Highlights from the 2024 HIV Research for Prevention (R4P) Conference

Beatriz Grinsztejn, MD

President, International AIDS Society (IAS)

Head of the STD/AIDS Clinical Research Laboratory

Evandro Chagas National Institute of Infectious Diseases (FIOCRUZ)

Rio de Janeiro, Brasil

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Disclosures

- Consultant/advisor: ViiV; Merck; Gilead.

Agenda

- Current situation of the HIV pandemic
- Expanding PrEP options
- Improving PrEP uptake
- Implementing PrEP options
- Final remarks

HIVR4P 2024

HIV pandemic

New HIV infections among adults and children

Globally

39%

fewer people acquired HIV in 2023 compared with 2010.

In 2023, there were still

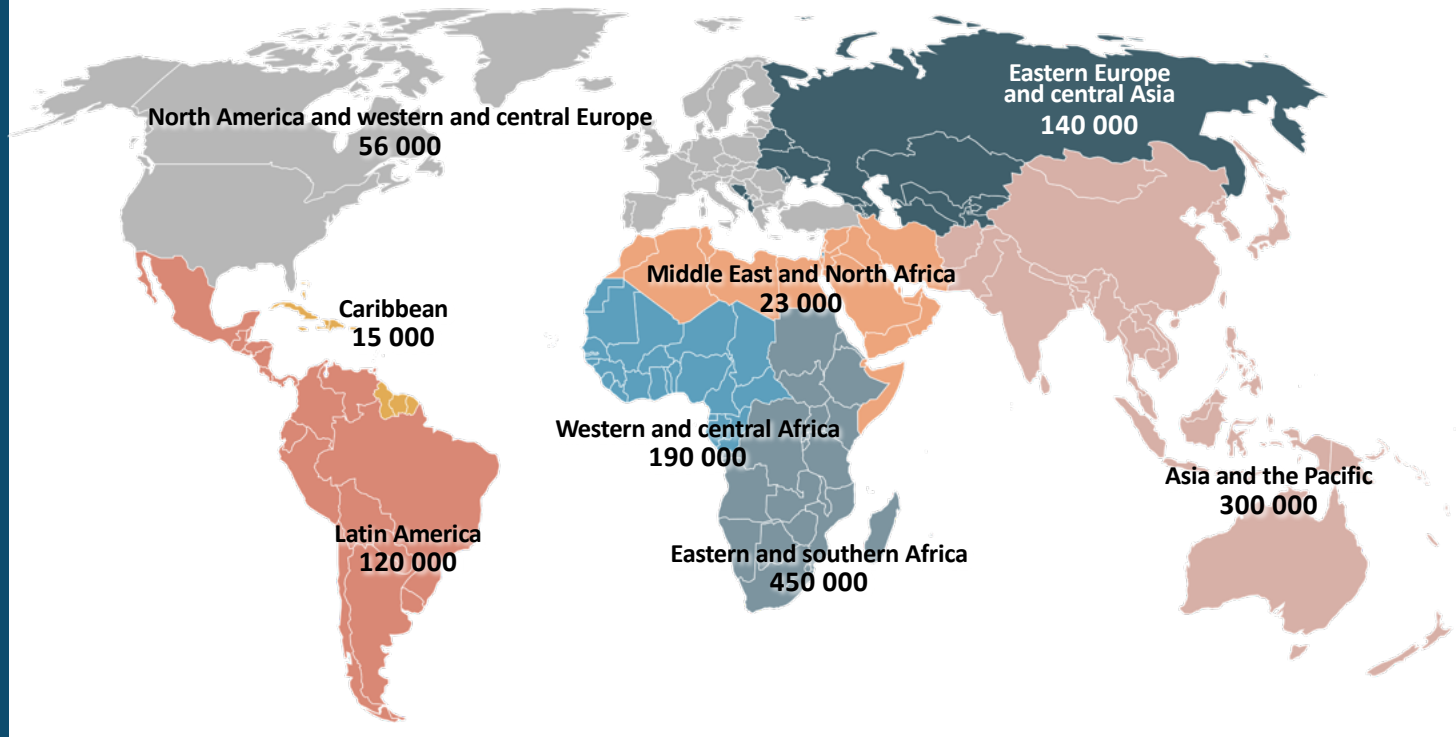
1.3M

new HIV infections.

This is

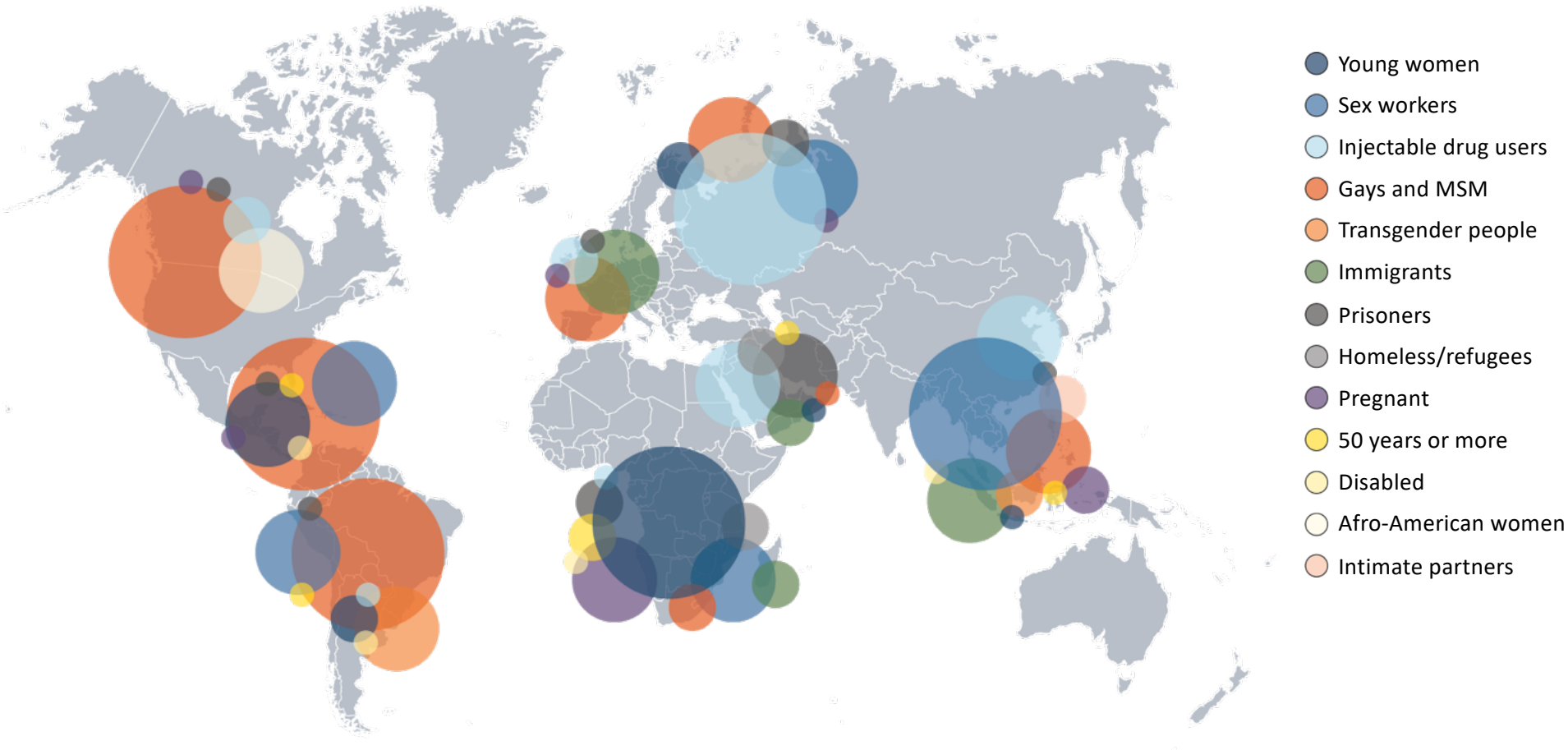
more than 3x

the 2025 UN target of no more than 370,000 new infections per year.

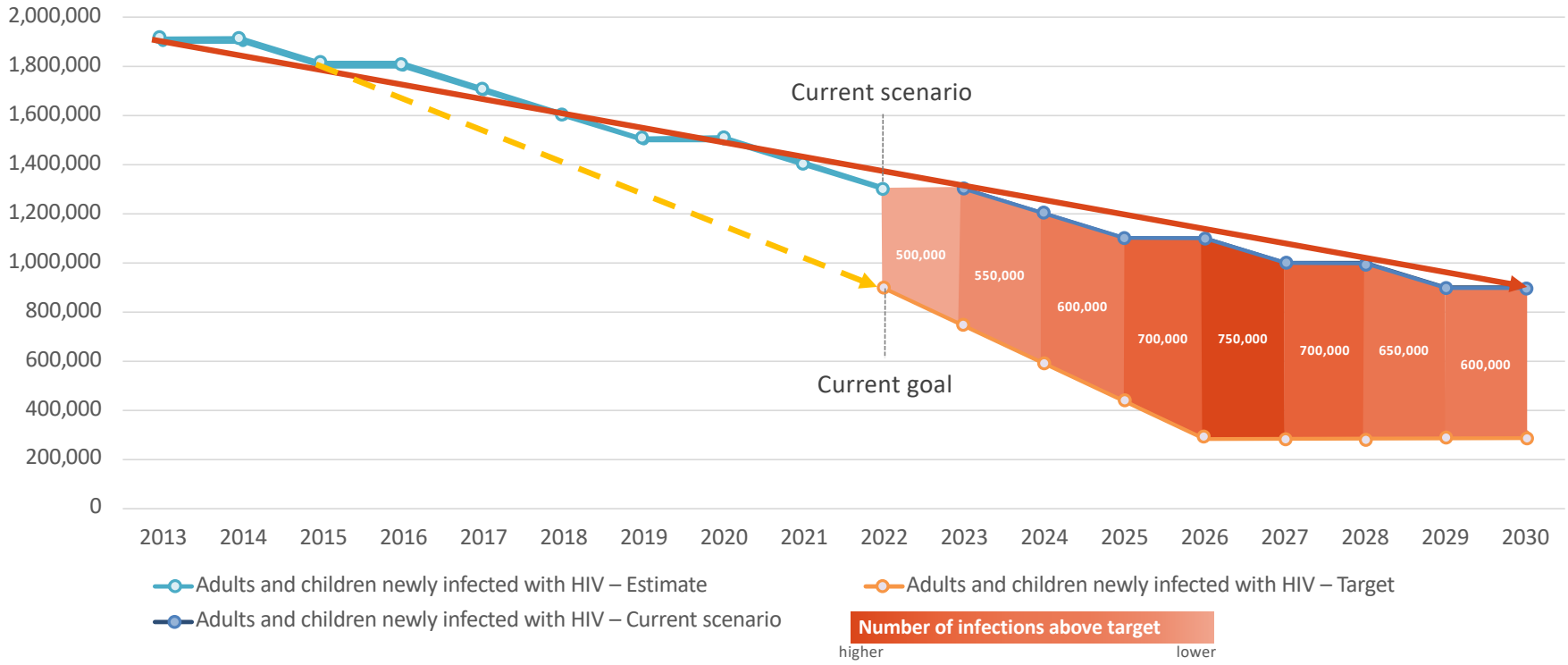


UNAIDS 2024.

Importance of location and population



HIV incidence – Not on track for 2030 UNAIDS targets

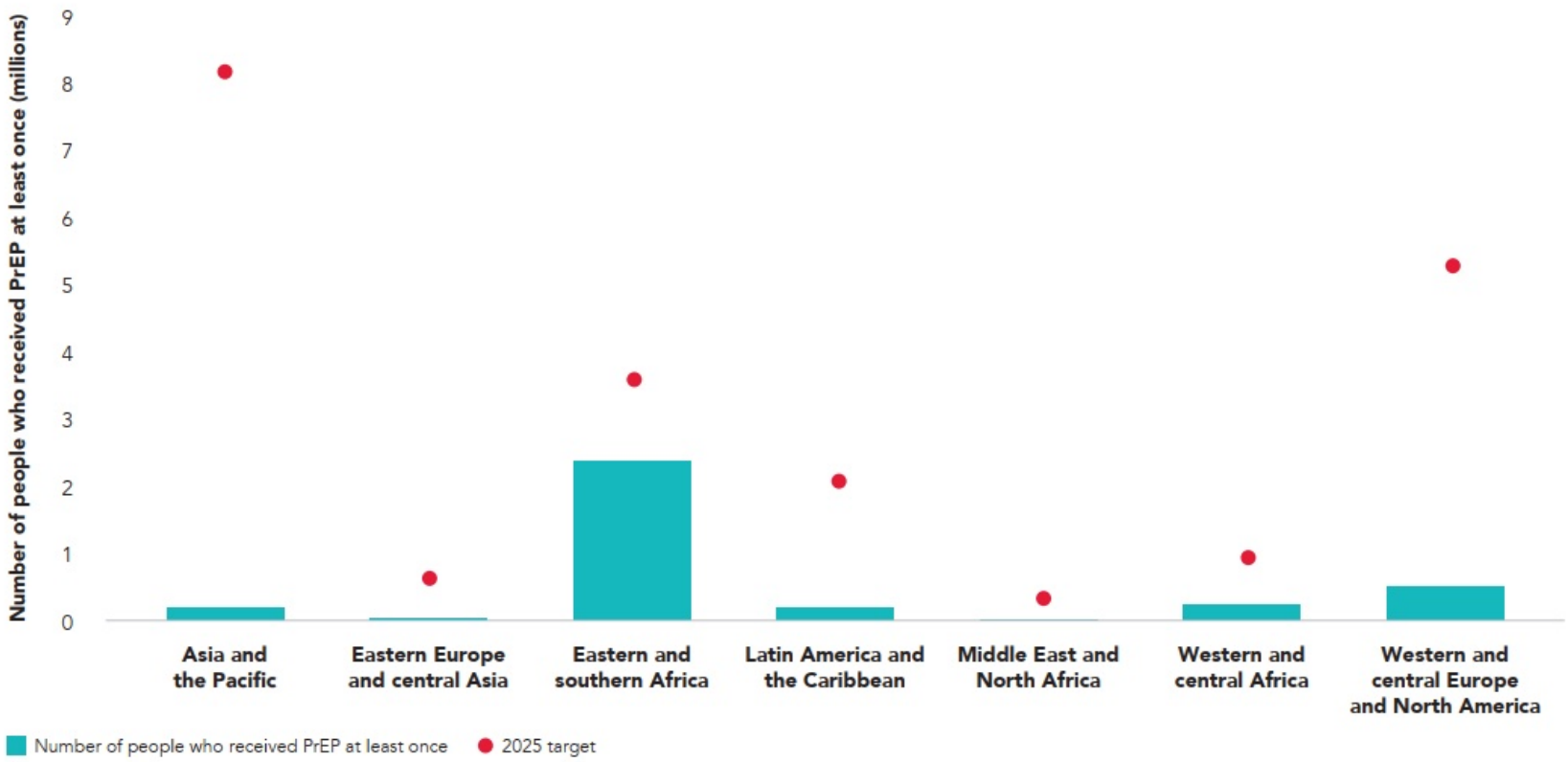


Huub Gelderblom, HVTN (personal comms)

https://www.unaids.org/en/resources/fact-sheet - 30 Nov 2023

PrEP use by region, 2023

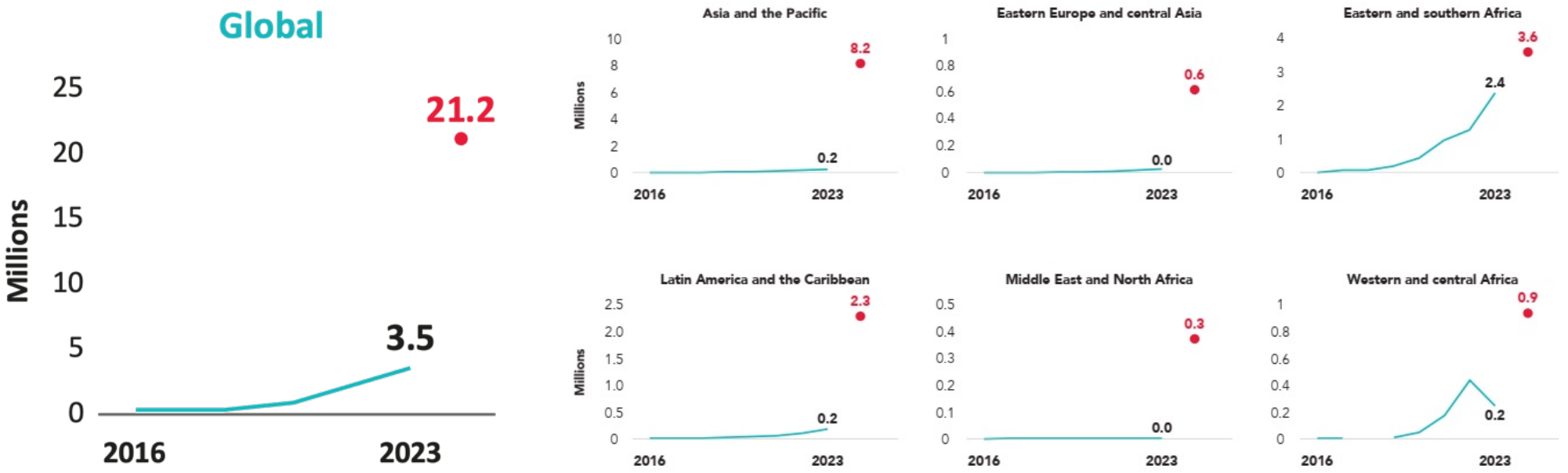
Number of people who used PrEP at least once in 2023, by region and 2025 target



UNAIDS 2024.

