

# Long-acting injectable PrEP

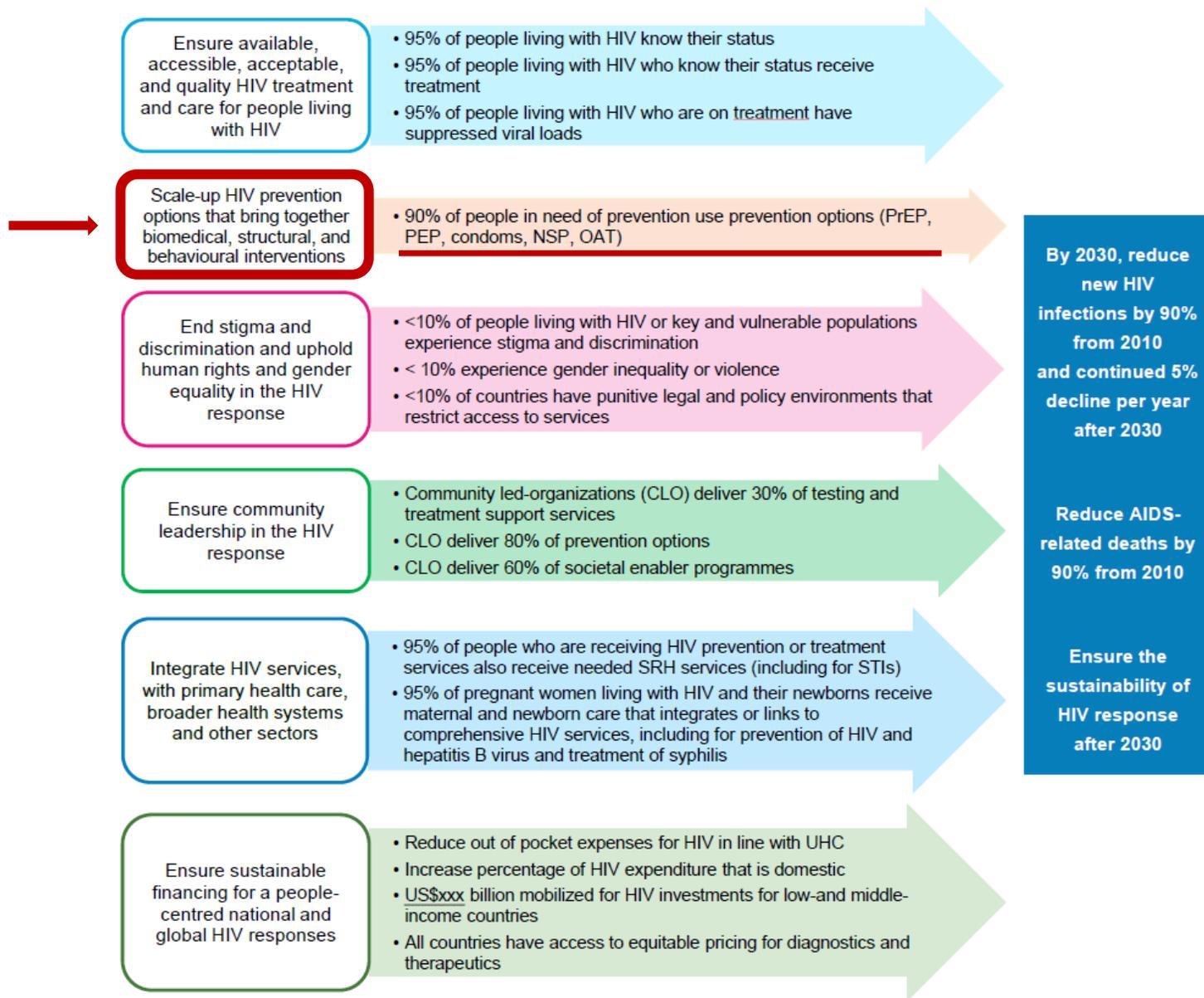
**Silvia Nozza**

04 February 2026

IRCCS San Raffaele di Milano

Università Vita-Salute San Raffaele

