SCUOLA DI SPECIALIZZAZIONE IN MALATTIE INFETTIVE E TROPICALI

PANDORA ID - 24

TIME TO WEBINAR IN INFECTIOUS DISEASES

PROGETTO DI FORMAZIONE

Novità in tema di prevenzione dell'infezione da HIV

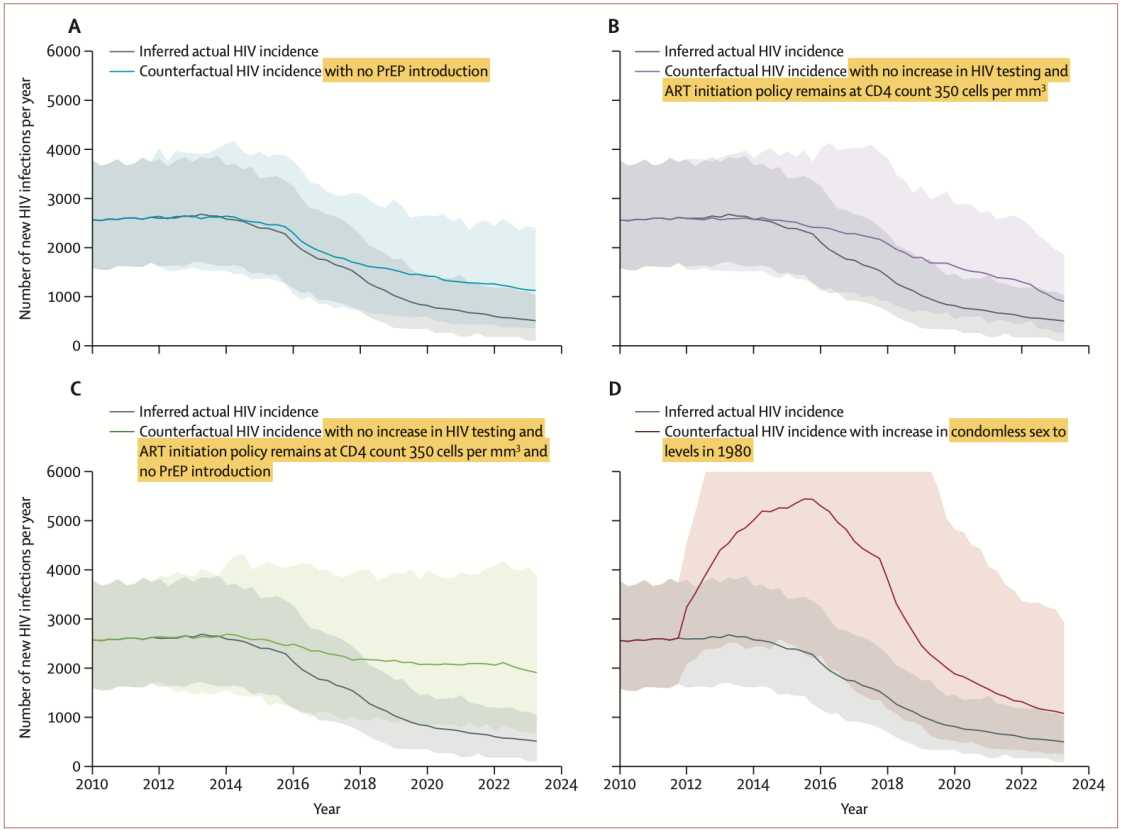
Dr. Davide Moschese

Luigi Sacco University Hospital
Milan, Italy

UNIVERSITÀ DEGLI STUDI DI MILANO

Sistema Socio Sanitario
Regione Lombardia
ASST Fatebenefratelli Sacco

Oral PrEP as a Game-Changer



Our model estimated a **77%** (90% uncertainty interval [UI] 61–88) **decline in HIV incidence since around 2014**, with an estimated 597 infections ([90% UI 312–956]; 1·1 per 1000 person-years [90% UI 0·6–1·8]) in men aged
15–64 years in 2022.

We estimate there would have been:
- ***Without PrEP introduction, 2·16 times the number of infections that actually occurred*** (90% UI 1·06–3·75) between 2012 and 2022;
- ***without increased HIV testing and ART initiation at diagnosis 2·18*** times the number of infections that actually occurred (1·18–3·60),
- and if ***condomless sex*** was at the levels before the HIV epidemic, ***2·27 times*** the number of infections that actually occurred (0·9–5·4).

INTEGRATING INNOVATIONS

1.3 million new HIV infections in 2023 despite expanded ART and PrEP.
HPTN 083 & 084: injectable long-ating CAB more effective than oral PrEP at reducing HIV infections
Oral PrEP programs exist in many countries but coverage remains sub-optimal

- HIV prevention has to “fit” with users’ needs:
  - Oral
  - Long-acting
  - Vaginal Rings
  - TasP
  - Condoms

- Role of the HCP:
  - Support
  - Guide in the Choice

- Challenges:
  - Regimens: singular or mixed
  - Upstart and discontinuation
  - Novel hurdles due to injection

Retrospective observational study (US)

Real-World Adherence of HIV-1 Oral PrEP Regimens
A Group-Based Trajectory Modeling Approach

N=76,212

People without HIV, aged ≥18 years, who were PrEP naïve prior to January 2021

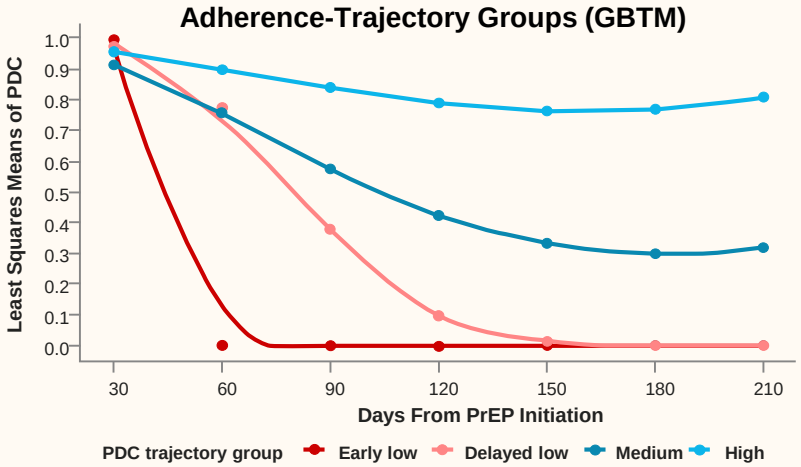
Outcomes

Population-based adherence; factors affecting adherence

January 2021–December 2022

Individuals were categorized into **four adherence-trajectory groups** using GBTM:

- **Early low: 15%**
- **Delayed low: 21%**
- **Medium: 26%**
- **High: 37%**



Potential Drivers of Adherence Trajectories

PrEP regimen was the most important factor associated with adherence trajectory

- Among **F/TAF only users**, **46%** were in the "high" and **12%** were in the "early low" group
- Among **F/TDF users**, **30%** were in the "high" and **19%** were in the "early low" group

Other factors, in order of importance, were gender identity, age, region and race/ethnicity

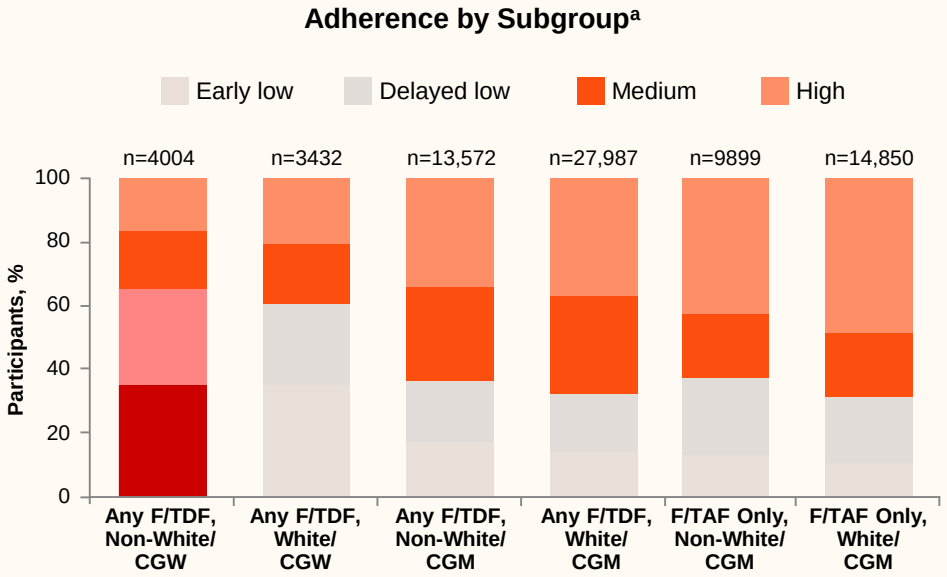
PrEP regimen was the most important factor associated with adherence trajectory, followed by gender identity, age, region and race/ethnicity

Adherence was evaluated by PDC over seven 30-day windows, based on prescription refill as an indirect measure; no objective measurement or validation of adherence was available
GBTM, group-based trajectory modeling; PDC, proportion of days covered

Tao L, et al. AIDS 2024, Poster THPEC172

Retrospective observational study (US)

Real-World Adherence of HIV-1 Oral PrEP Regimens: A Group-Based Trajectory Modeling Approach



Adherence in Selected Subgroups

When participants were grouped by regimen, gender identity and race/ethnicity:

- **CGM** using F/TAF only demonstrated the **highest adherence**
- **Most CGW using "any F/TDF"[a] had low adherence**

Among 26 subgroups defined by the top five drivers of adherence, the **four subgroups** with the **highest adherence were all CGM aged ≥35 years using F/TAF only**

- Included White and non-White participants from across the US

Most CGW aged <35 years using F/TDF had low adherence, suggesting this is a priority population for strategies to increase adherence and help reach HIV-1 prevention goals

