223555 Final Protocol

NON-INTERVENTIONAL STUDY PROTOCOL

STUDY DETAILS

UNIQUE IDENTIFIER (CTMS/OneCDP)	223555
TITLE	Frequency of HIV diagnoses among people using oral and LA PrEP
STUDY ACCOUNTABLE PERSON	PPD, ViiV Healthcare
SCIENTIFIC LEAD	PPD, ViiV Healthcare
CONTRIBUTING AUTHORS	PPD, Epividian PPD, Epividian PPD, ViiV Healthcare PPD, ViiV Healthcare PPD, ViiV Healthcare PPD, ViiV Healthcare
ASSET ID	GSK1265744
GSK or ViiV ASSET	Cabotegravir (Apretude)
EFFECTIVE DATE	02 October 2024
INDICATION	HIV pre-exposure prophylaxis

DATA COLLECTION TYPE	SECONDARY
SAFETY OBJECTIVE	NO
ASSET INVOLVEMENT	YES
TSS/PASS ASSESSMENT PERFORMED	YES
STUDY CLASSIFICATION	Voluntary TSS/PASS
EVALUATING A PRODUCT **(TIER TYPE)**	Tier 2
REGULATORY COMMITMENT	No

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TITLE PAGE

Study ID: 223555

Division: Global Medical

Information Type: Non-Interventional Study Protocol

Title:

Frequency of HIV diagnoses among people using oral and LA PrEP

Effective Date:

02 October 2024

Author(s):

PPD, Epividian

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STUDY INFORMATION

Title	Frequency of HIV diagnoses among people using oral and LA PrEP
Protocol version identifier	1.0
Date of last version of protocol	NA
EU PAS (ENCEPP) register number	TBD
Active substance	Cabotegravir
Medicinal product	Apretude
Product reference	N/A
Procedure number	N/A

Marketing authorisation holder(s)	ViiV Healthcare
Research question and objectives	1. Estimate the annual incidence of HIV diagnoses among all people without HIV in OPERA a. Among people with an incident HIV diagnosis, characterize history of PrEP use 2. Describe the demographic and clinical characteristics of people who initiate oral and LA PrEP 3. Estimate the frequency and rate of incident HIV diagnoses following index oral PrEP or LA PrEP initiation among people who initiate a PrEP regimen 4. Evaluate PrEP coverage within 12-months following index oral PrEP or LA PrEP initiation among people who initiate a PrEP regimen 5. Assess HIV testing and STI screening patterns at index oral or LA PrEP initiation and within 12-months following index PrEP initiation among people who initiate a PrEP regimen 6. Describe demographic and clinical characteristics, HIV testing and diagnoses, as well as STI screening and diagnoses over a 12-month period of follow-up among people who are not on PrEP but could benefit from PrEP
Country(-ies) of study	United States
Author	PPD

MARKETING AUTHORISATION HOLDER(S)

Marketing authorisation holder(s)	ViiV Healthcare Company 410 Blackwell St. Durham, NC 27701
MAH contact person	N/A

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LIST OF ABBREVIATIONS

AE	Adverse Event
CAB	Cabotegravir
CI	Confidence intervals
CMS	Centers for Medicare & Medicaid Services
EHR	Electronic health record
FTC	Emtricitabine
FU	Follow-up
GSK	GlaxoSmithKline
HBV	Hepatitis B virus
HCP	Healthcare provider
HCV	Hepatitis C virus
HPV	Human papilloma virus
HSV-2	Herpes Simplex-2
LA	Long acting
NA	Not applicable
Obj	Objective
PHI	Protected health information
PrEP	Pre-exposure prophylaxis
STI	Sexually transmitted infection
TAF	Tenofovir alafenamide
TDF	Tenofovir disoproxil fumarate
US	United States

TRADEMARK INFORMATION

Trademarks of the <<GSK\ViiV>> group of companies	Trademarks not owned by the <<GSK\ViiV>> group of companies
APRETUDE	OPERA

1. RESPONSIBLE PARTIES

MARKETING AUTHORISATION HOLDER
ViiV Healthcare Company

Sponsor Legal Registered Address:
ViiV Healthcare Company
410 Blackwell St.
Durham, NC 27701

1.1. Sponsor Signatory

Title: Frequency of HIV diagnoses among people using oral and LA PrEP

Compound Number: GSK1265744

PPD

12 September 2024

Leah Sadinski
Primary Author/NI Scientific Lead

Date (DD Month YYYY)

PPD

12 September 2024

Vani Vannappagari
VP and Global Head, Epidemiology and Real World Evidence

Date (DD Month YYYY)

PPD

02-Oct-2024

Nassrin Payvandi
VP & Head, Safety and Pharmacovigilance

Date (DD Month YYYY)

PPD

02-Oct-2024

Jens-Ulrich Stegmann
ViiV QPPV

Date (DD Month YYYY)

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1.2. Investigator Protocol Agreement Page

- I confirm agreement to conduct the study in compliance with the protocol.
- I acknowledge that I am responsible for overall study conduct. I agree to personally conduct or supervise the described study.
- I agree to ensure that all associates, colleagues, and employees assisting in the conduct of the study are informed about their obligations. Mechanisms are in place to ensure that site staff receive the appropriate information throughout the study.

Investigator Name:
Laurence Brunet

PPD

In

26 September 2024

Date (DD Month YYYY)

2. SYNOPSIS

Title Frequency of HIV diagnoses among people using oral and LA PrEP

Rationale and Background

In the US, out of approximately 1.2 million people who could benefit from pre-exposure prophylaxis (PrEP), it was estimated that approximately 30% had received a PrEP prescription in 2021. Oral PrEP has been shown to be an effective form of HIV prevention. When taken as prescribed, daily oral PrEP reduces the risk of HIV diagnosis by 99% compared to placebo or those who do not use PrEP among men who have sex with men. Tenofovir disoproxil fumarate (TDF)/emtricitabine (FTC) was approved for PrEP on 16JUL2012 and tenofovir alafenamide (TAF)/FTC was approved on 3OCT2019. The effectiveness of oral PrEP depends on the level of adherence to the daily pill regimen. Cabotegravir long-acting injectable (CAB LA) PrEP was approved on 20DEC2021 and has been shown to have superior efficacy compared to daily oral TDF/FTC. The CDC guidelines for PrEP indicate that HIV testing is required before PrEP initiation and recommended every 3 months (oral PrEP) or 2 months (CAB LA PrEP). The guidelines also recommend regular screening for syphilis, gonorrhea and chlamydia for PrEP users. It is important to understand patterns of PrEP use among people who acquire HIV to improve public health and clinical practice. This study will also provide crucial real-world evidence on HIV acquisition on PrEP, PrEP coverage, HIV testing and STI screening in individuals receiving either oral or LA PrEP.

Research Question and Objective(s)

Analyses to meet the study objectives below will be conducted twice during the study period. Analysis #1 will include data from 01JAN2021-31DEC2023 (Obj. 1) and from 21DEC2021-30JUN2024 (Obj. 2-6). Analysis #2 will be a repeat of Analysis #1 with data from 1JAN2021-31DEC2024 (Obj. 1) and from 21DEC2021-30JUN2025 (Obj. 2-6).

1. Estimate the annual incidence of HIV diagnoses among all people without HIV in OPERA
    a. Among people with an incident HIV diagnosis, characterize history of PrEP use
2. Describe the demographic and clinical characteristics of people who initiate oral and LA PrEP
3. Estimate the frequency and rate of incident HIV diagnoses following index oral PrEP or LA PrEP initiation among people who initiate a PrEP regimen
4. Evaluate PrEP coverage within 12-months following index oral PrEP or LA PrEP initiation among people who initiate a PrEP regimen
5. Assess HIV testing and STI screening patterns at index oral or LA PrEP initiation and within 12-months following index PrEP initiation among people who initiate a PrEP regimen
6. Describe demographic and clinical characteristics, HIV testing and diagnoses, as well as STI screening and diagnoses over a 12-month period of follow-up among people who are not on PrEP but could benefit from PrEP

Study Design
Design: Cohort study using secondary data from electronic medical records in the OPERA cohort.
Exposure groups: Oral PrEP, LA PrEP
Duration of study:

- Analysis #1: 2021 to 2023 (Obj 1-1a); 21DEC2021 to 30JUN2024 (Obj 2-6)
- Analysis #2: 2021 to 2024 (Obj 1-1a); 21DEC2021 to 30JUN2025 (Obj 2-6)

Population
(Obj 1) People in OPERA aged ≥18 years with ≥1 clinical encounter during the calendar year of interest and no evidence of prior HIV diagnosis.

(Obj 1a) People with an incident HIV diagnosis identified in Obj 1.

(Obj 2-5) People without HIV in OPERA aged ≥18 years who initiated any new PrEP formulation during the study period with or without prior PrEP use.

(Obj 6) People without HIV in OPERA aged ≥18 years who could benefit from PrEP and are not on PrEP

Variables
Exposures:

- PrEP use (never, use within ≤12 months before diagnosis, use >12 months before diagnosis)

- Time-updated PrEP type (oral or LA)

Outcomes:

- Incident HIV diagnosis: New HIV diagnosis *and/or* detectable HIV RNA *and/or* positive antigen/antibody test
- PrEP coverage: Proportion of days of access to oral PrEP or proportion of days of coverage by CAB LA
- HIV testing/STI screening: frequency and type of tests performed

Data Sources

OPERA cohort, a multi-site observational database built from the complete patient health records managed in electronic health record (EHR) systems throughout the US.

Study Size

Between 21DEC2021 and 30JUN2023 (Analysis # 1 inclusion period), 22,234 adults without HIV started a new PrEP formulation in OPERA. The first formulation used during the study period was TAF/FTC oral (n=12,110, 54%), TDF/FTC oral (n=9,740, 44%), or CAB LA (n=384, 2%). An additional 292 individuals switched to CAB LA PrEP later during the study period, for a total of 767 people receiving CAB LA injections during the Analysis #1 inclusion period.

Data Analysis

(Obj 1) For each calendar year (2021-2024), the number and percentage of incident HIV diagnoses will be reported out of all individuals receiving care at an OPERA clinic.

(Obj 1a) Among people with incident HIV diagnoses, PrEP use (never, use within ≤12 months before diagnosis, use >12 months before diagnosis) and PrEP characteristics will be described.

(Obj 2) Baseline demographic and clinical characteristics will be described for people initiating a PrEP regimen, by regimen type (oral or LA).

(Obj 3) The number, percentage, and incidence rate (per 100 person-years) of HIV diagnoses within 12-months following index oral or LA PrEP initiation and through study end will be described by regimen type (time-updated, oral or LA).