# 16 key objectives to achieve the UNAIDS targets by 2030.

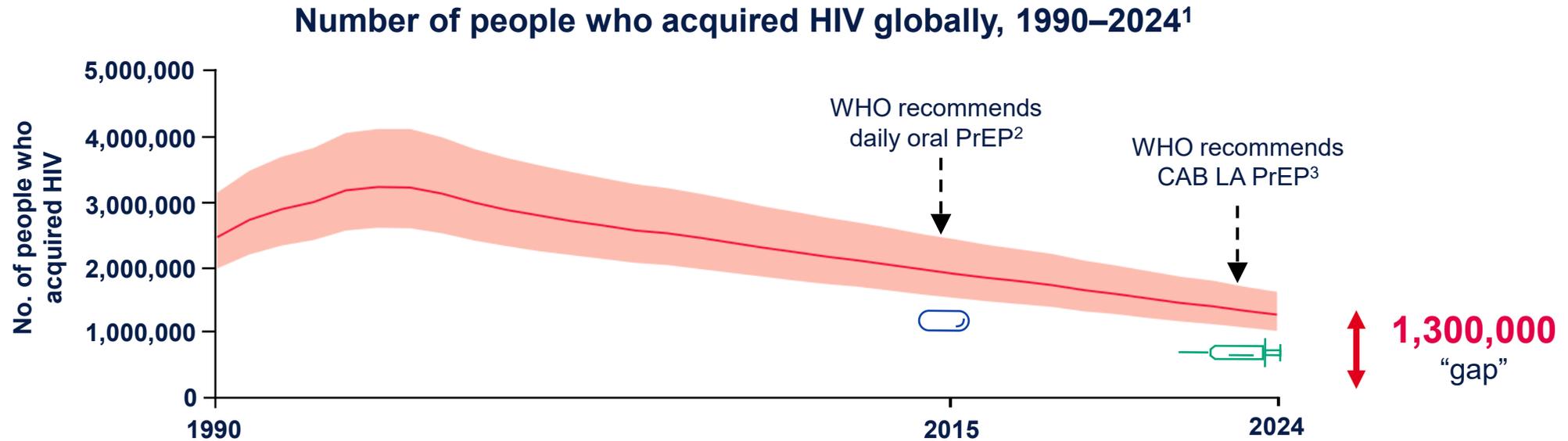


# RIAS Scale up HIV prevention on a large scale

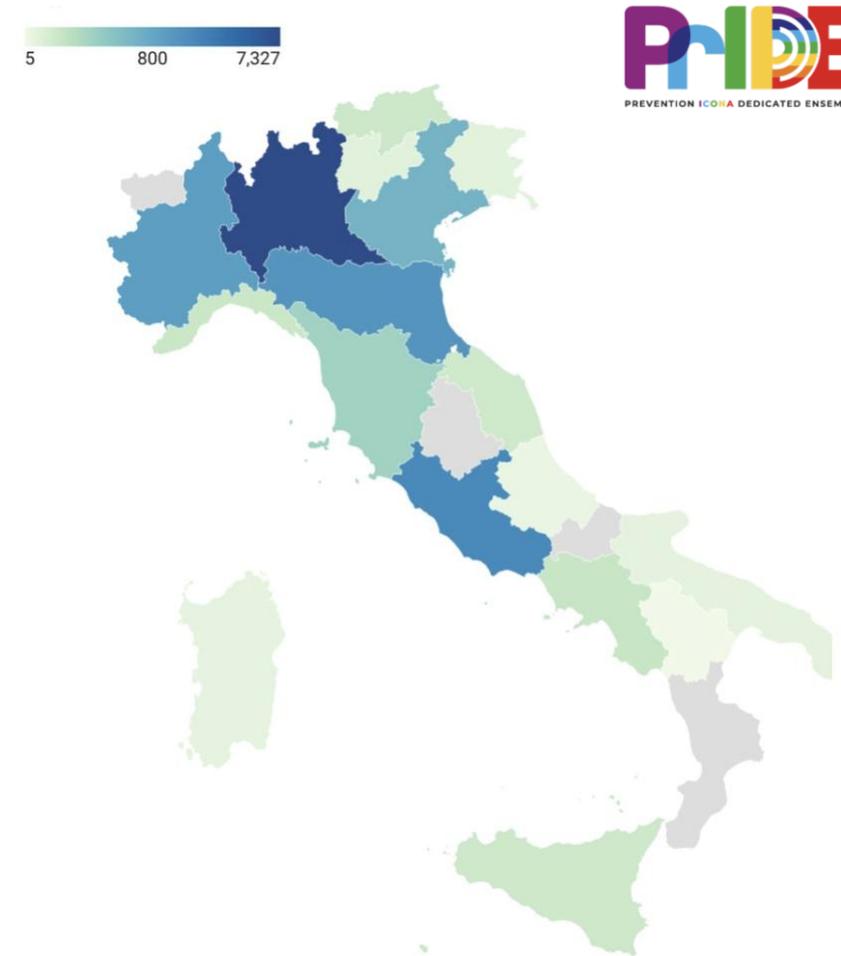
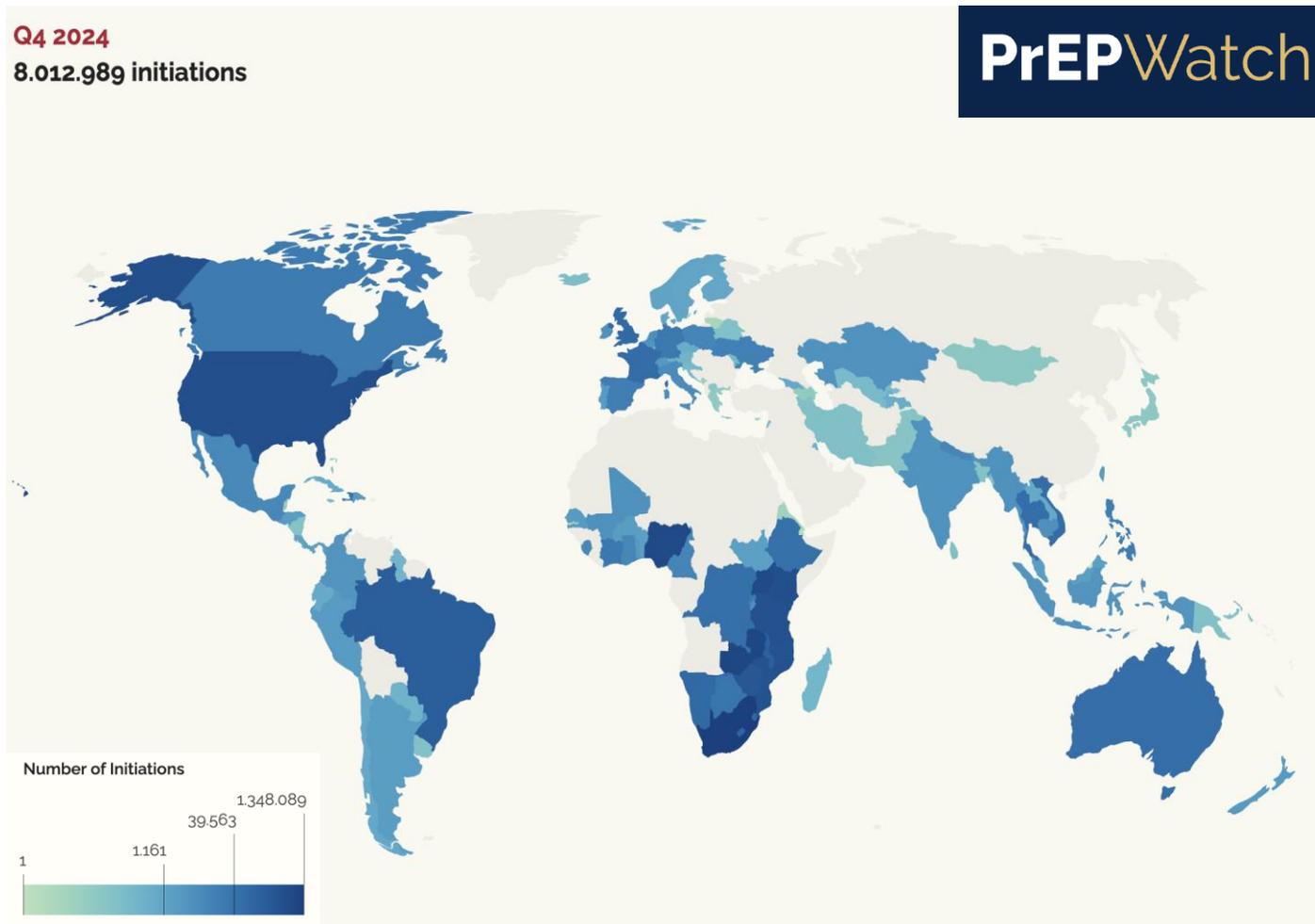


