Lo stato dell’arte della PrEP

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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 =	Placebo (n = 608)	62.2 (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.

Daily and on-demand HIV pre-exposure prophylaxis with emtricitabine and tenofovir disoproxil (ANRS PREVENIR): a prospective observational cohort study

*Jean-Michel Molina, Jade Ghosn, Lambert Assoumou, Constance Delaugerre, Michèle Algarte-Genin, Gilles Pialoux, Christine Katlama, Laurence Slama, Geoffroy Liegeon, Lydie Beniguel, Michel Ohayon, Hanane Mouhim, Lauriane Goldwirt, Bruno Spire, Bénédicte Loze, Laure Surgers, Juliette Pavie, Jérémy Lourenco, Mohamed Ben-Mechlia, Soizic Le Mestre, Daniela Rojas-Castro, Dominique Costagliola, on behalf of the ANRS PREVENIR Study Group**

Lancet HIV 2022; 9: e554–62

Published Online June 27, 2022

Between May 3, 2017, and May 2, 2019, 3082 people were assessed for eligibility and 3065 participants were enrolled. **3056 (99·7%) of 3065 participants reported using PrEP and were included in the analyses.**

Median follow-up was **22·1 months** (IQR 15·9–29·7) and incidence of **study discontinuation was 17·6** participants (95% CI 16·5–18·7) per 100 person-years.

At the data cutoff on Sept 30, 2020, there had been **six HIV-1 seroconversions** (three participants using daily PrEP and three using on-demand PrEP; all were MSM) over 5623 person-years.

Overall HIV-1 incidence was 1·1 cases (95% CI 0·4–2·3) per 1000 person-years, and did not differ between participants using daily PrEP and those using on-demand PrEP

	Person-years	Number of HIV-1 seroconversions	Incidence per 1000 person-years (95% CI)	p value
Overall	5623	6	1·1 (0·4–2·3)	..
PrEP regimen*	..	..	..	0·99
Daily	2713	3	1·1 (0·2–3·2)	..
On-demand	2723	3	1·1 (0·2–3·2)	..
Period of follow-up	..	..	..	0·69
1st year	2821	1	0·3 (0·0–2·0)	..
2nd year	2024	3	1·5 (0·3–4·3)	..
3rd and 4th years	778	2	2·6 (0·3–9·3)	..
Calendar period of follow-up	..	..	..	0·66
May, 2017–April, 2018	668	0	0·0 (0·0–5·5)	..
May, 2018–April, 2019	1975	2	1·0 (0·1–3·7)	..
May, 2019–September, 2020	2980	4	1·3 (0·4–3·4)	..

Data are n unless otherwise stated. HIV-1 incidences rates were calculated as the total number of infections over person-years of observation, and were compared between groups using a Poisson distribution. According to the type of dosing regimen used by participants between visits, the follow-up time per dosing regimen was calculated during the study period to assess HIV-1 incidence per dosing regimen. PrEP=pre-exposure prophylaxis. *Information on the PrEP dosing regimen was missing for seven participants.

Table 2: **HIV-1 incidence over time and by PrEP regimen**

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.

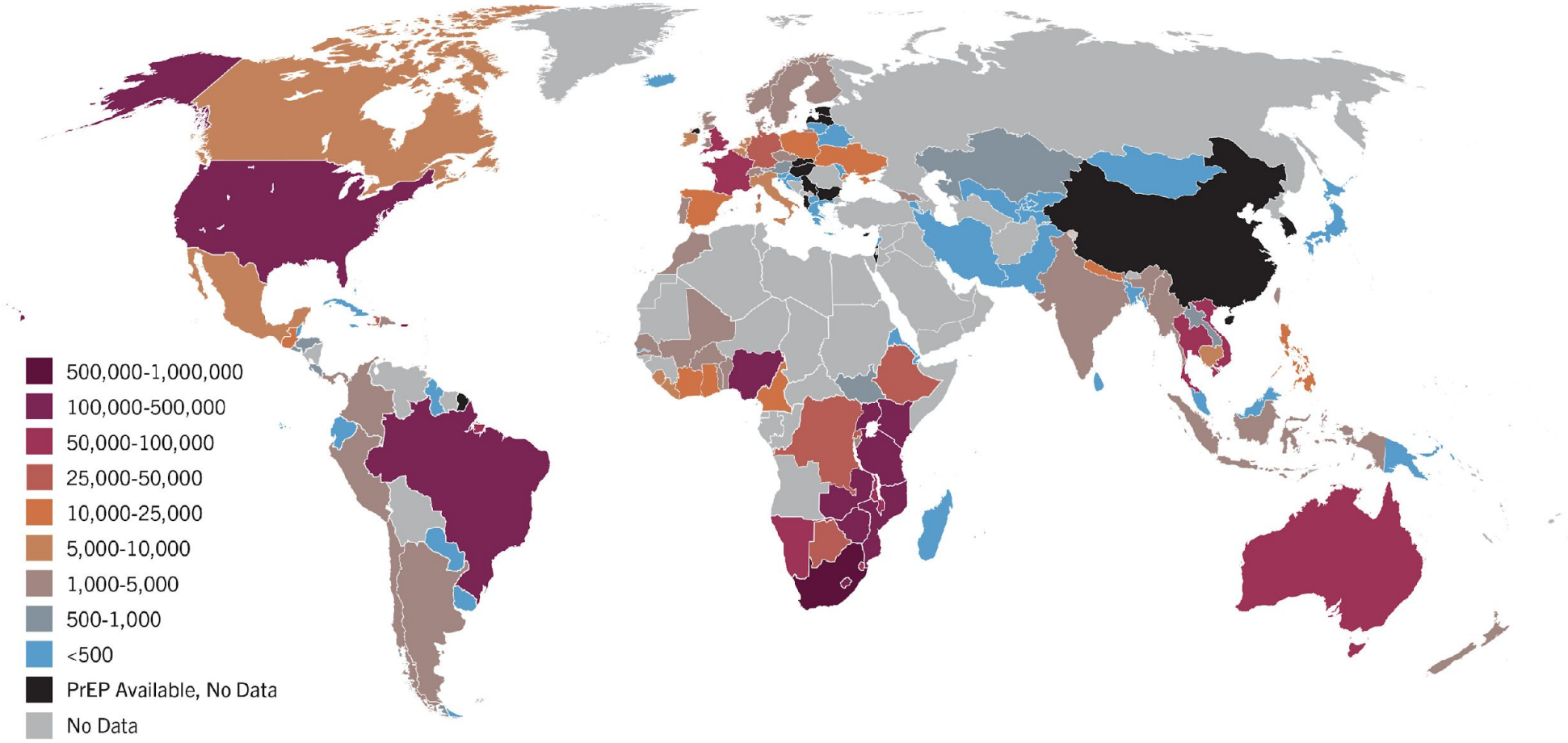
Table 4: Years since first dispensed PrEP, calendar period of follow-up, and mean MPR during follow-up and risk of HIV infection

PrEP Initiations by Country, August 2023

AVAC
Global Advocacy for HIV Prevention

Q2 2023 **203 projects**

4.929.732 PrEP initiations **64 countries approved selected products**



Source: AVAC Global PrEP Tracker, Q2 2023, https://www.prepwatch.org/data-by-country/

SERIE GENERALE

Spediz. abb. post. - art. 1, comma 1
Legge 27-02-2004, n. 46 - Filiale di Roma

Anno 164° - Numero 115

GAZZETTA UFFICIALE
DELLA REPUBBLICA ITALIANA

PARTE PRIMA Roma - Giovedì, 18 maggio 2023 SI PUBBLICA TUTTI I GIORNI NON FESTIVI

DETERMINA 8 maggio 2023.

Regime di rimborsabilità e prezzo, a seguito di nuove indicazioni terapeutiche, del medicinale per uso umano «Emtricitabina/Tenofovir Disoproxil Mylan». (Determina n. 349/2023).

Indicazione autorizzata:

Emtricitabina/Tenofovir disoproxil Mylan è indicato in combinazione con pratiche sessuali sicure per la profilassi pre-esposizione al fine di ridurre il rischio di infezione da HIV-1 sessualmente trasmessa in adulti e adolescenti ad alto rischio.

Indicazione rimborsata SSN:

Emtricitabina/Tenofovir disoproxil Mylan è rimborsato nell'indicazione della profilassi pre-esposizione di HIV unicamente in soggetti adulti ad alto rischio di acquisizione di HIV per via sessuale come definito nei seguenti criteri di rimborsabilità

Emtricitabina/tenofovir disoproxil deve essere utilizzato per la profilassi pre-esposizione solo come parte di una strategia globale di prevenzione dell'infezione da HIV-1, incluso l'uso di altre misure di prevenzione dell'HIV-1 (per es., l'uso costante e corretto del preservativo, la conoscenza dello stato HIV-1, l'analisi regolare per altre malattie sessualmente trasmesse) e nell'ambito del programma di gestione e implementazione della PrEP predisposto dal Ministero della Salute.