Adherence was evaluated by proportion of days covered over seven 30-day windows, based on prescription refill. [a]"Any F/TDF" includes F/TDF-only users and those with mixed use of F/TDF and F/TAF; the number of CGW using F/TAF only, and the number of transgender individuals, were too small to be shown. CGM, cisgender men; CGW, cisgender women

Tao L, et al. AIDS 2024, Poster THPEC172

Real-world study (US)

Assessment of Longitudinal Changes in Renal Function of HIV-1 Oral PrEP Users

N=12,183

People without HIV who had ≥1 eGFR measurement within 1 year pre- and post- oral PrEP initiation

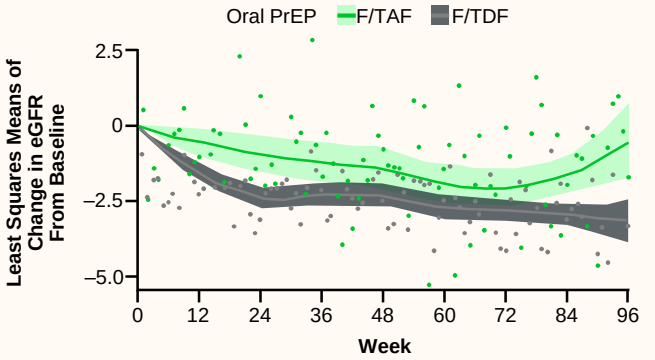
- Initiated F/TAF (n=2323)
- Initiated F/TDF (n=9860)

Outcome

Longitudinal change in eGFR from baseline following F/TAF and F/TDF initiation

January 2015–December 2023

eGFR Change From Baseline Over Time for F/TAF and F/TDF Users



Weeks (inclusive)	0	1–12	13–24	25–36	37–48	49–60	61–72	73–84	85–96
F/TAF, n	2323	873	839	682	510	400	287	245	177
F/TDF, n	9860	3420	3171	2674	2039	1745	1397	1240	1036

- Compared with F/TAF users, **F/TDF users had a greater mean decrease in eGFR through 96 weeks**
- eGFR decreased more rapidly in F/TDF than F/TAF users in the first 6 months of use

Likelihood of eGFR falling to <60 mL/min/1.73 m^2

•Overall, **F/TDF users had 67% higher odds of eGFR falling to <60 mL/min/1.73 m^2** vs. F/TAF users after adjusting for multiple factors (fully adjusted OR [95% CI]: 1.67 [1.16, 2.38])[a]

•Contributing factors included:

- **Age** (<40 vs. ≥40 years)
- **Sex at birth**
- **Baseline eGFR** (60–90 vs. >90 mL/min/1.73 m^2)
- **Chronic kidney disease**

In this real-world study, eGFR was less likely to be negatively impacted in individuals using F/TAF than in those using F/TDF[b]; findings are consistent with those from the DISCOVER trial[2]

[a]Users with eGFR <60 mL/min/1.73 m^2, n/N (%): F/TAF 57/1658 (3.4%), F/TDF 248/7382 (3.4%); [b]The absence of controls for baseline conditions and monitoring of other medical issues could introduce bias, thus caution should be taken when interpreting the study's findings

1. Huang X, et al. AIDS 2024, Poster TUPEC213; 2. Mayer KH, et al. *Lancet*. 2020;396:239-54

Questionnaire-based, cross-sectional study (Thailand)

PrEP Preferences Among Sex Workers

N=1511

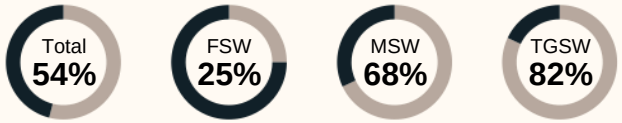
Thai adults, aged ≥18 years, who engaged in sex work within the past 3 months, with negative or unknown HIV status

Outcomes

Current PrEP uptake and preferred PrEP delivery

April 2023–December 2023

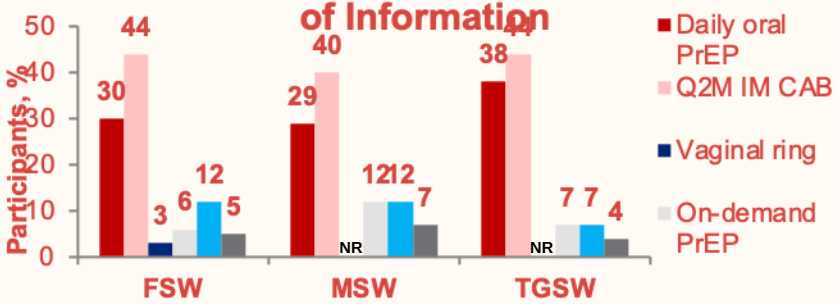
Participants Who Were Aware of PrEP



Participants Who Use PrEP

FSW were less likely to be aware of or report use of PrEP than MSW and TGSW

PrEP Options Preferred by SW After Provision of Information



- Of 1511 SW participants, 370 (25%) were not interested in PrEP
- After receiving further information, 72% selected a PrEP option
  - Of these, 40% stated a preference for Q2 IM CAB and 17% for daily oral PrEP

Provision of information to SW about PrEP options increased interest and demand among those previously reporting no interest, suggesting that investment in PrEP awareness is needed for PrEP scale-up in Thailand

FSW, female sex workers; MSW, male sex workers; NR, not reported; SW, sex workers; TGSW, transgender sex workers

Sukthongsa S, et al. AIDS 2024, Poster WEPEC221

The Chicago Study for HIV Prevention in Psychiatry: Survey-based study (US)[1]

PrEP Engagement and Preferences Among People With Mental Illness

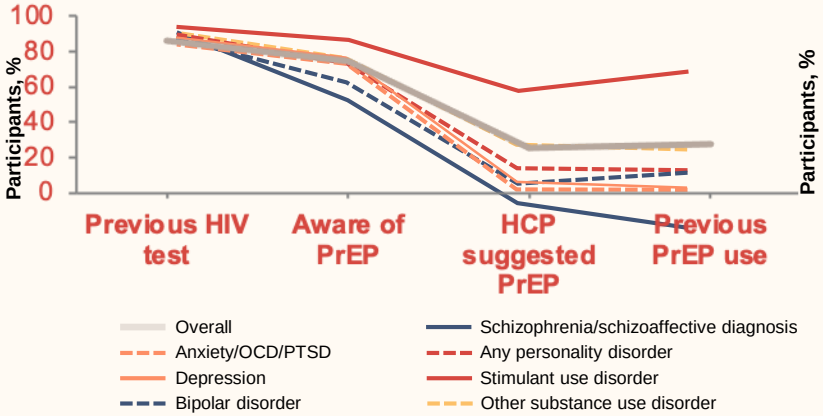
N=417[1]

Adult without HIV receiving outpatient psychiatric care, who were sexually active and/or injected drugs in the past year[1]

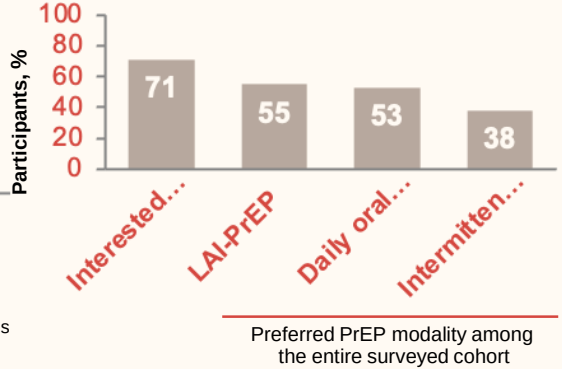
Outcomes[1]

- Engagement along the PrEP care continuum
- Preferred PrEP modalities and preferred PrEP prescribers

Engagement Along The PrEP Care Continuum Among PWMI (Overall and By Diagnosis)[1]



PrEP Preferences Among PWMI[1]



Preferred PrEP modality among the entire surveyed cohort

Qualitative Substudy Among Psychiatrists (N=30)[2]

- **56.5%** were interested in prescribing PrEP in the future
- **20.0%** had already prescribed PrEP
- **Training** is needed to support greater PrEP implementation in psychiatric practice

There is a need to increase implementation of PrEP by psychiatrists and engagement along the PrEP care continuum among PWMI

HCP, healthcare professional; LAI, long-acting injectable; OCD, obsessive compulsive disorder; PTSD, post-traumatic stress disorder; PWMI, people with mental illness

1. Bunting SR, et al. AIDS 2024, Poster TUPEE493; 2. Bunting SR, et al. AIDS 2024, Poster THPEE491

PROTECT Survey

- 74% of **MSM** showed interest in using LA-PrEP, 37% of MSM would prefer LA-PrEP over other HIV prevention methods

- **Heterosexual** cis-men and women: low level of HIV/STI testing and virtually no oral PrEP use, but interest in LA PrEP (albeit at a much lower level than key population!)