	Target	Data source	Previous target
1	<u>90% of people in need of prevention use appropriate, prioritized, person-centred and effective prevention options (pre-exposure prophylaxis (PrEP), post-exposure prophylaxis (PEP), condoms, needle/syringe programmes (NSPs), opioid agonist therapy (OAT) (topline).</u>	Population-based surveys	2025 target
2	<u>80% of people use a condom at last sex with a non-regular partner.</u>	GAM 1.14. Population-based surveys.	New
3	<u>50% of people at high risk of acquiring HIV (including key populations) use effective, ARV-based, prevention options: oral PrEP, long-acting PrEP, PEP (target levels in line with epidemiology and people's choices).</u>	Programme records.	New
4	95% of sex workers and their clients used a condom at last paid sex.	IBBS, population-based surveys.	New
5	95% of people who inject drugs used safe injecting equipment during their last injection.	GAM 1.8. IBBS.	New
6	50% use of opioid agonist maintenance treatment among people who inject opioids.	GAM 1.10. Programme data, IBBS.	2025 target
7	<u>95% of adolescent girls and young women, adult women, pregnant and breastfeeding women, and adolescent boys and men, effectively reached with people-centred HIV prevention programmes (HIV prevention related contact with health services, (including SRH quality services), community outreach, virtual interventions, schools or other providers).</u>	Population-based surveys or programme data.	New
8	<u>90% of schools provide life skills-based HIV and sexuality education.</u>	Annual School Census questionnaire or the UNESCO Institute for Statistics (UIS) Annual Survey of Formal Education questionnaire.	2025 target
9	<u>95% of key populations effectively reached with people-centred HIV prevention programmes.</u>	GAM 1.6, 1.7. Programme data, IBBS.	2025 target
10	95% of the estimated need for condoms is available and distributed.	Programme data versus needs estimates.	New
11	95% of the estimated need for PrEP is available and distributed.	Programme data versus needs estimates.	New
12	95% of the estimated need for PEP is available and distributed.	Programme data versus needs estimates.	New
13	95% of the estimated need for sterile syringes is available and distributed.	Programme data versus needs estimates.	New
14	<u>80% of people-centred HIV prevention programmes for key populations to be delivered by community-led organizations.</u>	Work is ongoing on measurement sources and methods. Policy data on the operating environment for community-led service delivery are being used as proxy measures.	2025 target
15	90% of all people living with HIV are virally suppressed by 2030, increasing to 95% by 2040.	GAM 2.3. Programme data plus epidemiological estimates.	New

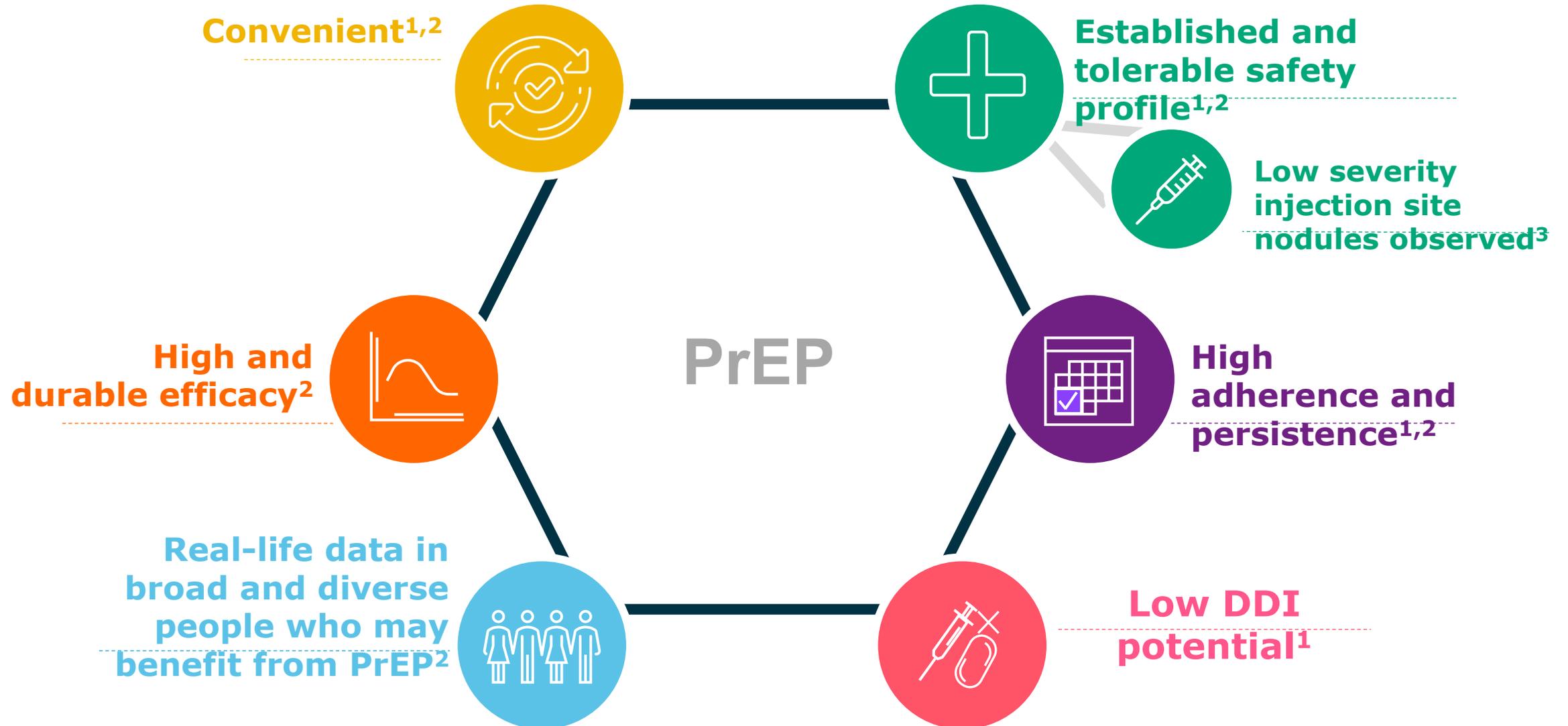
# Despite availability of PrEP, an estimated 1,300,000 people newly acquired HIV in 2024



