HIV Acquisition after PrEP Initiation: Quantifying Opportunities for Long-Acting Injectable Interventions Using Large-Scale Observational Data

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Introduction

Lenacapavir, a **long-acting injectable** (LAI) capable of preventing HIV infection for up to six months, represents a **major advance** in HIV **pre-exposure prophylaxis (PrEP)** & has been hailed as a breakthrough in the fight against HIV.

Despite PrEP's potential to **reduce infection risk by up to 99%** when taken as prescribed, adherence and persistence remain suboptimal for two daily oral regimens, tenofovir disoproxil fumarate (TDF) or tenofovir alafenamide (TAF) combined with emtricitabine (FTC), and the two-month LAI, cabotegravir.[1-3]

Globally, **more than 1.3 million people acquired HIV in the past year**,[3] yet within six months of starting, approximately **70%** of individuals prescribed PrEP had **suboptimal adherence** and **41% discontinued use completely**.[2]

Reasons for PrEP Discontinuation

Individual	- Low perceived risk of HIV infection - Experiencing side effects - Concern for long-term side effects - Pill burden - Choosing other prevention methods - Relocation - Misunderstanding of PrEP
Interpersonal	- Lack of family support - Lack of partner support - Concern about judgement from healthcare providers
Societal	- Stigma - Perceptions of PrEP in social or cultural groups
Structural	- Cost - Lack of health insurance - Inaccessibility to care - Housing instability

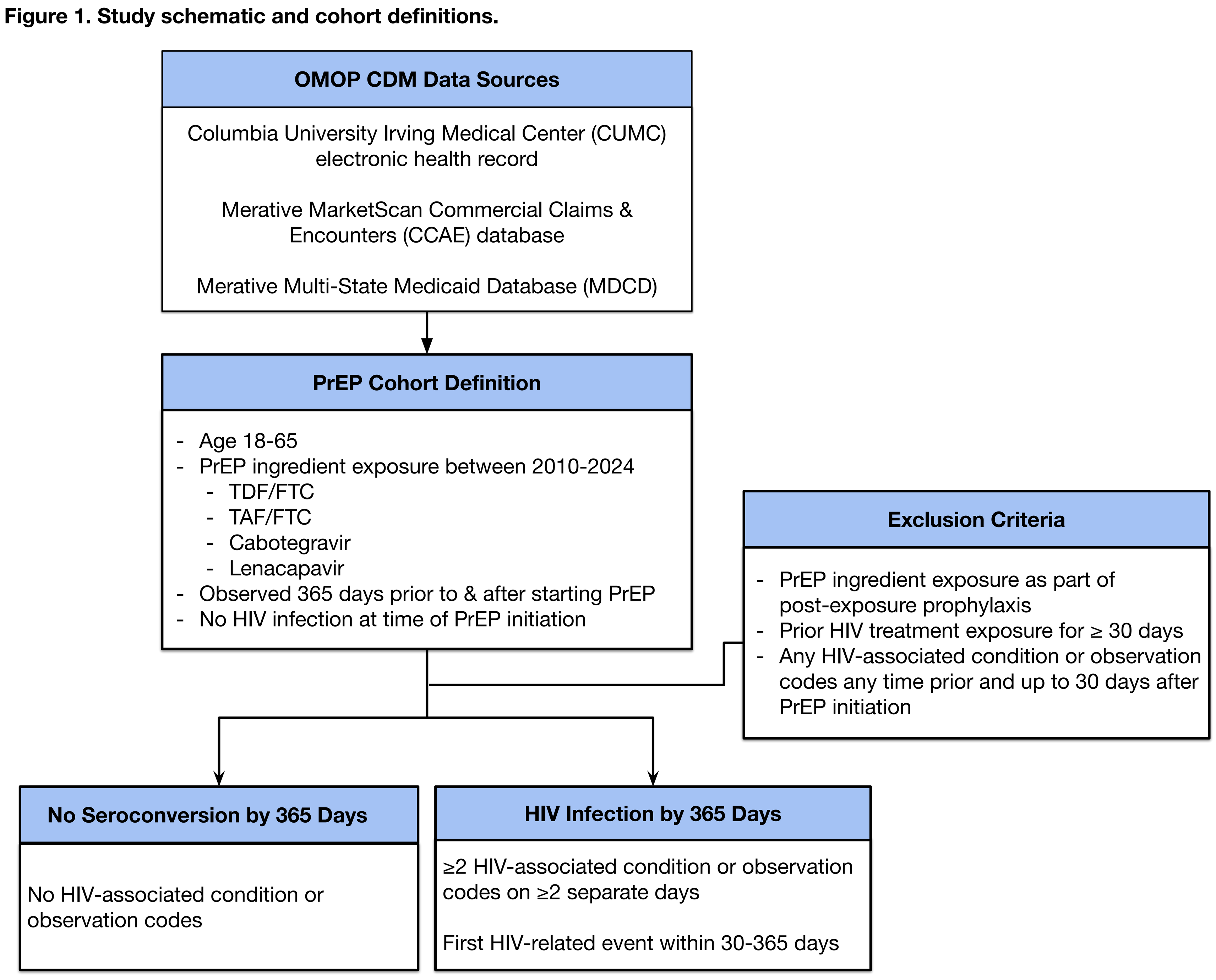
Large observational data networks, such as the **Observational Health Data Sciences and Informatics (OHDSI)** community, provide opportunities to study outcomes associated with these gaps.