- **Trans*** individuals are interested in LA PrEP, but may require support around perceived GAHT DDIs and impact of gluteal implants

-Many **PLWH** would prefer their partners to be on LA PrEP and are willing to co-pay

The PrEPARE Project

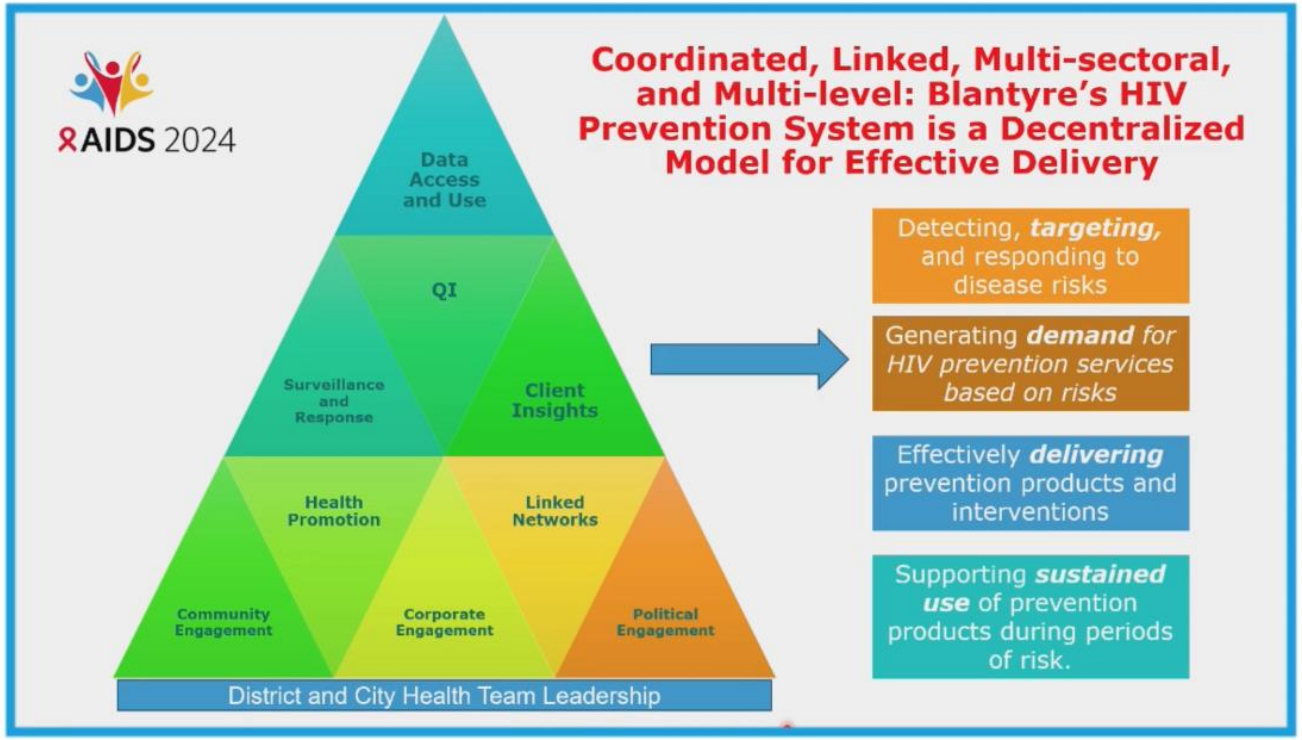
Most common reasons for not using PrEP	n=251
Not having enough sex	39%
Not comfortable talking to a doctor	34%
Using condoms	33%
Concerned about side effects	32%
Concerned about long-term medication	30%
Not knowing how to get PrEP	29%

THE PrEPARE PROJECT

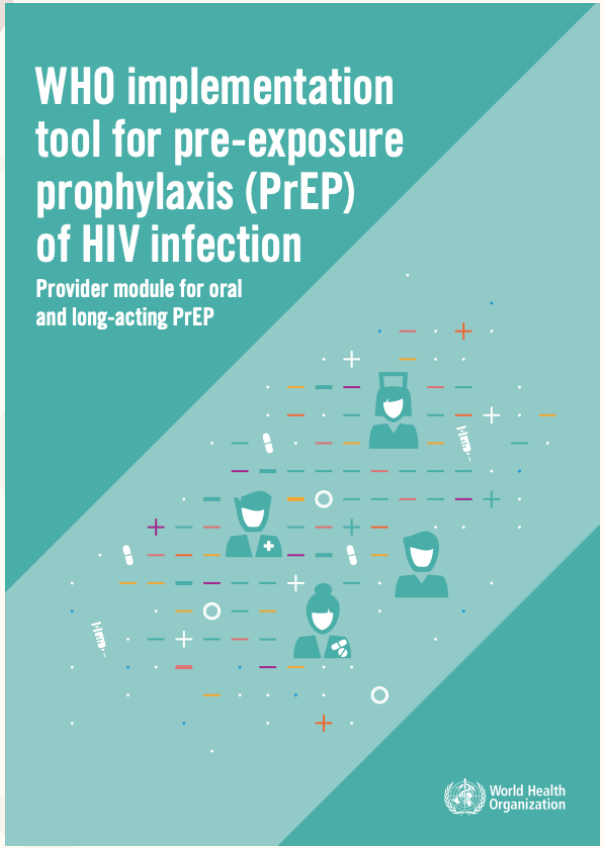
Most preferred strategy*	Non-PrEP-users n=960	PrEP users n=947	*p* value
Monthly pill	28%	29%	
Long-acting injection	16%	26%	
Event-driven/on demand dosing	31%	14%	<.001
Daily pills	9%	13%	
Long-acting removable implant	12%	17%	

*Participants were told to assume all methods were available and equally effective.

Implementation Strategies



WHO PrEP Implementation Tool



- WHO Guidance on:
    - differentiated and simplified PrEP services
    - guidelines on services for key populations
    - recommendations on the DVR and CAB-LA

- Support for providers

- Integrates guidance for all 3 WHO recommended PrEP prducts (oral, CAB-LA and DVR) to support choice
    - offering choice is crucial for person-centred services

WHO PrEP Implementation Tool

- Dosing and starting, stopping and restarting for oral PrEP
  - WHO no longer using the term «ED PrEP» to describe the dosing for cis-men or AMAB

- use of self-testing

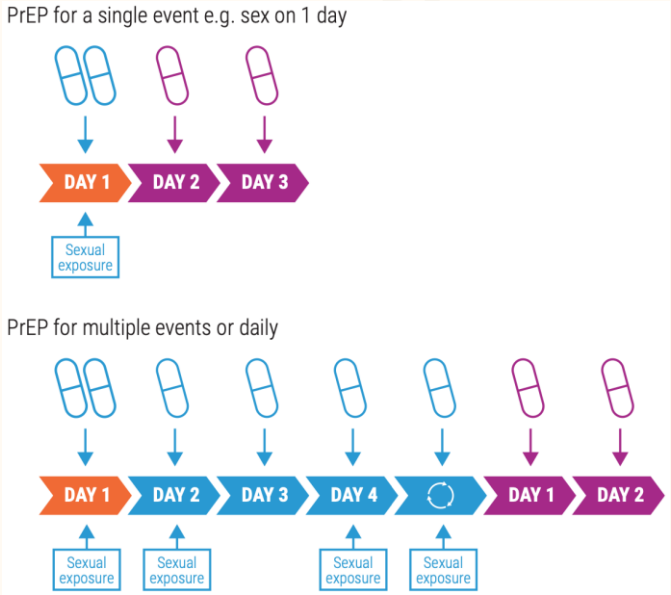
- minimum service packages

- risk assessment and eligibility

- same-day PrEP

- considerations for drug resistance

- PrEP in pregnancy and breast-feeding



STIs in PrEP

Baseline

8,528 participants tested for bacterial STI at baseline

Follow-up

7,558 participants were tested for any STI after PrEP initiation

Factors associated with incident STI in ImPrEP Study

		aHR (95%CI)	*p-value*
Country (reference: Brazil)	Mexico	1.54 (1.36-1.75)	<0.01
	Peru	0.82 (0.72-0.92)	<0.01
Age (years)	18-24	1.22 (1.10-1.35)	<0.01
Race/color	Black, mixed race or indigenous	1.13 (1.03-1.24)	0.01
Previous PEP use at baseline		1.18 (1.04-1.35)	0.01
Number of sex partners	2-3	1.47 (1.29-1.69)	0.04
	4+	1.75 (1.55-1.98)	<0.01
Sexual behavior	Condomless receptive anal sex	1.47 (1.33-1.62)	<0.01
Poppers use		1.18 (1.04-1.33)	<0.01
Any bacterial STI diagnosed at baseline		1.66 (1.51-1.82)	<0.01