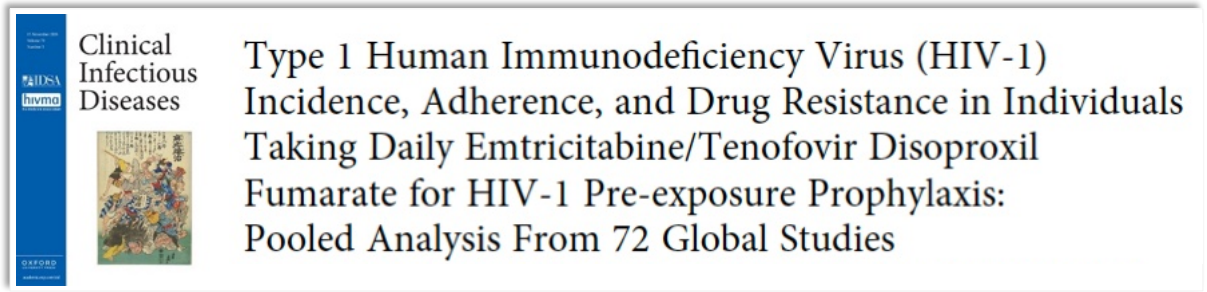
PrEP use by region, 2023

Trends in the number of people who received pre-exposure prophylaxis (PrEP) at least once during the reporting period, by region, 2016–2023, and 2025 target

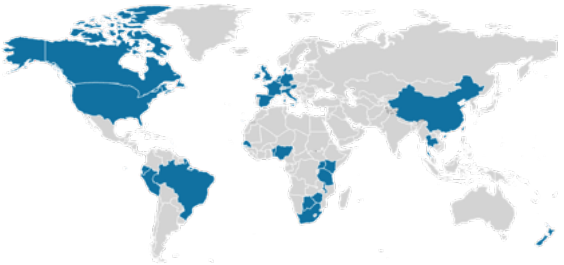


UNAIDS 2024.

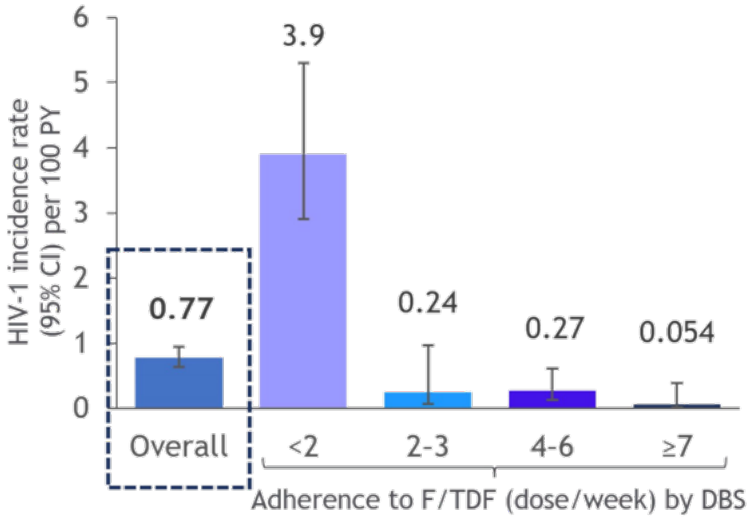
Oral PrEP use and HIV incidence

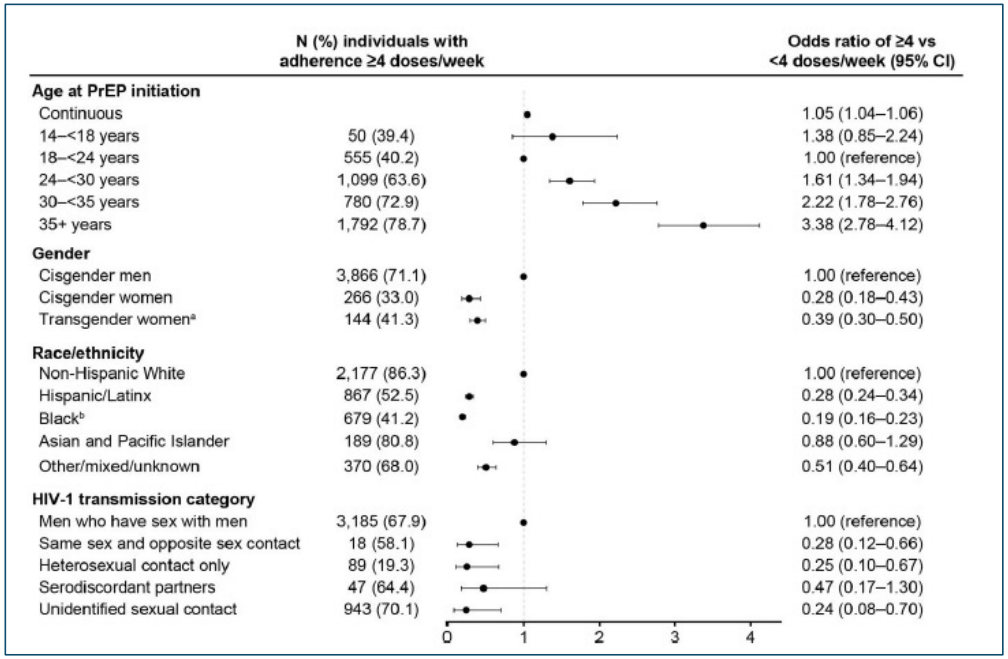


>17 000 people



HIV Incidence Rates





	N (%) individuals with adherence ≥4 doses/week	Odds ratio of ≥4 vs <4 doses/week (95% CI)
Age at PrEP initiation		
Continuous		1.05 (1.04–1.06)
14–<18 years	50 (39.4)	1.38 (0.85–2.24)
18–<24 years	555 (40.2)	1.00 (reference)
24–<30 years	1,099 (63.6)	1.61 (1.34–1.94)
30–<35 years	780 (72.9)	2.22 (1.78–2.76)
35+ years	1,792 (78.7)	3.38 (2.78–4.12)
Gender		
Cisgender men	3,866 (71.1)	1.00 (reference)
Cisgender women	266 (33.0)	0.28 (0.18–0.43)
Transgender women[a]	144 (41.3)	0.39 (0.30–0.50)
Race/ethnicity		
Non-Hispanic White	2,177 (86.3)	1.00 (reference)
Hispanic/Latinx	867 (52.5)	0.28 (0.24–0.34)
Black[b]	679 (41.2)	0.19 (0.16–0.23)
Asian and Pacific Islander	189 (80.8)	0.88 (0.60–1.29)
Other/mixed/unknown	370 (68.0)	0.51 (0.40–0.64)
HIV-1 transmission category		
Men who have sex with men	3,185 (67.9)	1.00 (reference)
Same sex and opposite sex contact	18 (58.1)	0.28 (0.12–0.66)
Heterosexual contact only	89 (19.3)	0.25 (0.10–0.67)
Serodiscordant partners	47 (64.4)	0.47 (0.17–1.30)
Unidentified sexual contact	943 (70.1)	0.24 (0.08–0.70)

Landovitz et al. Clinical Infectious Diseases, 2024.

Do vaginas demand perfection?

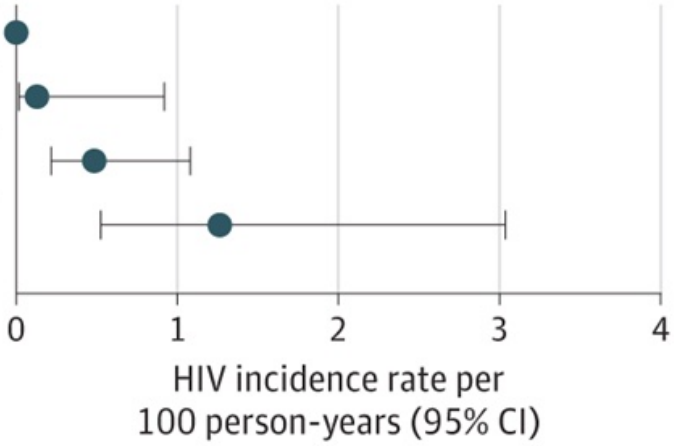
JAMA®
The Journal of the American Medical Association

HIV Preexposure Prophylaxis With Emtricitabine and Tenofovir Disoproxil Fumarate Among Cisgender Women

8-year pooled analysis: adherence and HIV incidence in >6,000 cis women on F/TDF for PrEP

HIV Incidence Rates Among Cisgender Women by Adherence Trajectory (n = 2954)

	Adherence	HIV incidence rate per 100 person-years (95% CI)
7 doses/week	Consistently daily	0 [Reference]
4-6 doses/week	Consistently high	0.13 (0.02-0.92)
	High but declining	0.49 (0.22-1.08)
	Consistently low	1.27 (0.53-3.04)

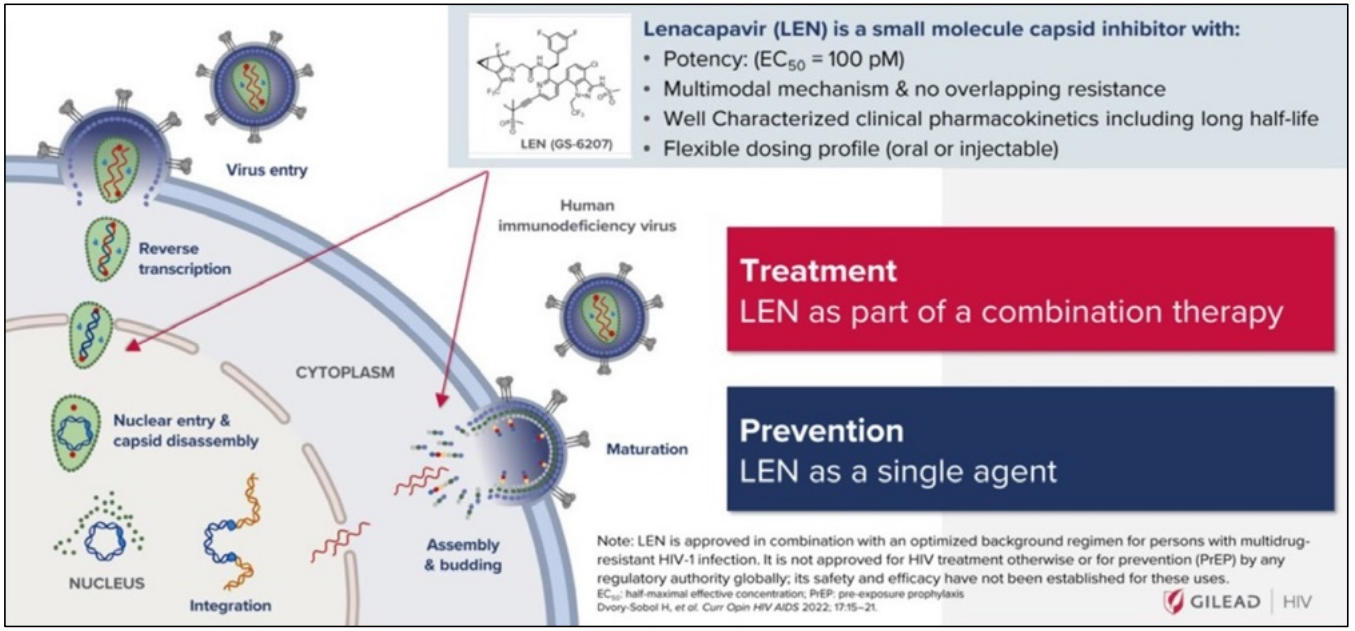


Marrazzo J, et al, 2024.

Expanding PrEP Options

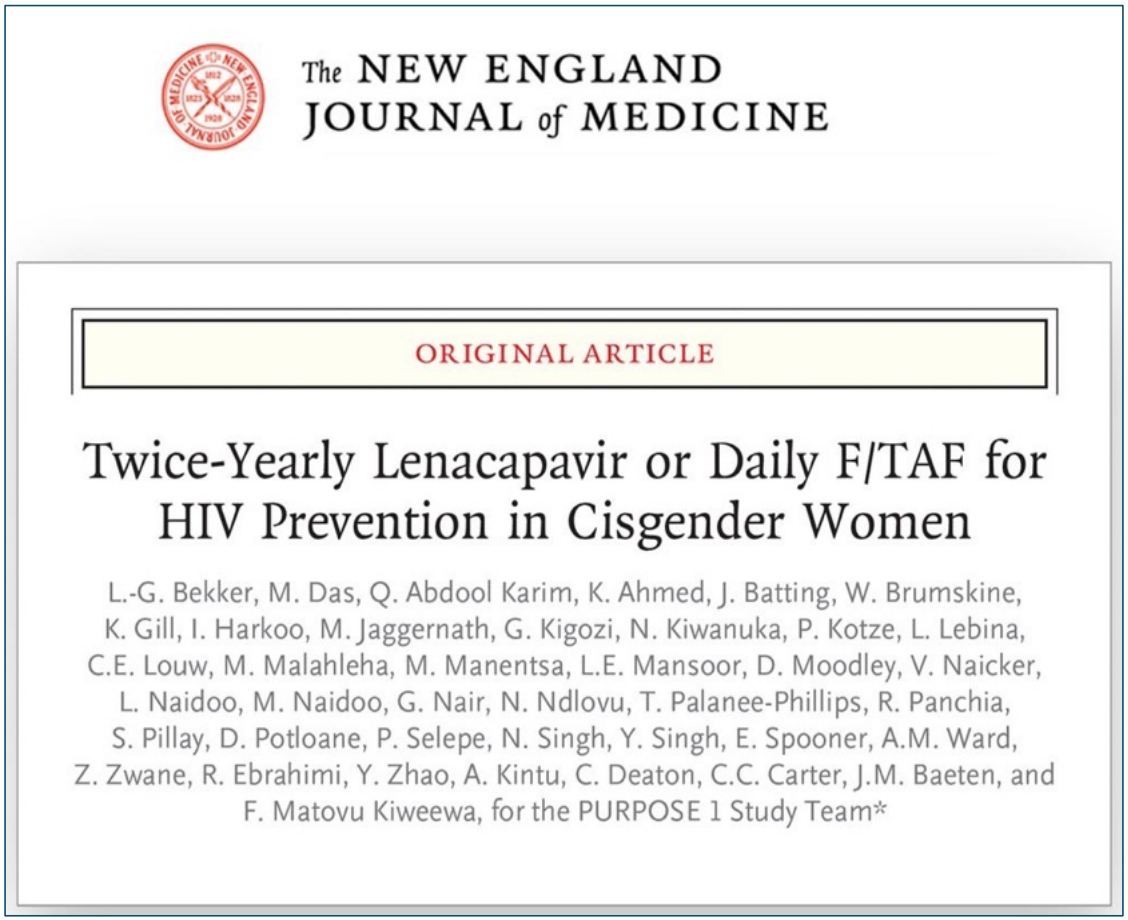
Lenacapavir

- First in class long-acting capsid inhibitor
- Administered via two subcutaneous injections in the abdomen once every 6 months
- Oral loading dose: 2 pills at the time of the first injection and 2 more on the following day