(Obj 4) The percentage of days with access to oral PrEP and the percentage of days with coverage by CAB LA PrEP will be described within 12-months following index PrEP initiation.

(Obj 5) The frequency, rate (per 100 person-years), and characteristics of HIV testing and STI screening at index oral or LA PrEP initiation and within 12-months following index PrEP initiation will be described by PrEP regimen type (oral or LA), type of healthcare provider (MD or DO, physician associate, nurse practitioner, other/unknown) and clinic type (healthcare center, wellness center, other).

(Obj 6) Baseline demographic and clinical characteristics will be described for all people who could benefit from PrEP but are not on PrEP. The frequency and rate (per 100 person-years) of HIV testing and diagnosis as well as STI screening and diagnosis will be estimates over a 12-month period of follow-up among people who could benefit from PrEP but are not on PrEP. Characteristics of the tests conducted will be described by type of healthcare provider (MD or DO, physician associate, nurse practitioner, other/unknown) and clinic type (healthcare center, wellness center, other).

3. AMENDMENTS AND UPDATES

Amendment or update no	Date	Section of study protocol	Amendment or update	Reason
<<1>>	<< Date (DD Month YYYY)>>	<<Text >>	<<Text>>	<<Text>>
<<2>>	<< Date (DD Month YYYY)>>	<<Text>>	<<Text>>	<<Text>>
<<n>>	<< Date (DD Month YYYY)>>	<<Text >>	<<Text>>	<<Text>>

4. MILESTONES

Milestone	Planned date
Draft protocol	July 2024
Protocol Review Committee	July 2024
Final Protocol	Effective Date
Analysis #1 results	October 2024
Analysis #2 results	September 2025
Final Study Report (Analysis #1-2 results)	October 2025

5. RATIONALE AND BACKGROUND

In the US, the yearly number of HIV diagnoses declined on average by 2-3% between 2016 and 2019, with a total of 36,585 diagnoses in 2019. In 2020, a 17% decline in HIV diagnosis were observed, down to 30,403 diagnoses as a result of disruptions in testing services during the COVID-19 pandemic.[1] The number of new HIV diagnoses rebounded to 36,136 in 2021 and 37,981 in 2022.[2] Of approximately 1.2 million people in the US who could benefit from pre-exposure prophylaxis (PrEP) in 2022, it was estimated that only around 36% had received a PrEP prescription (due to limitations with the numerator and denominator, PrEP coverage reporting by the CDC has been paused for one year)[3].[4]

Oral PrEP was introduced as a form of HIV prevention when the single tablet combination of tenofovir disoproxil fumarate (TDF) and emtricitabine (FTC) was approved by the FDA on 16JUL2012. A meta-analysis of 14 clinical trials, open-label extension studies or demonstration studies found an incidence of HIV of 1.1% (95% CI: 0.6, 2.0). Compared to the non-PrEP control groups, the relative risk for incident HIV was 0.24 (95% CI: 0.11, 0.54).[5] Of note, higher blood levels of TDF/FTC (indicating better adherence) were correlated with a lower incidence of HIV.[5] The second oral PrEP option, a single tablet combination of tenofovir alafenamide (TAF) and FTC was approved on 3OCT2019. TAF/FTC was demonstrated to be non-inferior to TDF/FTC in men in a clinical trial.[6] When taken as prescribed, daily oral PrEP reduces the risk of HIV diagnosis by 99% compared to placebo or those who do not use PrEP among men who have sex with men.[7] Of note, the efficacy of oral PrEP is highly correlated with adherence.[5,8] Cabotegravir long-acting injectable (CAB LA) PrEP was approved for the prevention of HIV by the FDA on 20DEC2021.[9] Clinical trials have demonstrated the superior efficacy of CAB LA PrEP over daily oral TDF/FTC for HIV prevention.[10, 11] CAB LA PrEP consists of intramuscular injections given by a healthcare professional and is considered directly observed prevention.

The CDC guidelines for PrEP indicate that HIV testing is required before PrEP initiation to confirm the person does not have HIV. When oral PrEP is used, it is recommended to repeat HIV testing every 3 months before refilling or reissuing the PrEP prescription. When CAB LA PrEP is used, HIV testing is recommended every 2 months, at the time the injection is administered.[7] HIV testing for PrEP should consist of a laboratory antigen/antibody test or a point-of-care fingerstick antigen/antibody test; rapid tests using oral fluids lack the sensitivity to detect recent infection.[7]

PrEP clinical care represents an opportunity to provide reproductive & sexual health-related services, such as STI screening. The CDC guidelines for PrEP recommends regular screening for syphilis, gonorrhea and chlamydia.[7] A systematic review of 91 PrEP programs implementing STI testing services in 32 countries found that only 70% of PrEP programs conducted STI screening before PrEP start, and 70% screened for STI every 3 months. However, in high-income countries, screening was high for gonorrhea (92%), chlamydia (92%) and syphilis (87%), but low for hepatitis A (18%) and hepatitis C (43%).[12] In the US, a survey study found that among 809 current or former PrEP users, 91% reported receiving HIV testing at every PrEP care visit. As for STI screening, a blood sample, urine/urethral swab or a rectal swab was collected at every PrEP care visit in 67%, 57% and 36% of participants, respectively.[13]

It is important to understand patterns of PrEP use among people with incident HIV diagnosis to

improve public health and clinical practice. This study will also provide crucial real-world evidence on incident HIV diagnoses on PrEP, PrEP coverage, HIV testing and STI screening in individuals on either oral or LA PrEP.

6. RESEARCH QUESTION AND OBJECTIVE(S)

Primary Objectives

1. Estimate the annual incidence of HIV diagnoses among all people without HIV in OPERA
    a. Among people with an incident HIV diagnosis, characterize history of PrEP use

2. Describe the demographic and clinical characteristics of people who initiate an oral or LA PrEP regimen

3. Estimate the frequency and rate of incident HIV diagnoses following index oral PrEP or LA PrEP initiation among people who initiate a PrEP regimen

4. Evaluate PrEP coverage within 12-months following index oral PrEP or LA PrEP initiation among people who initiate a PrEP regimen

5. Assess HIV testing and STI screening patterns at index oral or LA PrEP initiation and within 12-months following PrEP initiation, as well as the frequency and rate of STI diagnoses among people who initiate a PrEP regimen

6. Describe demographic and clinical characteristics, HIV testing, HIV diagnoses, STI screening and STI diagnoses over a 12-month period of follow-up among people who are not on PrEP but could benefit from PrEP

7. RESEARCH METHODS

7.1. Study Design

A cohort study using secondary data from the OPERA® (Observational Pharmaco-Epidemiology Research & Analysis) cohort will be used to answer the study objectives. OPERA is a multi-site observational database collecting data prospectively from the complete electronic health records (EHR) from clinical care throughout the US.

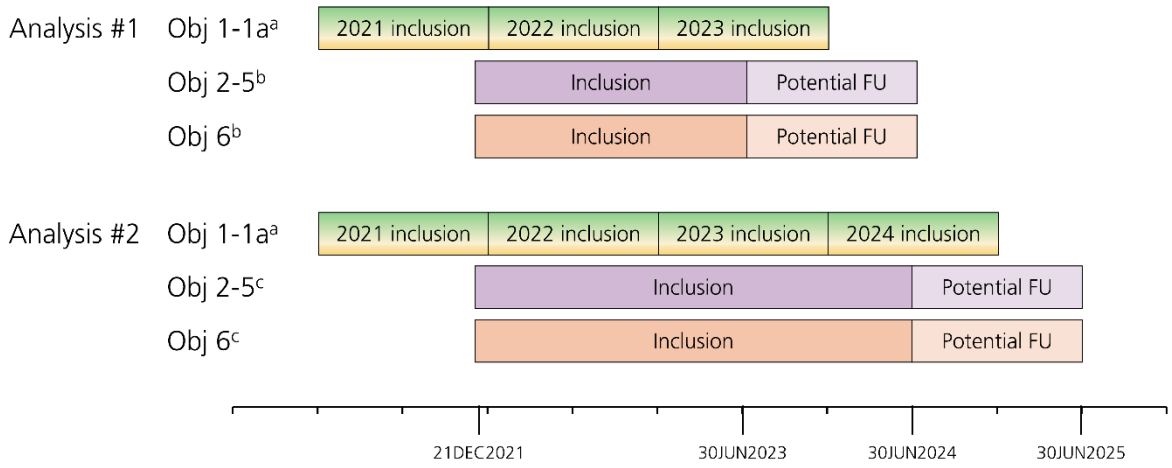
Analyses to meet the study objectives will be conducted twice during the study period. Analysis #1 will include data from 01JAN2021-31DEC20203 (Obj. 1-1a) and from 21DEC2021 to 30JUN2024 (Obj 2-6). Analysis #2 will be a repeat of Analysis #1 with data from 1JAN2021-31DEC2024 (Obj. 1-1a) and from 21DEC2021 to 30JUN2025 (Obj 2-6). A

summary of the study design is provided in Table 1 (exposure groups, index date, censoring criteria, endpoints) and in Figure 1 (timeline).

Table 1. Summary of study design

		Analysis #1	Analysis #2
Obj 1 Among all people without HIV in OPERA	**Exposure groups**	Calendar years	Calendar years
	Index date	NA	NA
	Censoring criteria	NA	NA
	Endpoints	HIV diagnosis	HIV diagnosis
Obj 1a Among people with a new HIV diagnosis	**Exposure groups**	PrEP use (never, use within ≤12 months before diagnosis, use >12 months before diagnosis)	PrEP use (never, use within ≤12 months before diagnosis, use >12 months before diagnosis)
	Index date	Date of HIV diagnosis	Date of HIV diagnosis
	Censoring criteria	NA	NA
	Endpoints	NA	NA
Obj 2-5 Among PrEP users	**Exposure groups**	Oral PrEP, CAB LA PrEP	Oral PrEP, CAB LA PrEP
	Index date	Start of first PrEP regimen during the study period	Start of first PrEP regimen during the study period
	Censoring criteria	Death, loss to follow-up (12 months after last clinical contact), study end (30JUN2024), 12 months after index date	Death, loss to follow-up (12 months after last clinical contact), study end (30JUN2025), 12 months after index date
	Endpoints	HIV diagnosis, PrEP coverage, HIV testing, STI screening, STI diagnoses	HIV diagnosis, PrEP coverage, HIV testing, STI screening, STI diagnoses
Obj 6 Among people who could benefit from PrEP	**Exposure groups**	NA	NA
	Index date	First OPERA visit with indication for PrEP during study period	First OPERA visit with indication for PrEP during study period
	Censoring criteria	Death, loss to follow-up, study end (30JUN2024), 12 months after index date, PrEP initiation	Death, loss to follow-up, study end (30JUN2025), 12 months after index date, PrEP initiation
	Endpoints	HIV testing, HIV diagnoses, STI screening, STI diagnoses	HIV testing, HIV diagnoses, STI screening, STI diagnoses