The NEW ENGLAND JOURNAL of MEDICINE

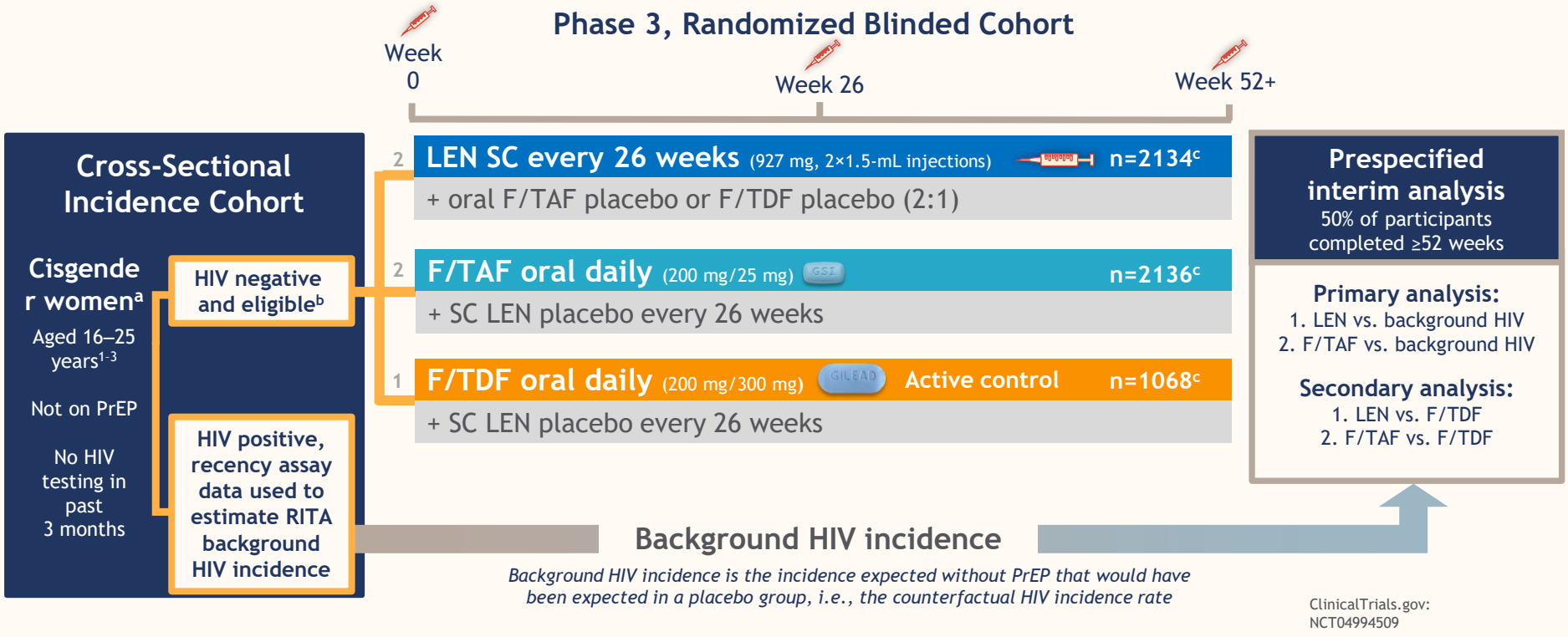
ORIGINAL ARTICLE

Twice-Yearly Lenacapavir or Daily F/TAF for HIV Prevention in Cisgender Women

L.-G. Bekker, M. Das, Q. Abdool Karim, K. Ahmed, J. Batting, W. Brumskine, K. Gill, I. Harkoo, M. Jaggernath, G. Kigozi, N. Kiwanuka, P. Kotze, L. Lebina, C.E. Louw, M. Malahleha, M. Manentsa, L.E. Mansoor, D. Moodley, V. Naicker, L. Naidoo, M. Naidoo, G. Nair, N. Ndlovu, T. Palanee-Phillips, R. Panchia, S. Pillay, D. Potloane, P. Selepe, N. Singh, Y. Singh, E. Spooner, A.M. Ward, Z. Zwane, R. Ebrahimi, Y. Zhao, A. Kintu, C. Deaton, C.C. Carter, J.M. Baeten, and F. Matovu Kiweewa, for the PURPOSE 1 Study Team*

PURPOSE 1

Study Design and Efficacy Outcomes



ClinicalTrials.gov: NCT04994509

[a]The first participant was screened in August 2021, the 50th percentile participant was randomized in May 2023, and the last participant was randomized in September 2023. [b]Eligibility criteria included: weight ≥35 kg, eGFR ≥60 mL/min, not pregnant. [c]n numbers represent the full analysis set for efficacy analyses. **1.** Bekker LG, et al. AIDS 2024, Oral SS0407. **2.** Bekker LG, et al. *N Engl J Med*. 2024;10.1056/NEJMoa2407001. **3.** NCT04994509. https://clinicaltrials.gov/study/NCT04994509?intr=NCT04994509 (accessed July 16, 2024)

Baseline Demographics and Clinical Characteristics

Characteristic	LEN, n=2138	F/TAF, n=2137	F/TDF, n=1070
Age, years, median (range)	21 (16–25)	21 (16–26)[a]	21 (16–25)
Age 16 to <18, years, n (%)	56 (2.6)	45 (2.1)	23 (2.1)
Black,[b] n (%)	2135 (99.9)	2136 (100)	1068 (99.8)
Highest education level college/university,[c] n (%)	183 (8.6)	198 (9.3)	109 (10.2)
Marital status, n (%)			
Married	26 (1.2)	30 (1.4)	17 (1.6)
Living with primary partner	148 (6.9)	132 (6.2)	73 (6.8)
STIs, n (%)			
Chlamydia trachomatis	520 (24.3)	562 (26.3)	263 (24.6)
Neisseria gonorrhoeae	197 (9.2)	178 (8.3)	90 (8.4)
Trichomonas vaginalis	154 (7.2)	165 (7.7)	82 (7.7)
Syphilis	57 (2.7)	63 (2.9)	29 (2.7)
Any prior use of PrEP, n (%)	143 (6.7)	121 (5.7)	71 (6.6)
Any prior HIV testing, n (%)	1713 (80.1)	1731 (81.0)	860 (80.4)
Median time since last HIV test, months (Q1, Q3)	6.8 (4.7, 11.5)	6.6 (4.8, 11.0)	6.5 (4.6, 11.0)

Participants

84.3%
South Africa

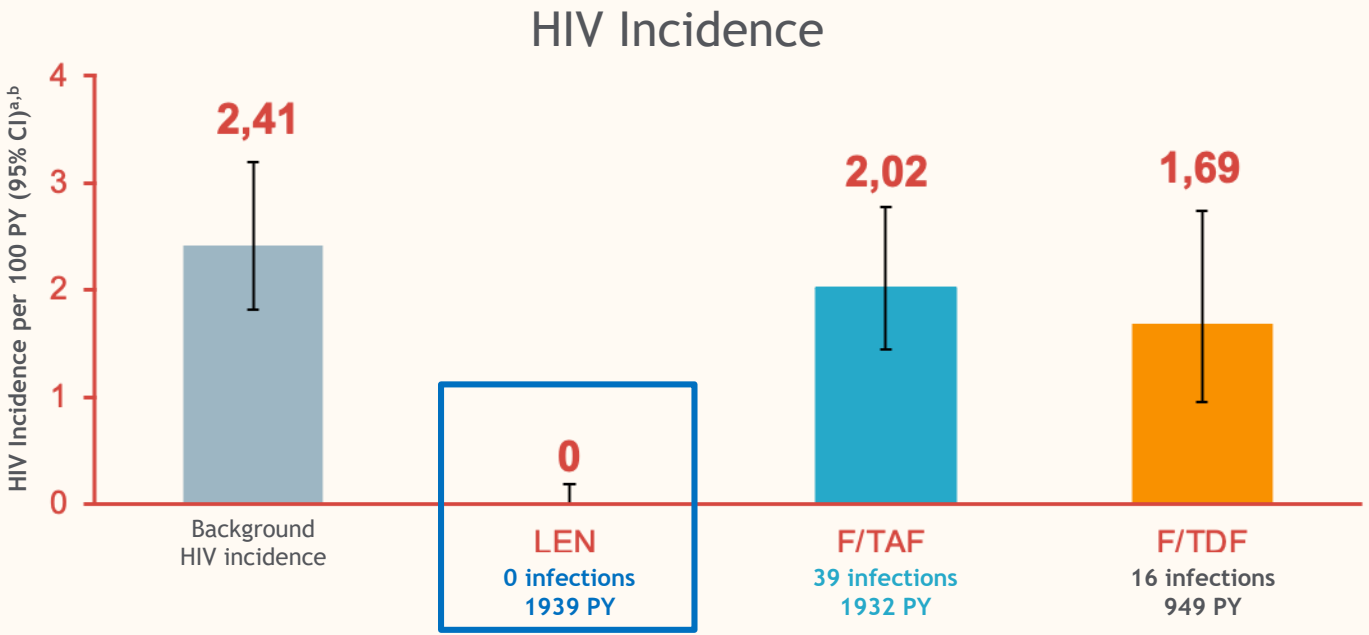
15.7%
Uganda

Baseline demographics and clinical characteristics were balanced across randomized groups

Seven participants were subsequently determined to have had HIV infection at the time of randomization, and thus 5338 were included in the modified intention-to-treat efficacy analysis. [a]One participant was aged 25 years at screening but turned 26 by randomization—this was not a violation of eligibility criteria. [b]All non-Black participants were multiracial. [c]Sample size: LEN 2136, F/TAF 2134, F/TDF 1069

1. Bekker LG, et al. AIDS 2024, Oral SS0407. **2.** Bekker LG, et al. *N Engl J Med.* 2024;10.1056/NEJMoa2407001

HIV Incidence



No incident HIV acquisitions were observed in the LEN group.
HIV incidence on F/TAF was not different from background HIV incidence

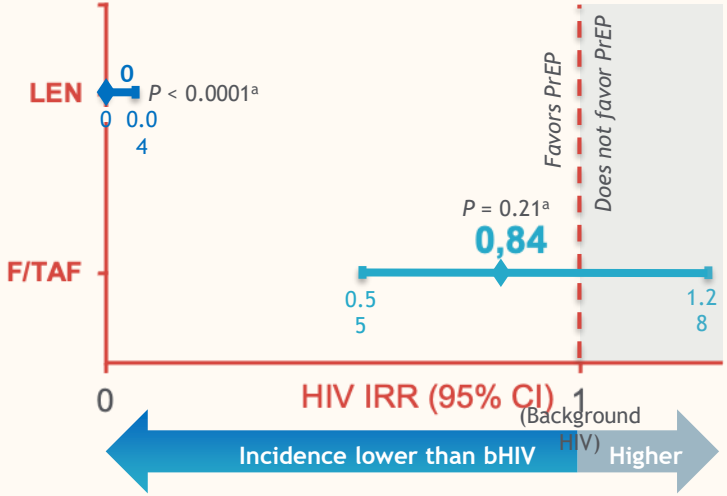
[a]Overall n: background HIV incidence group 8094, LEN 2134, F/TAF 2136, F/TDF 1068. [b]95% CIs: background HIV incidence group 1.82, 3.19, LEN 0, 0.19, F/TAF 1.44, 2.76. F/TDF 0.96, 2.74
PY, person-years

1. Bekker LG, et al. AIDS 2024, Oral SS0407. **2.** Bekker LG, et al. *N Engl J Med.* 2024;10.1056/NEJMoa2407001

HIV Incidence Rate Ratios in Primary and Secondary Analyses

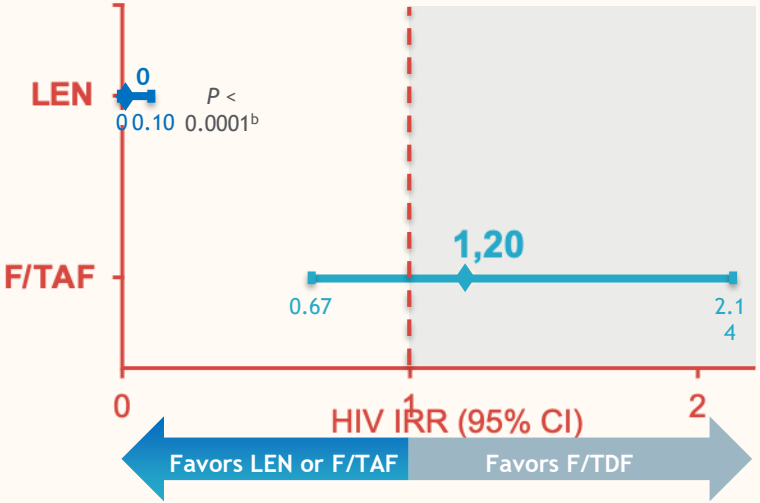
Primary Analysis

Efficacy Compared With Background HIV Incidence



Secondary Analysis

Relative Efficacy Compared With F/TDF



LEN reduced HIV incidence by 100% compared with background HIV; HIV incidence with F/TAF was not different from background HIV incidence