# IAS Worldwide uptake of PrEP



# IAS Key attributes of an effective PrEP option



# RIAS The following PrEP options are reflected in international clinical guidelines, but national clinical recommendations may vary between markets



## TDF/FTC

As daily oral PrEP for populations at risk of HIV acquisition\*<sup>1-3</sup>



## TDF/FTC

On-demand oral PrEP  
Event-driven<sup>1-3</sup>

*Off label, not recommended, for CGW*



## TAF/FTC

As daily oral PrEP for MSM/TGW only<sup>†1</sup>



## DPV

For CGW only as part of combination prevention approaches<sup>4</sup>



## CAB LA

As IM injections given every 2 months for eligible populations at risk of HIV acquisition<sup>1,2,5</sup>



## LEN LA

As SC injections given every 6 months for eligible populations at risk of HIV acquisition<sup>6,7</sup>

**PrEP is an important biomedical prevention strategy for people at risk of HIV acquisition and can significantly reduce HIV infections in at-risk groups, including MSM, TGW and PWID<sup>1-4</sup>**

1. Centers for Disease Control and Prevention (CDC). DHHS/CDC Clinical Practice Guideline: PrEP for the Prevention of HIV Infection in the United States. Available at: <https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf>. Accessed October 2025

2. Gandhi RT, et al. JAMA 2023;329:63-84

3. EACS. Guidelines. Version 12.0. Available at: <https://www.eacsociety.org/media/guidelines-12.0.pdf>. Accessed October 2025

4. WHO. Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: Recommendations for a public health approach. Available at: <https://www.who.int/publications/i/item/9789240031593#:~:text=Overview,on%20HIV%20produced%20since%202016>. Accessed October 2025

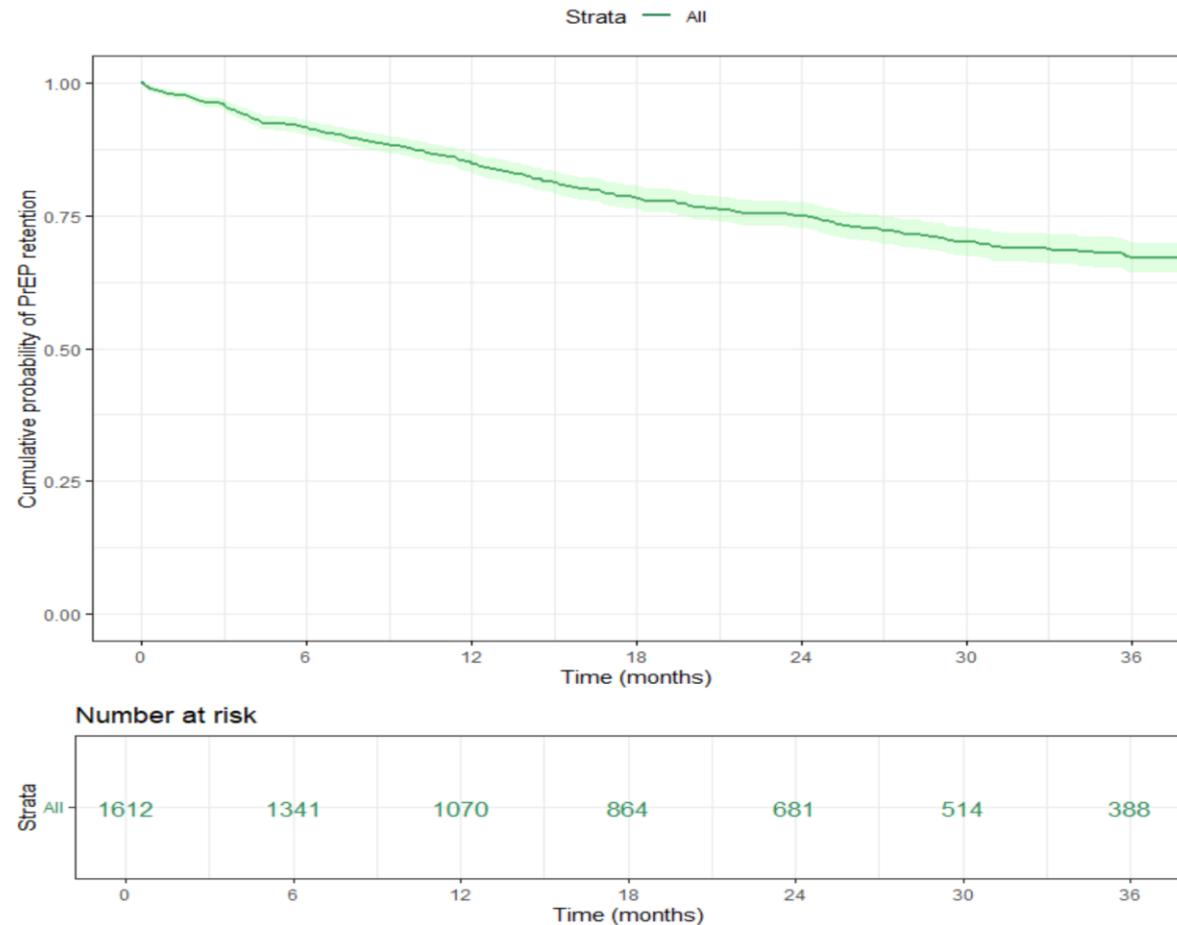
5. WHO. Guidelines on Long-acting injectable cabotegravir for HIV prevention. Available at: <https://www.who.int/publications/i/item/9789240054097>. Accessed October 2025

6. Yeztugo (lenacapavir). US Prescribing Information. June 2025

7. Gilead. Yeztugo® (Lenacapavir) Is Now the First and Only FDA-Approved HIV Prevention Option Offering 6 Months of Protection. 18 June 2025. Available at: <https://www.gilead.com/news/news-details/2025/yeztugo-lenacapavir-is-now-the-first-and-only-fda-approved-hiv-prevention-option-offering-6-months-of-protection>. Accessed October 2025