Figure 1. Study timeline



[a] Inclusion dates: 1JAN202X to 31DEC202X of each year
[b] Inclusion dates: 21DEC2021 to 30JUN2023, with potential follow-up through 30JUN2024
[c] Inclusion dates: 21DEC2021 to 31JUN2024 , with potential follow-up through 30JUN2025

7.2. Study Population and Setting

7.2.1. Inclusion Criteria

People without HIV in OPERA (Obj 1)

i. ≥1 clinical encounter in OPERA during the calendar year of interest
ii. ≥18 years old at the first clinical encounter during the calendar year of interest
iii. No evidence of prior HIV diagnosis

People with a new HIV diagnosis (Obj 1.a)

i. Incident HIV diagnosis (new HIV diagnosis/positive HIV test/detectable HIV RNA viral load) identified in Obj 1

PrEP users (Obj 2-5)

i. HIV-negative
ii. ≥18 years of age
iii. Started any new PrEP formulation
   - Analysis #1: between 21DEC2021 and 30JUN2023
   - Analysis #2: between 21DEC2021 and 30JUN2024
iv. With or without prior PrEP use (a different formulation or a gap ≥61 days without any PrEP immediately prior to the index PrEP; the same formulation may have been used ≥61 days before starting the index PrEP)

People who could benefit from PrEP (Obj 6)

i. HIV-negative
ii. ≥18 years of age

iii. ≥1 clinical encounter in OPERA during the inclusion period
- Analysis #1: between 21DEC2021 and 30JUN2023
- Analysis #2: between 21DEC2021 and 30JUN2024

iv. Any of the following indications for PrEP[11]:
- Bacterial STI in past 12 months[i] (gonorrhea, syphilis, chlamydia)[7]
- Alcohol use disorder[7]
- Illicit non-injection drug use[7]
- Injection drug use[7, 14]
- Black women[14]
- Transgender women[14]
- Men who have sex with men[14]
- All individuals aged 18-24 years[ii14]
- Any history of PrEP use

7.3. Variables

The following variables will be assessed at index date

- Demographic characteristics
  - Age (years)
  - Sex assigned at birth
  - Gender (trans, cis)
  - Race (African American/Black, Asian, White, Other Race)
  - Ethnicity (Hispanic, non-Hispanic)
  - Geographic Region (Northeast, Midwest, South, West, US Territories)
  - Marital status
  - Payer type (Medicaid, Medicare, Commercial insurance, Cash)

- Clinical characteristics
  - Time since first OPERA visit
  - Number of visits with OPERA healthcare provider (HCP) within 12 months prior to baseline
  - Prescriber specialty (MD or DO, physician associate, nurse practitioner, other/unknown)
  - Clinic type (healthcare center, wellness center, other)

- Sexual Behavior and Health
  - History of STI (ever)
    a) Syphilis
    b) Gonorrhea

[i] The CDC PrEP Clinical Practice Guideline recommends using an STI in the past 6 months as an indication for PrEP. This has been extended to an STI in the past 12 months for this protocol.
[ii] The National HIV/AIDS Strategy for the United States 2022–2025 identifies youth aged 12-24 as a priority population. This has been changed to individuals aged 18-24 in accordance with the study inclusion criteria

c) Chlamydia
d) Chancroid
e) Lymphogranuloma venereum
f) *Mycoplasma genitalium*
g) Herpes Simplex-2 (HSV-2) infection
h) Trichomoniasis infection
i) Human papilloma virus (HPV)/genital warts

- History of STI (past 3 months)
  a) Syphilis
  b) Gonorrhea
  c) Chlamydia
  d) Chancroid
  e) Lymphogranuloma venereum
  f) *Mycoplasma genitalium*
  g) HSV-2
  h) Trichomoniasis infection
  i) HPV/genital warts

7.3.1. Exposure definitions

People without HIV in OPERA (Obj 1)
Not applicable

People with a new HIV diagnosis (Obj 1.a)
PrEP use (never, use within ≤12 months before diagnosis, use >12 months before diagnosis)

- Formulation (TDF/FTC, TAF/FTC, CAB LA)
- Number of PrEP formulations
- Presence and duration of gaps without PrEP use

PrEP users (Obj 2-5)
Time-updated PrEP type (oral or LA).

People who could benefit from PrEP (Obj 6)
Not applicable

7.3.2. Outcome definitions

People without HIV in OPERA (Obj 1)
Incident HIV diagnosis

- New HIV diagnosis and/or detectable HIV RNA and/or positive antigen/antibody test
- All potential incident HIV diagnoses will be subject to a thorough chart review for confirmation

People with a new HIV diagnosis (Obj 1.a)
Not applicable

PrEP users (Obj 2-5)

Incident HIV diagnosis

- Frequency of new HIV diagnosis and/or detectable HIV RNA and/or positive antigen/antibody test
- Months from start of PrEP type (oral vs. LA) to HIV diagnosis
- Rate of incident HIV diagnoses per 100 person-years of follow-up
    - Within the first 12 months after index PrEP start
    - Through study end (Analysis #1: 30JUN2024; Analysis #2: 30JUN2025)
    - Follow-up (FU) will be censored at first of:
        - HIV diagnosis
        - Death
        - Study end (Analysis #1: 30JUN2024; Analysis #2: 30JUN2025)
        - Loss to follow-up (12 months after last clinical contact)
        - 12 months after index date
- All potential HIV acquisitions will be subject to a thorough chart review for confirmation
    - All lab results, diagnoses, ART prescriptions and clinician notes available in OPERA on or after the potential HIV acquisition was identified will be reviewed

PrEP coverage

- Oral PrEP coverage:
    - Proportion of days of access to oral PrEP in the 12-months following index PrEP initiation
    - Follow-up (FU) will be censored at first of:
        a) Death
        b) Study end (Analysis #1: 30JUN2024; Analysis #2: 30JUN2025)
        c) Loss to follow-up (12 months after last clinical contact)
        d) 12 months after index date
    - Access to oral PrEP will be determined based on the dates and days of supply for each prescription (e.g., a prescription for 30 pills/month with 3 refills provides 90 days of access)
        a) Each calendar day will only be counted once, even if there is an overlap between access from the prior prescription and start of the next prescription.

$$\%\ access = \frac{\sum Number\ of\ pills\ in\ each\ prescription}{Number\ of\ FU\ days} \times 100\%$$

- LA PrEP coverage:
    - Proportion of days of coverage by CAB LA over follow-up
    - Follow-up (FU) will be censored at first of:
        a) Death
        b) Study end (Analysis #1: 30JUN2024; Analysis #2: 30JUN2025)

c) Loss to follow-up (12 months after last clinical contact)
d) 12 months after index date

- Coverage by LA PrEP will be determined based on the duration of medication from injection date forward. The number of days of coverage per injection were derived from the CAB LA PrEP USPI label.[14]
  - 1st injection: coverage = 37 days (30 days of coverage + 7-day injection window)
  - Subsequent injections: coverage = 67 days (60 days of coverage + 7-day injection window)
  - Each calendar day will only be counted once, even if there is an overlap between coverage from the prior injection and date of the next injection.

$$\%\ coverage = \frac{\sum \min(coverage, days\ between\ injections)}{Number\ of\ FU\ days} \times 100\%$$

<u>HIV testing & STI screening</u>

- HIV testing
  - Assessed within 14 days before PrEP start and over the first 12 months after PrEP start
    - Frequency and rate (per 100 person years) of HIV tests over 12-month period
    - Type of HIV tests (RNA [quantitative, qualitative], antigen/antibody, rapid screen)
    - Timing of HIV tests as recommended by PrEP clinical guidelines[7]
      - Oral PrEP: on-schedule testing defined as receiving an HIV test ≤14 days before/at start, and 3 months (76-104 days) after each test
      - LA PrEP: on-schedule testing defined as receiving an HIV test ≤14 days before/at first injection, and ±14 days of each subsequent injection
    - HIV testing practices (type, frequency) by type of healthcare provider (MD or DO, physician associate, nurse practitioner, other/unknown)
    - HIV testing practices (type, frequency) by clinic type (healthcare center, wellness center, other)
- STI screening
  - Assessed within 14 days before PrEP start and over the first 12 months after PrEP start
    - Frequency and rate (per 100 person years) of STI testing events (testing for multiple STIs on the same day will count as 1 testing event)
    - Type of other STI tests
      - Syphilis
      - Gonorrhea
      - Chlamydia
      - Chancroid
      - Lymphogranuloma venereum

  - Mycoplasma genitalium
  - Hepatitis B virus (HBV)
  - Hepatitis C virus (HCV)
  - HSV-2
  - Trichomoniasis
  - HPV and/or genital warts
- Timing of STI tests as recommended by PrEP clinical guidelines[7]
  - Testing 3 months (76-104 days) after last test
  - Testing 6 months (168-196 days) after last test
  - Testing 12 months (351-379 days) after last test
- STI screening practices (type, frequency) by type of healthcare provider (MD or DO, physician associate, nurse practitioner, other/unknown)
- STI screening practices (type, frequency) by clinic type (healthcare center, wellness center, other)

- Crosstabulation of HIV and STI testing frequency
- STI diagnoses
  - New diagnosis of STI as noted in medical record or positive test result
  - STI diagnoses for
    - Syphilis
    - Gonorrhea
    - Chlamydia
    - Chancroid
    - Lymphogranuloma venereum
    - Mycoplasma genitalium
    - Hepatitis B virus (HBV)
    - Hepatitis C virus (HCV)
    - HSV-2
    - Trichomoniasis
    - HPV and/or genital warts

People who could benefit from PrEP (Obj 6)

<u>HIV testing & STI screening</u>

- HIV testing
  - Frequency and rate (per 100 person years) of HIV tests over 12-month period
  - Type of HIV tests (RNA [quantitative, qualitative], antigen/antibody, rapid screen)
  - HIV testing practices (type, frequency) by HCP type (MD or DO, physician associate, nurse practitioner, other/unknown)
  - HIV testing practices (type, frequency) by clinic type (healthcare center, wellness center, other)
- HIV diagnoses
  - Frequency of new HIV diagnosis and/or detectable HIV RNA and/or positive antigen/antibody test
  - Rate of incident HIV diagnoses per 100 person-years of follow-up
    - Within the first 12 months after index PrEP start
    - Through study end (Analysis #1: 30JUN2024; Analysis #2: 30JUN2025)