LEN was superior to F/TDF with 0 cases of HIV; F/TAF had numerically similar incidence to F/TDF

[a]HIV IRR LEN vs. background HIV assessed using a likelihood ratio test (LEN, due to zero infections) and a Wald test (F/TAF).[3,4] [b]HIV IRR LEN vs. F/TDF assessed using an exact conditional Poisson regression model (due to zero infections).**1.** Bekker LG, et al. AIDS 2024, Oral SS0407. **2.** Bekker LG, et al. *N Engl J Med.* 2024;10.1056/NEJMoa2407001. **3.** Shao Y, Gao F. *Stat Commun Infect Dis.* 2024;16:20230004. **4.** Gao F, et al. *Stat Commun Infect Dis.* 2021;13:20200009

Adherence and Matched Case–Control Analysis

Adherence to Injections

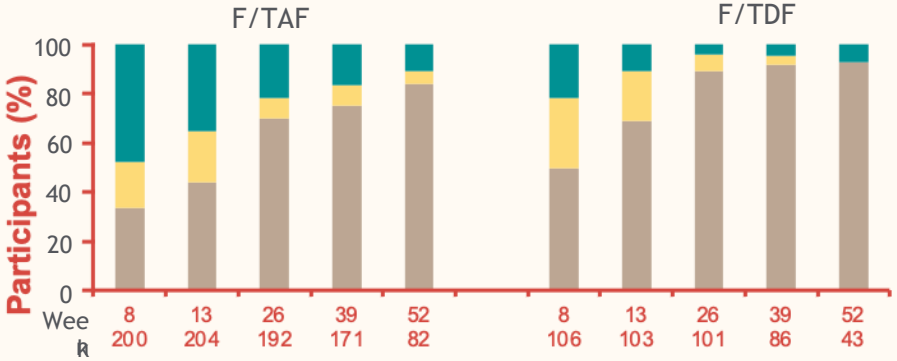
Injections were on time[a] for:

- **91.5% (4545/4967) at Week 26**
- **92.8% (2025/2181) at Week 52**

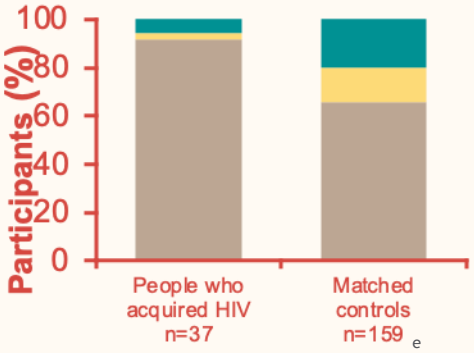
On-time injection similar on LEN and placebo (F/TAF and F/TDF)

Within the F/TAF group, those with medium or high adherence had a significantly lower likelihood of acquiring HIV than those with low adherence (odds ratio: 0.11; 95% CI: 0.012, 0.49; *P*=0.0006)

Adherence[b,c] to F/TAF and F/TDF



Matched Case–Control Analysis of Adherence[c,d] to F/TAF



On-time adherence to injections was high. Most participants in both the F/TAF and F/TDF groups overall had low adherence to oral tablets and adherence declined over time. Most infections on F/TAF occurred in those with low adherence

[a]Adherence to LEN defined as on-time injection (<28 weeks from the last injection) and participants who presented late required negative HIV testing to reinitiate study product which included reloading with oral LEN or placebo. [b]Preselected 10% sample of participants. [c]By TFV-DP DBS levels (adherence cutoffs for F/TAF: low <450, medium ≥450 to <900, high ≥900 fmol/punch and F/TDF: low <350, medium ≥350 to <700, high ≥700 fmol/punch); [d]Missing DBS concentrations imputed for participants with HIV infection based on last concentration prior to HIV diagnosis and decay rate based on the median half-life. [e]Available data shown in stacked bar
DBS, dried blood spot; TFV-DP, tenofovir diphosphate. **1.** Bekker LG, et al. AIDS 2024, Oral SS0407. **2.** Bekker LG, et al. *N Engl J Med.* 2024;10.1056/NEJMoa2407001

Safety Results

Adverse Events,[a] n (%)	LEN n=2138	F/TAF n=2137	F/TDF n=1070
Any	1631 (76.3)	1665 (77.9)	830 (77.6)
Grade ≥2	1111 (52.0)	1078 (50.4)	533 (49.8)
Grade ≥3	88 (4.1)	95 (4.4)	50 (4.7)
SAEs	59 (2.8)	85 (4.0)	35 (3.3)
AEs leading to discontinuation of study drug	5 (0.2)[b]	2 (<0.1)[c]	0
AEs occurring in ≥10% of participants, n (%)			
Headache	285 (13.3)	352 (16.5)	155 (14.5)
Urinary tract infection	307 (14.4)	305 (14.3)	163 (15.2)
Genitourinary chlamydia infection	300 (14.0)	317 (14.8)	129 (12.1)
Upper respiratory tract infection	271 (12.7)	274 (12.8)	121 (11.3)
Nausea	144 (6.7)	234 (10.9)	142 (13.3)
Vomiting	125 (5.8)	235 (11.0)	107 (10.0)
Laboratory abnormalities, n with ≥1 baseline result	2126	2113	1054
Any Grade ≥1, n (%)	1929 (90.7)	1904 (90.1)	959 (91.0)

Six deaths[d] all in the F/TAF group; none related to study drug per investigator

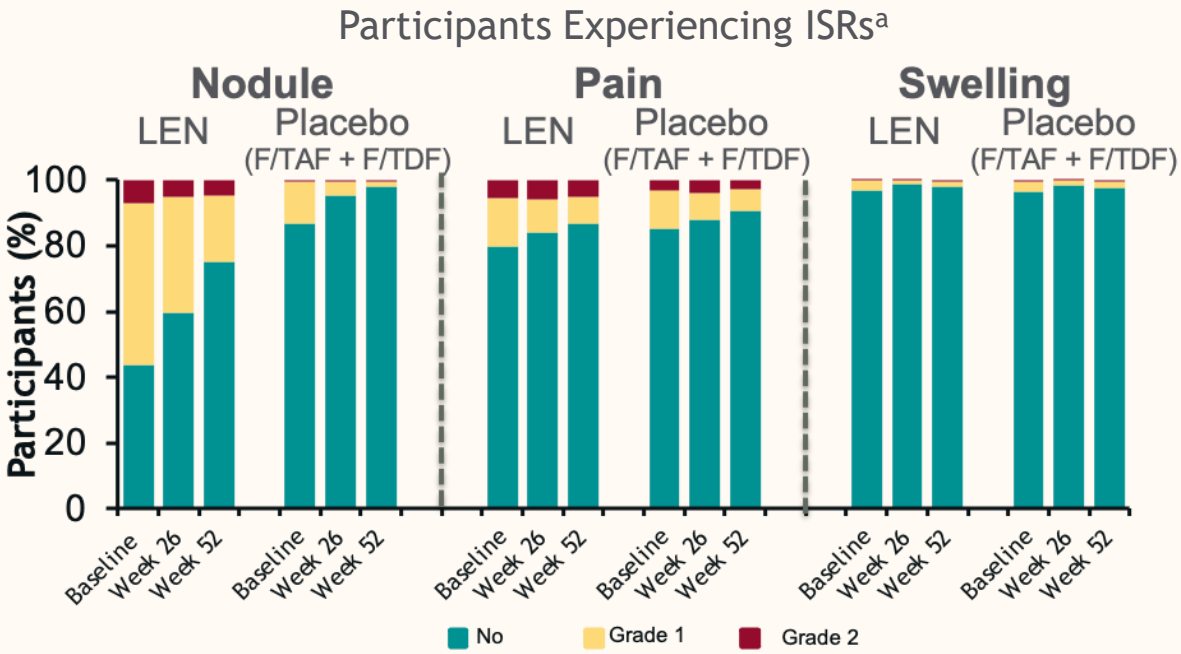
Adverse events were consistent with prior LEN, F/TAF and F/TDF trials[1-6]

Pediatric AEs, Version 2.1. [b]n=1 for each of: nausea, decreased creatinine renal clearance, increased hepatic enzyme, spontaneous miscarriage, suicide attempt/major depression. [c]n=1 for each of: suicide attempt/depressive symptoms/drug overdose, angioedema. [d]Asphyxia secondary to strangulation, non-accidental burns, knife stab to chest, hemorrhage due to traffic accident, autopsy-confirmed ischemic cardiomyopathy, and ovarian cancer

1. Bekker LG, et al. AIDS 2024, Oral SS0407. 2. Bekker LG, et al. *N Engl J Med.* 2024;10.1056/NEJMoa2407001. 3. Gupta SK, et al. *Lancet HIV.* 2023;10:e15-e23. 4. Ogbuagu O, et al. *Lancet HIV.* 2023;10:e497-e505. 5. Mayer KH, et al. *Lancet.* 2020;396:239-54. 6. Baeten JM, et al. *N Engl J Med.* 2012;367:399-410

Injection-Site Reaction Frequency

- LEN is injected into the SC space and forms a drug depot that may be palpable under the skin but is usually not visible
- As the drug elutes over time, the depot gets smaller and the nodules resolve or reduce in size substantially prior to the next injection
- ISRs, including nodules, decreased with subsequent doses (also observed in HIV treatment[3])