Condizioni cliniche e criteri di rimborsabilità

La persona candidata alla PrEP deve soddisfare tutte le condizioni sottostanti:

- età ≥18 anni
- negatività al test HIV Ab/Ag (test di 4° generazione o superiore)
- comportamento sessuale ad alto rischio di acquisizione di HIV per via sessuale, definito come aver avuto, negli ultimi 3 mesi:
  - Almeno un rapporto sessuale senza l'uso del preservativo con partner occasionale HIV-positivo o di siero-stato HIV ignoto (storia di uso inconsistente o non uso del profilattico);
  - Trattamento di una malattia sessualmente trasmissibile (MST);
  - Precedente utilizzo di profilassi post-esposizione (PEP);
  - Uso di droghe (cocaina, metamfetamina, GHB, MDMA, mefedrone, ketamina) durante i rapporti sessuali (*chemsex*).

La persona candidata alla PrEP non deve presentare nessuno dei seguenti criteri di esclusione:

- Persone con infezione da HIV;

SERIE GENERALE

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Valutazione clinica e monitoraggio ^

	Prima prescrizione	Ogni 3 mesi	Ogni 6 mesi
Visita clinica generale (raccolta dati demografici, clinici e sui comportamenti sessuali a rischio)	X		
Definizione dei criteri di eleggibilità	X		
Counseling sui comportamenti a rischio	X	X	X
Test HIV Ab/Ag (4° generazione o superiore)	X	X	X
Test per HBV (HBsAg, HBsAb e HBcAb)	X		X*
Sierologia per epatite C (HCV Ab)	X		X§
Sierologia per epatite A (HAV Ab)	X		X*
Screening per MST (sierologia per sifilide; tampone oro-faringeo, ano-rettale e raccolta urine spot per Chlamydia, Neisseria gonorrhoeae)	X	X	X
Determinazione della creatinina sierica e stima GFR	X		X
Misurazione dell'aderenza alla PrEP e interventi di supporto		X	X
Valutazione degli eventi avversi		X	X

^ Procedure definite in accordo al Documento sulla profilassi pre-esposizione per l'infezione da HIV (PrEP) redatto dalle Sezioni L e M per la lotta contro l'AIDS del Comitato Tecnico-Sanitario del Ministero della Salute.
* nei soggetti con sierologia negativa precedente, non vaccinati o non *responder* alla vaccinazione;
§ nei soggetti con sierologia negativa precedente.

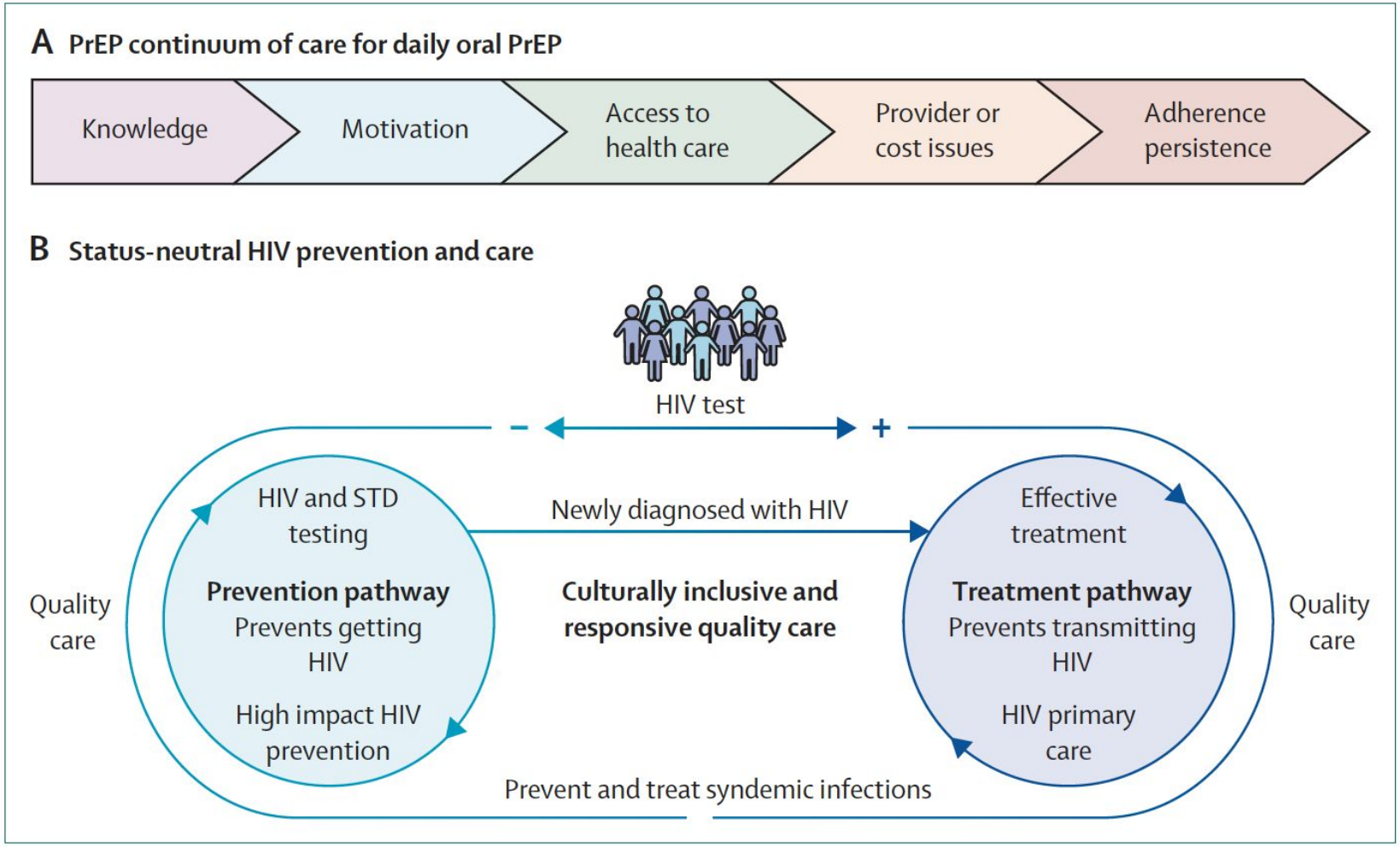
ITAPrEP

Main characteristics and HIV/STI events among 1,919 Italian PrEP users

HIV-seroconversions	5
Incidence Rate HIV	0.22 x 100 PYFU
C. trachomatis pos tests after first visit	551
Incidence Rate C. trachomatis	25.0 x 100 PYFU
N. gonorrhoeae pos test after first visit	424
Incidence Rate N. gonorrhoeae	20.1 x 100 PYFU
Syphilis pos test after first visit	321
Incidence Rate Syphilis	19.25 x 100 PYFU