The aim of this study was to leverage the OHDSI data network to **describe individuals who acquire HIV within six and twelve months of PrEP initiation,** and **quantify the proportion of individuals who acquire HIV and may benefit from this LAI** recently approved by the U.S. Food and Drug Administration.

Methods

We conducted a **retrospective observational cohort study** of **U.S. adults aged 18–65 prescribed PrEP** for the first time between 2010 and 2024 with at least a year of observation prior to and after starting PrEP (Figure 1)

Figure 1. Study schematic and cohort definitions.



Results

A total of 336 cases of incident HIV were identified across three databases in a combined cohort of N = 23,161 (Table 1)

The **median time to event ranged from 136-159 days** (Table 2)

The starting cohort was predominantly male (70-87%), between 18-40, and received TDF/FTC, but there were **higher proportions of women**, **older, Black, and Hispanic or Latino individuals in those with seroconversion**

Table 1. Demographic information for PrEP cohorts across three databases.

	CUMC N = 4,464ꝉ	CCAE N = 13,056ꝉ	MDCD N = 5,641ꝉ
Age (Years)	33 (27, 42)	37 (29, 46)	31 (24, 40)
Age Group			
18-24	542 (12%)	1,846 (14%)	1,469 (26%)
25-34	1,956 (44%)	3,894 (30%)	1,997 (35%)
35-44	1,040 (23%)	3,407 (26%)	1,205 (21%)
45-54	552 (12%)	2,790 (21%)	650 (12%)
55-64	374 (8.4%)	1,119 (8.6%)	320 (5.7%)
Gender			
Male	3,905 (87%)	11,148 (85%)	3,938 (70%)
Female	551 (12%)	1,908 (15%)	1,703 (30%)
Race			
American Indian or Alaska Native	11 (0.2%)	***	***
Asian	151 (3.4%)	***	***
Black or African American	695 (16%)	***	1,686 (30%)
Native Hawaiian or Other Pacific Islander	12 (0.3%)	***	***
White	1,822 (41%)	***	2,662 (47%)
Unknown	15 (0.3%)	***	***
NA	1,757 (39%)	13,056 (100%)	1,293 (23%)
Ethnicity			
Hispanic or Latino	1,225 (27%)	***	545 (9.7%)
Not Hispanic or Latino	2,311 (52%)	***	***
NA	928 (21%)	13,056 (100%)	5,096 (90%)

ꝉMedian (Q1, Q3); n (%); ***categories with fewer than 10 observations are not shown

Table 2. Incidence of HIV seroconversion across three databases.

	CUMC N = 4,464	CCAE N = 13,056	MDCD N = 5,641
Cases	41	179	116
Cumulative incidence (per 100,000 persons)			
Between 30 and 180 days of PrEP Initiation	694	996	1454
Between 30 and 365 days of PrEP Initiation	918	1370	2060
Incidence rate (per 100,000 person-years)			
Between 30 and 180 days of PrEP Initiation	1417	2037	2982
Between 30 and 365 days of PrEP Initiation	1227	1838	2768
Median time to seroconversion (Days)	136 (83, 239)	152 (73,254)	159 (108, 266)

Discussion

Incidence rates in all databases were higher than what would be expected if adherence were optimal, **particularly in the first 180 days after starting PrEP**

Over **50% of cases occurred between 30-180 days after initiating PrEP, indicating a potential benefit of LAIs**

HIV incidence was higher in women and **in Black, and Hispanic or Latino individuals,** groups previously identified as being less likely to stay on PrEP

Limitations

- Observational data with risk factors not readily available
- Complexity and missingness of health data introduces bias

Conclusions

Long-acting injectable PrEP regimens could help close the gap between efficacy and adherence, potentially preventing HIV infection.

Using informatics, we can identify groups who are likely to benefit from LAIs and prevent new HIV infections.

References

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