Among 25,329 injections, only 4 ISRs led to discontinuation

[a]Grade 1 and 2 ISRs are shown. ISR, injection-site reaction

1. Bekker LG, et al. AIDS 2024, Oral SS0407. 2. Bekker LG, et al. *N Engl J Med.* 2024;10.1056/NEJMoa2407001. 3. Kumar P, et al. AIDS 2022, Poster EPB184

Pregnancy Outcomes

Participants and pregnancies,[a] n (%)	LEN n=2138	F/TAF n=2137	F/TDF n=1070
Participants with confirmed pregnancies	184	208	95
Confirmed pregnancies	193	219	98
Completed pregnancies	105 (54.4)	119 (54.3)	53 (54.1)
Ongoing pregnancies	88 (45.6)	100 (45.7)	45 (45.9)
Births[a]	55 (28.5)	45 (20.5)	21 (21.4)
Interrupted pregnancies	50 (25.9)	74 (33.8)	32 (32.7)
Induced abortion	30 (15.5)	40 (18.3)	20 (20.4)
Spontaneous miscarriage[b]	20 (10.4)	34 (15.5)	12 (12.2)

Expected spontaneous miscarriage rate[3,4]:

- **10–20% of clinically recognized pregnancies**
- **~30% of biochemically detected pregnancies**

Available pregnancy outcomes were similar to those expected for the population[5]

[a]Completed uninterrupted pregnancies which includes lives births and eight still births: three in the LEN group, four in the F/TAF group, one in the F/TDF group. [b]Spontaneous miscarriage defined as occurring at <20 weeks' gestation

1. Bekker LG, et al. AIDS 2024, Oral SS0407. **2.** Bekker LG, et al. *N Engl J Med.* 2024;10.1056/NEJMoa2407001. **3.** ACOG Committee on Practice Bulletins—Gynecology. *Obstet Gynecol*. 2018;132:e197-e207. **4.** Wilcox AJ, et al. *N Engl J Med.* 1988;319:189-94. **5.** Mugo NR, et al. *JAMA.* 2014;312:362-71

September 12, 2024

Gilead's Twice-Yearly Lenacapavir for HIV Prevention Reduced HIV Infections by 96% and Demonstrated Superiority to Daily Truvada® in Second Pivotal Phase 3 Trial

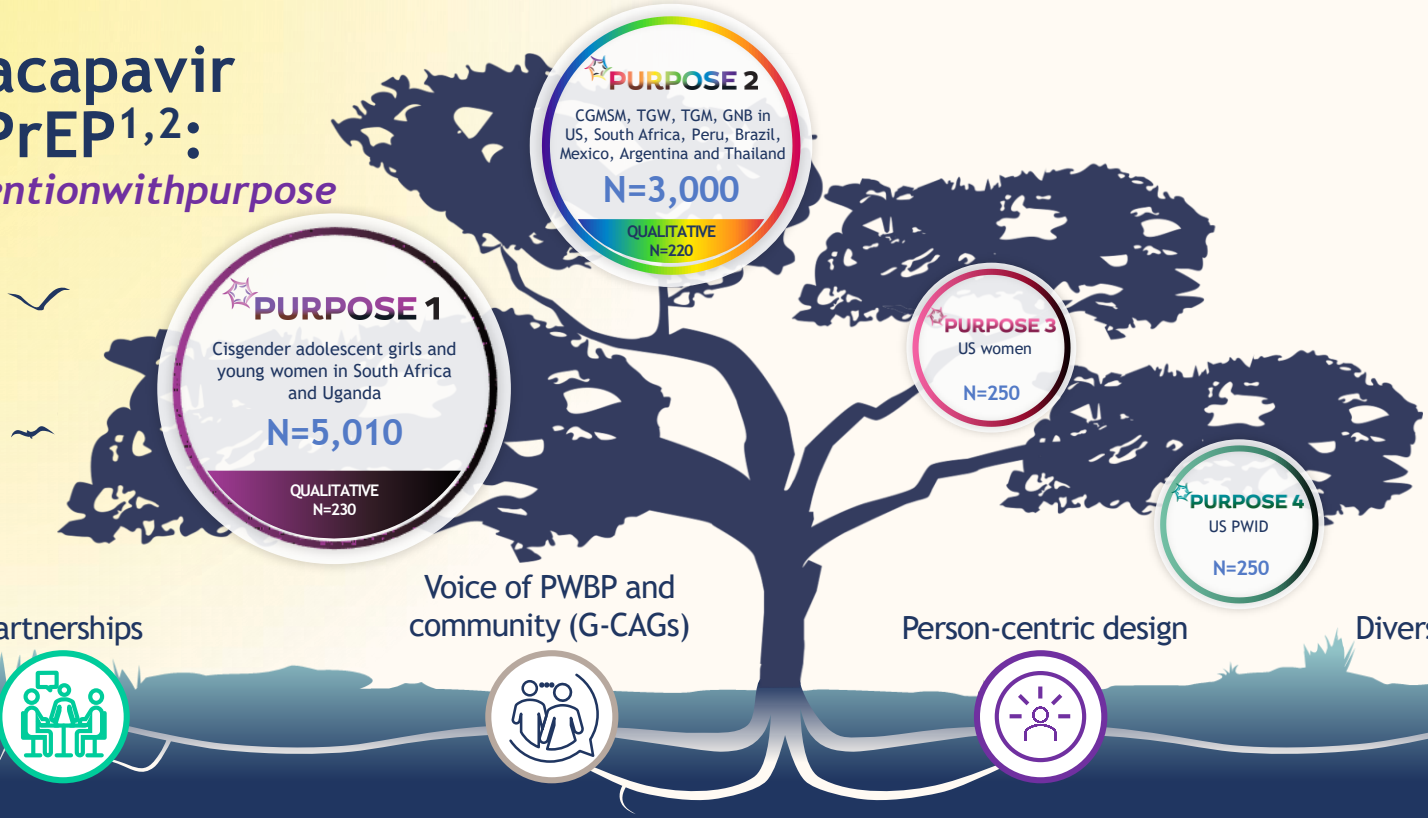
– 99.9% of Participants Did Not Acquire HIV Infection in the Lenacapavir Group, with 2 Incident Cases Among 2,180 Participants –

– PURPOSE 2 Trial Results for Cisgender Men and Gender-Diverse People Add to the Body of Evidence for the Investigational Use of Lenacapavir for HIV Prevention –

– Gilead Stopped the Blinded Phase of the Trial at Interim Analysis and Will Offer Open-Label Lenacapavir to All Participants –

Lenacapavir for PrEP[1,2]:

#preventionwithpurpose



Proof of concept that capsid inhibitors prevent SHIV in nonhuman primates[3-5]; Robust pharmacokinetic and safety database in persons with[6-10] and without HIV[11]

PURPOSE 1 NCT identifier: NCT04994509; PURPOSE 2 NCT identifier: NCT04925752.CGMSM, cisgender men who have sex with men; G-CAG, Global Community Advisory Group; GNB, gender nonbinary individuals; MDR, multidrug-resistant; PWBP, people who would benefit from PrEP; PWID, people who inject drugs; SHIV, simian-human immunodeficiency virus; TGM, transgender men; TGW, transgender women; Tx, treatment.1. Das et al, et al. IAS 2023, Symposium SY05; 2. Das et al, et al. IAS 2023, Satellite SAT050; 3.Bekerman E, et al, vCROI, 2021, Oral/Poster 717; 4. Bekerman E, et al, vIAS, 2021, PECLB24; 5. Swanstrom A, et al, CROI 2022, Poster 860; 6. Segal-Maurer S, et al, vCROI, 2021, Oral 127; 7. Molina JM, et al. vIAS, 2021, OALX01LB02; 8. Stellbrink H-J, et al. EACS, 2021, PE2/69; 9. Margot N, et al, EACS, 2021, OS1/1; 10. Gupta S, et al. vIAS, 2021, OALB0302; 11. Begley R, et al, AIDS, 2020, PEB0265

Purpose Studies. https://www.purposestudies.com/ (accessed July 31, 2023)

Oral FTC/TDF PrEP Efficacy in Placebo-controlled RCT

Population	Study	Phase	Participants		Efficacy for Reducing HIV Incidence, %
			Study Drug	Control	
MSM	iPrEx[1]	III	FTC/TDF (n = 1251)	Placebo (n = 1248)	44.0 (P = .005)
	IPERGAY[2]	**III**	**On-demand FTC/TDF (n = 199)**	**Placebo (n = 201)**	**86.0 (P = .002)**
HS men & women	Partners PrEP[3]	III	FTC/TDF (n = 1583)	Placebo (n = 1586)	75.0 (P < .001)
	TDF2[4]	II/III	FTC/TDF (n = 611)	Placebo (n = 608)	62.2 (P = .03)
PWID	BTS[5]	II/III	TDF (n = 1204)	Placebo (n = 1207)	48.9 (P = .01) If detectable TDF: 73.5 (P = .03)

Effectiveness in open-label/extension/demonstration project studies (MSM)

- iPrEx OLE: 49% reduction with vs without PrEP after adjusting for sexual practices[6]
- **PROUD: 86% reduction** with immediate vs deferred (12 mos) PrEP initiation (*P* = .0001)[7]
- Demo Project: 557 initiated PrEP, 437 retained 48 wks; 2 HIV infections occurred, both with TFV-DP levels consistent with < 2 doses/wk at seroconversion[8]
- **IPERGAY extension: 97% reduction with on-demand PrEP (vs placebo arm of randomized trial)[9]**

1. Grant. NEJM. 2010;363:2587. 2. Molina. NEJM. 2015;373:2237. 3. Baeten. NEJM. 2012;367:399. 4. Thigpen. NEJM. 2012;367:423. 5. Choopanya. Lancet. 2013;381:2083. 6. Grant. Lancet Infect Dis. 2014;14:820. 7. McCormack. Lancet. 2016;387:53. 8. Liu. JAMA Intern Med. 2016;176:75. 9. Molina. Lancet HIV. 2017;4:e402. 10. Mayer. Lancet. 2020;396:239. 11. Landovitz. AIDS 2020. Abstr OAXLB0101.