The Lens on LEN: The basics on injectable lenacapavir as PrEP, AVAC, July 2024

Lenacapavir for PrEP: Purpose 1



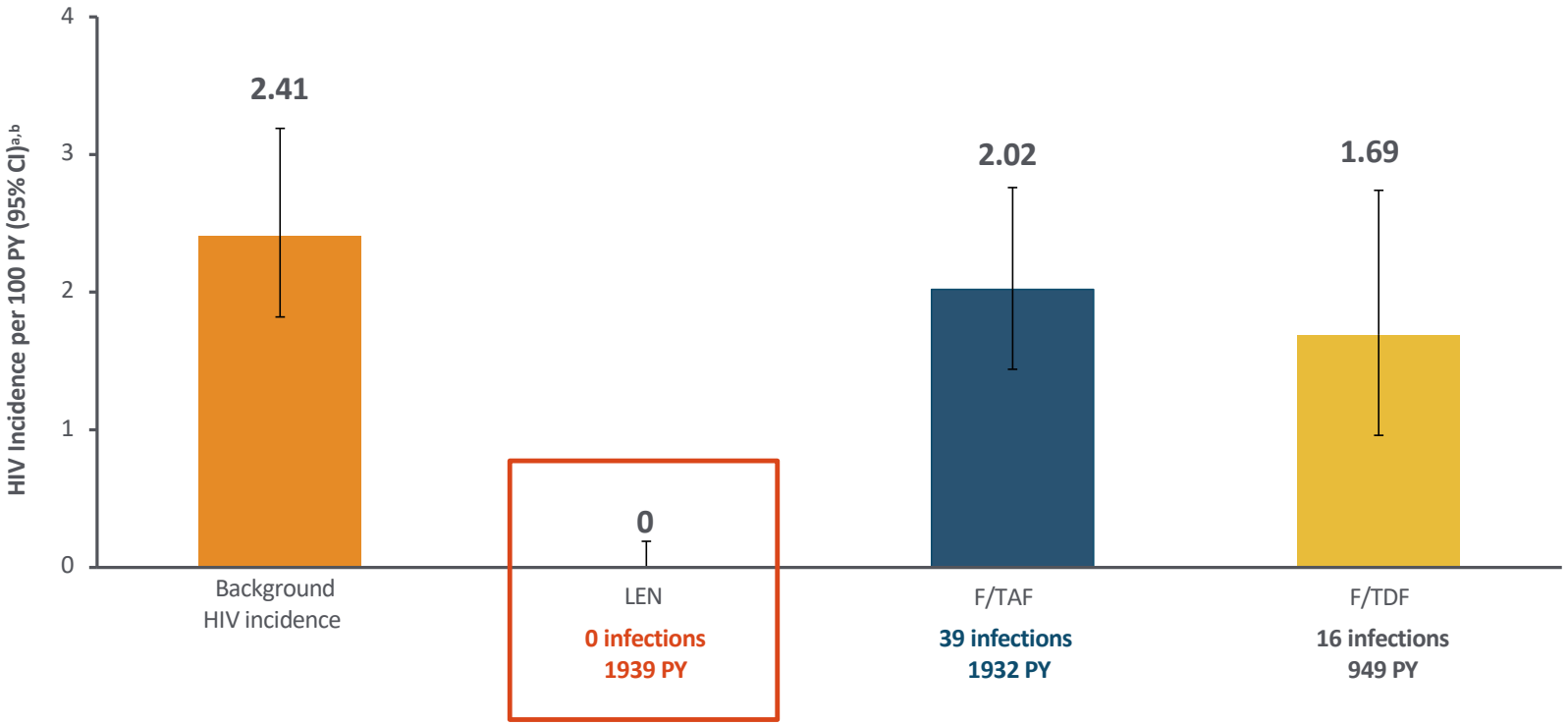
The NEW ENGLAND JOURNAL of MEDICINE

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*

Zero HIV infections among cisgender women receiving LEN

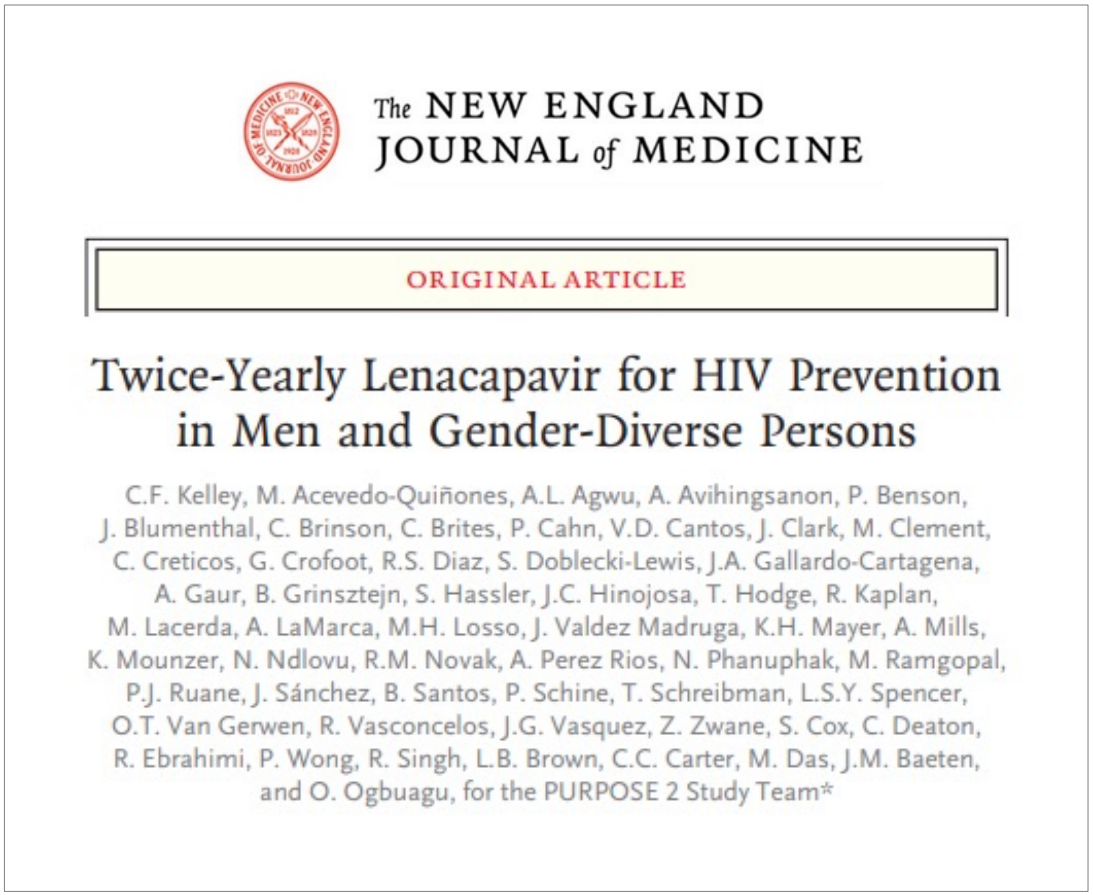


[a]*Overall n: background HIV incidence group 8094; LEN, 2134; F/TAF, 2136; F/TDF, 1068.* [b]*95% CIs: background HIV incidence group 1.82, 3.19, LEN 0, 0.19, F/TAF 1.44, 2.76. F/TDF 0.96, 2.74.*
CI, confidence interval; PY, person-years.

Bekker et al. AIDS 2024. Bekker et al, NEJM 2024.

Lenacapavir for PrEP: Purpose 2

PURPOSE 2



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Twice-Yearly Lenacapavir for HIV Prevention in Men and Gender-Diverse Persons

C.F. Kelley, M. Acevedo-Quiñones, A.L. Agwu, A. Avihingsanon, P. Benson, J. Blumenthal, C. Brinson, C. Brites, P. Cahn, V.D. Cantos, J. Clark, M. Clement, C. Creticos, G. Crofoot, R.S. Diaz, S. Doblecki-Lewis, J.A. Gallardo-Cartagena, A. Gaur, B. Grinsztejn, S. Hassler, J.C. Hinojosa, T. Hodge, R. Kaplan, M. Lacerda, A. LaMarca, M.H. Losso, J. Valdez Madruga, K.H. Mayer, A. Mills, K. Mounzer, N. Ndlovu, R.M. Novak, A. Perez Rios, N. Phanuphak, M. Ramgopal, P.J. Ruane, J. Sánchez, B. Santos, P. Schine, T. Schreibman, L.S.Y. Spencer, O.T. Van Gerwen, R. Vasconcelos, J.G. Vasquez, Z. Zwane, S. Cox, C. Deaton, R. Ebrahimi, P. Wong, R. Singh, L.B. Brown, C.C. Carter, M. Das, J.M. Baeten, and O. Ogbuagu, for the PURPOSE 2 Study Team*

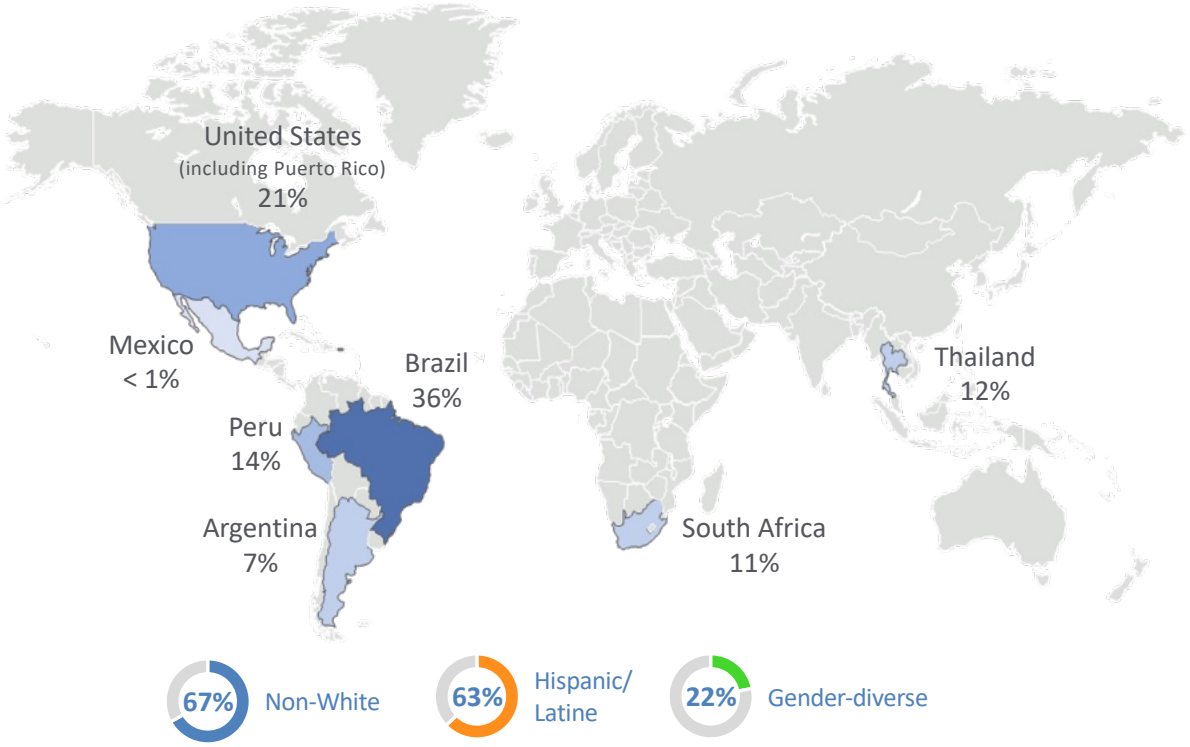
HIVR4P 2024

Lenacapavir for Prevention: Purpose

PURPOSE 1

Young women in Africa

PURPOSE 2



67% Non-White

63% Hispanic/ Latine

22% Gender-diverse

Young men, transgender women and men, non-binary people

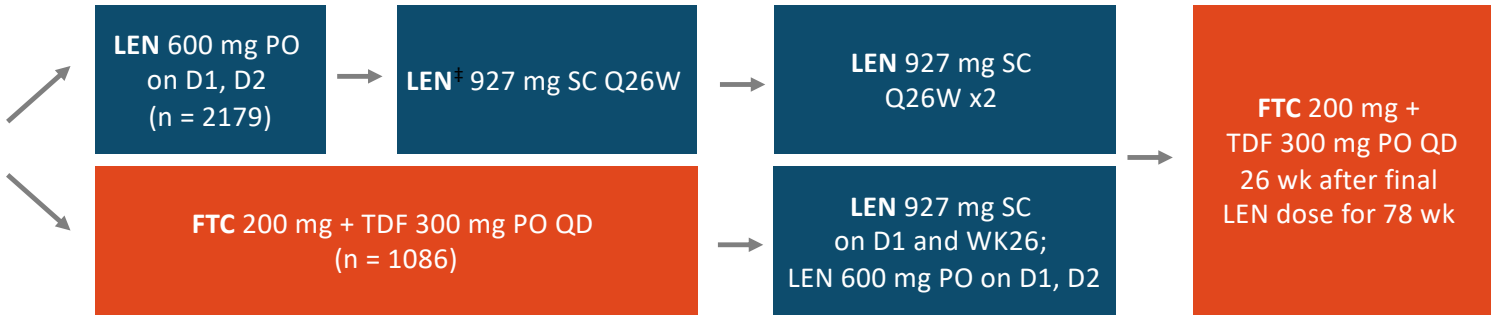
Darker shading corresponds to a higher proportion of participants.

Purpose 2

Q6M LEN as PrEP in Men, Transgender People, and Nonbinary People Who Have Sex With Men

- International, double-blind, randomized phase III trial

Cisgender men, transgender women, transgender men, and gender nonbinary people with unknown HIV status; aged ≥16 yr; sexually active with ≥1 partner who is assigned male sex at birth within last 12 mo and 1 risk factor[†]; no prior HIV testing or oral PrEP/PEP use in last 3 mo; no prior LA PrEP use
(N = 3295)



*Participants receiving LEN also received an oral placebo for FTC/TDF; participants receiving FTC/TDF also received a matched oral or SC placebo for LEN. [†]In last 3 mo, receipt of condomless anal sex with ≥2 partners or self-reported stimulant use with sex or, in last 6 mo, prior syphilis, rectal gonorrhea, or rectal chlamydia infection. [‡]Oral LEN is provided to participants when SC injections not available.

- Coprimary endpoints: background HIV incidence per 100-PY at screening, HIV incidence
- Key secondary endpoints: HIV incidence while adherence to study therapy, safety
- Interim analysis: LEN vs background HIV incidence, LEN vs FTC/TDF during blinding

Kelley CF, R4P, 2024. Kelley et al. NEJM 2024.

Purpose 2

Study design

4634 people tested for HIV

3271 people
HIV negative and received study drug

Group 1 (2183 people) → **Lenacapavir injections every 6 months** (and F/TDF placebo† tablet daily)

Group 2 (1088 people) → **F/TDF tablet once daily** (and lenacapavir placebo† injection every 6 months)

†Placebo tablets and injections contain an inactive substance and are not a medicine. They were used so that doctors and participants did not know which group they were in.

Week 0 — **12 months**

HIV positive: HIV test and recency test results from the beginning of the study were used to calculate the background HIV rate. These people were immediately referred to receive HIV care.

Prespecified interim analysis
50% of participants completed ≥ 52 weeks

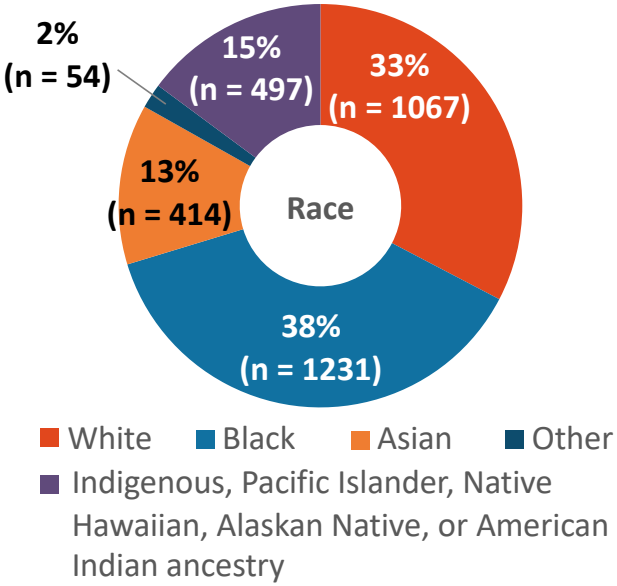
Primary analysis[d]:
LEN vs background HIV

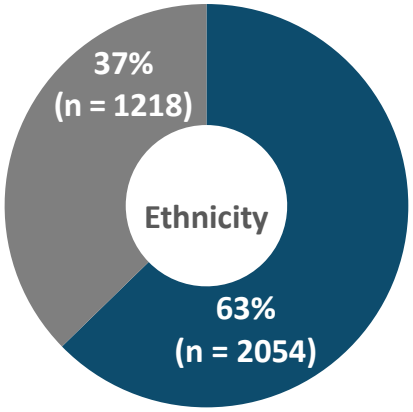
Secondary analysis[e]:
LEN vs F/TDF

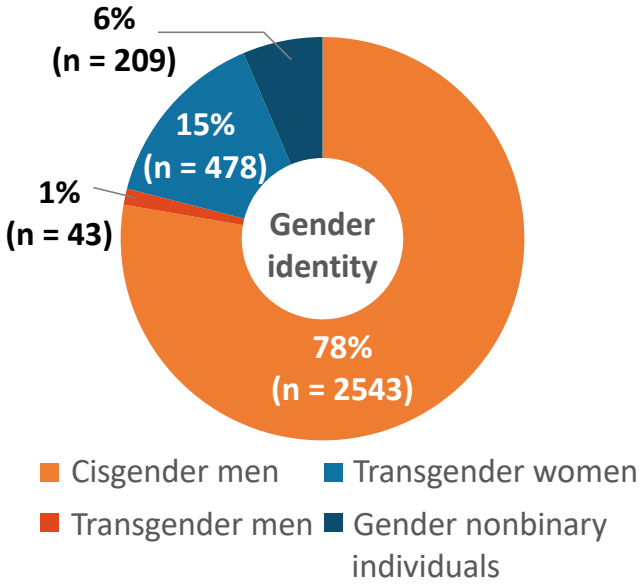
Kelley CF, R4P, 2024. Kelley et al. NEJM 2024.