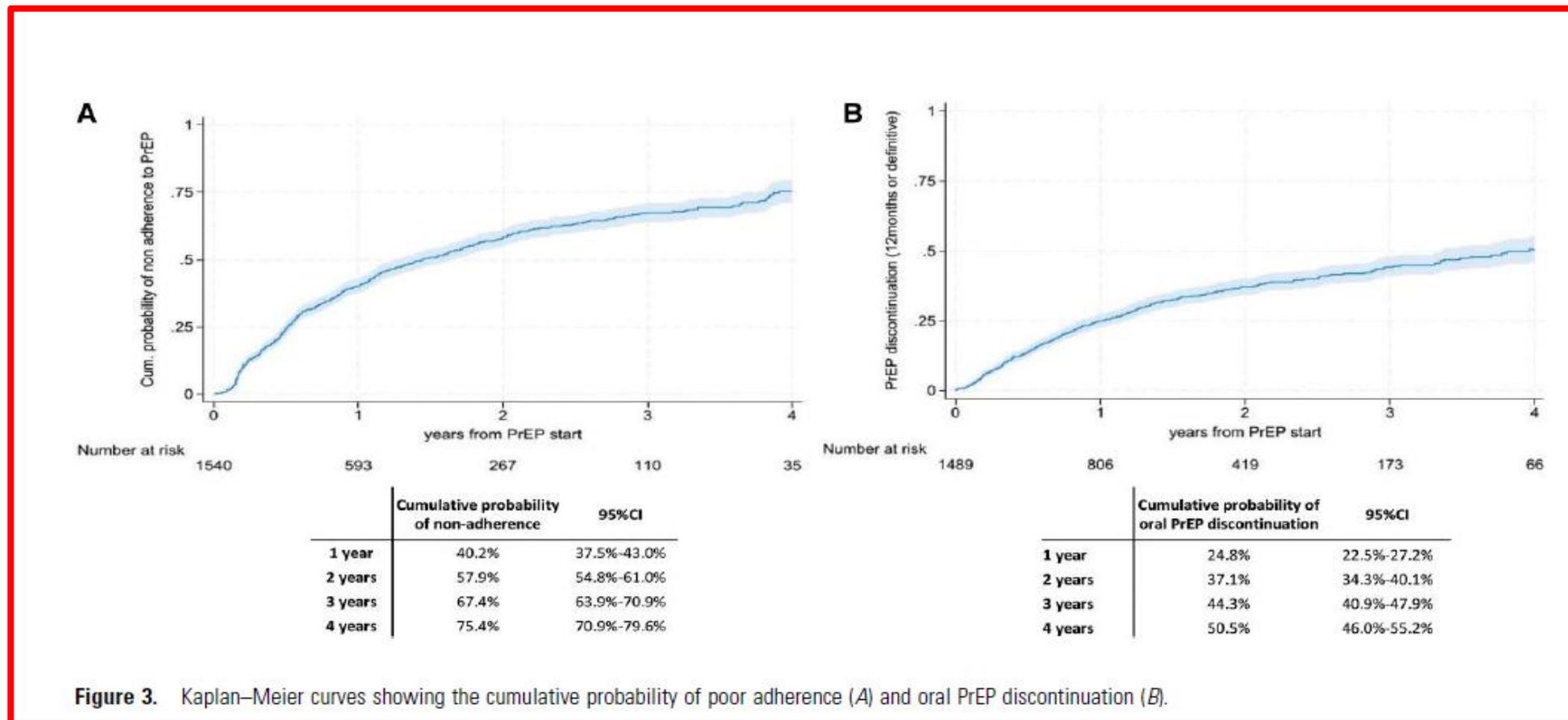
# Probability of retention in PrEP care over follow-up

Probability of PrEP care retention at:  
*-1 year: 84.7% (95%CI=82.9–86.6)*  
*-2 years: 74.9% (95%CI=72.6–77.4)*





# HIV Oral Pre-exposure Prophylaxis Effectiveness, Adherence, and Discontinuation in an Italian Multicentric Access Program: ItaPrEP Study





# LAIIs for PrEP : High directly-observed adherence in RCTs

## LAIIs for PrEP: CAB LA

RCTs: Proportion of observed person-time covered\*



**HPTN 083**<sup>1,2</sup>  
(Blinded phase)  
N=2,183 PY



**HPTN 084**<sup>3</sup>  
(Blinded phase)  
1,678/1,805 PY

## LAIIs for PrEP: LEN LA

RCTs: Proportion of on-time injections (<28 weeks from last injection)



**PURPOSE 1**<sup>4,5</sup>  
(Week 52)  
836/894



**PURPOSE 2**<sup>6,7</sup>  
(Week 52)  
678/727

\*CAB LA coverage was defined as injections received on time or with a delay of less than 2 weeks  
†Consistent with label group; ‡Number of injections not reported. Total participants, N=72  
HPTN, HIV Prevention Trials Network; PY, person-years; RCT, randomised controlled trial; RWE, real-world evidence