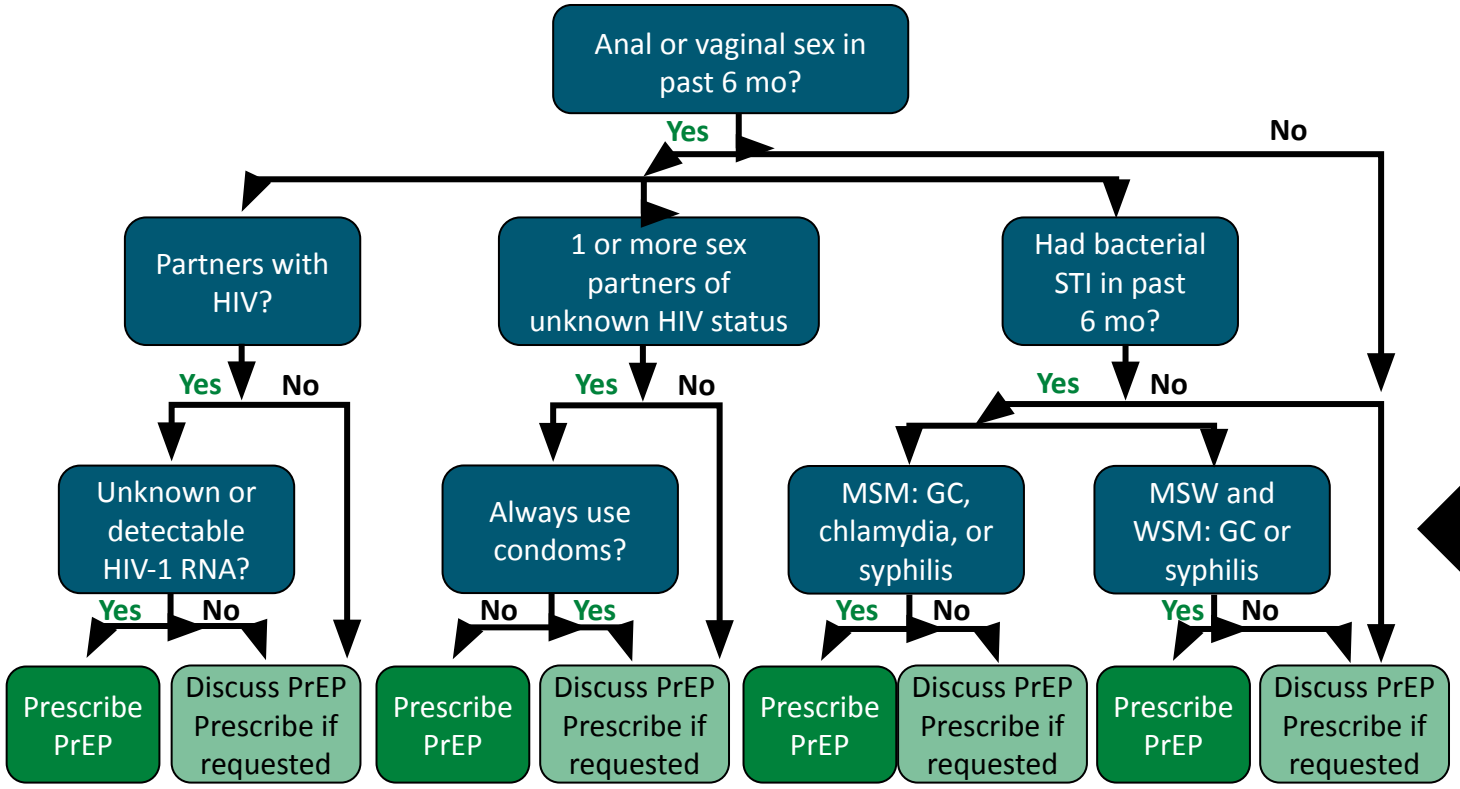
	Ita-PrEP users (N=1,919)	%
Age, Median (IQR)	36	31-44
<30	380	19,8
30-40	**781**	**40,7**
>40	**758**	**39,5**
Gender		
F	24	1,25
M	**1.873**	**97,6**
MtF	22	1,15
Sexual Orientation		
Bisexual	125	6,55
Heterosexual	46	2,41
MSM	**1.738**	**91,04**
Italian	**1585**	**82,6**
University	**1126**	**58,6**
Job		
Not-employed	223	11,6
Employed	**1476**	**76,9**
Sex worker	67	3,5
STIs baseline	**433**	**22,6**
Chemsex baseline	**333**	**17,3**
PEP baseline	**295**	**15,4**

The PrEP continuum of care model (A) and the HIV serostatus-neutral model (B)



PrEP Guidance: CDC

"All sexually active adults and adolescents should be informed about PrEP for prevention of HIV acquisition"



Anyone who requests PrEP should be prescribed PrEP

All pathways lead to prescribing or discussing PrEP!

CDC. PrEP Guidelines. 2021.

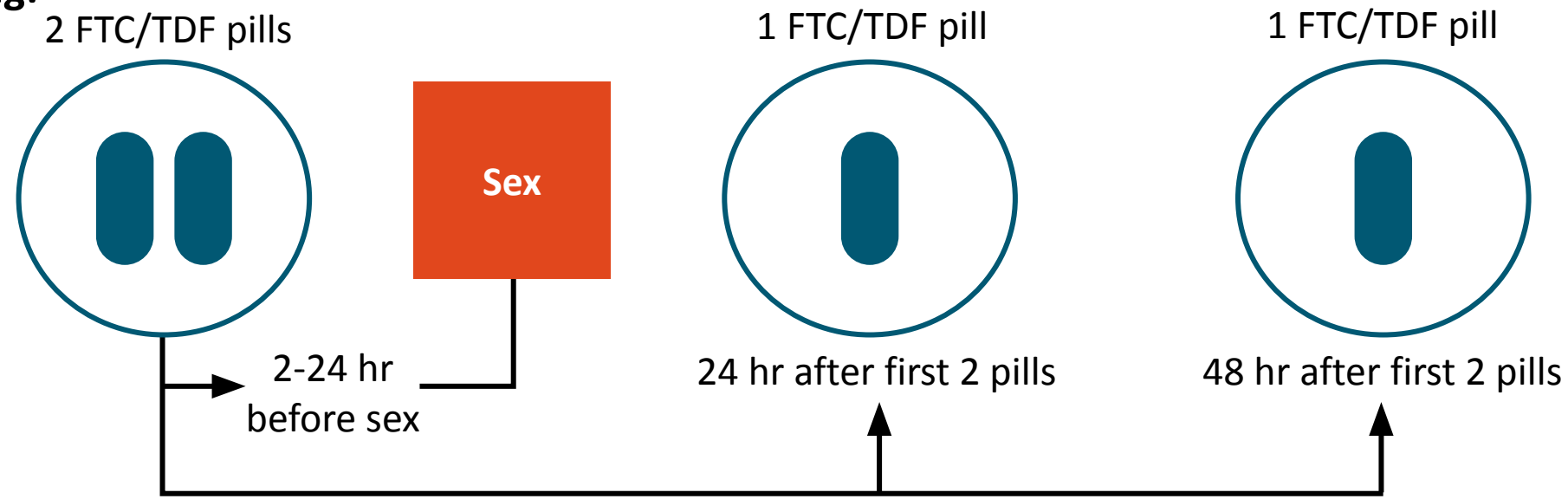
How effective is PrEP?

PrEP is highly effective for preventing HIV.

- PrEP reduces the risk of getting HIV from sex by about 99% when taken as prescribed.

On-Demand "2-1-1" PrEP Regimen

- **Dosing:**



- **On-demand FTC/TDF should not be used for men who have sex with men** with HBV infection and/or who may have difficulty adhering to complex dosing regimen
  - **Use with caution in transgender women receiving GAHT**
- Drug monitoring similar to daily PrEP

CDC PrEP guidelines. 2021.

Prevention-effective adherence paradigm

Defining success with HIV pre-exposure prophylaxis: a prevention-effective adherence paradigm

Jessica E. Haberer[a,b], David R. Bangsberg[a,b], Jared M. Baeten[c,d], Kathryn Curran[e], Florence Koechlin[e], K. Rivet Amico[f], Peter Anderson[g], Nelly Mugo[c,h], Francois Venter[i], Pedro Goicochea[j,k], Carlos Caceres[k,l] and Kevin O'Reilly[e]