Long-term protection from HIV infection with oral HIV pre-exposure prophylaxis in gay and bisexual men: findings from the expanded and extended EPIC-NSW prospective implementation study

Andrew E Grulich, Fengyi Jin, Benjamin R Bavinton, Barbara Yeung, Mohamed A Hammoud, Janaki Amin, Gesalit Cabrera, Shawn Clackett, Erin Ogilvie, Stefanie Vaccher, Tobias Vickers, Anna McNulty, David J Smith, Nila J Dharan, Christine Selvey, Cherie Power, Karen Price, Iryna Zablotska, David A Baker, Mark Bloch, Katherine Brown, Christopher J Carmody, Andrew Carr, Daniel Chanisheff, Nicholas Doong, Robert Finlayson, David A Lewis, Josephine Lusk, Sarah Martin, Catriona Ooi, Phillip Read, Nathan Ryder, Don Smith, Clara Tuck Meng Soo, David J Templeton, Emmanuel Vlahakis, Rebecca Guy, for the Expanded PrEP Implementation in Communities New South Wales (EPIC-NSW) research group*

Lancet HIV 2021; 8: e486–94

Published Online
July 1, 2021

In this cohort of almost **10 000 mostly gay and bisexual men** who were dispensed PrEP and **followed up for up to 3 years**, there were **only 30 new HIV infections**, with a **very low HIV incidence of 1·61 per 1000 person years**.

This incidence was 92% less than the expected incidence of at least 20 per 1000 person-years in the absence of PrEP.

	Number of HIV sero-conversions	Incidence per 1000 person-years	Incidence rate ratio (95% CI)	p value
Years since first PrEP dispensed				
<1	10	1·09	1 (ref)	0·086*
1–2	14	2·10	1·93 (0·86–4·35)	..
2–3	6	2·18	2·01 (0·73–5·53)	..
Calendar period of follow-up				
Year 1 (March, 2016–February, 2017)	1	0·38	1 (ref)	0·018*
Year 2 (March, 2017–February, 2018)	8	1·20	3·15 (0·39–25·21)	..
Year 3 (March, 2018–March, 2019)	21	2·24	5·88 (0·79–43·69)	..
Mean MPR†				
<0·6	17	4·76	1 (ref)	<0·0001
0·6–1·0	5	0·39	0·08 (0·03–0·22)	..

MPR=medication possession ratio. PrEP=pre-exposure prophylaxis. *p_{trend}. †Mean MPR during follow-up was calculated for participants with at least 6 months of adherence data available.

Table 4: **Years since first dispensed PrEP, calendar period of follow-up, and mean MPR during follow-up and risk of HIV infection**

HPTN 083 and 084: LA IM CAB Q2M vs Daily Oral FTC/TDF for PrEP

- International, randomized, double-blind phase IIb/III (083) and phase III (084) trials
- LA IM CAB met criteria for **superiority** vs daily oral FTC/TDF in both trials

HPTN 083[1]

- N = 4566 MSM and TGW
- 13 incident infections with LA CAB vs 39 with oral FTC/TDF
  - **4 with on-time CAB injections**
  - 1 CAB infection later determined to be baseline infection
- HR for CAB vs FTC/TDF:
  0.34 (95% CI: 0.18-0.62)

HPTN 084[2]

- N = 3224 cisgender women
- 4 incident infections with LA CAB vs 36 with oral FTC/TDF
  - **0 with on-time CAB injections**
  - 1 CAB infection later determined to be baseline infection
- HR for CAB vs FTC/TDF:
  0.12 (95% CI: 0.05-0.31)

1. Landovitz. NEJM. 2021;385:595. 2. Delany-Moretlwe. Lancet. 2022;399:1779.

Performance characteristics of HIV RNA screening with long-acting injectable cabotegravir (CAB-LA) pre-exposure prophylaxis (PrEP) in the multicenter global HIV Prevention Trials Network 083 (HPTN 083) Study

RESULTS: This analysis included 27,335 visits conducted for 2,620 participants through 11/30/23. Twenty-nine participants acquired HIV during the OLE. In 5/29 (17.2%), HIV infection was first identified by an isolated positive RNA test result (true positives, Table); in 2 of these cases, HIV infection was first identified at OLE enrollment. Twenty-three additional participants had an isolated positive RNA test result (22 HIV negative [false positives], 1 HIV status indeterminant). The PPV for detecting infection by RNA screening for participants with vs. without CAB-LA in the past 6 months was 9.1% (95% CI 1.6, 30.6) vs. 60% (95% CI 17, 92.7), respectively. The FPR and sensitivity for RNA screenir for participants with vs. without CAB-LA in the past 6 months were: FPR: 0.08 (95% CI 0.05, 0.13) vs. 0.06 (95% CI 0.01, 0.24); sensitivity: 87.5% (95% CI 46.7, 99.3) vs. 100% (95% CI 80, 100), respectively.

CONCLUSIONS: HIV RNA screening performed poorly for detecting HIV infection during CAB-LA PrEP injections; performance was better immediately prior to CAB-LA initiation. Although infrequent, most isolated positive RNA test results while on CAB-LA were false-positive results. Guidelines for HIV testing algorithms designed to screen for long-acting PrEP failure should consider these performance characteristics.

Initial evaluation of injectable cabotegravir (CAB-LA) safety during pregnancy in the HPTN 084 open-label extension

CONCLUSIONS: CAB-LA was well tolerated in pregnant women. Maternal and pregnancy outcomes were consistent across non-randomized exposure groups and with expected background rates. These data provide reassurance regarding use of CAB in pregnancy.

CONCLUSIONS: Initial analyses suggest that CAB concentrations decrease throughout pregnancy; however, concentrations largely remain above protocol-defined exposure targets. While dose modifications are unlikely to be required for those who continue CAB-LA during pregnancy, additional analyses are required.

HIV-PROTECTION HABITS OF MSM ON PrEP TEND TO BE STABLE AND WHEN THEY EVOLVE, IT'S TOWARDS PrEP-EXCLUSIVE COVERAGE.

Characteristics at Inclusion

- **Age:** 36 (IQR: 30-44)
- ≥ High school: 87%
- **PrEP naive**: 42%
- Comfortable financial situation: 72%
- Perception of **taking risks in sexual life**: 60%

Time-dependent Characteristics at M3

- **Known partner*:** 56%
- **On-demand PrEP** (last 3 months): 48%
- **Chemsex*:** 14%

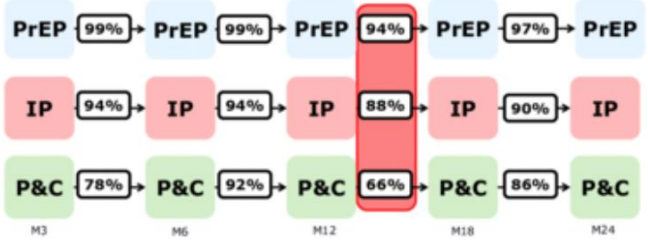
*Last sexual encounter

Results

Latent States

Description of estimated latent states	Prevalence M3 → M24	Factors associated with membership
PrEP **Optimal PrEP :** 90% **Condom use :** 6%	45% → 58%	Ref.
Inefficiently Protected (IP) **Sub-optimal PrEP :** 71% **Condom use :** 31%	42% → 35%	**Age :** ↓ **Takes risks in sexual life:** ↓
PrEP & Condoms (P&C) **Optimal PrEP :** 76% **Condom use :** 70%	13 % → 7%	**Age :** ↓ **Takes risks in sexual life:** ↓

Probability of staying in the same state



Adjusted for Age, PrEP Naive, Perception of taking risks in sexual life, PrEP on-demand, chemsex, and known partner

- **Largest probabilities of transition between M12→M18**
- **Most transitions → PrEP**
- Factors associated with **transitioning towards Inefficiently Protected:**
  - **PrEP on-demand increases odds of transitioning**
  - **Known partner & Chemsex**
    - **Decrease** odds of transitioning, between **M3-M18**
    - **Increase** odds of transitioning between **M18-M24**

Take Away

→ **3 states** of HIV protection (PrEP, IP, and P&C)

→ **Extremely stable HIV-Protection habits**, BUT **when individuals transition, they tend towards an exclusive use of PrEP**

→ Potential **PrEP-fatigue starting around M18**

What can be done?

→ **Offer education and support at inclusion,** particularly for those who are **young, who don't consider they take risks in their sexual life,** and those taking **PrEP on-demand**

→ **Education and support** should be **renewed at M18**

Waiting for a PrEP appointment: how many people have seroconverted?