Purpose 2: Study Recruitment

- Most racially, ethnically, and gender-diverse PrEP trial, representing 7 countries (Argentina, Brazil, Peru, Mexico, South Africa, Thailand, US)





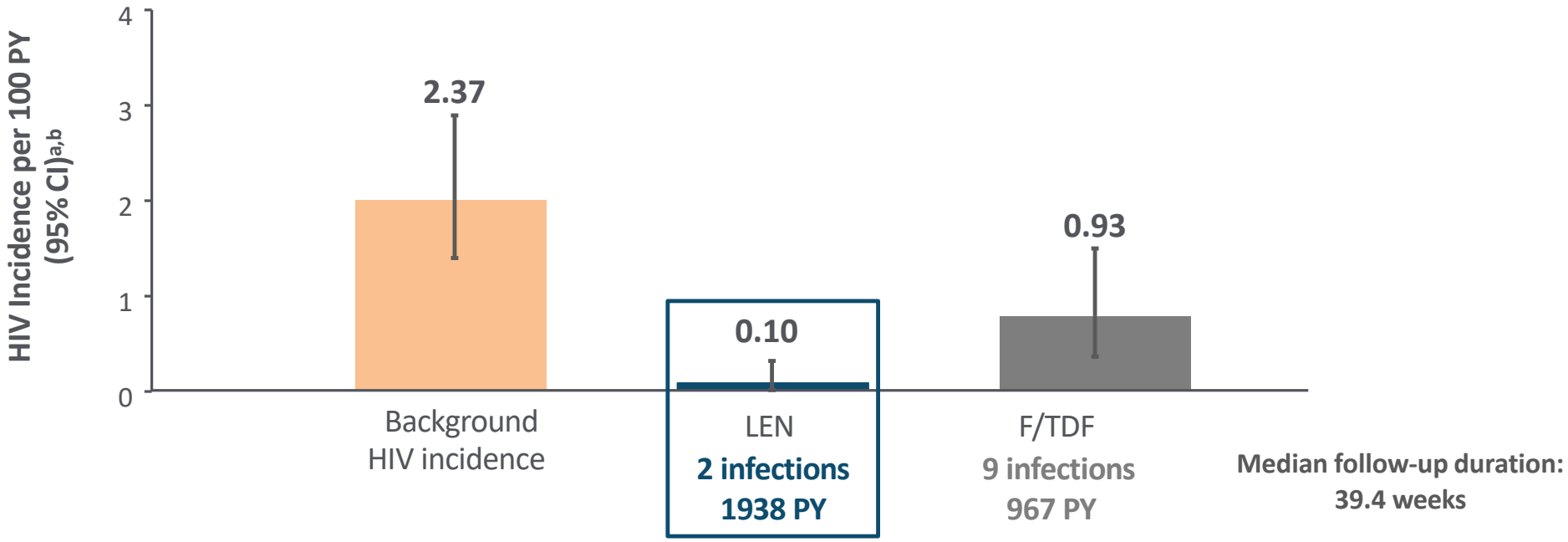


- Strategies used to optimize enrollment: global community advisory group, consultation with key stakeholders, purposeful site selection and recruitment

Gallardo-Cartagena. HIVR4P 2024. Abstr OA0207.; Kelley CF, R4P, 2024. Kelley et al. NEJM 2024.

Purpose 2: Results from the interim analysis

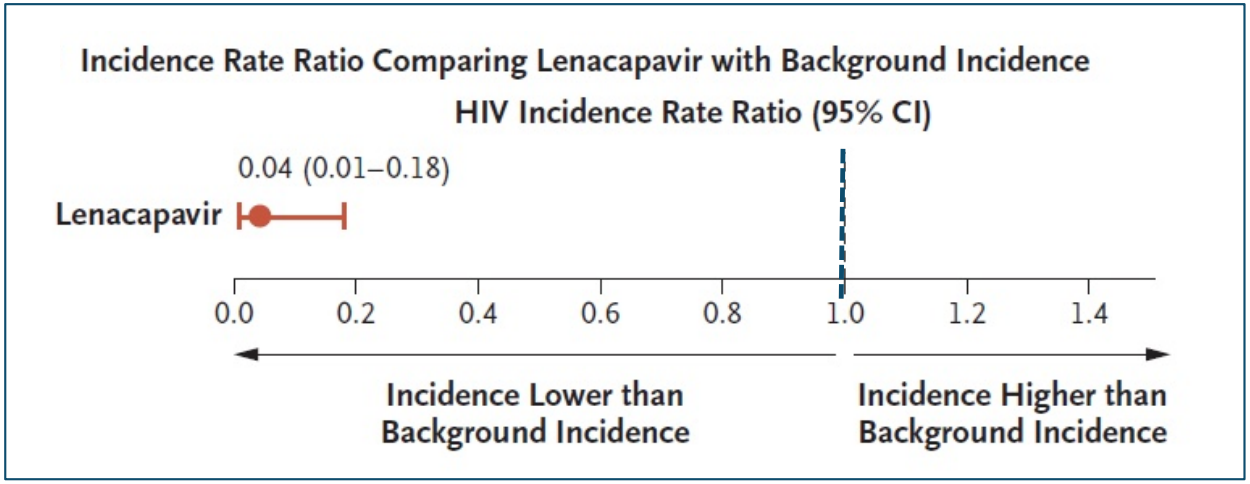
Lenacapavir reduced the risk of acquiring HIV by 96% when compared with the background HIV rate

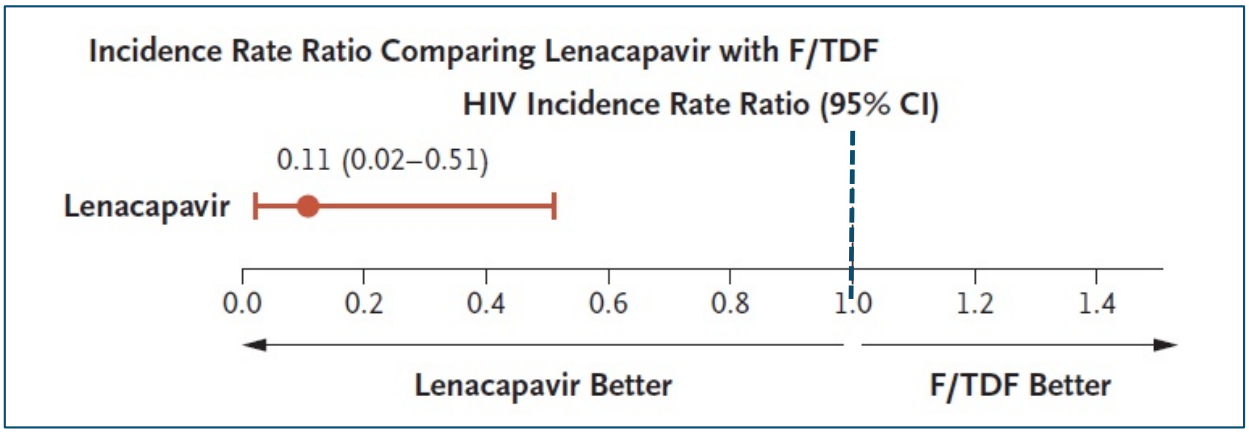


Lenacapavir was also **89%** more effective than **F/TDF** at preventing people from acquiring HIV

Kelley CF, R4P, 2024. Kelley et al. NEJM 2024.

Purpose 2: Results from the interim analysis



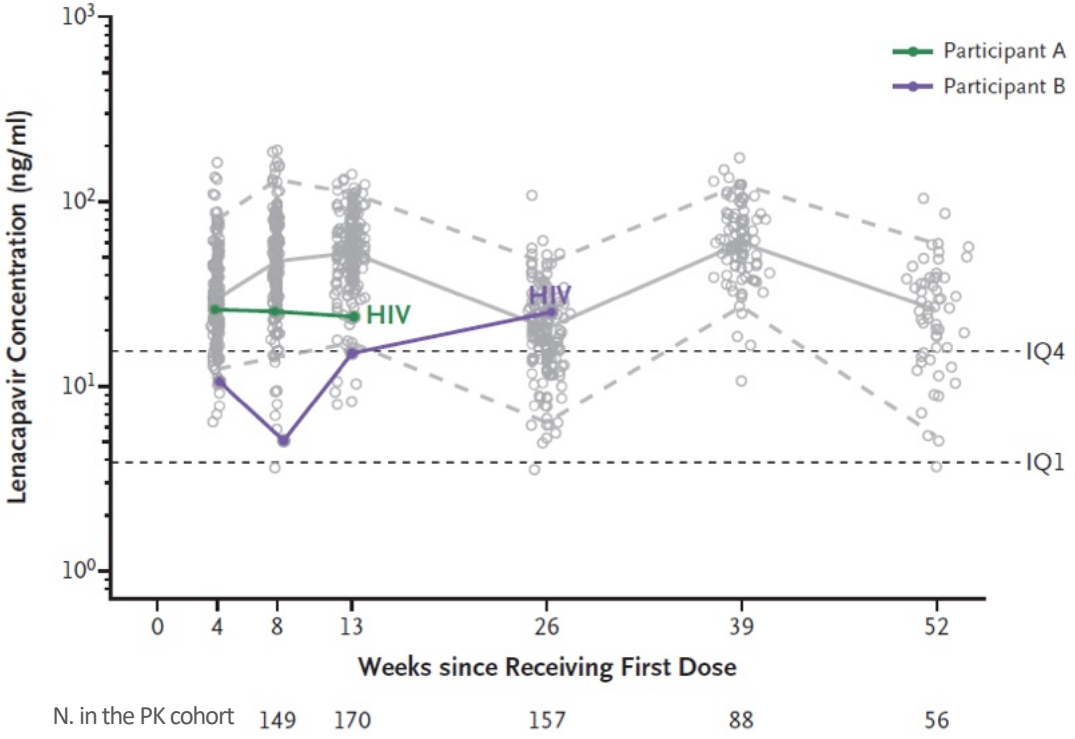


Kelley CF, R4P, 2024. Kelley et al. NEJM 2024.

Purpose 2: Results from the interim analysis

- LEN concentrations within the range of the overall LEN concentrations in the PK cohort.
- No delayed diagnosis.
  - Retrospective HIV-1 RNA single-copy testing positive only for Participant A at week 8.
- Both participants had the N74D capsid resistance mutation found at their HIV diagnosis visit.
- Neither participant reported symptoms of HIV seroconversion

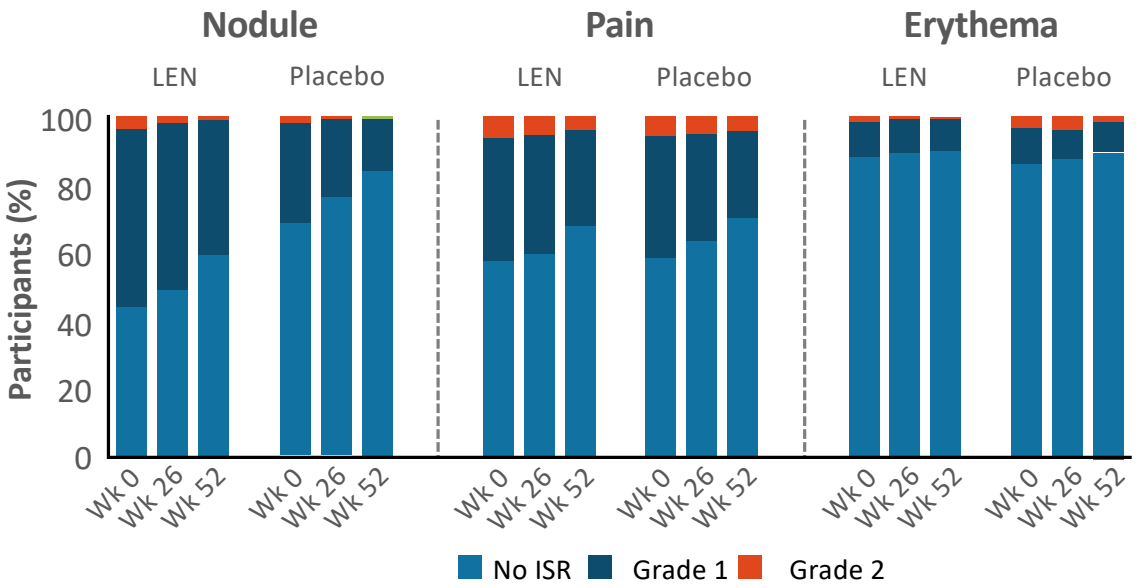
LEN plasma concentrations in the PK cohort and in the two participants in the LEN group who acquired HIV infection



Kelley et al. NEJM 2024.

Purpose 2: Safety

- Among 15,239 LEN or placebo injections, 29 participants discontinued for ISR AEs (LEN: n = 26; FTC/TDF: n = 3)
- AE rates similar between groups except for eGFR changes:
  - Wk 26: +1.2 mL/min with LEN vs -3.0 mL/min with FTC/TDF (*P* <.0001)
  - Wk 52: +0.6 mL/min with LEN vs -2.9 mL/min with FTC/TDF (*P* = .0024)

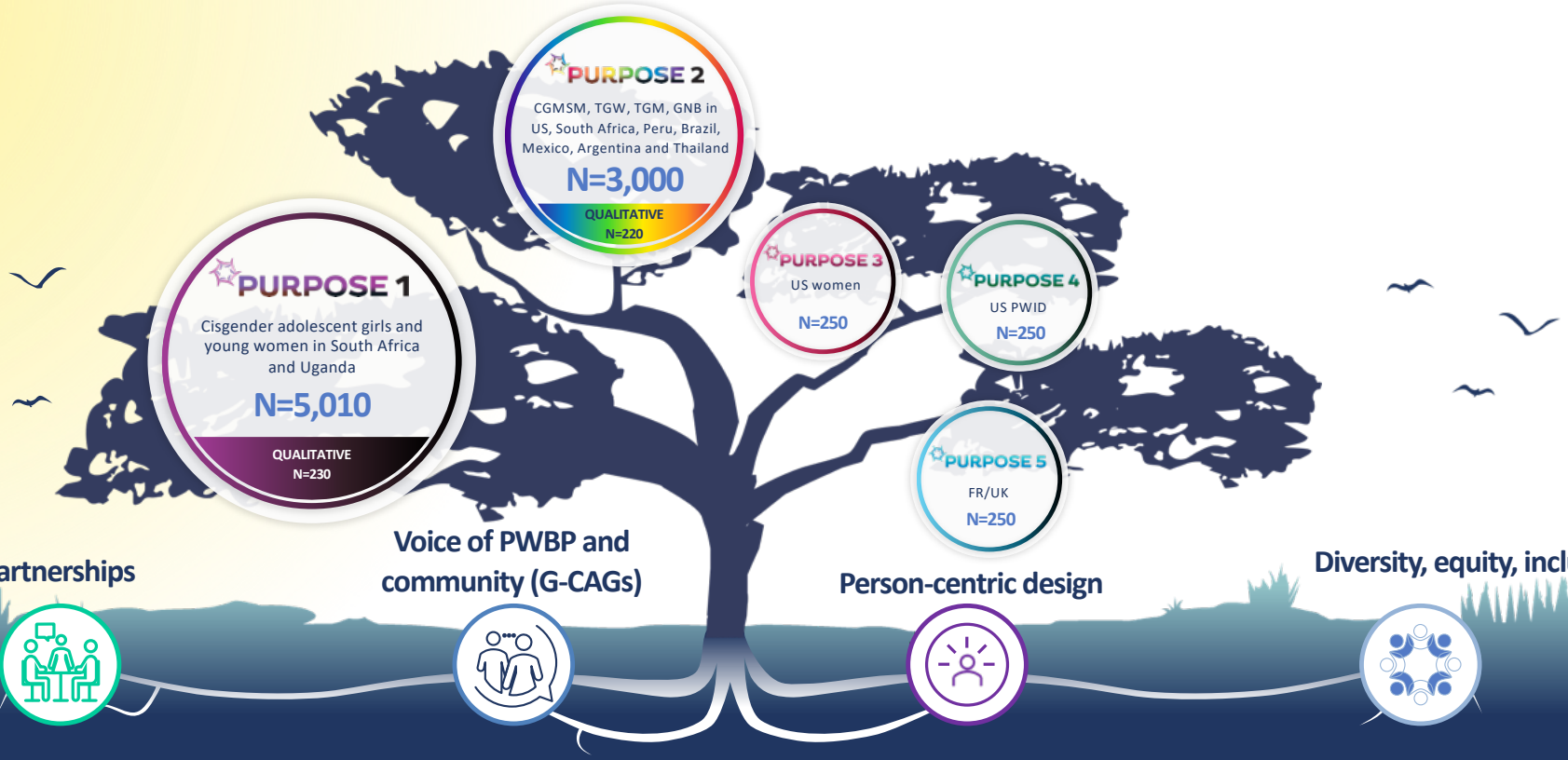


- ISR frequency decreased with subsequent doses

Kelley. HIVR4P 2024. Abstr 0208.

https://www.science.org/content/article/breakthrough-2024#section_breakthrough

Lenacapavir for PrEP: #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 Islatravir for PrEP