AIDS 2015, **29**:1277–1285

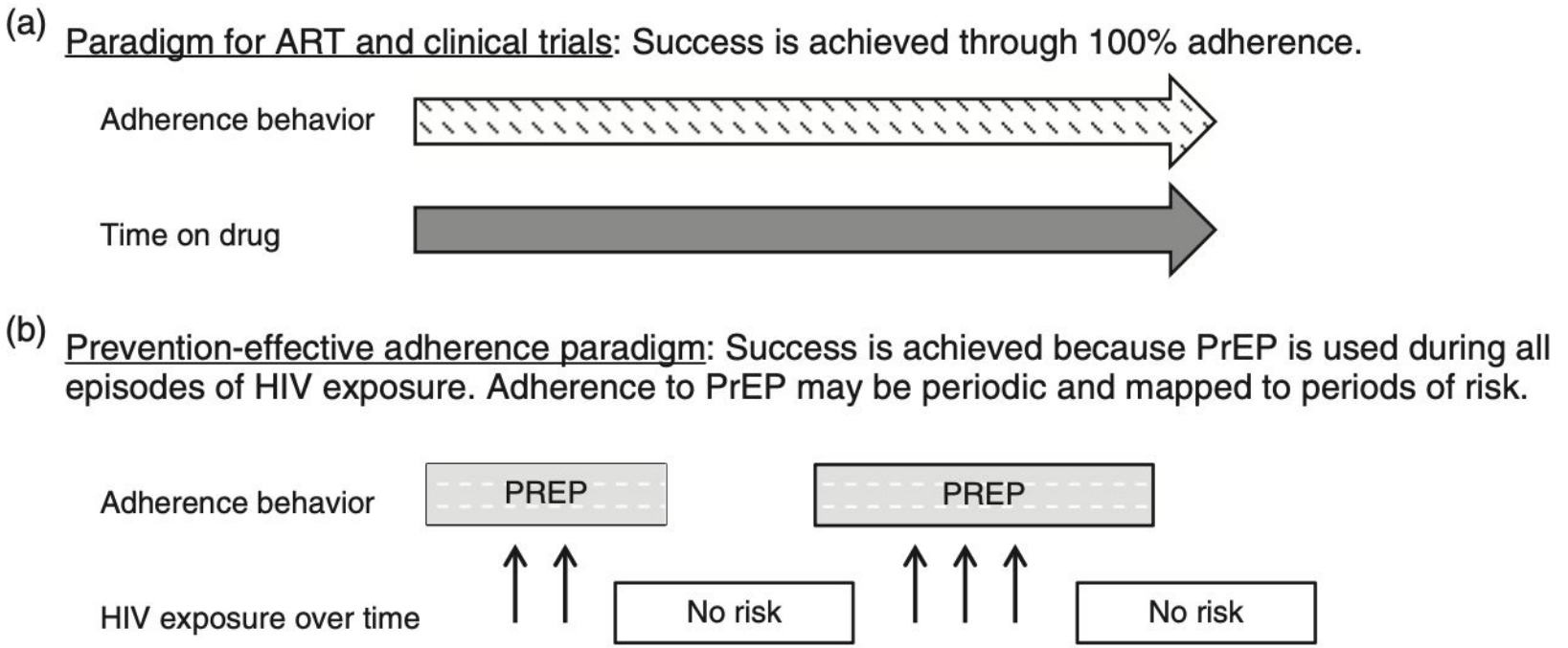


Fig. 1. Adherence success by adherence paradigm. The paradigm of consistently high adherence for all individuals applies to ART and PrEP in clinical trials (panel a). The prevention-effective paradigm applies to PrEP in demonstration projects and wider implementation (panel b). ART, antiretroviral therapy; PrEP, pre-exposure prophylaxis.

IAS-USA Recommendations for PrEP by Population and Transmission Risk Behavior

Population and Risk Behavior	Oral TDF/FTC		Oral QD TAF/FTC	IM CAB
	QD	2:1:1		
Cisgender men/women				
▪ Insertive sex (vaginal/anal)	Yes	Yes	Yes	Yes
▪ Receptive anal sex	Yes	Yes	Yes	Yes
▪ Receptive vaginal sex	Yes	Insufficient data	Insufficient data	Yes
▪ Injection drug use	Yes	Insufficient data	Insufficient data	Insufficient data
Transgender women				
▪ Insertive sex (vaginal/anal)	Yes	Yes	Yes	Yes
▪ Receptive anal sex	Yes	Yes	Yes	Yes
▪ Receptive (neo) vaginal sex	Yes	Insufficient data	Insufficient data	Yes
▪ Injection drug use	Yes	Insufficient data	Insufficient data	Insufficient data
Transgender men				
▪ Receptive anal sex	Yes	Yes	Yes	Yes
▪ Receptive vaginal (“front hole”) sex	Yes	Insufficient data	Insufficient data	Yes
▪ Injection drug use	Yes	Insufficient data	Insufficient data	Insufficient data

Gandhi. JAMA. 2023;329:63.

Key Take-home Points

PrEP should be offered to *any* person who is (or plans to be) sexually active

- To improve conversations on PrEP, HCPs should:
  - **Avoid stigmatizing language**
  - **Provide person-centered care**
  - **Use shared decision-making**
  - **Set up safe clinic spaces** (eg, promote representation of racial and ethnic minority and transgender people, wear pride pin on clothing, add your pronouns on ID tag)
- **HCPs should avoid asking for unnecessary information when taking a sexual history**
- Several safe and effective PrEP options are available based on type of sex (or orifice used)
- **Best PrEP regimen = a regimen the patient/client will use**

Stigmatizing Language: Commonly Used Terminology to Avoid and Suggested Alternatives

	Term to Avoid	Alternative
Person-first terminology	Drug user HIV infected, HIV patient Mentally ill	Person who injects (or uses) drugs Person with HIV Person with mental illness
Terminology to use when reporting on race, ethnicity and structural inequities	Blacks Caucasians Hispanics Latinos Poor, poverty stricken, poverty ridden, third world	Black people White people Hispanic people Latino, Latina (if referring to women only), or Latinx (gender-neutral term) people Resource limited
Terminology to use when reporting on sex, gender, and sexuality	Biologically male/female Cisgendered/transgendered Homosexual men	Assigned male/female at birth Cisgender/transgender Men who have sex with men

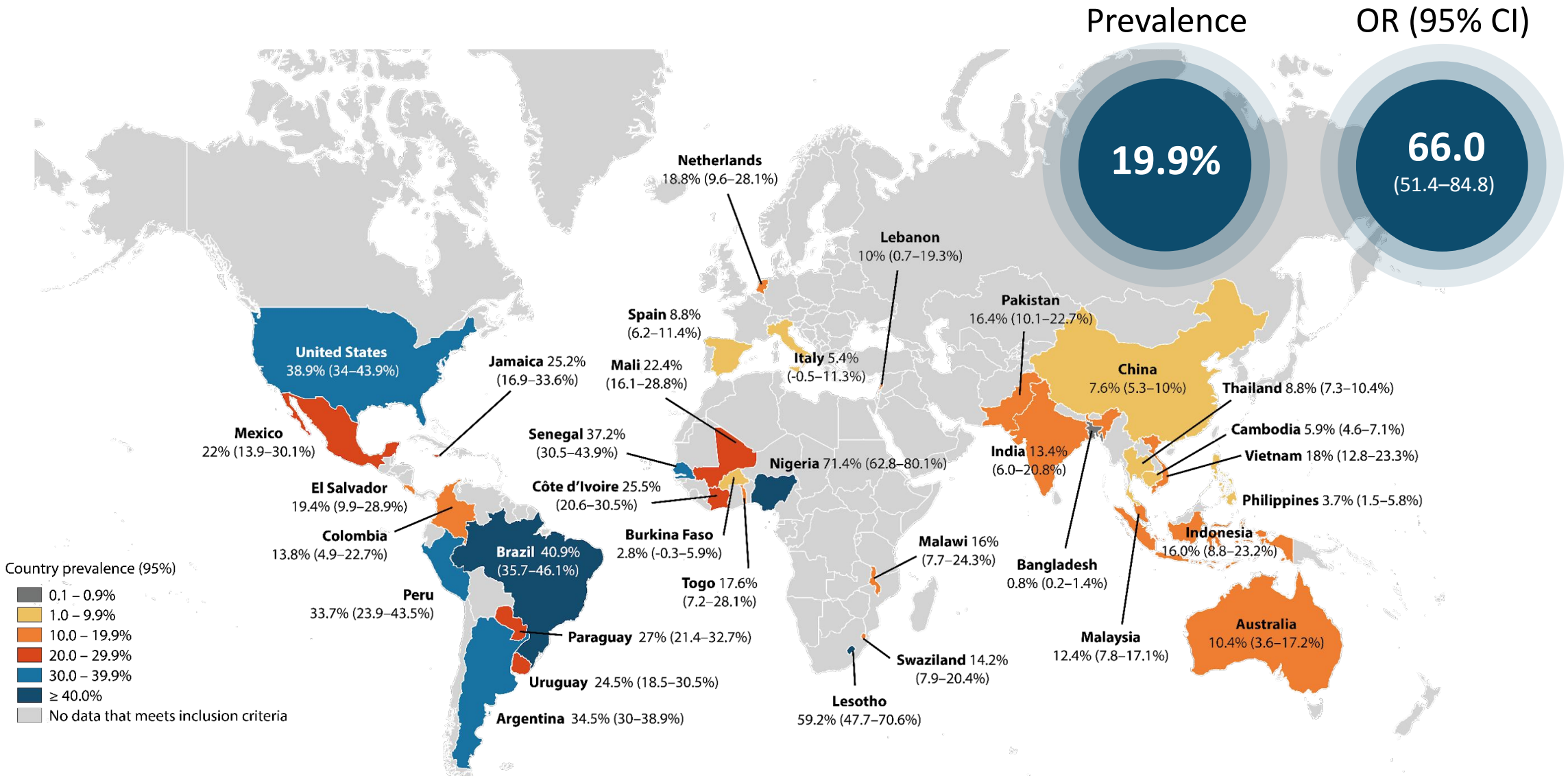
Bares. Clin Infect Dis. 2023;76:1860.

Tips on Taking a Sexual History

- Promote a **comfortable** and **nonjudgmental environment**
- **Do not assume** gender, gender identity, pronouns, sexual orientation of the patient or their partners, or types of sexual activity that they are engaging in
- **Avoid asking unnecessary information** (eg, number of partners, frequency of sex)
  - Instead, ask, **"Are you having sex, or do you want to be having sex? What type of sex, or what body parts are used?"**

cdc.gov/hiv/clinicians/transforming-health/health-care-providers/sexual-history.html.