  - Follow-up (FU) will be censored at first of:
    - HIV diagnosis
    - Death
    - Study end (Analysis #1: 30JUN2024; Analysis #2: 30JUN2025)
    - Loss to follow-up (12 months after last clinical contact)
    - 12 months after index date
  - All potential HIV acquisitions will be subject to a thorough chart review for confirmation
    - All lab results, diagnoses, ART prescriptions and clinician notes available in OPERA on or after the potential HIV acquisition was identified will be reviewed
- STI screening
  - Frequency and rate (per 100 person years) of STI testing events (testing for multiple STIs on the same day will count as 1 testing event)
  - Type of other STI tests
    - Syphilis
    - Gonorrhea
    - Chlamydia
    - Chancroid
    - Lymphogranuloma venereum
    - Mycoplasma genitalium
    - Hepatitis B virus (HBV)
    - Hepatitis C virus (HCV)
    - HSV-2
    - Trichomoniasis
    - HPV and/or genital warts
  - Timing of STI tests as recommended by PrEP clinical guidelines[7]
    - Testing 3 months (76-104 days) after last test
    - Testing 6 months (168-196 days) after last test
    - Testing 12 months (351-379 days) after last test
  - STI screening practices (type, frequency) by HCP type type (MD or DO, physician associate, nurse practitioner, other/unknown)
  - STI screening practices (type, frequency) by clinic type (healthcare center, wellness center, other)
- Crosstabulation of HIV and STI testing frequency
- STI diagnoses
  - New diagnosis of STI as noted in medical record or positive test result
  - STI diagnoses for
    - Syphilis
    - Gonorrhea
    - Chlamydia
    - Chancroid
    - Lymphogranuloma venereum
    - Mycoplasma genitalium
    - Hepatitis B virus (HBV)
    - Hepatitis C virus (HCV)
    - HSV-2

- Trichomoniasis
- HPV and/or genital warts

7.3.3. Confounders and effect modifiers

Not applicable; this study is descriptive in nature.

7.4. Data sources

All data used for this study will be obtained from the OPERA cohort, which is a multi-site observational database built from the complete patient health records managed in EHR systems from more than 850 participating caregivers at over 150 separate locations throughout the US. Through their membership in OPERA, medical practices meet the Centers for Medicare & Medicaid Services (CMS) MIPS Incentive Program for Integration with a Specialized Registry. OPERA-participating physicians and ancillary healthcare providers have documented the care of over 1 million patients in their EHRs, including over 710,000 people without HIV (~40% women). The OPERA database is refreshed from these EHR systems at each clinic daily providing up-to-date data to both clinicians and researchers. The average years of follow-up (years of documenting patient visits prospectively in the EHR) for patients in OPERA is 1.2 years and there are over 64,000 people without HIV who have 5 years or more of follow-up.

Table 2. Characteristics of the OPERA cohort as of June 2024

	People with HIV		People without HIV	
	All N=152,761	Active[a] N=85,396	All N=720,581	Active[a] N=294,314
Age (years)				
< 1	22 (0%)	13 (0%)	12,211 (2%)	8,217 (38%)
13-25	4,768 (3%)	4,036 (5%)	109,459 (15%)	67,250 (23%)
26-49	79,361 (52%)	48,838 (57%)	464,982 (64%)	174,683 (59%)
50+	68,610 (45%)	32,509 (38%)	133,910 (19%)	44,156 (15%)
Sex				
Male	127,238 (83%)	71,051 (83%)	438,539 (61%)	179,309 (61%)
Female	25,339 (17%)	14,339 (17%)	281,588 (39%)	114,935 (39%)
Unknown	184 (0%)	6 (0%)	454 (0%)	70 (0%)
Transgender	4,122 (3%)	2,326 (3%)	4,805 (1%)	2,251 (1%)
Race				
African American	64,078 (42%)	37,915 (44%)	260,654 (36%)	111,307 (38%)
American Indian/ Alaska Native	1,188 (1%)	912 (1%)	6,642 (1%)	3,437 (1%)
Asian	2,301 (2%)	1,518 (2%)	26,545 (4%)	11,170 (4%)
Multiracial[b]	1,486 (1%)	872 (1%)	13,051 (2%)	8,030 (3%)
Native Hawaiian/ Other Pacific Islander	371 (0%)	239 (0%)	3,699 (1%)	1,817 (1%)
White	69,411 (45%)	37,972 (44%)	288,323 (40%)	110,059 (37%)
Other	2,706 (2%)	2,033 (2%)	17,073 (2%)	11,701 (4%)
Unknown	11,220 (7%)	3,935 (5%)	104,594 (14%)	36,793 (12%)
Ethnicity				
Not Hispanic	118,624 (78%)	62,550 (73%)	555,069 (77%)	219,604 (75%)
Hispanic	34,137 (22%)	22,846 (27%)	165,512 (23%)	74,710 (25%)

[a] Active defined as having at least one contact (visit, med, lab, diagnosis) in the previous 24 months

[b] Multiracial includes any combination of races or no race specified just multiracial indicated

7.5. Study size

Between 21DEC2021 and 30JUN2023 (Analysis #1 inclusion period), 22,234 adults without HIV started a new PrEP formulation in OPERA. The first formulation used during the study period was TAF/FTC oral (n=12,110, 54%), TDF/FTC oral (n=9,740, 44%), or CAB LA (n=384, 2%). An additional 292 individuals switched to CAB LA PrEP later during the study period, for a total of 767 people receiving CAB LA injections during the Analysis #1 inclusion period. Table 2 presents the precision estimates for proportions using a 95% confidence level, calculated using the standard confidence intervals equation [$p \pm 1.96\sqrt{((p*(1-p)/N)}$]. In both oral PrEP groups, the confidence interval width ranges from 0.01 to 0.02 for all proportions evaluated. For the CAB LA PrEP group, the confidence interval width ranges from 0.04 to 0.07 for all proportions evaluated.

Table 3. Precision estimates based on sample size and event proportions, using a 95% confidence level

PrEP formulation	Sample Size	Event Proportion	Lower Limit	Upper Limit	CI Width
CAB LA	767	0.1	0.08	0.12	0.04
	767	0.2	0.17	0.23	0.06
	767	0.3	0.27	0.33	0.06
	767	0.4	0.37	0.43	0.07
	767	0.5	0.46	0.54	0.07
	767	0.6	0.57	0.63	0.07
	767	0.7	0.67	0.73	0.06
	767	0.8	0.77	0.83	0.06
	767	0.9	0.88	0.92	0.04
TDF/FTC	9740	0.1	0.09	0.11	0.01
	9740	0.2	0.19	0.21	0.02
	9740	0.3	0.29	0.31	0.02
	9740	0.4	0.39	0.41	0.02
	9740	0.5	0.49	0.51	0.02
	9740	0.6	0.59	0.61	0.02
	9740	0.7	0.69	0.71	0.02
	9740	0.8	0.79	0.81	0.02
	9740	0.9	0.89	0.91	0.01
TAF/FTC	12110	0.1	0.09	0.11	0.01
	12110	0.2	0.19	0.21	0.01
	12110	0.3	0.29	0.31	0.02
	12110	0.4	0.39	0.41	0.02
	12110	0.5	0.49	0.51	0.02
	12110	0.6	0.59	0.61	0.02
	12110	0.7	0.69	0.71	0.02
	12110	0.8	0.79	0.81	0.01
	12110	0.9	0.89	0.91	0.01

7.6. Data management

EHR data from participating clinics are encrypted, extracted and processed daily. High levels of encryption are employed to ensure the security and confidentiality of protected health information (PHI). Data are deidentified for inclusion in the OPERA database.

7.7. Data analysis

All analyses conducted for this study will be descriptive and will aim at estimating frequencies of outcomes. Analyses to meet the study objectives will be conducted twice during the study period. Analysis #1 will include data from 01JAN2021-31DEC2023 (Obj. 1-1a) and from 21DEC2021 to 30JUN2024 (Obj 2-6). Analysis #2 will be a repeat of analysis #1 with data from 1JAN2021-31DEC2024 (Obj. 1-1a) and from 21DEC2021 to 30JUN2025 (Obj 2-6).

7.7.1. Primary analysis

7.7.1.1. Main Analytical approach

People without HIV in OPERA (Obj 1)
For each calendar year, the number and percentage of new HIV diagnoses will be reported out of all individuals receiving care at an OPERA clinic.

People with a new HIV diagnosis (Obj 1.a)
Among newly diagnosed people with HIV, PrEP use (never, use within ≤12 months before diagnosis, use >12 months before diagnosis) and PrEP characteristics will be described using counts and proportions for categorical variables and median and interquartile ranges for continuous variables.

PrEP users (Obj 2-5)
(Obj 2) Baseline demographic and clinical characteristics will be described at the start of PrEP use during the study period, by regimen type (oral or LA), using median and interquartile ranges for continuous variables and counts and proportions for categorical variables. Individuals contributing to both the oral and CAB LA PrEP groups may be included in both groups.

(Obj 3) The number, percentage, and incidence rate (per 100 person-years) of incident HIV diagnoses within 12 months of starting index PrEP and through study end will be described by route of administration (time-updated, oral or LA). The timing of HIV testing relative to PrEP start and HIV diagnosis will be described to assess to possibility of attributing HIV acquisition to the correct PrEP type. Incidence rates of HIV diagnoses (per 100 person-years) within 12 months of start and through study end will be estimated using time-updated univariate Poisson regression for each regimen type (time-updated, oral vs LA) to account for varying duration of follow-up.

(Obj 4) The percentage of days with access to oral PrEP and the percentage of days with coverage by CAB LA PrEP will be described over the first 12 months after index PrEP initiation.

(Obj 5) The frequency and rate (per 100 person-years) of HIV testing, STI screening, and STI diagnoses at index PrEP initiation and in the 12-months after index PrEP initiation. Characteristics of the tests conducted will also be described. Frequency and type of tests

performed will be described by type of healthcare provider ordering the test and clinic type. Rates of HIV and STI tests over the first 12 months will be estimated using time-updated univariate Poisson regression for each regimen type (oral vs LA).