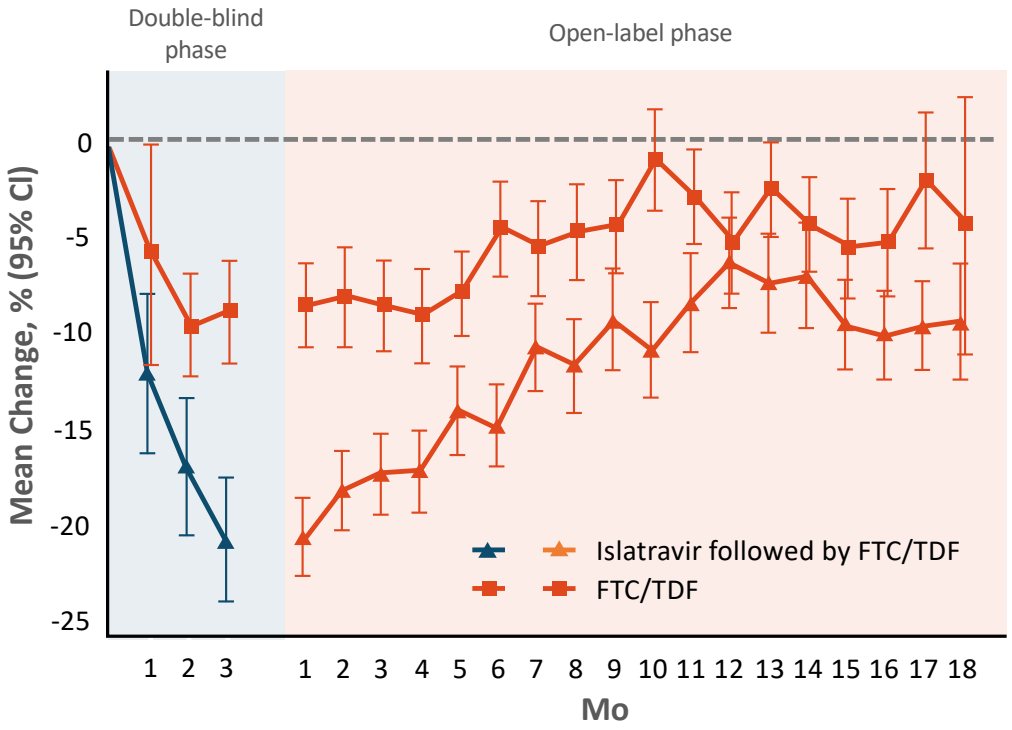
- **Islatravir:** first in class nucleoside reverse transcriptase translocation inhibitor (NRTTI), with very long half life (192 hours) → monthly PO administration
- Assessed for efficacy for PrEP in two phase 3 studies:
  - IMPOWER 22: cisgender women in Sub-Saharan Africa
  - IMPOWER 24: cisgender men and trans women (> 50% in the US)
- Both compared to oral F/TDF
  - 2021: FDA place a full clinical hold on both studies after ~ 1 year due to dose/exposure-related decreases in total lymphocytes and CD4 counts across the islatravir trials.
  - **@R4P:** full safety data for IMPOWER 22 and 24

IMPOWER-22: Safety

- Most AEs grade 1/2; 1 drug-related SAE (ALT increase) in ISL arm resulting in drug discontinuation

Mean % Change in Total Lymphocyte Counts per Initial Intervention Assignment	ISL	FTC/TDF
Double-blind Mo 3	-20.8% (n = 159)	-8.9% (n = 280)
Open-label Mo 12	-6.3% (n = 322)	-5.3% (n = 295)

- In ISL arm throughout double-blind phase or within 42 days after discontinuation of blinded intervention
  - No cases of grade ≥3 total lymphocyte counts (<500 cells/mm^3)
  - No cases of grade ≥3 CD4+ T-cell counts (<200 cells/mm^3)



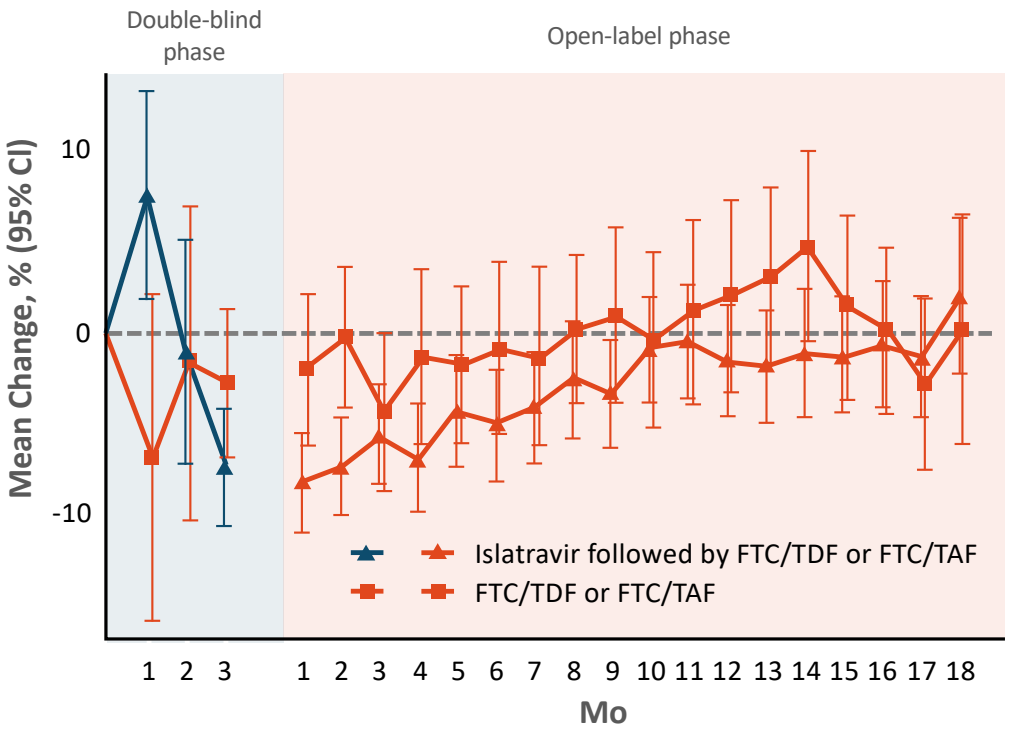
Delany-Moretlwe. HIVR4P 2024. Abstr OA0202.

IMPOWER-24: Safety

- Most AEs grade 1/2; no SAEs deemed related to study intervention

Mean % Change in Total Lymphocyte Counts per Initial Intervention Assignment	ISL	FTC/TDF or FTC/TAF
Double-blind Mo 3	-7.4% (n = 200)	-2.7% (n = 133)
Open-label Mo 10	0.9% (n = 263)	-0.4% (n = 124)

- 2 patients in ISL arm with grade 3 lymphocyte counts (<500 cells/mm^3)
  - Not deemed serious or related to study intervention per investigator
- No cases of CD4+ T-cell counts <200 cells/mm^3 throughout double-blind phase or within 42 days after discontinuation



Landovitz. HIVR4P 2024. Abstr OA02023.

IMPOWER-22 and IMPOWER-24: HIV Acquisition During Study

- No HIV infections through 42 days post discontinuation in either double-blind phase
- HIV acquisition during open-label phase:
  - IMPOWER-22: 3.3% of participants
    - 17 participants initially in ISL arm and 6 participants initially in FTC/TDF arm
  - IMPOWER-24: 1.5% of participants
    - 5 participants initially in ISL arm and 2 participants initially in FTC/TAF and FTC/TDF arm
- HIV-1 infection detected 99-473 days after final ISL dose

Delany-Moretlwe. HIVR4P 2024. Abstr OA0202. Landovitz. HIVR4P 2024. Abstr OA02023.

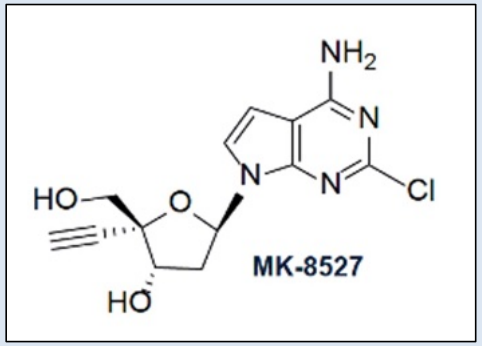
Islatravir summary

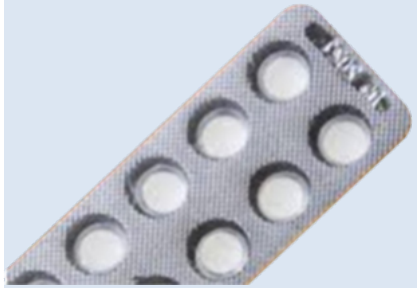
- Despite no HIV seroconversions in the blinded phase of both studies, islatravir for PrEP is no longer pursued due to concerns about lymphopenia
- Lower doses of islatravir continue to be evaluated for HIV treatment

- **ISL no longer under development for oral or implantable PrEP**
- MK-8527, a different investigational NRTTI, is being evaluated as potential oral QM PrEP in phase II study

Agent class:

Nucleoside Reverse Transcriptase Translocation Inhibitor (NRTTI)

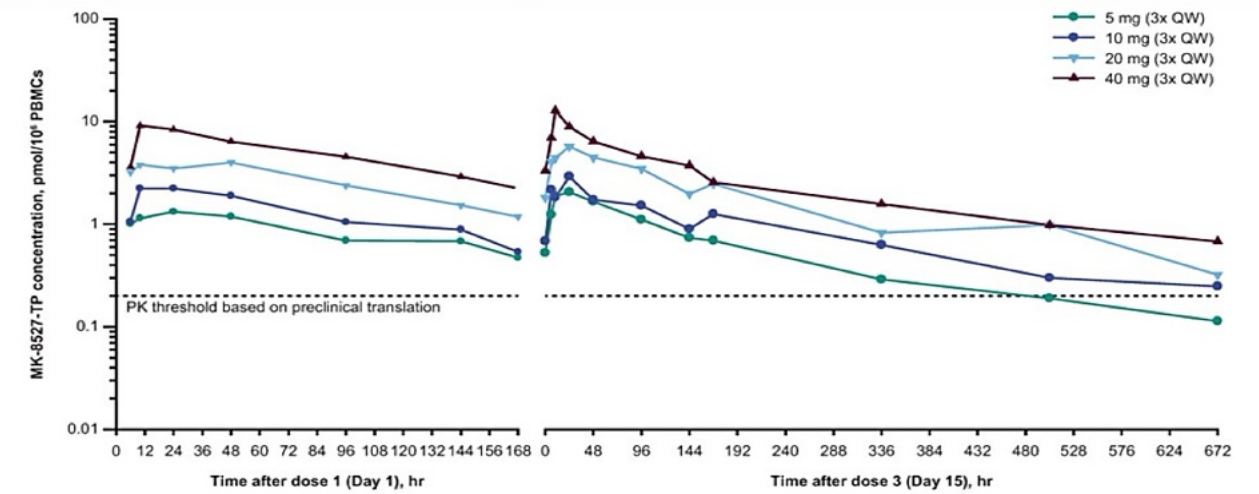




Long half life favours Monthly pill dosing

Perspectives in DPP

Mean MK-8527-TP concentrations after ascending multiple doses of MK-8527 (trial B)



Pharmacokinetics (PK) data from multiple doses of MK8527 with potential once monthly (QM) for HIV pre-exposure prophylaxis (PrEP)

- After multiple doses of MK-8527 (3x QW), the true geometric mean C_{168} of MK-8527-TP was >0.2 pmol/10^6 PBMCs for all dose levels.
- Accumulation of intracellular MK-8527-TP was modest (range of C_{max} and $AUC_{0\text{-}168}$ ratios was 1.1-1.6).
- Across all dose levels, the range of MK-8527-TP apparent terminal half-life was 216-291 hours

Single (0.5–200 mg) and multiple (QW) doses (up to 40 mg) of MK-8527 administered to adults without HIV were generally well tolerated. The safety and pharmacokinetic profiles of MK-8527 support continued clinical investigation.

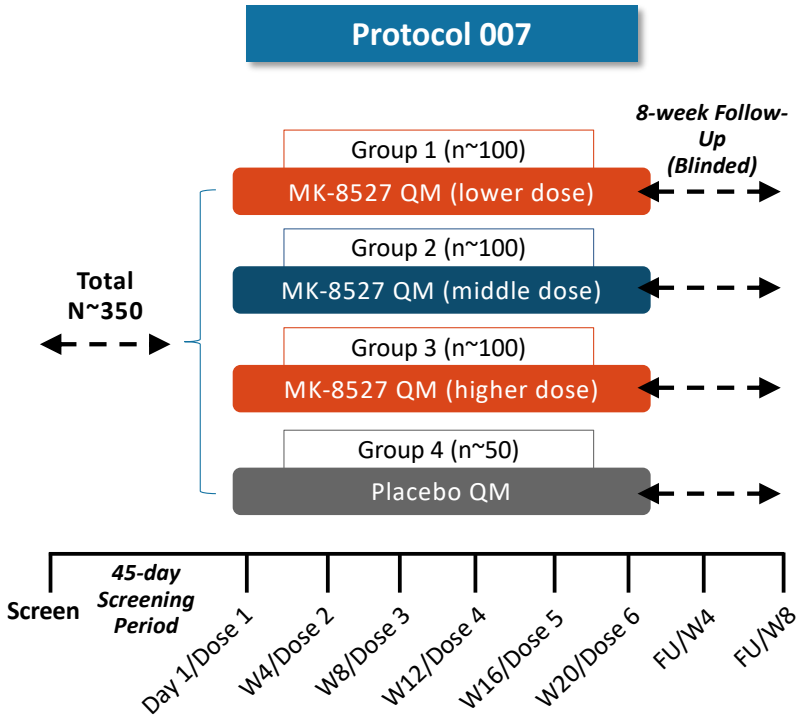
Gillespie et al. CROI 2024. C_{168} - concentration at 168 hours post dose.

Ongoing Phase 2 Study of MK-8527 in Individuals at Low Risk of Exposure to HIV-1, Fully Enrolled

Phase 2 randomized (2:2:2:1), double-blind, dose-ranging study of monthly oral MK-8527

Key Inclusion Criteria

- Confirmed HIV-uninfected
- 18–65 years old
- Low-risk of HIV exposure
- Not pregnant or breastfeeding
- No prior use of ISL or MK-8527



Primary Endpoints

- Safety and tolerability of MK-8527 QM of different doses

Secondary Endpoints

- Plasma pharmacokinetic profile of MK-8527 QM at different doses

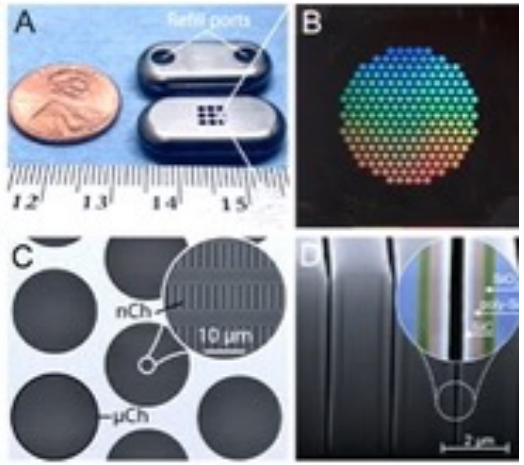
Phase 3s opening in 2025

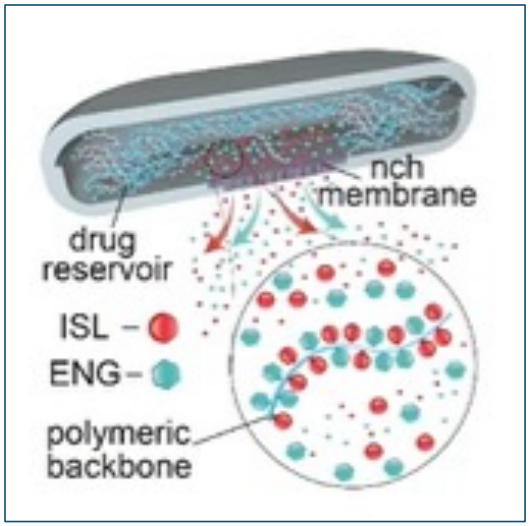
Clinicaltrials.gov NCT06045507

Slide : Rebeca Planc

Nanofluidic implants for ultra-long-acting ARV for PrEP

- Transcutaneously refillable
- Stable concentrations of islatravir in NHP over 2 years, without changes in total lymphocytes and CD4 counts (N=4)
- PK studies in rats using MK-8527 are on-going
- “drug-agnostic” technology: developing polymeric prodrug formulations for hydrophilic drugs such as bictegravir, LEN, DTG
- Ability to load ART and etonogestrel (contraceptive) into a polymeric backbone, into the nanofluidic implant





Pons-Faudoa et al, R4P, 2024

MTN-025/HOPE OLE:
Dapivirine Ring for PrEP During First Trimester of Pregnancy

- Multination study in Africa assessing PrEP ring safety in 1456 HIV-negative individuals, not pregnant or breastfeeding (on contraception)
  - First 3 mo, ring received monthly, then quarterly thereafter (3 rings dispensed)
  - Pregnancy testing: every follow-up visit; ring discontinued when pregnancy identified
  - Pregnancies followed to term

Pregnancy Characteristics	Outcome
Total pregnancies, n	72
Incidence, pregnancies/100 PY	5.0
Median gestational age, days (IQR)	45 (30-64)
PrEP ring exposure, %	82
Outcomes available, n	70

Mayo. HIVR4P 2024. Abstr OA2302.