### References:

1. Landovitz RJ, et al. Lancet HIV 2023;10:e767-78
2. Landovitz RJ, et al. N Engl J Med 2021;385:595-608
3. Delany-Moretlwe S, et al. Lancet 2022;399:1779-89
4. Bekker LG, et al. HIV Glasgow 2024. Oral presentation O48
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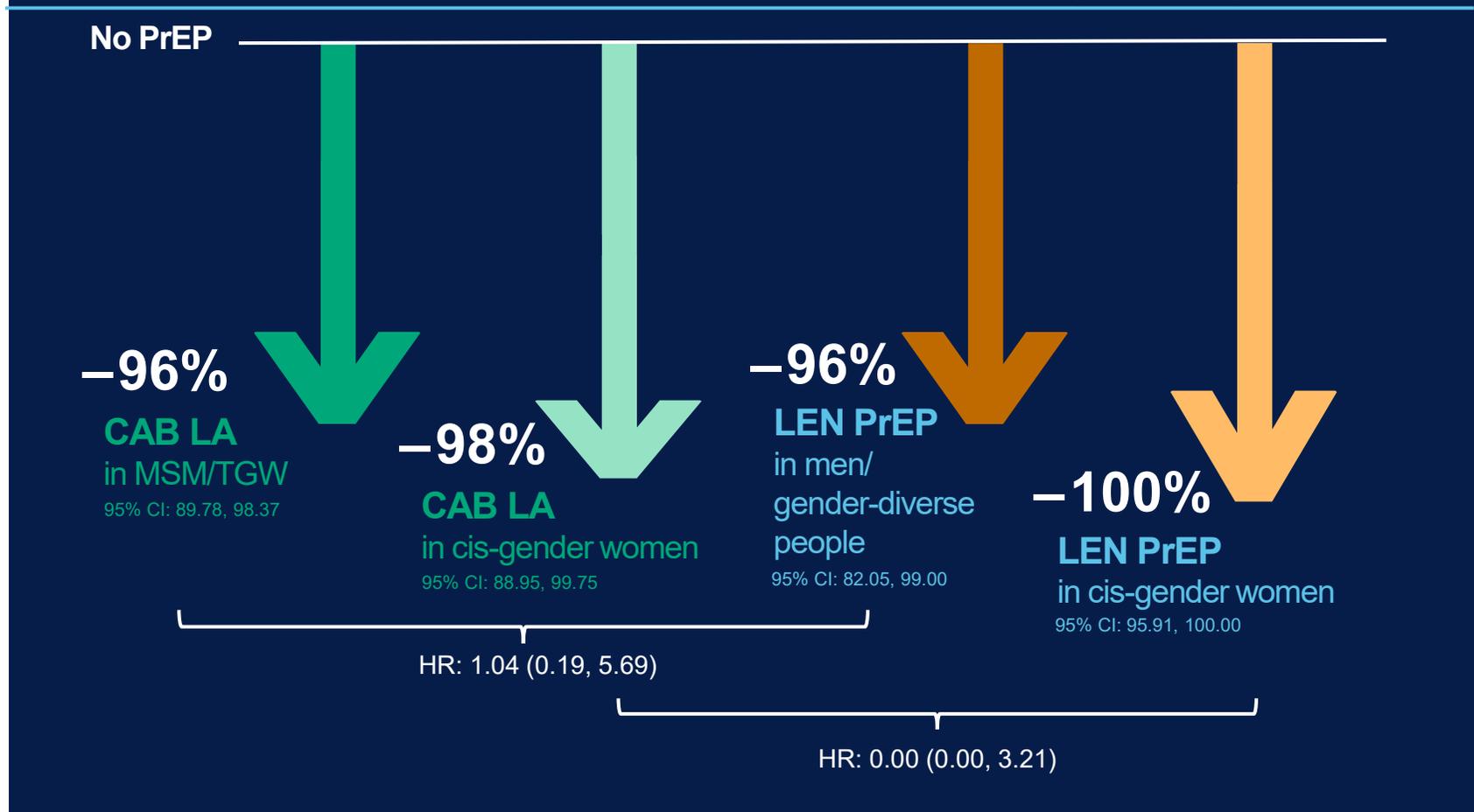


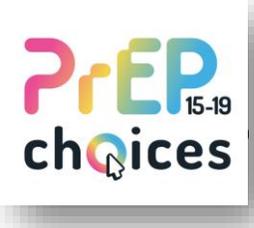
# Indirect treatment comparison : efficacy of CAB LA PrEP and LEN PrEP

## Study population and design

- An indirect treatment comparison was conducted to assess efficacy of CAB LA PrEP and LEN PrEP and provide insight into their relative clinical value
- Efficacy inputs included published efficacy data from the HPTN and PURPOSE trials identified through a systematic literature review
- CAB and LEN were compared using no PrEP as a common comparator

## Predicted efficacy of CAB LA PrEP and LEN PrEP in reducing HIV acquisition risk



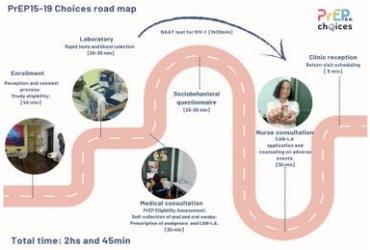


**PrEP15-19 Choices is a multisite, prospective implementation study evaluating three PrEP modalities - long-acting injectable cabotegravir, daily and on-demand oral TDF/FTC - among adolescent cisgender MSM, TGW and non-binary (assigned male at birth) aged 15 to 19 years**

Dourado, I et al. *BMJ open*, v. 15, n. 1, p. e083146, 2025



The study surpassed its target enrollment (120%; 660/550). To date, 384 (58%) participants have received at least one Cab-LA injection, and for 309 participants (47%), Cab-LA was their preferred choice (77% MSM, 15% TGW/M, 8% Non-binary). The Cab-LA arm reported only 5 discontinuations and 3 incident infections (one per site), compared to 5 incident infections in the Oral PrEP arm.



Adolescents initially prefer oral PrEP (6 in 10). However, the switch rate from oral PrEP to Cab-LA was seven times higher than the reverse (14% vs 2%). This trend, which was most evident in vulnerable groups, ultimately balanced the proportion of participants in each study arm. The Cab-LA initiation visit requires 2 hours and 45 minutes (1.5 h dedicated to GeneXpert result waiting time).

NAAT	4th-generation RT		Total
	Positive	Negative	
Positive	7	0	7
Negative	0	245	245
NAAT	Oral ST		Total
	Positive	Negative	
Positive	7	0	7
Negative	0	245	245
<b>Total</b>	<b>7</b>	<b>245</b>	<b>252</b>

We compared the accuracy of 3 HIV tests for Cab-LA initiation visits from the first twelve months of the study. Among 252 participants (April 2024 to May 2025), absolute concordance was demonstrated among the results of the oral fluid ST and the 4th Generation RT (Ag/Ab) when both were compared against GenXpert as the reference standard. Sensitivity and Specificity were greater than 99.9%, with a Kappa value of 1.0 (p < 0.001).