People who could benefit from PrEP (Obj 6)

Baseline demographic and clinical characteristics will be described at the first OPERA visit with a PrEP indication, using median and interquartile ranges for continuous variables and counts and proportions for categorical variables. The frequency and rate (per 100 person-years) of HIV testing, HIV diagnoses, STI screening, and STI diagnoses will be described at the first OPERA visit with a PrEP indication and in the 12-months after the first indication. Characteristics of the tests conducted will also be described. Frequency and type of tests performed will be described by type of healthcare provider ordering the test and clinic type. Rates of HIV tests and diagnoses as well as STI tests and diagnoses over the first 12 months will be estimated using time-updated univariate Poisson regression

7.7.1.2. Data handling conventions

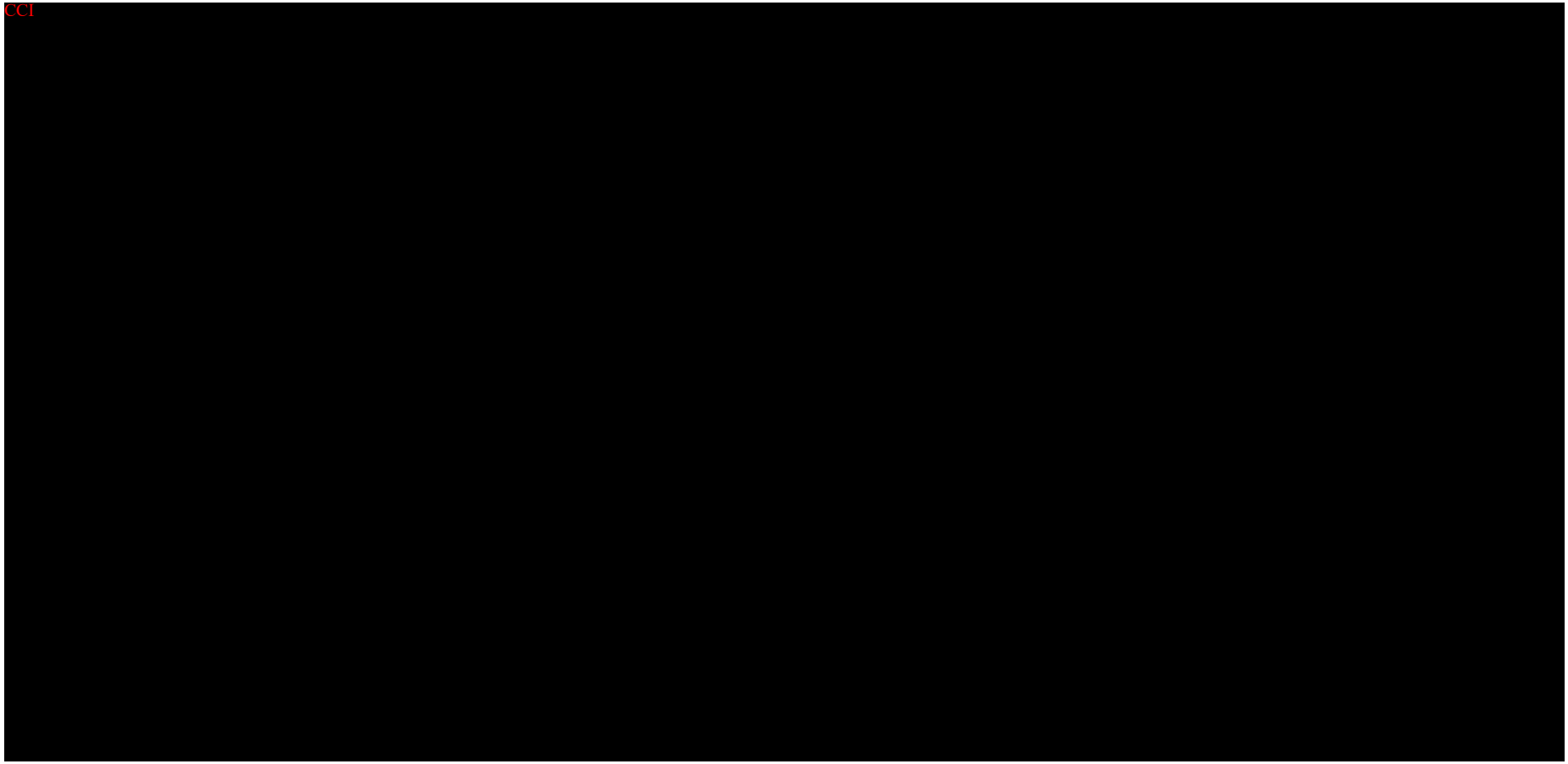
The data used for this research study are not identifiable by the research staff. However, all data, even when stripped of identifiers, are handled and treated, in motion and at rest, as though the data could be identified. All data are managed according to U.S. regulations such as HIPAA and HITECH. These regulations and guidelines expand upon the ethical principles detailed in the 1964 Declaration of Helsinki.

7.8. Quality control and Quality Assurance

This study will be conducted according to local quality control processes. This procedure requires documented evidence that the study protocol has been correctly interpreted and executed.
Epividian has working practices & procedures governing the use of observational data, the development of analysis specifications and plans, the development of analytical programming and the analytical quality assurance (QA) process and the scientific review of reports as well as clinical advisory charters for the clinical review of output intended for public domain. Working practices for the development of analysis specifications include basic identifying information, background material, relevant definitions of key study variables, population definitions, baseline definitions, specific requirements for dataset creation, and statistical requirements such as eligibility criteria, exposures, outcomes and model fitting. Working practices for programming include naming conventions, proper code documentation and commentary, content, appearance, efficiencies (i.e. use of macros), and organization of output, maintainability and generalizability. Working practices for programming QA include self-reviews of observational counts, missing data values, many-to-many merges, variable formatting, numeric-character & character-numeric conversions, uninitialized variables, unresolved macro references, report completeness and report-to-specification correspondence, and system errors and logs. The QA team review may include small sample spot-checking, coding log reviews, complete coding review, selected observations from intermediary dataset reviews, and/or independent programming to reproduce the results. Documentation of non-public domain reports includes market, scientific, statistical, and clinical review. Documentation of scientific protocols, reports and manuscripts intended for

public domain follows two sequential steps: an internal-to-Epividian epidemiological, statistical, and clinical review, followed by a clinical/epidemiological external advisory board review.

All analytical data, coding algorithms, QA documentation and report outputs will be retained per Epividian standard practices. Figure 2 presents an overview of study processes.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7.9. Limitations of the research methods

CAB LA PrEP is directly observed; thus, injection records in the EHR provide certainty that PrEP was received and the exact timing of injections. However, oral PrEP use and timing cannot be ascertained with as much precision because only prescription records are available in the EHR. Incident HIV diagnosis can only be ascertained if tests are administered. Therefore, information on incident HIV diagnosis and exact timing may be subject to measurement error. Additionally, EHR data do not contain the following information to identify people who could benefit from PrEP: Other indications cannot be assessed in EHR data (HIV+ partner, ≥1 sex partner of unknown HIV status, inconsistent condom use, sex work)
Issues confronting population-level assessments include such aspects as differential medical care by practice size and specialty, academic and research orientation of the health care practitioner, ethnic-based & gender-based attitudes and geographic regional health care practices. OPERA clinical data is collected at point-of-care and is subject to the record-keeping practices of each healthcare provider and the standards of each clinic or organization. Patients may see multiple physician practices for various conditions, which may result in incomplete case ascertainment. Data is collected for the medical management of patients and is not directly intended for research purposes, but rather for the care and management of individual patients and patient populations.

7.9.1. Study closure/uninterpretability of results

Not applicable: observational study.

8. PROTECTION OF HUMAN SUBJECTS

8.1. Ethical approval and subject consent

This study will comply with all applicable laws regarding participant privacy. No direct subject contact or primary collection of individual human subject data will occur. Study results will be in tabular form and aggregate analyses that omits subject identification, therefore informed consent, ethics committee or IRB approval are not required. Any publications and reports will not include subject identifiers.

Clinical information is originally compiled into separate CHORUS™ databases for each clinic. This protected health information (PHI) is used in the creation of the CHORUS™ analytics and reporting used by each practice and its providers as part of Quality Improvement activities in an effort to improve care of patients. The data collection occurs via a secure and encrypted connection as part of Epividian's privacy and security policies and systems, which are routinely reviewed by a third-party privacy and security advisory organization.

Subsequently, the clinical data in each CHORUS™ database is de-identified and aggregated

into the OPERA® Database following the guidelines of the Health Insurance Portability and Accountability Act (HIPAA) and the Health Information Technology for Economic and Clinical Health Act (HITECH).

Business Associate Agreements (BAA) in place between Epividian and all medical practices govern, following the guidelines established in HIPAA and HITECH, the encryption, transportation, aggregation, de-identification and use of all clinical data in either the CHORUS™ reporting platform or the OPERA® Database. All medical practices are responsible for obtaining proper HIPAA consent for their patients. With BAAs in place and subsequent de-identification, a separate informed consent for each individual, non-interventional study is not required. Additionally, investigational review board (IRB) approval has been granted for the processes of data extraction, transmission, management, analysis and reporting of healthcare data from OPERA® by Advarra IRB.

8.2. Subject confidentiality

All clinical data in CHORUS™ is PHI and managed as such according to HIPAA, HITECH and relevant state regulations. The CHORUS™ portal, as a Quality Improvement activity, is accessed securely by clinic staff to view PHI for only those patients seen at the practice. All clinical data is subsequently de-identified as per HIPAA and HITECH in OPERA® with all reports submitted at the aggregated population level in OPERA®. No personally identifiable information is available in the OPERA® Database. The OPERA® Epidemiology & Clinical Advisory Board (ECAB) provides clinical and methodological review & oversight.

9. LEGAL BASIS FOR PROCESSING INDIVIDUAL HUMAN DATA

The authors confirm that study data is Individual Human Data (IHD) not owned by GSK, but that the proposed use of the IHD aligns with the 'purpose of use' outlined in the source contract and/or the terms and conditions of use of the data source and it will comply with any specified prohibitions of use.

10. MANAGEMENT AND REPORTING OF ADVERSE EVENTS/ADVERSE REACTIONS

The study design includes analysis of secondary data, which includes data that were previously collected for other purposes e.g., routine healthcare encounters. There is no potential to collect serious and non-serious AEs, pregnancy exposures, or incidents related to any GSK/ViiV product during the conduct of this research, as the minimum criteria of identifiable patient, reporter, exposure and event, needed to collect and report individual case safety reports are not present in the data source. The study is based on secondary anonymised healthcare data which lack an identifiable patient and reporter and are insufficient to establish attribution between a potential safety event and an individual patient using a GSK/ViiV product.

11. PLANS FOR DISSEMINATING AND COMMUNICATING STUDY RESULTS

The target audience for these data includes healthcare providers, health plan population-based decision-makers, and regulatory and health authorities.

Results will be published via study reports. Study results will be presented at scientific conferences and published in peer reviewed journal publication.

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ANNEX 1 TABLES

Table shells for Analysis #1 are presented. Tables will be identical for Analysis #2, with the exception that study periods will be updated.