HIV Epidemic Among Transgender Women 1995-2016



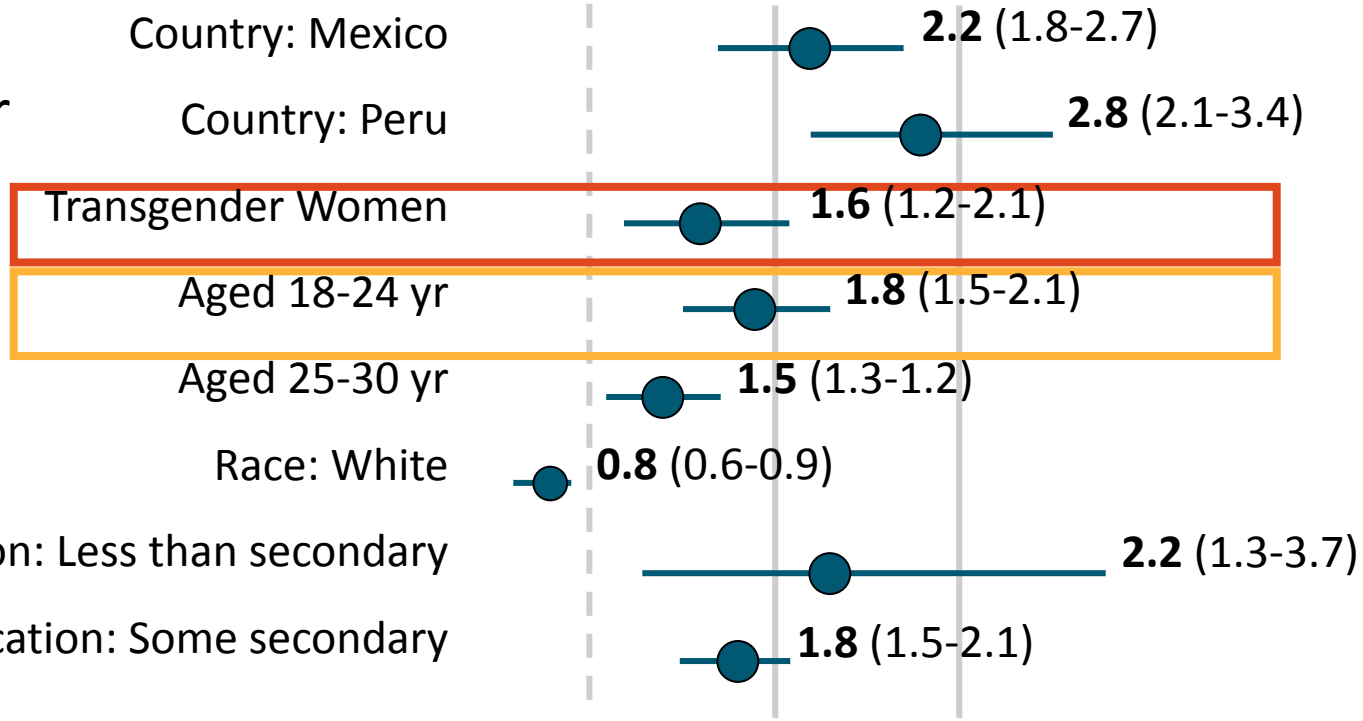
Adapted from: Stutterheim. Plos One. 2021;16:e0260063.

ImPrEP: PrEP Implementation Study in Cisgender Men Who Have Sex With Men and Transgender Women

- **Single-arm, open-label, multicenter, implementation study of same-day oral FTC/TDF PrEP (N = 9509) in Brazil, Mexico, and Peru (2018-2021)**

- **8.4%** did not show up after enrollment

Factors Associated With Early Loss to Follow-up



- Transgender women had **increased** odds of **early loss to follow-up**

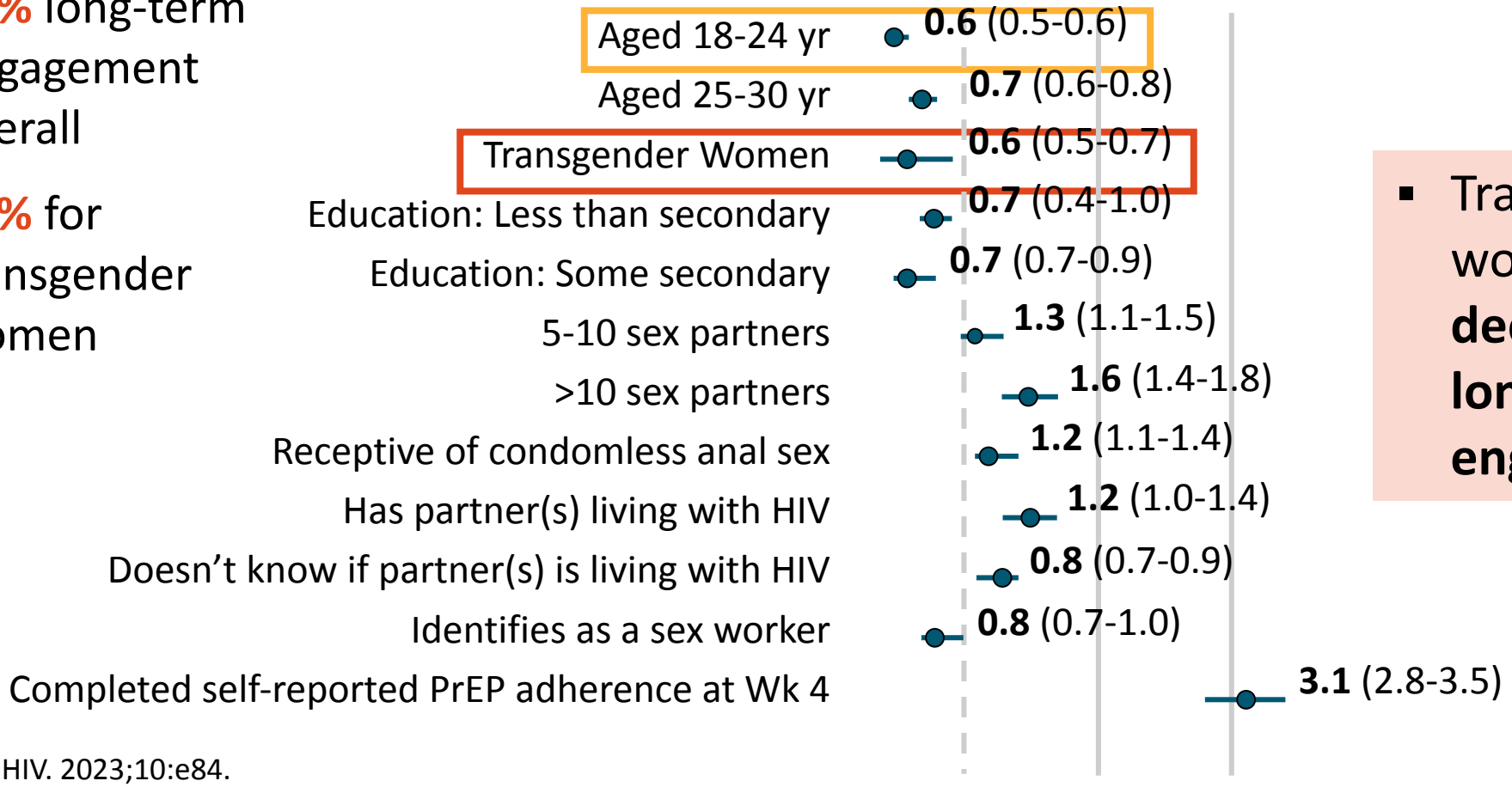
Veloso. Lancet HIV. 2023;10:e84.