MTN-025/HOPE OLE: Pregnancy Outcomes

Pregnancy Outcomes,[1] n (%)	No Ring (n = 12)	Ring (n = 58)
Full term birth (≥37 wk)	8 (67)	36 (62)
Preterm birth (<37 wk)	0 (0)	3 (5)
Stillbirth/intrauterine fetal demise (≥20 wk)	0 (0)	3 (5)
Spontaneous abortion (<20 wk)	3 (25)	11 (19)
Therapeutic/elective abortion	1 (8)	5 (9)
Ectopic pregnancy	0 (0)	0 (0)

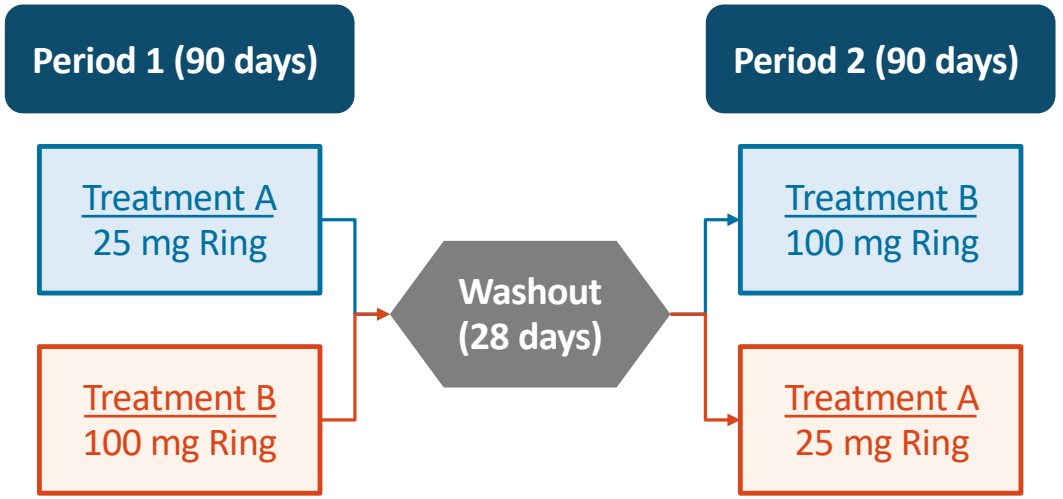
- **Pregnancy complications:** 4 cases (6%) with gestational hypertension; no other complications reported
- **Infant outcomes:**
  - Median birthweight 3.3 kg (IQR: 2.8-3.7) with 5 babies <2.5 kg (11%)
  - No congenital anomalies reported

- Similar findings to MTN-020/ASPIRE with 181 pregnancy outcomes[2]

1. Mayo. HIVR4P 2024. Abstr OA2302 2. Makanani. JAIDS. 2018;79:566.

IPM 054: 1-Mo vs 3-Mo Dapivirine Vaginal Ring Pharmacokinetic Study in South Africa

- Monthly (25 mg) DPV ring approved for use in limited areas (not in US)
- **IPM 054:** open-label, randomized, crossover phase I study of 124 HIV-negative women
- **Primary endpoint:** plasma DPV concentration at Day 90 (prior to removal)
  and exposure during last 30 days
  - Lower bound LS mean ratio 90% CI >0.95 (noninferiority) and >1 (superiority)



Nuttal. HIVR4P 2024. Abstr OA0802LB.

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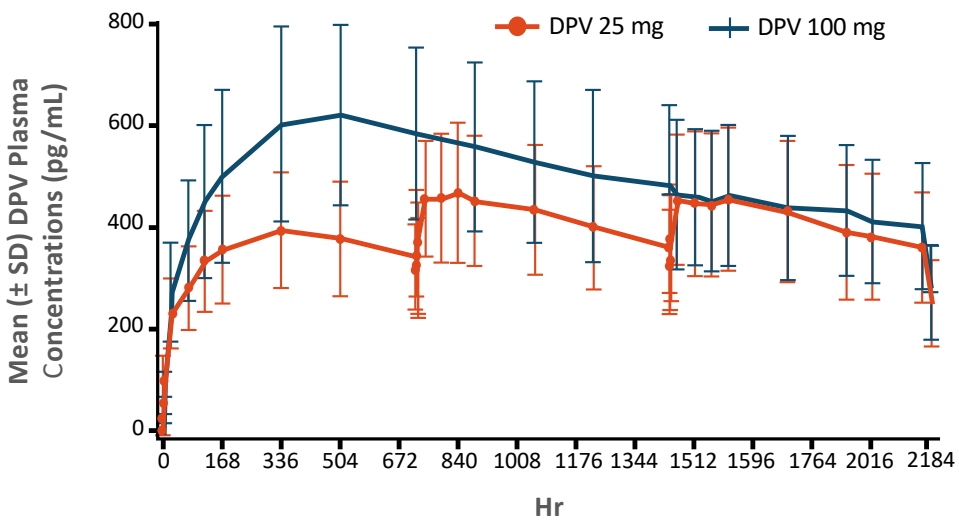
- 3-mo (100 mg) ring noninferior and **superior** to 1-mo (25 mg) ring
- **No differences** in treatment-emergent AEs (eg, discharge, VVC and BV)



Nuttal. HIVR4P 2024. Abstr OA0802LB.

HPTN 084 Substudy: LA CAB or FTC/TDF and Hormonal Contraceptives DDI Assessment

- HPTN 084 demonstrated superiority of Q2M LA CAB vs QD oral TDF/FTC for PrEP in cisgender women
- Substudy of 170 participants taking hormonal contraceptives (ETO, MPA, NOR); drug levels assessed by LC-MS/MS through Wk 73
  - No difference in ETO, MPA, and NOR concentrations between LA CAB and FTC/TDF arms

LA CAB

- Interactions with ETO, MPA, and NOR not observed
- Concentration-time profiles comparable with participants receiving ETO, MPA, or NOR
  - Geometric mean trough concentrations >4x PA-IC_{90} during the injection phase of study

FTC/TDF

- Associations with contraceptive concentrations could not be effectively evaluated because of low adherence

ETO, etonogestrel; MPA, medroxyprogesterone acetate; NOR, norethindrone or norethisterone enanthate

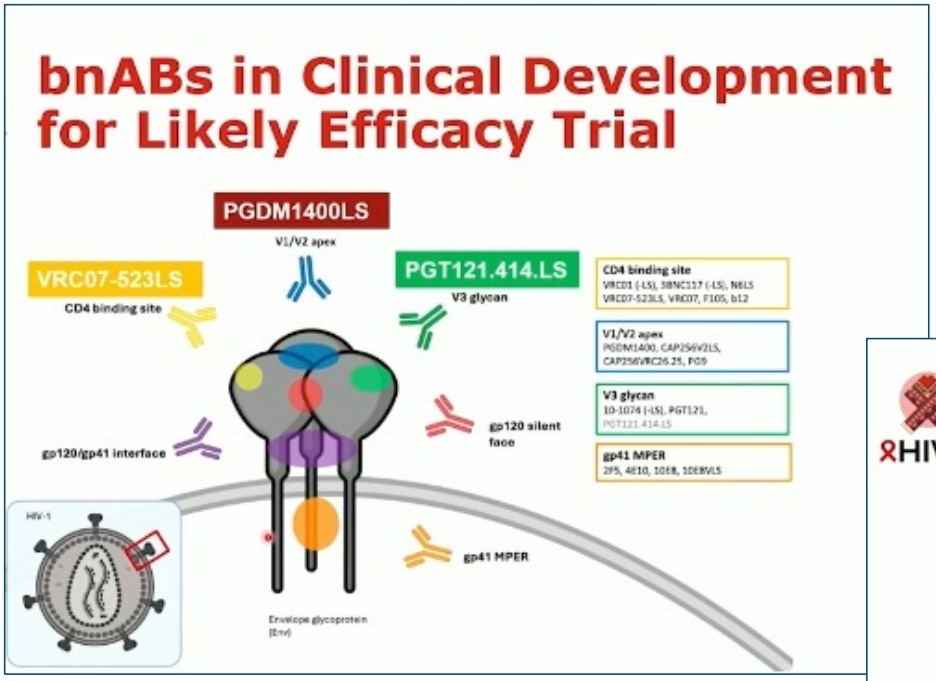
Marzinke. HIVR4P 2024. Abstr OA2306.

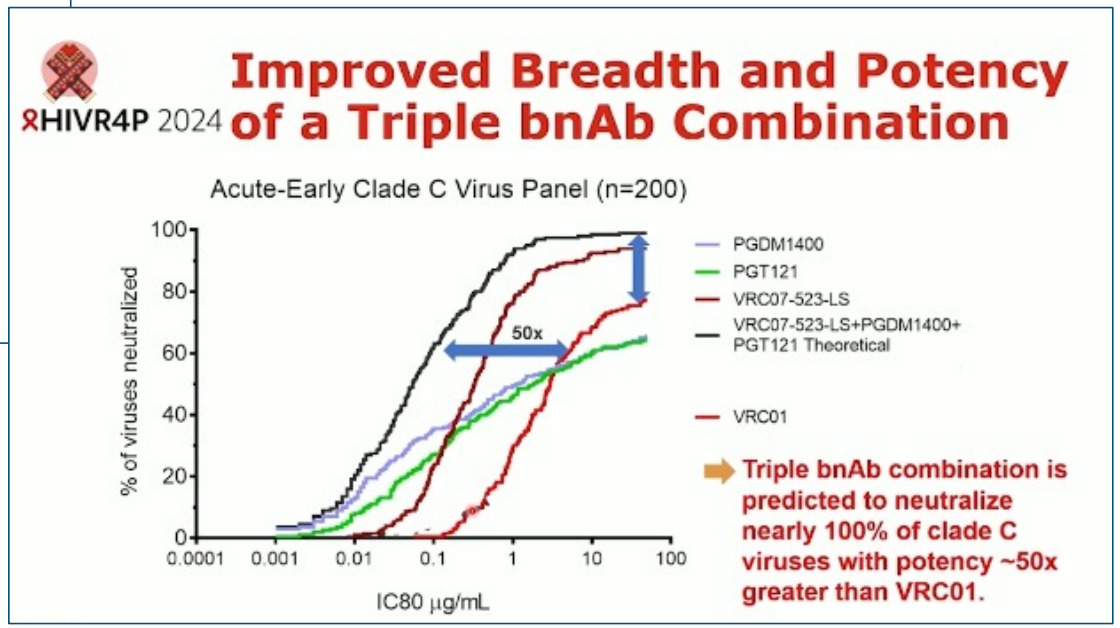
On-demand tenofovir rectal douche for PrEP

- **ATN 163**: phase I trial, assessing PK, PD, and acceptability of single dose TFV rectal douche
- N=8, surveys and IDI following dose. 75% of them: douching prior to study
- Overall acceptability: 9/10
- 100% would recommend to others
- 80% would prefer TFV douche over daily oral PrEP
- Appreciated behavioral congruence of a PrEP modality that aligns with their sexual preparation routines
- Douche was overall well tolerated
- **HPTN 106**: phase 2 crossover study
  - On-demand TFV douche vs. oral F/TDF 2-1-1 for PrEP

Bauermeister J et al, R4P, 2024

Broadly neutralizing antibodies for PrEP (bnAbs)

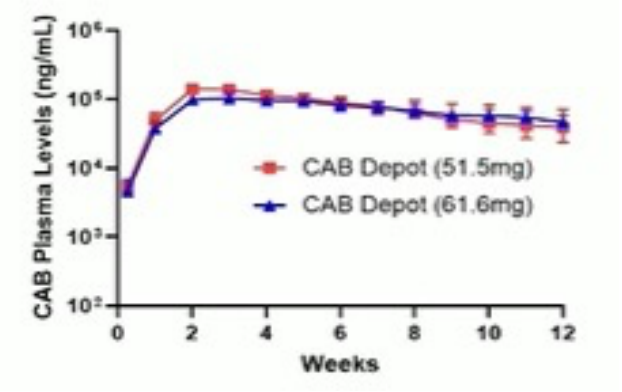


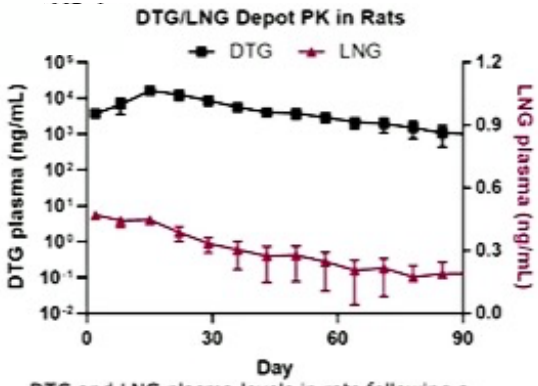


Scott H, R4P, 2024

Multipurpose prevention (MTP)

- Pre-clinical development of long-acting, silica-based, biodegradable, co-formulated, hydrogel depot for prevention of HIV (CAB or DTG) and/or pregnancy (levonorgestrel)
- Designed for > 3m drug delivery
- High drug concentrations in small volumes
- Acts like a fluid when it's being injected through a small-gauge needle → forms a gel in the SC space
- Administered to rats to assess PK, DDI, and ISR





DTG and LNG plasma levels in rats following a single 0.1mL subcutaneous injection

Peet M, R4P, 2024

Multipurpose Prevention Technologies Supported by NIAID Funding

HIVR4P 2024

Institution	PI	Title	Delivery Platform	Duration	Drugs
Population Council	Angsantikul	Novel Pre-coital, Non-hormonal Multipurpose Prevention Technology (MPT)	Fast-dissolving insert	4 hours	Amphora & QGRFT
Oak Crest Institute of Science	Baum	Next Generation Multipurpose Prevention Technology: An Intravaginal Ring for HIV Prevention and Nonhormonal Contraception	*Intravaginal ring *Funded by NICHD	30 days	mAb against CD52g (sperm target) & TDF
Univ. North Carolina Chapel Hill	Benhabbour	Next Generation Multipurpose Intravaginal Ring Technology Using Innovative CLIP 3D Printing	3D-printed intravaginal ring	≥90 days	ENG/EE & EFdA
Methodist Hospital Research Institute	Grattoni	Long-Acting Multi-prevention Implant for 2-year Contraception and HIV PrEP	NanoMPI: subcutaneous nanofluidic multipurpose implant	2 years	ENG & ISL or LEN "drugamer"

Cummins J, R4P, 2024

Improving PrEP Uptake

PrEP initiations

PrEP-to-Need Ratios

Calculation:

# of PrEP initiations

Estimated HIV incidence

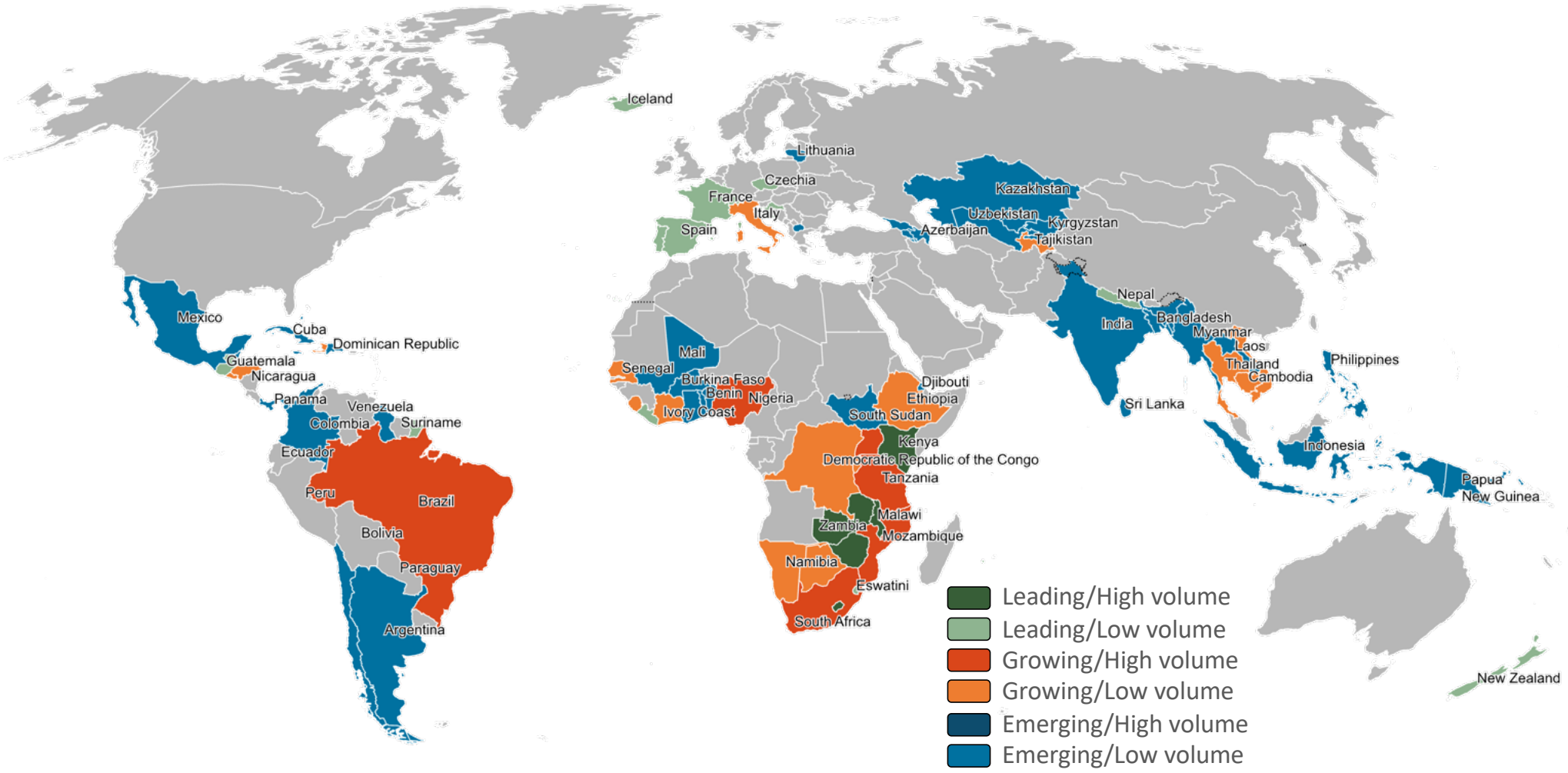
Volume of PrEP Distributed

of cumulative PrEP initiations from start of PrEP programme to end of 2023

	PrEP Distributed by Country	
Country PrEP-to-Need Ratio	**High: >100,000 Initiations**	**Low: <100,000 Initiations**
Leading: >5	Leading, High Volume	Leading, Low Volume
Growing: 1- 4.99	Growing, High Volume	Growing, Low Volume
Emerging: <1	Emerging, High Volume	Emerging, Low Volume

Verde Hashim et al. HIV R4P 2024.