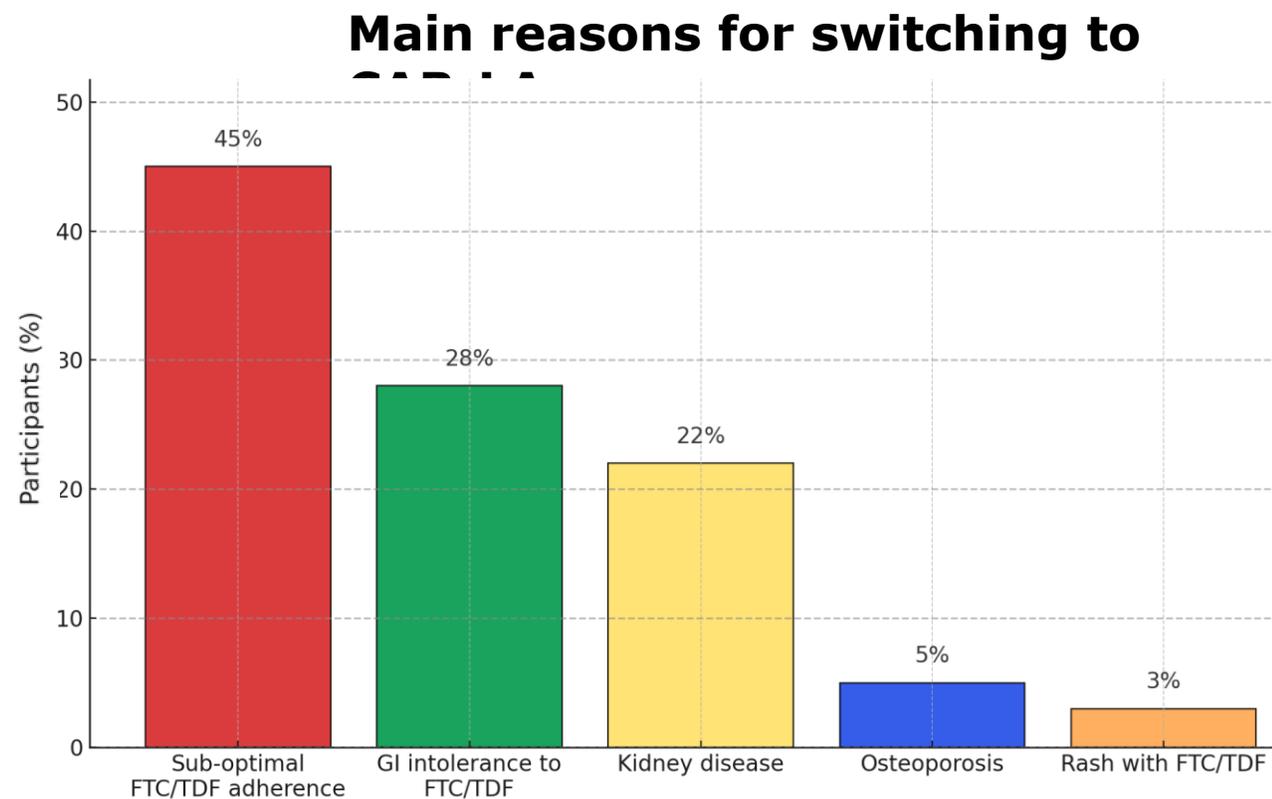


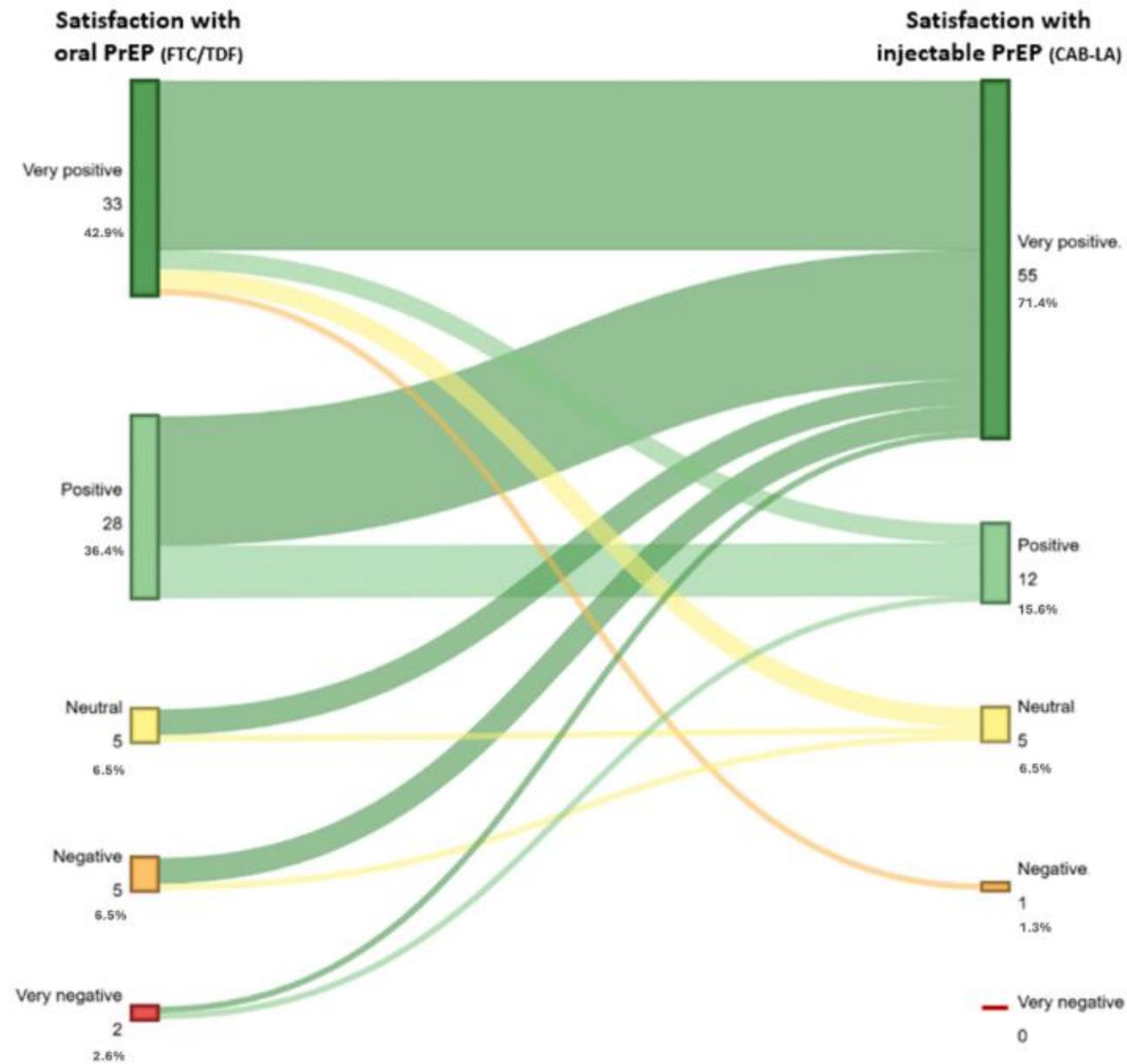
Over the 18-month provision of Cab-LA, a total of 44 SAEs were reported across both study arms. Of these, 21 constituted Grade 3-4 suicidality events, 17 occurring in the Cab-LA arm. Suicide risk screening criteria were subsequently implemented for Cabotegravir initiation in February 2025 and no further suicidality events have been reported in the Cab-LA arm, whereas four such events were documented in the oral arm between April and August 2025.