ImPrEP: Long-term Engagement

- Defined as attendance at Wk 4 visit and ≥2 quarterly visits within 52 wk

- **70%** long-term engagement overall
- **49%** for transgender women

Factors Associated With Long-term Engagement, aOR (95% CI)



- Transgender women had **decreased** odds of **long-term PrEP engagement**

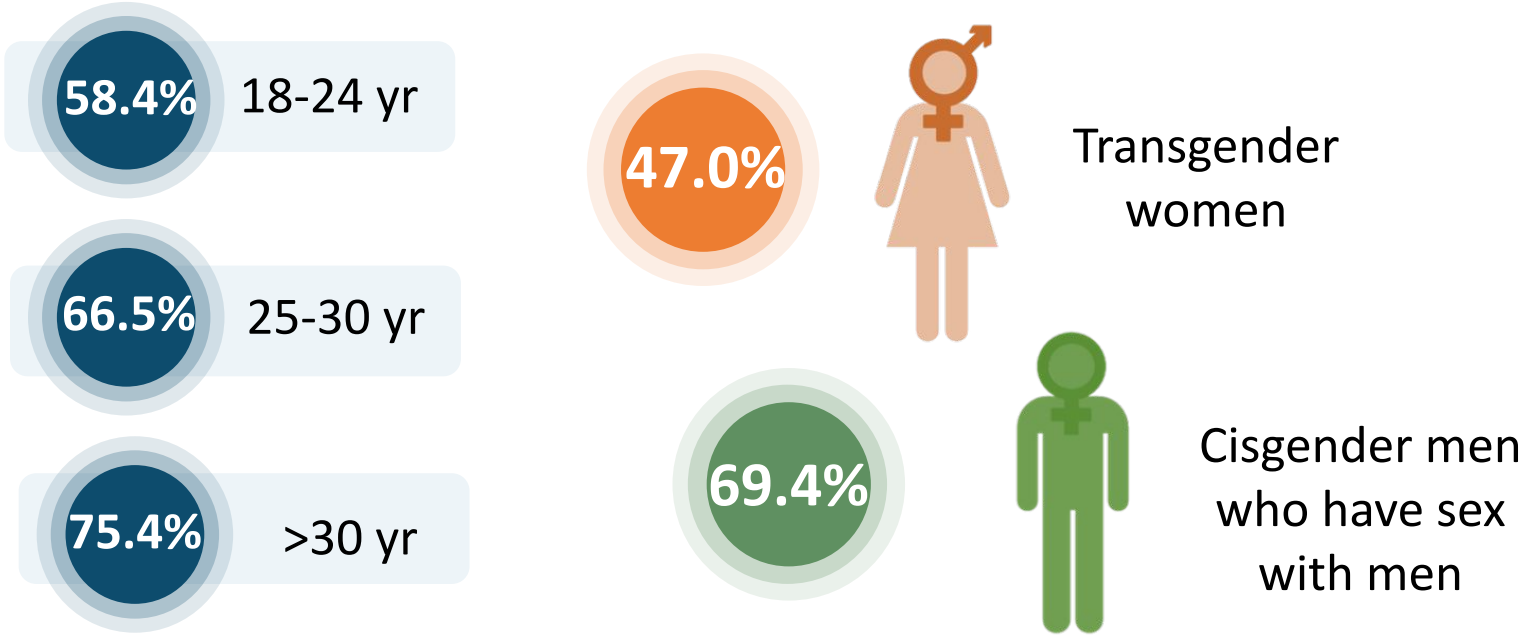
Veloso. Lancet HIV. 2023;10:e84.

ImPrEP: Adherence

- **Adherence measured by MPR*:**

MPR = No. of FTC/TDF pills dispensed during the study □ MPR ≥0.6 = 4 pills/wk
No. of days between enrollment and last visit

Percentage of People With an MPR ≥0.6



- Transgender women had **decreased** odds of **PrEP adherence**

*MPR, medication possession ratio

Veloso. Lancet HIV. 2023;10:e84.

Barriers to PrEP Uptake and Adherence for Transgender Women

- In a subgroup analysis of transgender women in the iPrEX study (n = 339), FTC/TDF was not more effective than placebo, likely due to low adherence[1]

PrEP Uptake and Adherence Barriers Among Transgender Women[2]		
Individual Factors	**Interpersonal and Community Factors**	**Structural Factors**
▪ Cost concerns ▪ Mental health concerns ▪ Substance use ▪ PrEP adverse events ▪ **FHT interaction concerns*** ▪ Past experiences of violence	▪ Romantic partner influence ▪ Patient–provider communication ▪ Discrimination and stigma ▪ Negative community opinions ▪ Negative experiences in healthcare settings	▪ Employment ▪ Transportation ▪ Housing insecurity ▪ Food insecurity ▪ Limited access to health services

*FHT, feminizing hormone therapy

1. Deutsch. Lancet HIV. 2015;2: e512. 2. Ogunbajo. AIDS Behav. 2021;25:2301.

Drug–Drug Interactions With FHT*

- **Concerns about FHT–PrEP interaction is a barrier to PrEP uptake and adherence for transgender women[1]**

- Recent **reassuring** drug–drug interaction data between FHT and PrEP:
  - In a nested PK study in Brazil (PrEParadas), **FHT did not significantly affect FTC/TDF[2] and estradiol PK was not significantly affected by FTC/TDF[3]**
  - In a US study, **FHT had no significant effect on TFV-DP concentrations** nor were there perceived changes in gender-affirming effects of FHT in those receiving FTC/TDF PrEP[4]
  - In a substudy from HPTN 083, **FHT did not affect CAB concentrations[5]**

Current data limitations may not refrain healthcare professionals from providing FHT to transgender women concomitantly with daily oral PrEP

*FHT, feminizing hormone therapy

1. Ogunbajo. AIDS Behav. 2021;25:2301. 2. Cattani. J Antimicrob Chemother. 2022;77:2729. 3. Cattani. Clin Pharmacokinet. 2023;62:1031. 4. Blumenthal. CROI 2022. Abstr 84. 5. Marzinke. Lancet HIV. 2023:S2352-3018(23)00200-X.

HIV Incidence and PrEP Uptake in Cisgender Women

Women accounted for 19% of new HIV diagnoses in 2019

- **Rates of new HIV diagnoses:**
  - **Black women**: 55% (13% of female population)
  - **White women**: 22% (62% of the female population)
  - **Hispanic/Latina women**: 18% (17% of the female population)

Based on CDC data, of women who could benefit from PrEP, only 10% were prescribed PrEP in 2019

cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-surveillance-report-2018-updated-vol-32.pdf.
cdc.gov/hiv/group/gender/women/prep-coverage.html. Guest. IAC 2020. Abstr OAC0804.

Barriers to PrEP Uptake in Cisgender Women

- **Low awareness**
- Lack of available resources on PrEP education
  - **Few commercials or marketing campaigns about PrEP with women**
- **Low perceived risk for HIV**
- Competing priorities
- Preference for barrier protection against STIs and unwanted pregnancy
- Concerns about adverse events, disclosure and stigma, financial challenges, potential increase in risk behavior
- **Limited options for PrEP**
- **Lack of knowledge from HCPs**
- **Lack of available HCPs who prescribe PrEP for women**
- Perceived complexity of PrEP monitoring and follow-up

Baldwin. Arch Sex Behav. 2021;50:1713. Goparaju. J AIDS Clin Res. 2015;6:1. Hirschhorn. J Acquir Immune Defic Syndr. 2020;84:497.
Pasipanodya. BMC Womens Health. 2021;21:220. cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf.

PrEP Barriers for Adolescents

Lower levels of medication adherence reported by young people[1]

Adolescent Barriers[2,3]

- **Adverse events**
- **Dissatisfaction with HCPs**
- Depression
- Social stigma
- **Lack of support**
- Substance use
- Lower health literacy and navigation skills

HCP Barriers[4]

- **Unaware of PrEP or indication for youths**
- Discomfort performing sexual history
- Implicit bias about who should start PrEP
- **Discomfort prescribing PrEP/ unaware of how to start (labs to order, etc)**
- **Concerns about risk compensation**

1. Velloza. AIDS. 2021;35:463. 2. Hightow-Weidman. JMIR Res Protoc. 2018;7:e10365.
3. Okafor. J Acquir Immune Defic Syndr. 2020;85:23. 4. Yusuf. JAMA Pediatr. 2020;174:1102.

Possible Solutions to PrEP Barriers for Adolescents

- **Increasing awareness of PrEP and how to access it**
- Meeting youth where they are for marketing, advertising, outreach
- **Education and training for healthcare professionals on how to talk to and provide PrEP for adolescents**
- Knowing where and how adolescents can get PrEP care confidentially and free in your area

Structural Barriers to PrEP: Informed Consent for Minors

- "As of 2022, all jurisdictions have laws that explicitly allow a minor of particular age (as defined by each state) to give informed consent to receive STD diagnosis and treatment services"
- **Consent laws vary among states**
  - In some states, minors are allowed to give informed consent to receive specific STI or HIV services, including PrEP
- Parental insurance usually **does not guarantee confidentiality** for minors
- HCPs should **be familiar with their local/state policies**, including **age of consent** and permitted **treatment/services**

cdc.gov/hiv/policies/law/states/minors.html
Society for Adolescent Health and Medicine; American Academy of Pediatrics. J Adolesc Health. 2016;58:374.