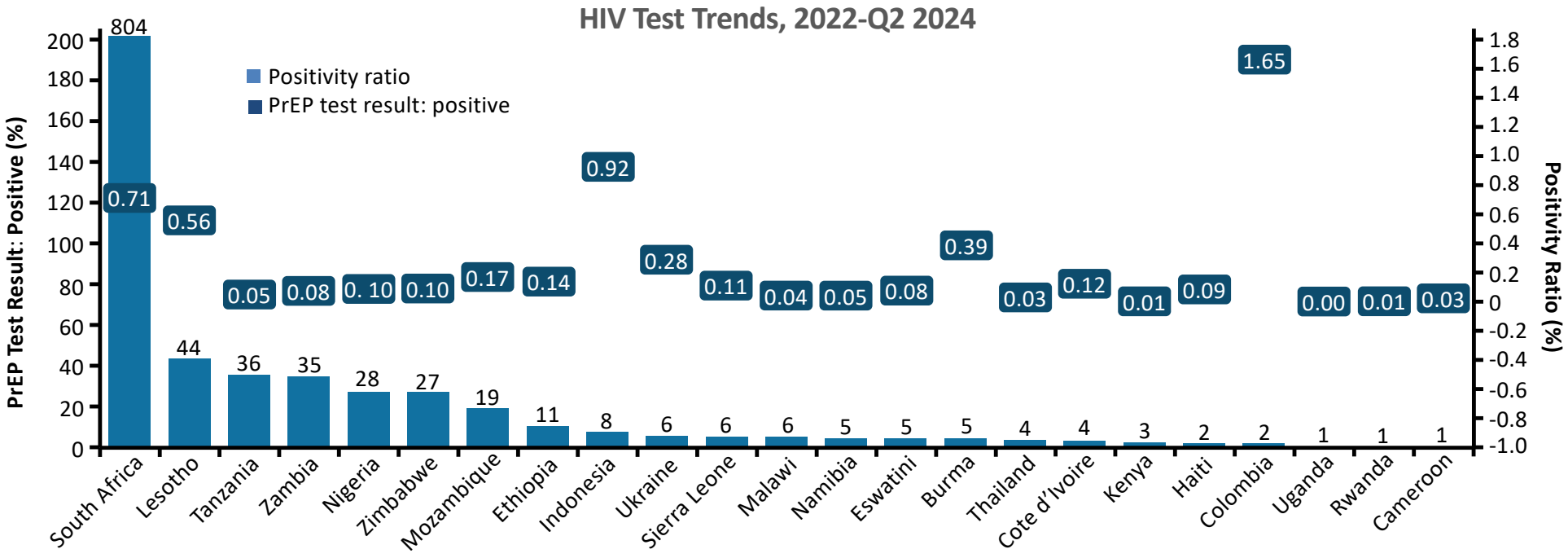
PrEP initiations



Verde Hashim et al. HIV R4P 2024.

PEPFAR: Large-Scale PrEP Implementation Successful in Reducing HIV Incidence

- US President's Emergency Plan for AIDS Relief; provided PrEP since 2015
  - 2017-Q2 2024: 6,176,046 PrEP initiations in PEPFAR countries



Akom. HIVR4P 2024. Abstr OA0102.

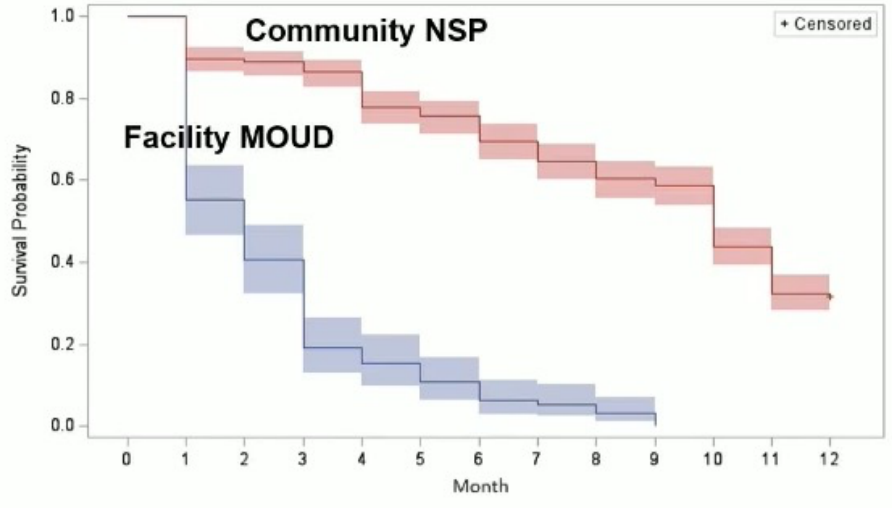
PrEP integration into harm reduction services

Greater PrEP use in a community-based needle and syringe programme versus facility-based medication foropioid use disorder programme for people who use drugs in Uganda

PrEP dispensations according to harm-reduction service, Uganda

	Facility MOUD			Community NSP		
	30 pills	60 pills	90 pills	30 pills	60 pills	90 pills
Individuals attended	130	62	36	389	118	431
Expected for a refill	178	82	48	397	122	1638
Refill visit: No attendance	46%	60%	67%	6%	2%	29%
Attendance within 30 days	41%	6%	0%	76%	1%	0%
Attendance within 60 days	5%	12%	6%	11%	84%	2%
Attendance within 90 days	4%	7%	13%	1%	9%	56%
Attendance within 120-180 days	4%	10%	8%	6%	5%	12%

Time to first PrEP discontinuation



Heffron et al. HIV R4P 2024.

PrEP use and mental health and substance use

Unravelling PrEP persistence: mental health and substance use among South African adolescent girls and young women enrolled in a PrEP implementation programme

Age-stratified log-binomial regression analysis for the association between mental health and substance use exposures and retention and persistence outcomes

	Programme retention (attended first follow-up visit)		
Exposures	**15-19 years PR (95% CI)**	**20-24 years PR (95% CI)**	**25-29 years PR (95% CI)**
Moderate-severe depression/anxiety	1.45 (1.15, 1.82)	1.20 (0.92, 1.57)	1.05 (0.79, 1.40)
Alcohol misuse	1.58 (1.18, 2.11)	1.11 (0.95, 1.30)	1.15 (0.97, 1.37)
	PrEP persistence (PrEP dispensed at first follow-up visit)		
Exposures	**15-19 years PR (95% CI)**	**20-24 years PR (95% CI)**	**25-29 years PR (95% CI)**
Moderate-severe depression/anxiety	1.45 (1.10, 1.93)	1.02 (0.72, 1.44)	0.97 (0.68, 1.37)
Alcohol misuse	1.59 (1.19, 2.13)	1.06 (0.88, 1.27)	1.13 (0.92, 1.38)

Models adjusted for mobile vs. clinic enrollment location

- AGYW facing mental health and substance use challenges may have found support withing the FastPrEP programme, enhancing their engagement

Giovenco et al. HIV R4P 2024.

SPrEP: Online PEP and PrEP: First Online Platform for Access to HIV Prophylaxes in Brazil

- SPrEP: platform hosted in e-saúdeSP app, run by Municipal Health Department of São Paulo
  - **Consultation request choices:** (1) I want PrEP; (2) I want a PrEP follow-up; (3) I want PEP; (4) I have questions
  - **Teleconsultation:** 3 physicians available 7 days/wk
  - **PrEP and PEP prescriptions:** filled/dispensed by pharmacists, nurses, dentists, or physicians at multiple sites including some 24-hr sites and dispensing machines
- For PrEP: proof of HIV-negative test within past 7 days or negative self-test image required

da Silva. HIVR4P 2024. Abstr OA0402.

SPrEP: Online PEP and PrEP: Access From June 2023 to September 2024

- People accessing services through SPrEP: 61% White, 22% Pardo, and 9% Black; majority of people <35 yr of age
  - More cisgender men started PrEP (85%) or PEP (72%) via SPrEP than others; cisgender women were 10.9% of people starting PEP (only 0.6% starting PrEP)
  - <1% of transgender men and women, nonbinary, or travesti individuals used SPrEP

SPrEP Use	People
PrEP, n	1129
PEP, n	955
Preferred medication dispensed at 24-hr units, %	52
Consultation follow-ups, n	571

Automated Machines Use, n	People
Prescriptions dispensed, n • PrEP • PEP	>500 343 172
Self-test, n	>500

da Silva. HIVR4P 2024. Abstr OA0402.

PrEP expansion in São Paulo, Brazil

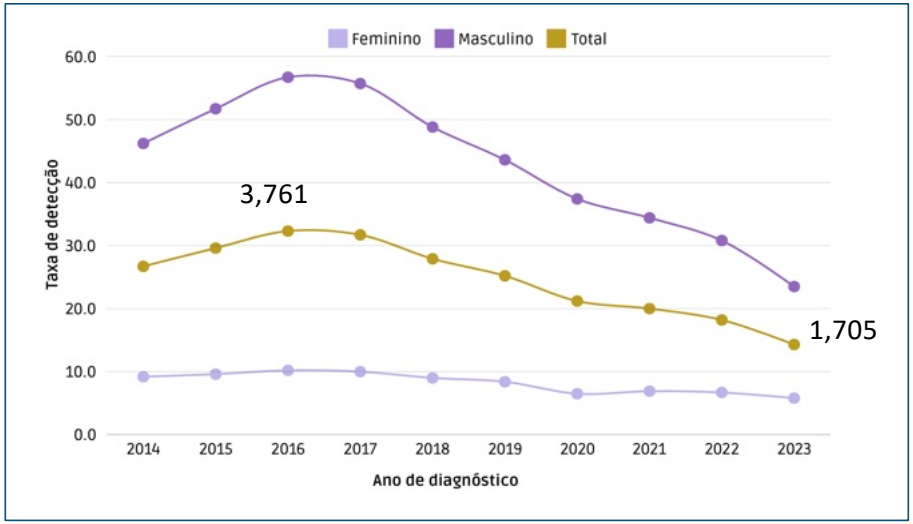
At the **Prevention Station Jorge Beloqui**
From Tuesday to Saturday
5 PM to 11 PM

At one of the **24-hour units** as indicated
Everyday
24 hours

One of the **conventional units** of the specialized network
From Monday to Friday
7 AM to 7 PM

At the **City's CTA**
From Thursday to Saturday
5 PM to 10 PM

Or collect from one of the **Dispensing machines**
Everyday
4:40 AM to 12PM



Casos de infecção por HIV na cidade de SP tiveram queda de 54% nos últimos 7 anos; redução está associada ao aumento no uso de PrEP

Cases of HIV infection in São Paulo city reduced by 54% in the last 7 years; reduction is associated to increase in PrEP use

Abbate et al. HIV R4P 2024; https://g1.globo.com/sp/sao-paulo/noticia/2024/09/18/casos-de-infeccao-por-hiv-na-cidade-de-sp-tiveram-queda-de-54percent-nos-ultimos-7-anos-reducao-esta-associada-ao-aumento-no-uso-de-prep.ghtml

Implementing PrEP options

CATALYST: PrEP Choice for Women With PrEP Ring vs Oral PrEP

- Implementation study that provided informed choice of PrEP to women at public sector PEPFAR delivery sites[1]
  - 2 stages: (1) PrEP ring and oral PrEP; (2) CAB PrEP, PrEP ring, and oral PrEP
- 3967 women enrolled in Stage 1: 66% oral PrEP; 30% PrEP ring, 4% no PrEP[2]
  - **More likely to use PrEP ring:** >1 partner in prior 3 mo and contraceptive use
  - **Less likely to use PrEP ring:** younger women, new PrEP users, pregnant and breastfeeding women

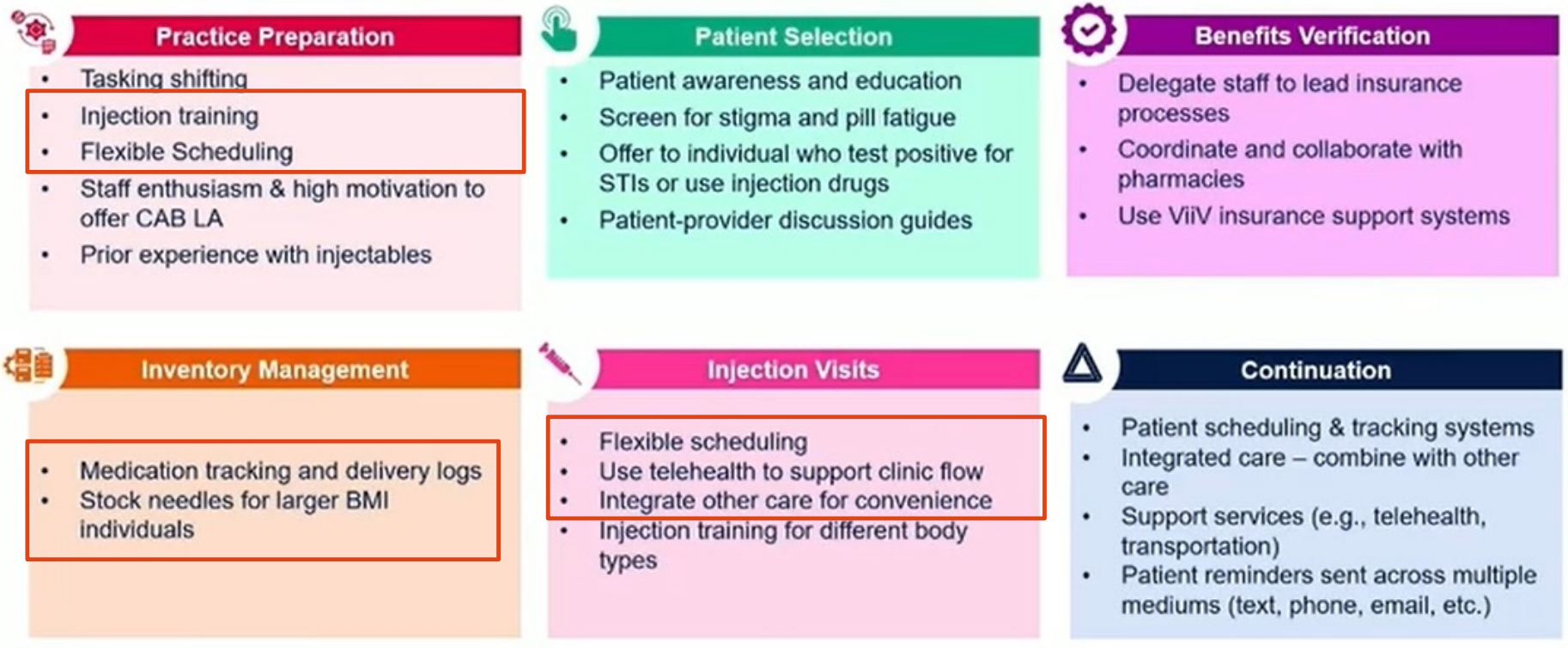
Reason for PrEP Choice[2]	PrEP Users, %
Oral PrEP	
• Ease of use	59
• Works well	32
• No need for something in body	11
• In charge when used	9
• Prior use	8
PrEP ring	
• Ease of use	57
• No need to swallow pills	53
• Prefer dose schedule	18
• Discretion	14
• Works well	9

Kiruki. HIVR4P 2024. Abstr OA2403. Irungu. HIVR4P 2024. Abstr OA2402.