Table 1. Identification of the population of people without HIV in OPERA (Analysis #1)

	Included N (%)	Excluded N (%)
All individuals in OPERA		
≥1 clinical encounter between 01JAN2021 and 31DEC2021		
≥18 years old at first clinical encounter in 2021		
No evidence of HIV diagnosis before the first clinical encounter in 2021 [2021 pop]		
≥1 clinical encounter between 01JAN2022 and 31DEC2022		
≥18 years old at first clinical encounter in 2022		
No evidence of HIV diagnosis before the first clinical encounter in 2022 [2022 pop]		
≥1 clinical encounter between 01JAN2023 and 31DEC2023		
≥18 years old at first clinical encounter in 2023		
No evidence of HIV diagnosis before the first clinical encounter in 2023 [2023 pop]		

Table 2. Annual HIV incidence among people without HIV (Analysis #1)

	People without HIV, N	Incident HIV,[a] n (%)
2021		
2022		
2023		

[a] New HIV diagnosis or positive HIV test (RNA, antigen/antibody)

Table 3. PrEP use among people with incident HIV (Analysis #1)

	People with incident HIV[a] N =
Never received PrEP, n (%)	
Ever received PrEP, n (%)	
Total number of days on PrEP, median (IQR)[b]	
Number of PrEP formulations received	
1, n (%)	
2, n (%)	
3, n (%)	
Any gaps between formulations, n (%)[c]	
Duration of gaps between formulations, median (IQR)	
PrEP use within ≤12 months before/on HIV diagnosis, n (%)	
Oral PrEP, n (%)	
TDF/FTC, n (%)	
TAF/FTC, n (%)	
CAB LA, n (%)	
Past PrEP use >12 months before HIV diagnosis, n (%)	
Oral PrEP, n (%)	
TDF/FTC, n (%)	
TAF/FTC, n (%)	
CAB LA, n (%)	

[a] New HIV diagnosis or positive HIV test (RNA, antigen/antibody)

[b] Including all formulations; gaps without PrEP do not count toward the total number of days on PrEP

[c] Gap ≥31 days after oral PrEP, gap ≥37 days after first CAB LA injection, or gap ≥67 days after 2nd or subsequent CAB LA injection

Table 4. Identification of the PrEP users population

	Included N (%)	Excluded N (%)
All individuals in OPERA		
Ever received a PrEP prescription/injection in OPERA while HIV negative		
Start a new PrEP formulation (TDF/FTC, TAF/FTC, CAB LA)[a] between 21DEC2021 and 30JUN2023		
≥18 years old at start of index PrEP regimen		

[a] Switch from one formulation to another or return to the same formulation after a pause ≥61 days without PrEP

Table 5. PrEP formulations used among PrEP users

	PrEP users
PrEP formulation at index, N	
Oral, n (%)	
TDF/FTC, n (%)	
TAF/FTC, n (%)	
CAB LA, n (%)	
Switch from oral to CAB LA PrEP within 12 months of initiating index oral PrEP, n (%)	
Switch from CAB LA to oral PrEP within 12 months of initiating index CAB LA, n (%)	

Table 6. Demographic characteristics at start of PrEP regimen[a] among PrEP users

	Oral PrEP N=	CAB LA PrEP N=
Age		
Median (IQR)		
18-29		
30-39		
40-49		
50-59		
≥60		
Sex		
Female		
Male		
Unknown		
Transgender, n (%)[b]		
Race		
Black		
Asian		
White		
Mixed or Other races		
Unknown race		
Hispanic ethnicity		
US Region		
Northeast		
South		
Midwest		
West		
US Territories		
Marital status		
Single		
Married/Domestic Partner		
Widowed		
Separated/divorced		
Unknown		
Payer[c]		
Medicaid		
Medicare		
Commercial Insurance		
Other		
Unknown		

[a] Individuals who switched PrEP type during follow-up are included in both groups

[b] Gender identity is not reported by all clinics and physicians; available data may be insufficient to infer cisgender identity.

[c] Payer categories are not mutually exclusive.

Table 7. Clinical care characteristics at start of PrEP regimen[a] among PrEP users

	Oral PrEP N=	CAB LA PrEP N=
Months since first OPERA visit, median (IQR)		
Any visits with OPERA provider within 12 months prior to start, n (%)		
Number of visits, median (IQR)		
Prescriber specialty, n (%)		
Infectious diseases		
General practice		
Other		
Unknown		
Clinic type, n (%)		
Healthcare center		
Wellness center		
Other		

[a] Individuals who switched PrEP type during follow-up are included in both groups

Table 8. Sexual health characteristics at start of PrEP regimen[a] among PrEP users

	Oral PrEP N=	CAB LA PrEP N=
History of STI (ever)		
Syphilis		
Gonorrhea		
Chlamydia		
Chancroid		
Lymphogranuloma venereum		
Mycoplasma genitalium		
Herpes Simplex-2		
Trichomoniasis		
Human papilloma virus/genital warts		
History of STI (past 3 months)		
Syphilis		
Gonorrhea		
Chlamydia		
Chancroid		
Lymphogranuloma venereum		
Mycoplasma genitalium		
Herpes Simplex-2		
Trichomoniasis		
Human papilloma virus/genital warts		

[a] Individuals who switched PrEP type during follow-up are included in both groups

Table 9. Incident HIV[a] within 12 months of index and through study end among PrEP users

	Oral PrEP N=	CAB LA PrEP N=
Within 12 months of index		
HIV diagnosis, n (%)		
Months from start of PrEP type to HIV diagnosis, median (IQR)		
Negative HIV test within 2 weeks before/on start of PrEP type, n (%)		
Through study end		
HIV diagnosis, n (%)		
Months from start of PrEP type to HIV diagnosis, median (IQR)		
Negative HIV test within 2 weeks before/on start of PrEP type, n (%)		

[a] Incident HIV is only counted for the PrEP type used at the time of diagnosis

Table 10 Incidence rate of HIV[a] within 12 months of index and through study end among PrEP users

	Oral PrEP N=	CAB LA PrEP N=
Within 12 months of index		
HIV diagnosis, n (%)		
Person-years of follow-up		
IR per 100 py (95% CI)		
Through study end		
HIV diagnosis, n (%)		
Person-years of follow-up		
IR per 100 py (95% CI)		

[a] Incident HIV is only counted for the PrEP type used at the time of diagnosis

Table 11. Oral PrEP coverage within 12 months of index among **oral** PrEP users

	Oral PrEP N=
Mean # pills prescribed (SD)	
Median # of pills prescribed (IQR)	
Mean days of follow-up on oral PrEP[a] (SD)	
Median days of follow-up on oral PrEP[a] (IQR)	
Mean % access (total pills prescribed/days of follow-up) (SD)	
Median % access (total pills prescribed/days of follow-up) (IQR)	

[a] If index PrEP is oral: shortest of (a) days from index to first CAB LA injection or (b) 12 months after index; if index PrEP is CAB LA injections: shortest of (a) days from start of switch to oral PrEP to study end or (b) 12 months after index

Table 12. CAB LA PrEP coverage within 12 months of index among **CAB LA** PrEP users

	CAB LA PrEP N=
Mean days covered[a] (SD)	
Median days covered[a] (IQR)	
Mean days of follow-up on CAB LA PrEP[b] (SD)	
Median days of follow-up on CAB LA PrEP[b] (IQR)	
Mean % coverage (days covered/days of follow-up) (SD)	
Median % coverage (days covered/days of follow-up) (IQR)	

[b] Total days between injections, up to 37 days between the first 2 injections or up to 67 days between subsequent injections

[a] If index PrEP is oral: shortest of (a) days from index to first CAB LA injection or (b) 12 months after index; if index PrEP is CAB LA injections: shortest of (a) days from first CAB LA injection to study end or (b) 12 months after index

Table 13. Incidence rate of HIV testing events within 12 months of index among PrEP users[a]

	Oral PrEP N=	CAB LA PrEP N=
Total # HIV testing events within 12 months of index, n		
Person-years of follow-up		
IR per 100 py (95% CI)		

[a] HIV testing events are only counted for the PrEP type used at the time of diagnosis

Table 14. Frequency and type of HIV testing among PrEP users[a]

	Oral PrEP N=	CAB LA PrEP N=
HIV test within 14 days before/on day of PrEP type start, n (%)		
Test type		
RNA only, n (%)		
Quantitative RNA test, n (%)		
Qualitative RNA test, n (%)		
Ag/Ab only, n (%)		
Rapid test only, n (%)		
Both RNA and Ag/Ab, n (%)		
Quantitative RNA test, n (%)		
Qualitative RNA test, n (%)		
Both RNA and rapid test, n (%)		
RNA, Ab/Ag and rapid tests, n (%)		
Days from test to PrEP type start, median (IQR)		
Any HIV test within 12 months after PrEP type start, n (%)		
Total number of testing events[b], N		
Test type		
RNA only, n (%)		
Quantitative RNA test, n (%)		
Qualitative RNA test, n (%)		
Ag/Ab only, n (%)		
Both RNA and Ag/Ab, n (%)		
Quantitative RNA test, n (%)		
Qualitative RNA test, n (%)		
Number of HIV testing events[b] per person, median (IQR)		
Average testing interval per person (#testing events /weeks on PrEP type), median (IQR)		
Testing on schedule (oral: every 3 months (76-104 days); CAB LA: ±14 days of each injection), n (%)		

[a] Tests are only counted for the PrEP type used at the time of diagnosis

[b] Multiple HIV tests on the same day count as one testing event

Table 15. Frequency and type of HIV tests among oral PrEP users, by healthcare provider type [a]

	MD or DO	Physician Assistant	Nurse Practitioner	Other/unknown
Total number of HIV testing events[b] ordered				
Test type				
RNA only, n (%)				
Quantitative RNA test, n (%)				
Qualitative RNA test, n (%)				
Ag/Ab only, n (%)				
Rapid test only, n (%)				
Both RNA and Ag/Ab, n (%)				
Quantitative RNA test, n (%)				
Qualitative RNA test, n (%)				
Both RNA and rapid test, n (%)				
RNA, Ab/Ag and rapid tests, n (%)				
Testing on schedule (≤14 days before/at start or 3 months (76-104 days) after the last test, as applicable), n (%)				

[a] Assessed at the test-level

[b] Multiple HIV tests on the same day count as one testing event

Table 16. Frequency and type of HIV tests among CAB LA PrEP users, by healthcare provider type[a]

	MD or DO	Physician Associate	Nurse Practitioner	Other/unknown
Total number of HIV testing events[b] ordered				
Test type				
RNA only, n (%)				
Quantitative RNA test, n (%)				
Qualitative RNA test, n (%)				
Ag/Ab only, n (%)				
Rapid test only, n (%)				
Both RNA and Ag/Ab, n (%)				
Quantitative RNA test, n (%)				
Qualitative RNA test, n (%)				
Both RNA and rapid test, n (%)				
RNA, Ab/Ag and rapid tests, n (%)				
Testing on schedule (≤14 days before/at first injection or ±14 days of each subsequent injection, as applicable), n (%)				

