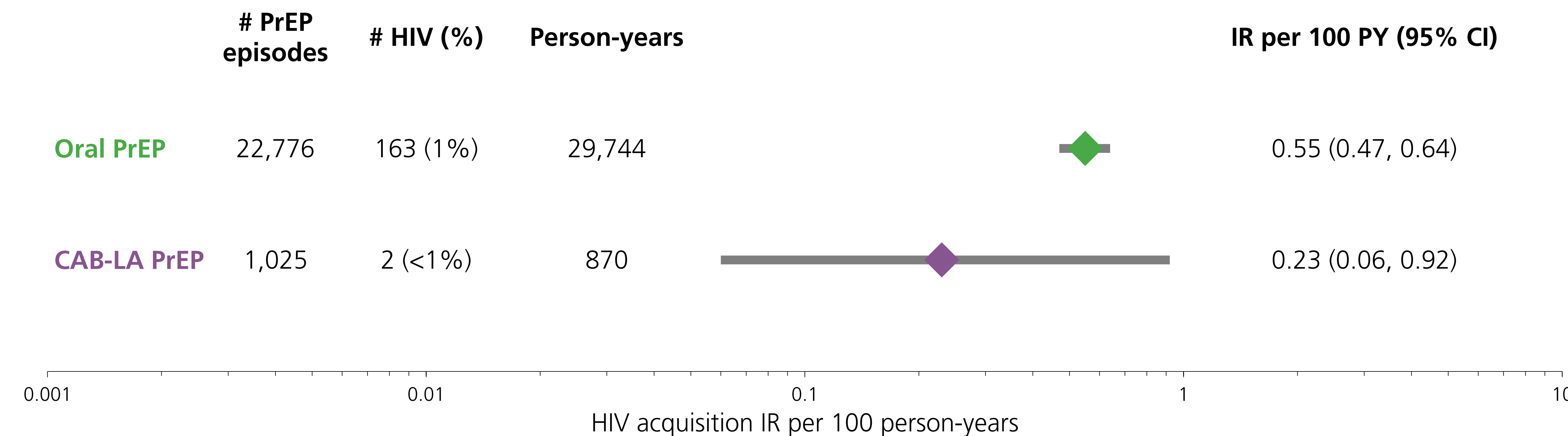### Figure 2. Incidence of HIV acquisition during oral PrEP or CAB-LA PrEP use

	# PrEP episodes	# HIV (%)	Person-years	IR per 100 PY (95% CI)
Oral PrEP	22,776	163 (1%)	29,744	0.55 (0.47, 0.64)
CAB-LA PrEP	1,025	2 (<1%)	870	0.23 (0.06, 0.92)

HIV acquisition IR per 100 person-years

Table 2. HIV testing and PrEP characteristics among people with incident HIV

	HIV diagnosis during oral PrEP episodes N = 163	HIV diagnosis during CAB-LA PrEP episodes N = 2
Months from start of PrEP episode to HIV diagnosis, median (IQR)	8 (4, 12)	12 (3, 21)
Any HIV test ≤2 weeks before/at PrEP episode start, n (%)	82 (50)	0 (0)
Any HIV test during PrEP episode before HIV diagnosis, n (%)	66 (40)	1 (50)
Direct switch from other PrEP type, n (%)	5 (3)	2 (100)

Abbreviations:
CAB-LA, cabotegravir long-acting; CI, confidence interval; HR, hazard ratio; IR, incidence rate; N, number; PrEP, pre-exposure prophylaxis; PY, person-years; RR, risk ratio; STI, sexually transmitted infection; TAF/FTC, tenofovir alafenamide/emtricitabine; TDF/FTC, tenofovir disoproxil fumarate

Discussion

- In the OPERA cohort, 22,538 individuals received PrEP during the study period, some received both oral and CAB-LA PrEP (Fig 1)
- Oral and CAB-LA PrEP were used by distinct populations
  - CAB-LA PrEP users were more likely to be women, Black or on Medicaid, to have commercial insurance, and to have a history of STI compared to oral PrEP users (Table 1)
- The incidence rate of HIV acquisition was low during both oral and CAB-LA PrEP use, (Fig 2)
  - The incidence rate was numerically lower on CAB-LA PrEP than oral PrEP
  - Overlapping confidence intervals due to the wide CAB-LA PrEP confidence intervals (small number of person-years)
- Among individuals who acquired HIV during PrEP use, a large proportion did not receive HIV testing either before or during the PrEP episode during which acquisition was recorded (Table 2)
- Strengths
  - Large study population
  - Includes all PrEP use during the study period (not limited to first use)
  - Chart reviews conducted to confirm all HIV diagnoses
- Limitations
  - Uncertainty around timing of HIV acquisition due to the absence of HIV testing; misclassification may have occurred
  - Reasons for discontinuation or switch are unknown

Key Findings

- In this real-world US study of PrEP use, rates of HIV diagnosis were low, and were numerically lower with CAB LA than oral PrEP use
- Testing before and during PrEP episode was low in people who acquired HIV, hindering early and accurate identification of HIV acquisition
- CAB-LA PrEP users represented a more vulnerable population than oral PrEP users, highlighting the importance of options to better meet the needs of different populations

References

1. Centers for Disease Control and Prevention. HV Surveillance Supplemental Report: Monitoring Selected National HIV Prevention and Care Objectives by Using HIV Surveillance Data United States and 6 Territories and Freely Associated States, 2022.
2. Huang X, et al. Efficacy and Safety of Oral TDF-Based Pre-exposure Prophylaxis for Men Who Have Sex With Men: A Systematic Review and Meta-Analysis. Frontiers in Pharmacology. 2018; 9.
3. Chen X, et al. Efficacy and safety of long-acting cabotegravir versus oral tenofovir disoproxil fumarate-emtricitabine as HIV pre-exposure prophylaxis: A systematic review and meta-analysis. Reviews in Medical Virology. 2023;33(4):e2460.

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