Background

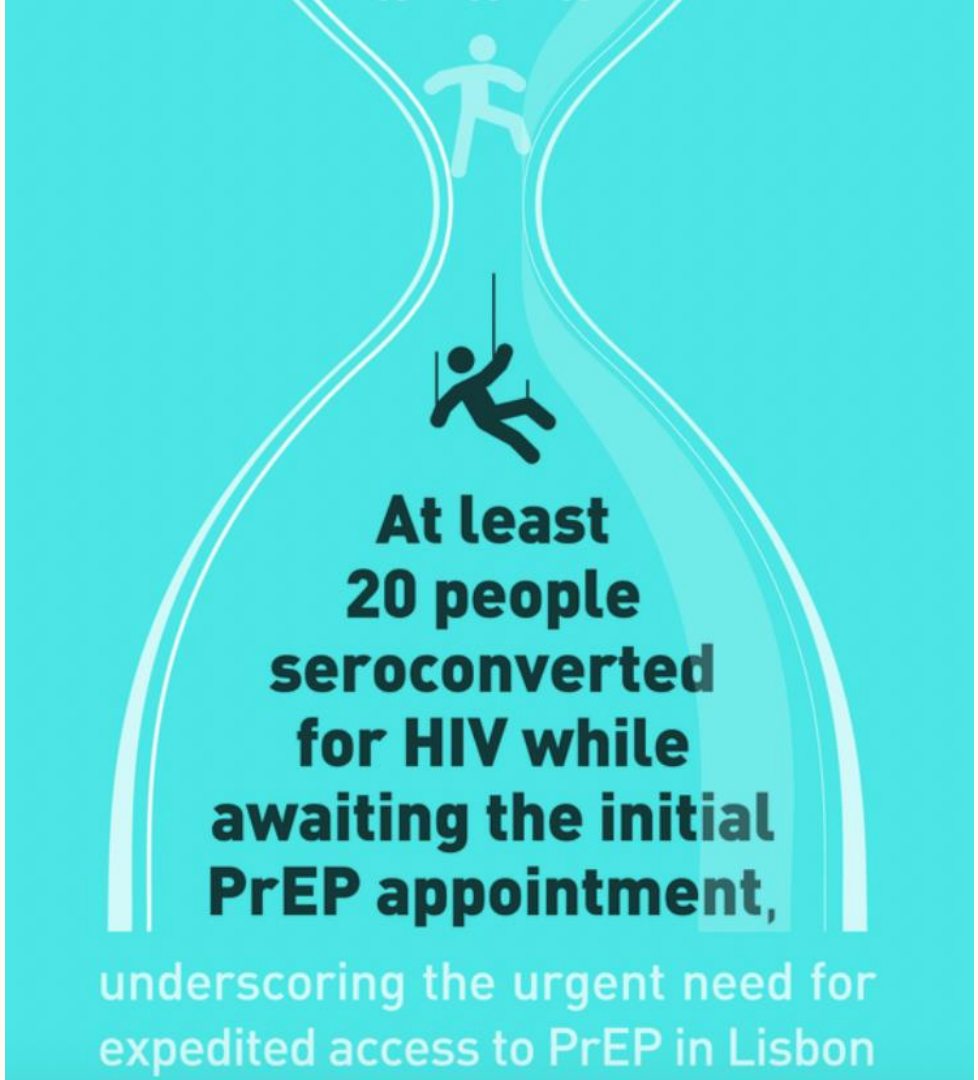
- In Portugal, both **HIV Pre-Exposure Prophylaxis (PrEP) and Treatment as Prevention (TasP) are available through National Health Service (NHS) HIV hospital units, which must complete the first medical appointment within 30 days of referral.**
- The Treatment Activists Group (GAT) offers STI screenings and refers individuals to the NHS in the Lisbon and Tagus Valley region based on their needs.
- Since PrEP referrals are for those at high risk of HIV, we aim to **estimate the number of people who seroconverted before accessing their initial PrEP appointment.**

Methods

- Community health workers (CHWs) provide combination prevention based on HIV status determined by antibody testing.
- Referrals for PrEP and TasP are sent to the NHS HIV hospital unit's appointment booking email.
- An electronic health record (EHR) tool recorded CHW referrals from 2019 to 2023.
- **We analyzed** these referrals for age, gender, country of birth, and key populations, isolating **sequential referrals from PrEP to TasP and calculating the days between referral dates.**
- Seroconversions were classified as "before the first PrEP appointment," "after the first PrEP appointment," or "undetermined," with counts and proportions performed.

Results

- We referred 8136 people to PrEP, to 27 different PrEP provision points country-wise, but mostly in the Lisbon and Tagus Valley region (97%).
- We identified 53 (0.65%) people referred for TasP after a previous PrEP referral: **20 were cases of seroconversion "before the first PrEP appointment,"** 27 "after the first PrEP appointment," and 6 were "undetermined."
  - The distribution of cases by calendar year (2019 to 2023) in the "before the first PrEP appointment" group was 0, 3, 2, 4, and 11.
  - The average (minimum-maximum) interval of **consecutive days between referrals in the "before the first PrEP appointment" group was 139 (58-300).**
- Overall, cases had a median (1Q-3Q) age of 29 (25-31) and occurred mainly in cis men (92.5%) who had sex with men (90.6%) born in Brazil (58.5%).



At least 20 people seroconverted for HIV while awaiting the initial PrEP appointment,

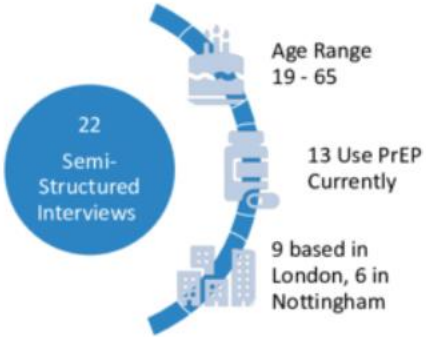
underscoring the urgent need for expedited access to PrEP in Lisbon

'Why are PrEP Gays always like this…'

Psychosocial influences on U.K. based MSM's perceptions and use of HIV Pre-Exposure Prophylaxis

Pre-Exposure Prophylaxis (PrEP) is a cost efficient, highly effective biomedical intervention used to prevent the spread of Human Immunodeficiency Virus (HIV). However, many individuals still report a range of barriers that limit their access to PrEP. The current study aimed further explore the range of psychosocial factors that increase/decrease MSM's PrEP usage.

And then this one guy was like, 'oh why are PrEP Gays always like'...' these PrEP Gays.' It was like, 'oh, all of a sudden, like, you take a pill. And that means that you can just do whatever the fuck you want. And you don't have to do condoms. I think everyone should be having condoms.'' (Alfie, 29, Gay, PrEP User)

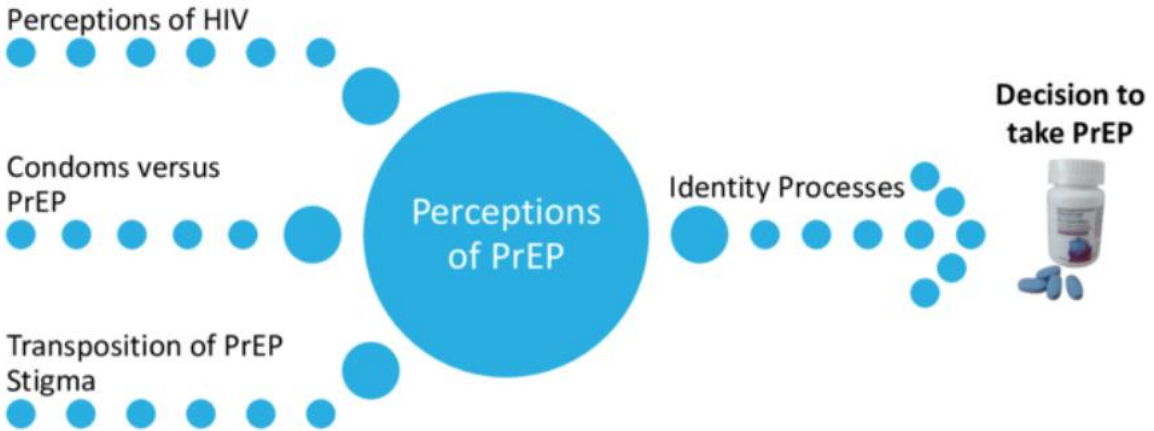


Reflexive Thematic Analysis

(Braun & Clarke, 2021)

'I hate to use the term lifestyle drug. But... I think... there does need to be an education piece of both. It's a bit like the conversation that consultant almost had with me about PEP, 'do you really need this?'' (Andy, 41, Gay, Non-PrEP User)

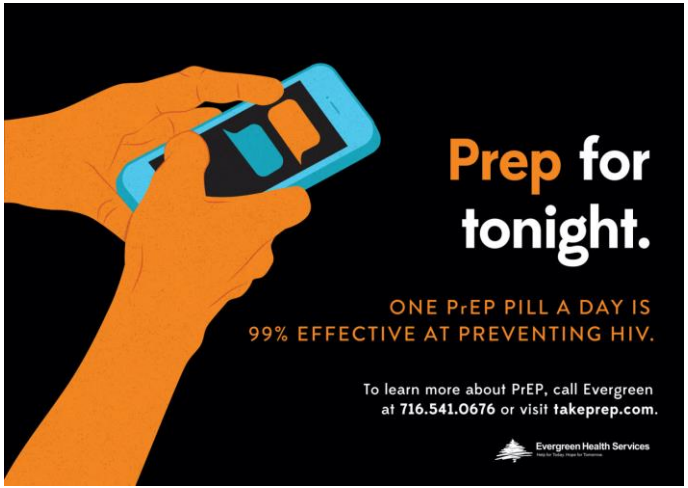
This study highlights current psychosocial barriers to PrEP, as well as the benefits (e.g., reduced HIV anxiety) that PrEP usage brings. Three superordinate themes describe how PrEP use is influenced by perceptions of HIV and condom use preferences. These homogenise into an identity of a 'PrEP User', shaping how stigmas associated with PrEP are then both attributed and mitigated. This is beneficial for informing future PrEP public health campaigns.



NTU

Anthony Gifford*, Rusi Jaspal, Beth Jones, Daragh McDermott

Psychology, Nottingham Trent University, Nottingham, United Kingdom, Vice-Chancellor's Office, University of Brighton, Brighton, United Kingdom.
**All correspondence regarding this poster should be directed to Anthony Gifford (anthony.gifford2021@my.ntu.ac.uk)*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PrEP 99+%*
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PrEP WORKS
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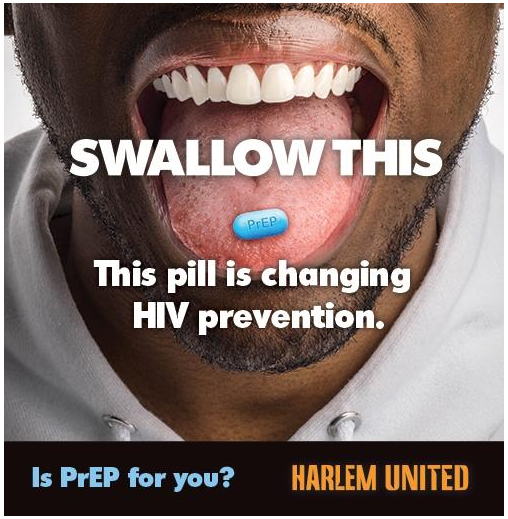
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