[a] Assessed at the test-level

[b] Multiple HIV tests on the same day count as one testing event

Table 17. Frequency and type of HIV tests among **oral** PrEP users, by healthcare clinic type[a]

	Healthcare center	Wellness center	Other
Total number of HIV testing events[b] ordered			
Test type			
RNA only, n (%)			
Quantitative RNA test, n (%)			
Qualitative RNA test, n (%)			
Ag/Ab only, n (%)			
Rapid test only, n (%)			
Both RNA and Ag/Ab, n (%)			
Quantitative RNA test, n (%)			
Qualitative RNA test, n (%)			
Both RNA and rapid test, n (%)			
RNA, Ab/Ag and rapid tests, n (%)			
Testing on schedule (≤14 days before/at first injection or ±14 days of each subsequent injection, as applicable), n (%)			

[a] Assessed at the test-level

[b] Multiple HIV tests on the same day count as one testing event

Table 18. Frequency and type of HIV tests among **CAB LA** PrEP users, by healthcare clinic type[a]

	Healthcare center	Wellness center	Other
Total number of HIV testing events[b] ordered			
Test type			
RNA only, n (%)			
Quantitative RNA test, n (%)			
Qualitative RNA test, n (%)			
Ag/Ab only, n (%)			
Rapid test only, n (%)			
Both RNA and Ag/Ab, n (%)			
Quantitative RNA test, n (%)			
Qualitative RNA test, n (%)			
Both RNA and rapid test, n (%)			
RNA, Ab/Ag and rapid tests, n (%)			
Testing on schedule (≤14 days before/at first injection or ±14 days of each subsequent injection, as applicable), n (%)			

[a] Assessed at the test-level

[b] Multiple HIV tests on the same day count as one testing event

Table 19. Incidence rate of STI screening events within 12 months of index among PrEP users[a]

	Oral PrEP N=	CAB LA PrEP N=
Total # STI screening events within 12 months of index, n		
Person-years of follow-up		
IR per 100 py (95% CI)		

Table 20. Frequency and type of STI screening among PrEP users[a]

	Oral PrEP N=	CAB LA PrEP N=
STI screening within 14 days before/on day of PrEP type start, n (%)		
STI tested, n (%)		
Syphilis		
Gonorrhea		
Chlamydia		
Chancroid		
Lymphogranuloma venereum		
Mycoplasma genitalium		
Herpes Simplex-2		
Trichomoniasis		
Human papilloma virus/genital warts		
HBV		
HCV		
Days from test to PrEP type start, median (IQR)		
Any STI screening within 12 months after PrEP type start, n (%)		
Number of STI screening events[b], median (IQR)		
Syphilis, n (%)		
Gonorrhea, n (%)		
Chlamydia, n (%)		
Chancroid, n (%)		
Lymphogranuloma venereum, n (%)		
Mycoplasma genitalium, n (%)		
Herpes Simplex-2, n (%)		
Trichomoniasis, n (%)		
Human papilloma virus/genital warts, n (%)		
HBV, n (%)		
HCV, n (%)		
Average screening interval per person (# screening events/weeks on PrEP type), median (IQR)		
Testing every 3 months (76-104 days)[c], n (%)		
Testing every 6 months (168-196 days)[d], n (%)		
Testing every 12 months (351-379 days)[e], n (%)		

[a] Tests are only counted for the PrEP type used at the time of diagnosis

[b] Multiple STI tests on the same day count as one screening event

[c] Recommended gonorrhea, chlamydia and syphilis screening interval for MSM and transgender women who have sex with men

[d] Recommended gonorrhea and syphilis screening interval for heterosexual women and men
[e] Recommended chlamydia screening interval for heterosexual women and men

Table 21. Frequency and type of STI screening among **oral** PrEP users, by healthcare provider type[a]

	MD or DO	Physician Associate	Nurse Practitioner	Other/unknown
Total number of STI screening events[b] ordered				
STI tested, n (%)				
Syphilis				
Gonorrhea				
Chlamydia				
Chancroid				
Lymphogranuloma venereum				
Mycoplasma genitalium				
Herpes Simplex-2				
Trichomoniasis				
Human papilloma virus/genital warts				
HBV				
HCV				
Testing 3 months (76-104 days) after last test[c], n (%)				
Testing 6 months (168-196 days) after last test[d], n (%)				
Testing 12 months (351-379 days) after last test[d], n (%)				

[a] Assessed at the test-level
[b] Multiple STI tests on the same day count as one screening event
[c] Recommended gonorrhea, chlamydia and syphilis screening interval for MSM and transgender women who have sex with men
[d] Recommended gonorrhea and syphilis screening interval for heterosexual women and men
[e] Recommended chlamydia screening interval for heterosexual women and men

Table 22. Frequency and type of STI screening among **CAB LA** PrEP users, by healthcare provider type[a]

	MD or DO	Physician Associate	Nurse Practitioner	Other/unknown
Total number of STI screening events[b] ordered				
STI tested, n (%)				
Syphilis				
Gonorrhea				
Chlamydia				
Chancroid				
Lymphogranuloma venereum				
Mycoplasma genitalium				
Herpes Simplex-2				
Trichomoniasis				
Human papilloma virus/genital warts				
HBV				
HCV				
Testing 3 months (76-104 days) after last test[c], n (%)				
Testing 6 months (168-196 days) after last test[d], n (%)				
Testing 12 months (351-379 days) after last test[d], n (%)				

[a] Assessed at the test-level

[b] Multiple STI tests on the same day count as one screening event

[c] Recommended gonorrhea, chlamydia and syphilis screening interval for MSM and transgender women who have sex with men

[d] Recommended gonorrhea and syphilis screening interval for heterosexual women and men

[e] Recommended chlamydia screening interval for heterosexual women and men

Table 23. Frequency and type of STI screening among **oral** PrEP users, by clinic type[a]

	Healthcare Center	Wellness Center	Other
Total number of STI screening events[b] ordered			
STI tested, n (%)			
Syphilis			
Gonorrhea			
Chlamydia			
Chancroid			
Lymphogranuloma venereum			
Mycoplasma genitalium			
Herpes Simplex-2			
Trichomoniasis			
Human papilloma virus/genital warts			
HBV			
HCV			
Testing 3 months (76-104 days) after last test[c], n (%)			
Testing 6 months (168-196 days) after last test[d], n (%)			
Testing 12 months (351-379 days) after last test[d], n (%)			

[a] Assessed at the test-level
[b] Multiple STI tests on the same day count as one screening event
[c] Recommended gonorrhea, chlamydia and syphilis screening interval for MSM and transgender women who have sex with men
[d] Recommended gonorrhea and syphilis screening interval for heterosexual women and men
[e] Recommended chlamydia screening interval for heterosexual women and men

Table 24. Frequency and type of STI screening among **CAB LA** PrEP users, by clinic type type[a]

	Healthcare Center	Wellness Center	Other
Total number of STI screening events[b] ordered			
STI tested, n (%)			
Syphilis			
Gonorrhea			
Chlamydia			
Chancroid			
Lymphogranuloma venereum			
Mycoplasma genitalium			
Herpes Simplex-2			
Trichomoniasis			
Human papilloma virus/genital warts			
HBV			
HCV			
Testing 3 months (76-104 days) after last test[c], n (%)			
Testing 6 months (168-196 days) after last test[d], n (%)			
Testing 12 months (351-379 days) after last test[d], n (%)			

[a] Assessed at the test-level
[b] Multiple STI tests on the same day count as one screening event
[c] Recommended gonorrhea, chlamydia and syphilis screening interval for MSM and transgender women who have sex with men
[d] Recommended gonorrhea and syphilis screening interval for heterosexual women and men
[e] Recommended chlamydia screening interval for heterosexual women and men

Table 25. Correspondence between HIV testing and STI screening schedule among PrEP users

	Oral PrEP N=	CAB LA PrEP N=
HIV testing on schedule (oral: every 3 months (76-104 days); CAB LA: ±14 days of each injection), n (%)		
STI screening every 3 months (76-104 days)[c], n (%)		
STI screening every 6 months (168-196 days)[d], n (%)		
STI screening every 12 months (351-379 days)[e], n (%)		
HIV testing NOT on schedule (oral: every 3 months (76-104 days); CAB LA: ±14 days of each injection), n (%)		
STI screening every 3 months (76-104 days)[c], n (%)		
STI screening every 6 months (168-196 days)[d], n (%)		
STI screening every 12 months (351-379 days)[e], n (%)		

Table 26. STI diagnoses among PrEP users[a]

	Oral PrEP N=	CAB LA PrEP N=
STI diagnosis within 14 days before/on day of PrEP type start, n (%)		
Any, n (%)		
Syphilis, n (%)		
Gonorrhea, n (%)		
Chlamydia, n (%)		
Chancroid, n (%)		
Lymphogranuloma venereum, n (%)		
Mycoplasma genitalium, n (%)		
Herpes Simplex-2, n (%)		
Trichomoniasis, n (%)		
Human papilloma virus/genital warts, n (%)		
HBV, n (%)		
HCV, n (%)		
STI diagnosis within 12 months after PrEP type start, n (%)		
Any, n (%)		
Syphilis, n (%)		
Gonorrhea, n (%)		
Chlamydia, n (%)		
Chancroid, n (%)		
Lymphogranuloma venereum, n (%)		
Mycoplasma genitalium, n (%)		
Herpes Simplex-2, n (%)		
Trichomoniasis, n (%)		
Human papilloma virus/genital warts, n (%)		
HBV, n (%)		
HCV, n (%)		

[a] Tests are only counted for the PrEP type used at the time of diagnosis

Table 27. Incidence rate of STI diagnoses within 12 months of index among PrEP users[a]

	Oral PrEP N=	CAB LA PrEP N=
Total # STI diagnoses within 12 months of index, n		
Person-years of follow-up		
IR per 100 py (95% CI)		

Table 28. Identification of the people who could benefit from PrEP population

	Included N (%)	Excluded N (%)
All individuals in OPERA		
≥1 clinical encounter between 21DEC2021 and 30JUN2023		
≥18 years old at first clinical encounter in study period		
Any indication for PrEP[a]		
No PrEP use between 21DEC2021 and 30JUN2023		

[a] Bacterial STI in past 12 months (gonorrhea, syphilis, chlamydia), alcohol use disorder, illicit non-injection drug use, injection drug use. Black woman, transgender woman, men who have sex with men, aged 18-24 years, any history of PrEP use

Table 29. Distribution of PrEP indication/priority group membership[a] among people who could benefit from PrEP

	People who could benefit from PrEP N=
Bacterial STI in past 12 months (gonorrhea, syphilis, chlamydia), n (%)	
Alcohol use disorder, n (%)	
Illicit non-injection drug use, n (%)	
Injection drug use, n (%)	
Black women, n (%)	
Transgender women, n (%)	
Men who have sex with men, n (%)	
Individuals aged 18-24 years, n (%)	
Any history of PrEP use, n (%)	

[a] Groups are not mutually exclusive

Table 30. Demographic characteristics at the first OPERA visit with indication for PrEP during study period among people who could benefit from PrEP

	People who could benefit from PrEP N=
Age	
Median (IQR)	
18-29	
30-39	
40-49	
50-59	
≥60	
Sex	
Female	
Male	
Unknown	
Transgender, n (%)[b]	
Race	
Black	
Asian	
White	
Mixed or Other races	
Unknown race	
Hispanic ethnicity	
US Region	
Northeast	
South	
Midwest	
West	
US Territories	
Marital status	
Single	
Married/Domestic Partner	
Widowed	
Separated/divorced	
Unknown	
Payer[c]	
Medicaid	
Medicare	
Commercial Insurance	
Other	
Unknown	

[a] Individuals who switched PrEP type during follow-up are included in both groups

[b] Gender identity is not reported by all clinics and physicians; available data may be insufficient to infer cisgender identity.