CAB-LA implementation

- The PILLAR study

12-month, Phase 4, open-label, two-arm study
MSM and transgender men in the US
Different strategies for delivering CAB LA for PrEP
Dynamic and Routine implementation



Khan et al. HIV R4P 2024.

USAID DISCOVER-Health LA CAB Demonstration Project in Zambia

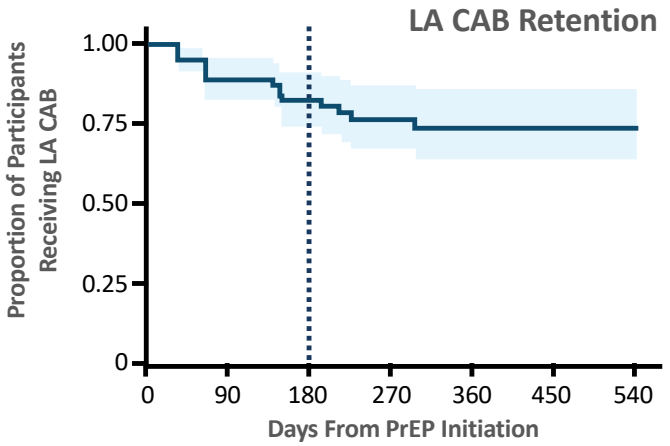
- PEPFAR LA CAB pilot demonstration project implemented in 6 sites in 2 districts evaluating LA CAB adherence in real-world pilot implementation (N = 609)
  - Mean age: 24.4 yr
  - 55.8% female, 32.5% adolescent girls/young women, 21.5% adolescent boys/young men
  - 6.9% key populations
  - 39.1% represented other high-risk populations

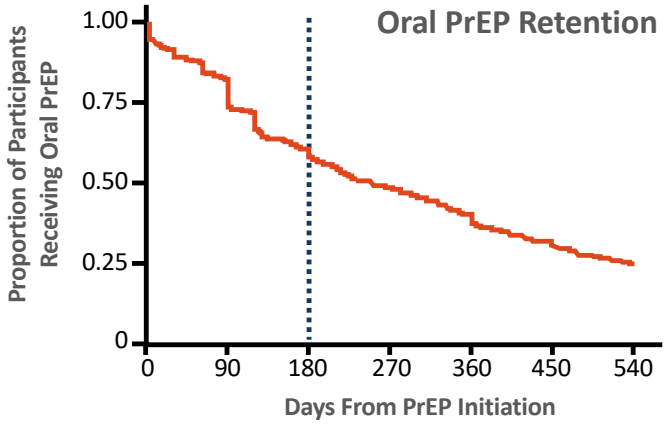
Characteristic, n (%)	Population (N = 609)
Eligible for second injection at 1 mo	406 (67.0)
Second injection results • **Received reinjection** • Pending review • Discontinued LA CAB	 **371 (91.0)** 35 (9.0) 24 (3.9)
Reasons for discontinuations (n = 24) • **HBV infection** • Pregnancy • Severe rash • Severe injection-site pain	 **20 (83.3)** 2 (8.3) 1 (4.2) 1 (4.2)
Outcome after discontinuation (n = 24) • Switch to oral PrEP • Started ART after positive HIV test	 22 (92.0) 2 (8.3)
Initiated on ART after HIV acquisition	2 (8.3)

Ndhlovu. HIVR4P 2024. Abstr OA0504.

LA CAB PrEP Rapid Start Model in San Francisco Public Health Clinics From March 2022 to May 2024

- LA CAB initiated at 8 clinics in San Francisco's Dept of Public Health, serving those with public insurance
  - Drop-in appt with same-day PrEP start and e-referral program
- Baseline characteristics: mean age 37 yr; 65% cis men, 19% cis women, 10% nonbinary, 5% trans women
  - 57% with mental health diagnosis, 51% reported substance use, 36% reported unstable housing
- 32% participants seen at Ward 86 began LA CAB within 24 hr of initial appointment
- 85% of injections were on-time (n = 507)
- No seroconversions, but 3 false-positive HIV RNA-1 tests
- **6-mo retention higher with LA CAB (83%) vs oral PrEP (~60% at same clinic network 2012 to 2017, 48%-63% at other sites)**

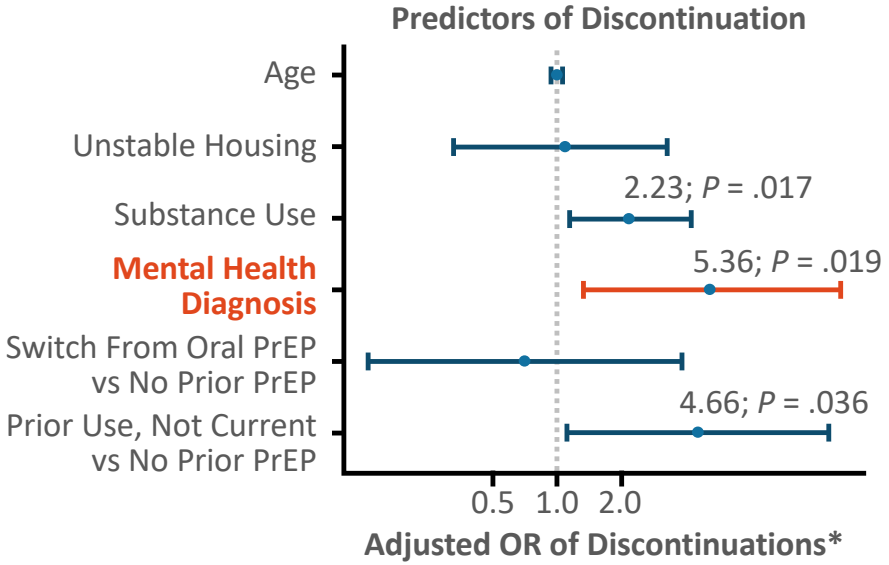


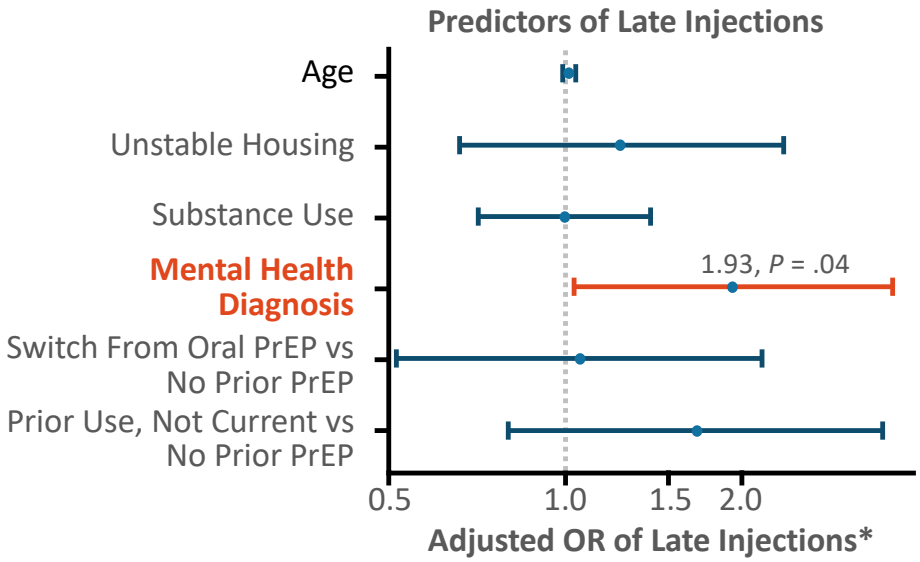


Heise. HIVR4P 2024. Abstr OA0503.

LA CAB PrEP Rapid Start Model: Predictors of Late Injections and Discontinuations

- 19 participants discontinued CAB (low self-perceived risk [n = 6], AE [n = 4], lost to follow-up [n = 6])
- **Mental health diagnosis associated with late injections and discontinuation**; substance use associated with discontinuation
  - Housing instability associated with neither late injections nor discontinuation





*OR was adjusted for age, gender, race.

Heise. HIVR4P 2024. Abstr OA0503.

SeroPrEP: HIV Treatment After LA CAB PrEP

- Incident HIV infections with LA CAB PrEP rare; limited data on optimal HIV treatment
- SeroPrEP: ongoing observational study enrolling persons in routine clinical care on oral or injectable PrEP who acquire HIV infection while on PrEP
- 3 cases of HIV infection with on-time LA CAB injections
  - All cisgender men: multiple sexual partners, no IDU, prior oral PrEP, undetectable HIV-1 RNA at initiation

Characteristic	Case 1	Case 2	Case 3
Age, yr	40	31	67
BMI, kg/m²	24	31	35.5
LA CAB injections, no.	5	6	13
HIV-1 RNA at diagnosis, c/mL	4880	3490	2.43 million
Ag/Ab at HIV diagnosis	POC test neg	POC test neg	Reactive test
CAB concentration, µg/mL	0.69	2.6	1.05
PA-IC_{90}	~4X	~16X	~6X
Time after last injection, days	42	21	55
Sample type	Random	Random	Trough

DHHS ART Guidelines. 2024. WHO CAB Guidelines. 2022. Parikh. HIVR4P2024. Abstr OA507LB.

SeroPrEP: INSTI Mutations and ART Regimen Selection

- No INSTI mutations detected by Sanger genotype

Single Genome Sequencing	Case 1	Case 2	Case 3
• Day after diagnosis • Signature INSTI mutations detected (n/N sequences) • Accessory INSTI mutations detected (n/N sequences)	NA (HIV-1 RNA 3 c/mL by sample collection)	7 E138K (1/56) N155K (1/43)	10 Q148R (10/33) None

- All patients started on DRV/COBI/FTC/TAF following diagnosis
  - Case 1 and 2 with undetectable HIV-1 RNA at 5-6 mo and 10 mo post-ART start, respectively
  - Case 3 switched to BIC/FTC/TAF due to DDIs and intolerance
    - HIV-1 RNA 4 copies/mL 6 mo after switch

Short-term follow-up period; more data needed to determine optimal HIV treatment regimen following LA CAB PrEP

Parikh. HIVR4P2024. Abstr OA507LB.

Final remarks

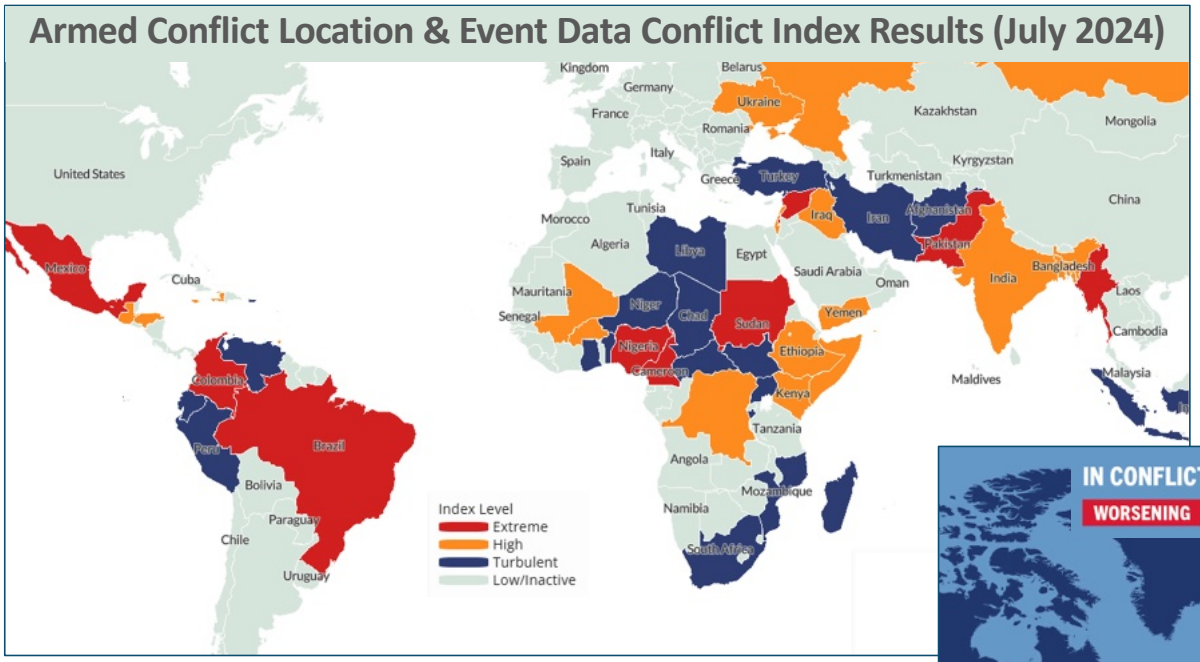
Option

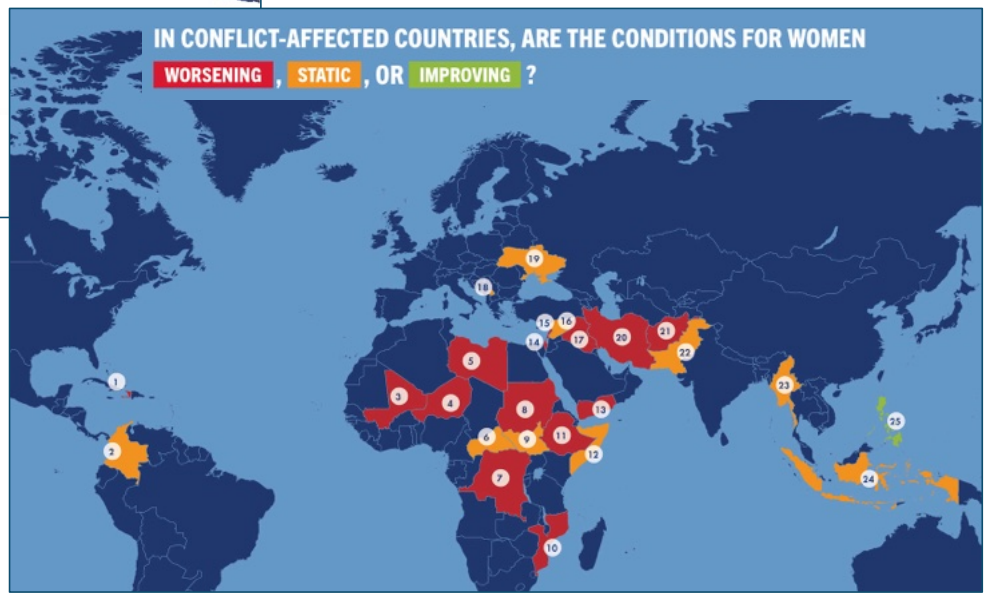
vs

Choice

WHO is choosing WHAT?

Adapted from:
African Women's HIV Prevention Community Accountability Board (AWPCAB) 2023. The HIV prevention choice manifesto. Gallardo-Cartagena. HIV R4P 2024.





Adapted from:
https://acleddata.com/conflict-index/index-july-2024/
https://www.carnegie.org/our-work/article/tracking-wars-disproportionate-impacts-on-women/
Marazzo. HIV R4P 2024.

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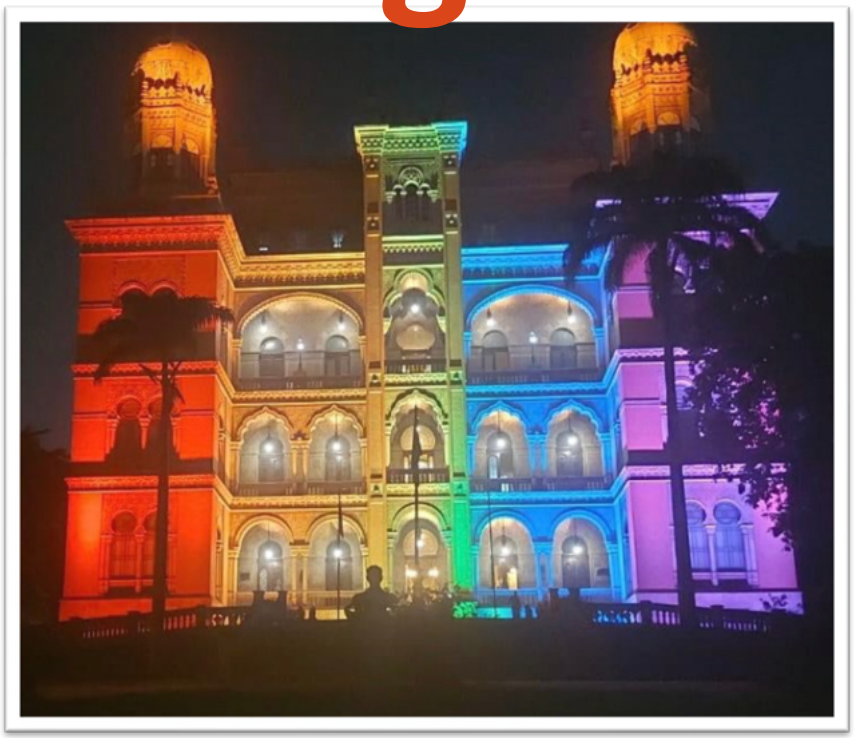
Obrigada!



Beatriz Grinsztejn gbeatriz@ini.fiocruz.br
www.fiocruz.br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