Summary of PrEP Eligibility by Regimen

Risk Group*	Daily FTC/TDF	On-Demand (2:1:1) FTC/TDF	Daily FTC/TAF	Injectable Long-acting CAB	DPV Monthly Vaginal Ring
MSM	**FDA approved, guideline recommended[1-5]**	**Off label, IAS-USA and WHO guideline recommended[2,9]**	**FDA approved, guideline recommended[2,5]**	**FDA approved, guideline recommended[2,5,7,10]**	**N/A**
TGW		**Off label, not recommended[2,3,5,9]**			
Heterosexual men					
Heterosexual women			**Off label, not recommended, studies underway[5]**	**FDA approved, guideline recommended (except in pregnancy)[5,7,10]**	**Unavailable in US, EMA-positive opinion in high-burden settings, WHO recommended[8]**
Transgender men			**Off label, not recommended (unless risk from anal sex only)[6]**		

*For PWID, sexual risk should be assessed and considered. **CDC guidelines state that PWID are likely to benefit from any FDA-approved medication for PrEP with or without a sexual risk indication.[5]**

1. FTC/TDF PI. 2. Saag. JAMA. 2020;324:1651. 3. Tan. CMAJ. 2017;189:E1448. 4. WHO implementation tool for pre-exposure prophylaxis (PrEP) of HIV infection. 2018. 5. CDC PrEP guidelines. 2021. 6. FTC/TAF PI. 7. CAB extended-release injectable suspension PI. 8. who.int/news/item/26-01-2021-who-recommends-the-dapivirine-vaginal-ring-as-a-new-choice-for-hiv-prevention-for-women-at-substantial-risk-of-hiv-infection. 9. WHO. WHAT'S THE 2+1+1? 2019.

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)**

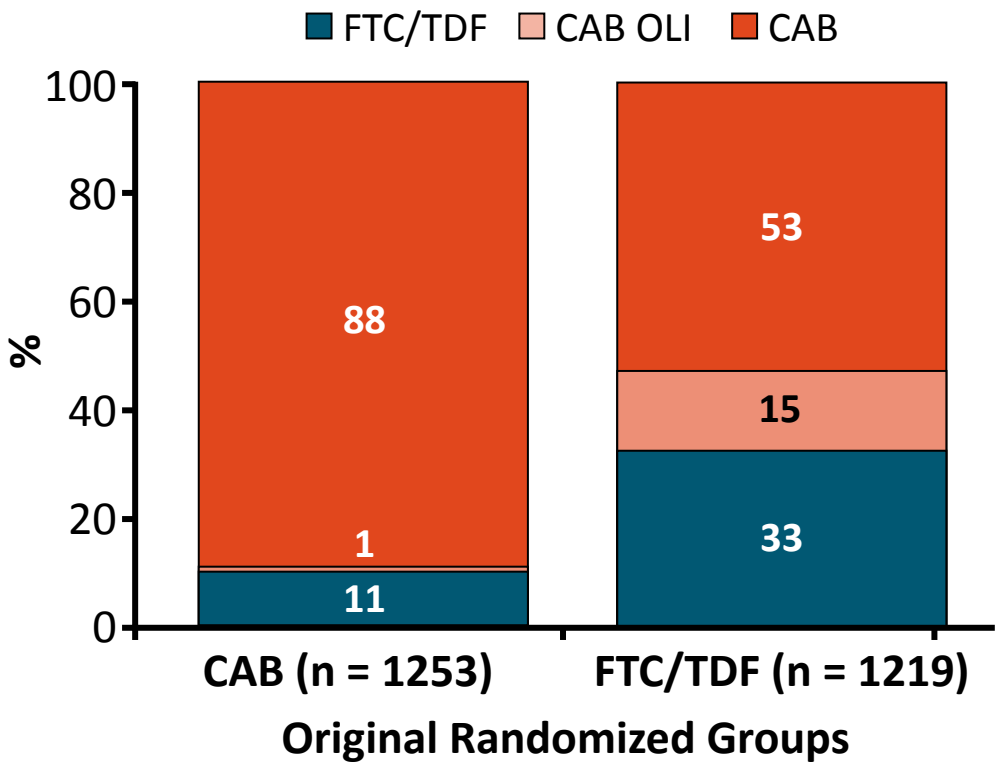
HPTN 084[2]

- 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)**

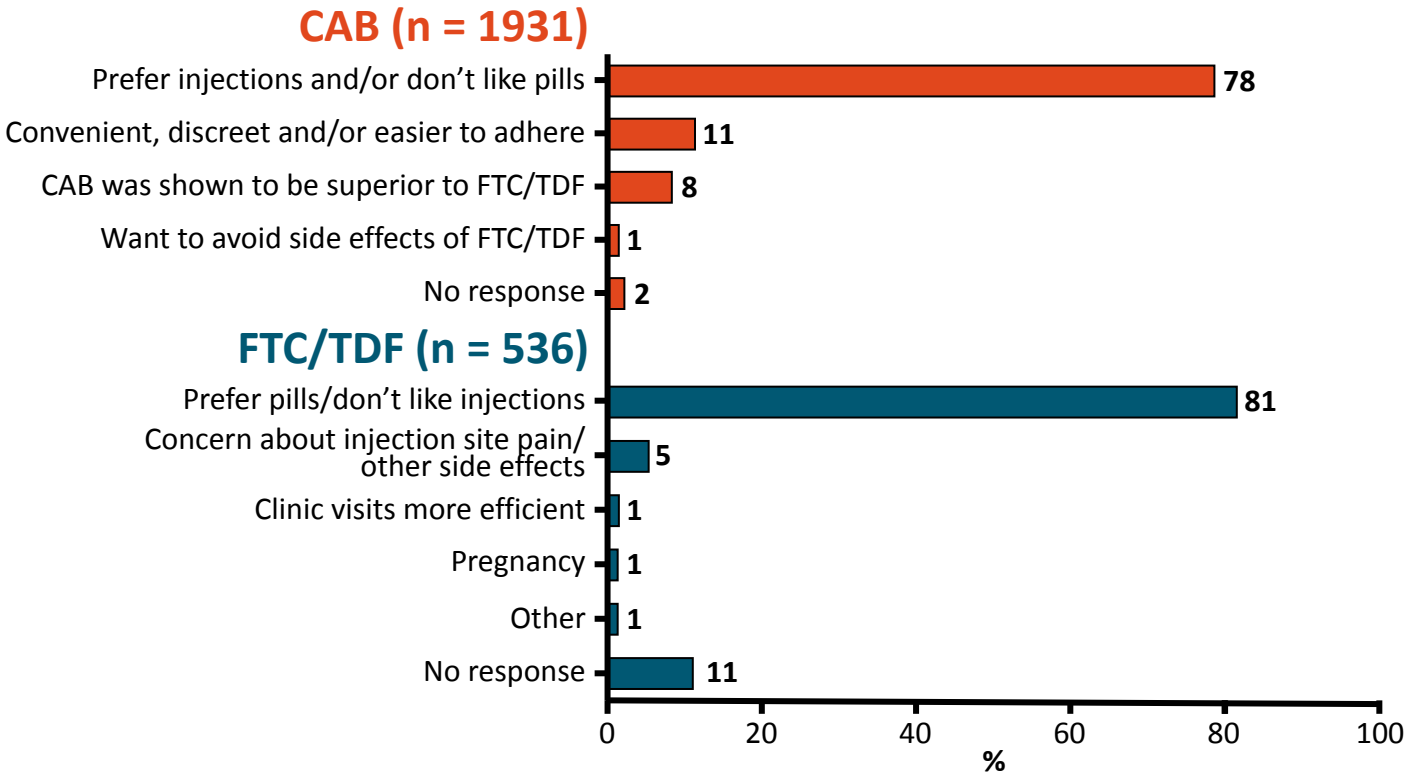
1. Landovitz. NEJM. 2021;385:595. 2. Delany-Moretlwe. Lancet. 2022;399:1779.

HPTN 084 Open-Label Extension: PrEP Product Choice

- **78% of participants chose CAB**



- Reasons for PrEP product choice



- **Participants who chose CAB were less likely to live with partners and more likely to have experienced recent physical intimate partner violence and to have been paid for sex**

Delany-Moretlwe. IAS 2023. Abstr OALBX0203.

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

20 July 2023
EMA/327881/2023
Committee for Medicinal Products for Human Use (CHMP)

Summary of opinion[1] (initial authorisation)

Apretude

cabotegravir

On 20 July 2023, the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion, recommending the granting of a marketing authorisation for the medicinal product Apretude, intended for prevention of sexually acquired HIV-1 in combination with safer sex practices. The applicant for this medicinal product is ViiV Healthcare B.V.