[c] Payer categories are not mutually exclusive.

Table 31. Clinical care characteristics at the first OPERA visit with indication for PrEP during study period among people who could benefit from PrEP

	People who could benefit from PrEP N=
Months since first OPERA visit, median (IQR)	
Any visits with OPERA provider within 12 months prior to start, n (%)	
Number of visits, median (IQR)	
Prescriber specialty, n (%)	
Infectious diseases	
General practice	
Other	
Unknown	
Clinic type, n (%)	
Healthcare center	
Wellness center	
Other	

Table 32. Sexual health characteristics at the first OPERA visit with indication for PrEP during study period among people who could benefit from PrEP

	People who could benefit from PrEP N=
History of STI (ever)	
Syphilis	
Gonorrhea	
Chlamydia	
Chancroid	
Lymphogranuloma venereum	
Mycoplasma genitalium	
Herpes Simplex-2	
Trichomoniasis	
Human papilloma virus/genital warts	
History of STI (past 3 months)	
Syphilis	
Gonorrhea	
Chlamydia	
Chancroid	
Lymphogranuloma venereum	
Mycoplasma genitalium	
Herpes Simplex-2	
Trichomoniasis	
Human papilloma virus/genital warts	

Table 33. HIV testing among people who could benefit from PrEP

	People who could benefit from PrEP N=
HIV test within 14 days before/on day of PrEP type start, n (%)	
Test type	
RNA only, n (%)	
Quantitative RNA test, n (%)	
Qualitative RNA test, n (%)	
Ag/Ab only, n (%)	
Rapid test only, n (%)	
Both RNA and Ag/Ab, n (%)	
Quantitative RNA test, n (%)	
Qualitative RNA test, n (%)	
Both RNA and rapid test, n (%)	
RNA, Ab/Ag and rapid tests, n (%)	
Days from test to PrEP type start, median (IQR)	
Any HIV test within 12 months after PrEP type start, n (%)	
Total number of testing events[b], N	
Test type	
RNA only, n (%)	
Quantitative RNA test, n (%)	
Qualitative RNA test, n (%)	
Ag/Ab only, n (%)	
Both RNA and Ag/Ab, n (%)	
Quantitative RNA test, n (%)	
Qualitative RNA test, n (%)	
Number of HIV testing events[b] per person, median (IQR)	
Average testing interval per person (#testing events /weeks on PrEP type), median (IQR)	
Testing on schedule (every 3-6 months (76-196 days)), n (%)	

[b] Multiple HIV tests on the same day count as one testing event

Table 34. Incidence rate of HIV testing events and HIV diagnosis within 12 months of index among people who could benefit from PrEP

	People who could benefit from PrEP N=
Total # HIV testing events within 12 months of index, n	
Person-years of follow-up	
IR per 100 py (95% CI)	

Table 35. Incident HIV[a] within 12 months of index among people who could benefit from PrEP

	Oral PrEP N=
HIV diagnosis, n (%)	
Months from start of PrEP type to HIV diagnosis, median (IQR)	
Negative HIV test within 2 weeks before/on start of PrEP type, n (%)	
Person-years of follow-up	
IR per 100 py (95% CI)	

Table 36. Frequency and type of HIV tests among people who could benefit from PrEP, by healthcare provider type[a]

	MD or DO	Physician Associate	Nurse Practitioner	Other/unknown
Total number of HIV testing events[b] ordered				
Test type				
RNA only, n (%)				
Quantitative RNA test, n (%)				
Qualitative RNA test, n (%)				
Ag/Ab only, n (%)				
Rapid test only, n (%)				
Both RNA and Ag/Ab, n (%)				
Quantitative RNA test, n (%)				
Qualitative RNA test, n (%)				
Both RNA and rapid test, n (%)				
RNA, Ab/Ag and rapid tests, n (%)				
Testing 3-6 months (76-196 days) after last test, n (%)				

[a] Assessed at the test-level

[b] Multiple HIV tests on the same day count as one testing event

Table 37. Frequency and type of HIV tests within 12 months of index among people who could benefit from PrEP, by clinic type[a]

	Healthcare Center	Wellness Center	Other
Total number of HIV testing events[b] ordered			
Test type			
RNA only, n (%)			
Quantitative RNA test, n (%)			
Qualitative RNA test, n (%)			
Ag/Ab only, n (%)			
Rapid test only, n (%)			
Both RNA and Ag/Ab, n (%)			
Quantitative RNA test, n (%)			
Qualitative RNA test, n (%)			
Both RNA and rapid test, n (%)			
RNA, Ab/Ag and rapid tests, n (%)			
Testing 3-6 months (76-196 days) after last test, n (%)			

[a] Assessed at the test-level

[b] Multiple HIV tests on the same day count as one testing event

Table 38. STI screening among people who could benefit from PrEP

	People who could benefit from PrEP N=
STI screening within 14 days before/on day of PrEP type start, n (%)	
STI tested, n (%)	
Syphilis	
Gonorrhea	
Chlamydia	
Chancroid	
Lymphogranuloma venereum	
Mycoplasma genitalium	
Herpes Simplex-2	
Trichomoniasis	
Human papilloma virus/genital warts	
HBV	
HCV	
Days from test to PrEP type start, median (IQR)	
Any STI screening within 12 months after PrEP type start, n (%)	
Number of STI screening events[b], median (IQR)	
Syphilis, n (%)	
Gonorrhea, n (%)	
Chlamydia, n (%)	
Chancroid, n (%)	
Lymphogranuloma venereum, n (%)	
Mycoplasma genitalium, n (%)	
Herpes Simplex-2, n (%)	
Trichomoniasis, n (%)	
Human papilloma virus/genital warts, n (%)	
HBV, n (%)	
HCV, n (%)	
Average screening interval per person (# screening events/weeks on PrEP type), median (IQR)	
Testing every 3 months[c], n (%)	
Testing every 6 months[d], n (%)	
Testing every 12 months[e], n (%)	

[a] Tests are only counted for the PrEP type used at the time of diagnosis
[b] Multiple STI tests on the same day count as one screening event
[c] Recommended gonorrhea, chlamydia and syphilis screening interval for MSM and transgender women who have sex with men
[d] Recommended gonorrhea and syphilis screening interval for heterosexual women and men
[e] Recommended chlamydia screening interval for heterosexual women and men

Table 39. Incidence rate of STI screening events within 12 months of index among people who could benefit from PrEP

	People who could benefit from PrEP N=
Total # STI screening events within 12 months of index, n	
Person-years of follow-up	
IR per 100 py (95% CI)	

Table 40. Frequency and type of STI screening among people who could benefit from PrEP, by healthcare provider type[a]

	MD or DO	Physician Associate	Nurse Practitioner	Other/unknown
Total number of STI screening events[b] ordered				
STI tested, n (%)				
Syphilis				
Gonorrhea				
Chlamydia				
Chancroid				
Lymphogranuloma venereum				
Mycoplasma genitalium				
Herpes Simplex-2				
Trichomoniasis				
Human papilloma virus/genital warts				
HBV				
HCV				
Testing 3 months (76-104 days) after last test[c], n (%)				
Testing 6 months (168-196 days) after last test[d], n (%)				
Testing 12 months (351-379 days) after last test[d], n (%)				

[a] Assessed at the test-level

[b] Multiple STI tests on the same day count as one screening event

[c] Recommended gonorrhea, chlamydia and syphilis screening interval for MSM and transgender women who have sex with men

[d] Recommended gonorrhea and syphilis screening interval for heterosexual women and men

[e] Recommended chlamydia screening interval for heterosexual women and men

Table 41. Frequency and type of STI screening among people who could benefit from PrEP, by clinic type[a]

	MD or DO	Physician Associate	Nurse Practitioner	Other/unknown
Total number of STI screening events[b] ordered				
STI tested, n (%)				
Syphilis				
Gonorrhea				
Chlamydia				
Chancroid				
Lymphogranuloma venereum				
Mycoplasma genitalium				
Herpes Simplex-2				
Trichomoniasis				
Human papilloma virus/genital warts				
HBV				
HCV				
Testing 3 months (76-104 days) after last test[c], n (%)				
Testing 6 months (168-196 days) after last test[d], n (%)				
Testing 12 months (351-379 days) after last test[d], n (%)				

[a] Assessed at the test-level

[b] Multiple STI tests on the same day count as one screening event

[c] Recommended gonorrhea, chlamydia and syphilis screening interval for MSM and transgender women who have sex with men

[d] Recommended gonorrhea and syphilis screening interval for heterosexual women and men

[e] Recommended chlamydia screening interval for heterosexual women and men

Table 42. STI diagnoses within 12 months of index among people who could benefit from PrEP

	People who could benefit from PrEP N=
STI diagnosis during follow-up, n (%)	
Any, n (%)	
Syphilis, n (%)	
Gonorrhea, n (%)	
Chlamydia, n (%)	
Chancroid, n (%)	
Lymphogranuloma venereum, n (%)	
Mycoplasma genitalium, n (%)	
Herpes Simplex-2, n (%)	
Trichomoniasis, n (%)	
Human papilloma virus/genital warts, n (%)	
HBV, n (%)	
HCV, n (%)	

Table 43. Incidence rate of STI diagnoses within 12 months of index among people who could benefit from PrEP

	Oral PrEP N=	CAB LA PrEP N=
Total # STI diagnoses within 12 months of index, n		
Person-years of follow-up		
IR per 100 py (95% CI)		