# Results: OSR experience

Individuals Characteristics*	Overall n=87
<b>DoxyPEP Use</b>	73 (83.9%)
<b>Previous Chlamydia</b>	48 (55.2%)
<b>Previous Gonorrhoea</b>	58 (66.7%)
<b>Previous Mpox</b>	13 (14.9%)
<b>Previous Mgen</b>	15 (17.2%)
<b>Previous Syphilis</b>	48 (55.2%)
<b>Sexual Partners<sup>^</sup></b>	
1-5	36 (41.4%)
6-10	22 (25.3%)
11-30	17 (19.5%)
Over 30	12 (13.8%)
<b>Chemsex Use</b>	28 (32.2%)
Sometimes	18 (20.7%)
Frequently	7 (8.0%)
Always	3 (3.4%)

\*At baseline ^ Previous 2 months





**FIGURE 1** Reported satisfaction with oral PrEP (FTC/TDF) at first CAB-LA injection and reported satisfaction with injectable PrEP (CAB-LA) at month 5 (fourth injection). Oral-PrEP experienced individuals who received four CAB-LA injections included ( $n = 73$ ). The colour gradient, ranging from green to red, indicates the transition from lower to higher satisfaction levels (tending towards green) and from higher to lower satisfaction levels (tending towards red).



# PrEP monitoring

Open-label randomized trial of 469 people on PrEP (99% MSM, median age 36 years).  
Comparison of follow-up every 3 vs. 6 months and in-clinic vs. online monitoring.

**Monitoring every 6 months** is non-inferior to monitoring every 3 months (IRR 0.96; 95% CI 0.84–1.11).

**Online monitoring** is non-inferior to in-clinic monitoring (IRR 0.83; 95% CI 0.72–0.95).

	Total	Monitoring frequency		Monitoring modality	
		3-monthly (Arm 1 + Arm 3)	6-monthly (Arm 2 + Arm 4)	In clinic (Arm 1 + Arm 2)	Online (Arm 3 + Arm 4)
<b>N</b>	469	236	233	231	238
<b>Follow-up time, PY</b>	605	305	300	307	298
<b>N with an unprotected sex act</b>	816	419	397	452	364
<b>IR of unprotected sex acts (95% CI), instances per PY</b>	1.3 (1.2–1.4)	1.4 (1.2–1.5)	1.3 (1.2–1.5)	1.5 (1.3–1.6)	1.2 (1.1–1.4)
<b>IR ratio of unprotected sex act (95% CI) (noninferiority margin = 1.8)</b>	N/A	<b>0.96 (0.84–1.11) (noninferior)</b>		<b>0.83 (0.72–0.95) (noninferior)</b>	

# IAS-USA policy change in December 2024

*No longer requiring NAT for LA-PrEP at all times*

JAMA | Special Communication

## Antiretroviral Drugs for Treatment and Prevention of HIV in Adults 2024 Recommendations of the International Antiviral Society-USA Panel

Rajesh T. Gandhi, MD, Raphael J. Landovitz, MD, Paul E. Sax, MD, Davey M. Smith, MD, Sandra A. Springer, MD, Huldrych F. Günthard, MD, Melanie A. Thompson, MD, Roger J. Bedimo, MD, Constance A. Benson, MD, Susan P. Buchbinder, MD, Brenda E. Crabtree-Ramirez, MD, Carlos del Rio, MD, Ellen F. Eaton, MD, Joseph J. Eron Jr, MD, Jennifer F. Hoy, MBS, Clara Lehmann, MD, Jean-Michel Molina, MD, Donna M. Jacobsen, BS, Michael S. Saag, MD

**IMPORTANCE** New data and new antiretroviral drugs and formulations continue to become available for the prevention and management of HIV infection.

**OBJECTIVE** To provide updated recommendations for HIV treatment and clinical management and HIV prevention.

**METHODS** A panel of volunteer expert physician scientists were appointed to provide updated consensus recommendations for 2024. Relevant evidence in the literature since the last report was identified from PubMed and Embase searches (which initially yielded 3998 unique citations, of which 249 were considered relevant); from ongoing monitoring of the literature by the panel members; from data submitted by product manufacturers; and from studies presented at peer-reviewed scientific conferences between June 2022 and October 2024.

**FINDINGS** Antiretroviral therapy continues to be recommended for all individuals with HIV. For most people with HIV, initial regimens composed of an integrase strand transfer inhibitor (INSTI), specifically bictegravir or dolutegravir, with 2 (and in some cases 1) nucleoside or nucleotide reverse transcriptase inhibitors are recommended. Recommendations are made for those with particular clinical circumstances, such as pregnancy and active opportunistic diseases, as well as for those unable to take INSTIs. Regimens may need to be changed for virologic failure, adverse effects, convenience, or cost, among other reasons. Lone-active

Editorial  
Multimedia  
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## IAS-USA revised their policy, stating:

- **At initiation or after a long hiatus**, HIV testing should include **an HIV RNA test** and a **lab-based Ag/Ab test**
  - If **RNA testing** is unavailable, initiation of PrEP after a **rapid HIV test** and while awaiting a laboratory-based Ag/Ab test result.
- **For CAB-LA continuation**, a **rapid HIV test and lab-based Ag/ab test**, **not routine RNA testing**



# KEY POINTS

- HIV prevention gap persists despite oral PrEP availability.
- WHO endorses long-acting injectable PrEP to accelerate impact.
- Long-acting PrEP improves adherence and persistence vs daily oral regimens.
- CAB-LA and LEN-LA show high, durable efficacy and favorable safety profiles.
- Strong uptake and retention observed in real-world and adolescent populations.
- Reduced monitoring frequency supports scalable, differentiated care models.
- Long-acting PrEP is essential to achieving UNAIDS 2030 targets.



Name of the Speaker

Topic Lore Ipsum