Apretude will be available as a 30 mg film-coated tablet and a 600 mg prolonged-release suspension for injection. The active substance of Apretude is cabotegravir, an antiviral for systemic use (ATC code: J05AJ04). Cabotegravir is an integrase inhibitor of HIV-1 which inhibits HIV integrase by binding to the integrase active site and blocking the strand transfer step of retroviral DNA integration, which is essential for the HIV replication cycle.

The benefit of Apretude was a demonstrated superiority of injections every 2 months over a daily oral regimen of tenofovir disoproxil fumarate plus emtricitabine (TDF/FTC) in preventing acquisition of HIV-1 infection, with a 69% and an 90% risk reduction, as shown in two double-blind safety and efficacy studies. The most common side effects are injection site reactions, headache, diarrhoea, and increased transaminase levels.

The full indication is:

> Apretude is indicated in combination with safer sex practices for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 infection in high-risk adults and adolescents, weighing at least 35 kg (see sections 4.2, 4.4 and 5.1).

Apretude should be prescribed by physicians experienced in the treatment of HIV.

Detailed recommendations for the use of this product will be described in the summary of product characteristics (SmPC), which will be published in the European public assessment report (EPAR) and made available in all official European Union languages after the marketing authorisation has been granted by the European Commission.

Authorisation details

Product details	
Name	Apretude
Agency product number	EMEA/H/C/005756
Active substance	Cabotegravir
International non-proprietary name (INN) or common name	cabotegravir
Therapeutic area (MeSH)	HIV Infections
Anatomical therapeutic chemical (ATC) code	J05AJ04

Publication details	
Marketing-authorisation holder	ViiV Healthcare B.V.
Date of issue of marketing authorisation valid throughout the European Union	15/09/2023

Lenacapavir for PrEP[1,2]:

#preventionwithpurpose

PURPOSE 1
Cisgender adolescent girls and young women in South Africa and Uganda
N=5,010
QUALITATIVE N=230

PURPOSE 2
CGMSM, TGW, TGM, GNB in US, South Africa, Peru, Brazil, Mexico, Argentina and Thailand
N=3,00
QUALITATIVE N=220

PURPOSE 3
US women
N=250

PURPOSE 4
US PWID
N=250

Partnerships

Voice of PWBP and community (G-CAGs)

Person-centric design

Diversity, equity, inclusion

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)

Victorian PrEPX: Mathematical modeling study (Victoria, Australia)

Combination of PrEP and Improvements in HIV Care Cascade Projected to Decrease HIV Incidence

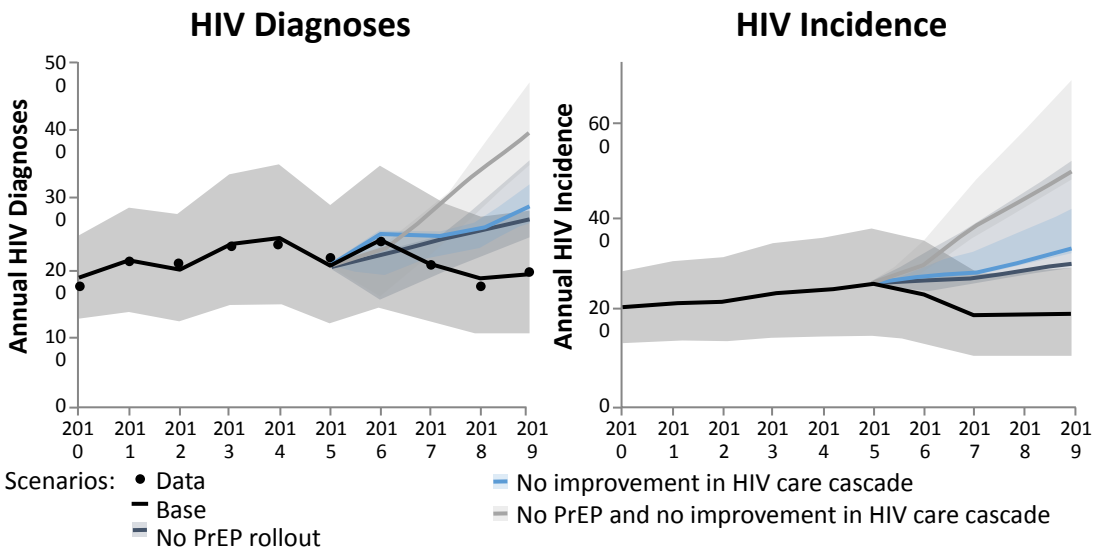
People at low and high chance of HIV acquisition and people using PrEP

Outcome

- Annual HIV diagnoses and incident HIV transmissions (2010–2019)
- Estimated relative decline in incident HIV transmissions post-PrEP vs. pre-PrEP

2010–2019

Model Projections for Annual HIV Diagnoses and Incidence Among MSM in Victoria (2010–2019)



Annual Number of Incident Transmissions and Cumulative 2017–2019 Difference Between Scenarios (Model Results)

Scenario	Incident HIV transmissions				
	Projected			Counterfactual scenarios vs. status quo (2017–2019)	
	2014–2016	2017–2019	% change	Additional*	Relative increase*
Status quo†	746	583	-21.8	–	–
No PrEP rollout‡	774	861	11.2	278	32.3%
No improvement in HIV care cascade	778	925	18.9	342	37.0%
No PrEP rollout,‡ no improvement in HIV care cascade	808	1,323	63.7	740	55.9%

Estimated reductions in incident HIV transmission (2017–2019)

- **32%** due to PrEP rollout
- **37%** due to improvements in treatment cascade
- **56%** due to combined PrEP rollo and treatment cascade of care

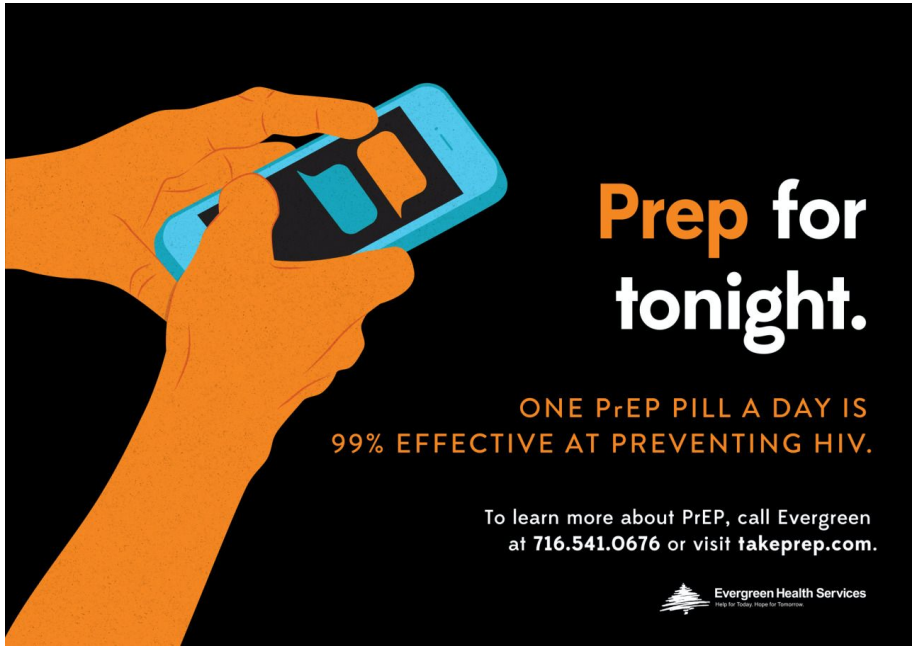
This mathematical modeling study suggests that the combination of PrEP and improvement in HIV care cascade are needed to substantially reduce HIV incidence

*Estimated; †Victorian PrEPX study PrEP rollout (PrEP obtained via the PrEPX study and PBS) and HIV care cascade indicators remain unchanged; ‡Via the PrEPX study and PBS from 2015. PBS, [Australian] Pharmaceutical Benefits Scheme

Wright W, et al. IAS 2023, Poster MOPEC22

THE PATH THAT ENDS AIDS

2023 UNAIDS Global AIDS Update


Prep for tonight.
ONE PrEP PILL A DAY IS
99% EFFECTIVE AT PREVENTING HIV.
To learn more about PrEP, call Evergreen at 716.541.0676 or visit takeprep.com.
Evergreen Health Services

"Lista y preparada para triunfar."
VIVA PrEP
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UNA VEZ AL DIA
PREVIENE EL VIH

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ticketmaster
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PrEP
BETTER THAN A CONDOM
PrEP 99+%*
Condom 72-91%*
* HIV risk reduction
PrEP WORKS
ONE PILL A DAY
concerned about STIs?
check out 100mg doxycyline daily
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BLACK WOMEN PREP
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