



PrEPping for the Future: The Era of Choice

Linda-Gail Bekker

Desmond Tutu Health Foundation & HIV Centre

Lock Lecture, Glasgow.

November 2024



Relevant disclosures

- DTHF has received grants and research product from Johnson and Johnson and Johnson and ViiV Healthcare
- LGB has served on advisories for
 - ViiV Healthcare
 - Merck Pty LTD
 - Gilead sciences
 - Cepheid



Places and times.....



The Glasgow Lock Hospital (1846)
for “unfortunate females.”
Venereal diseases

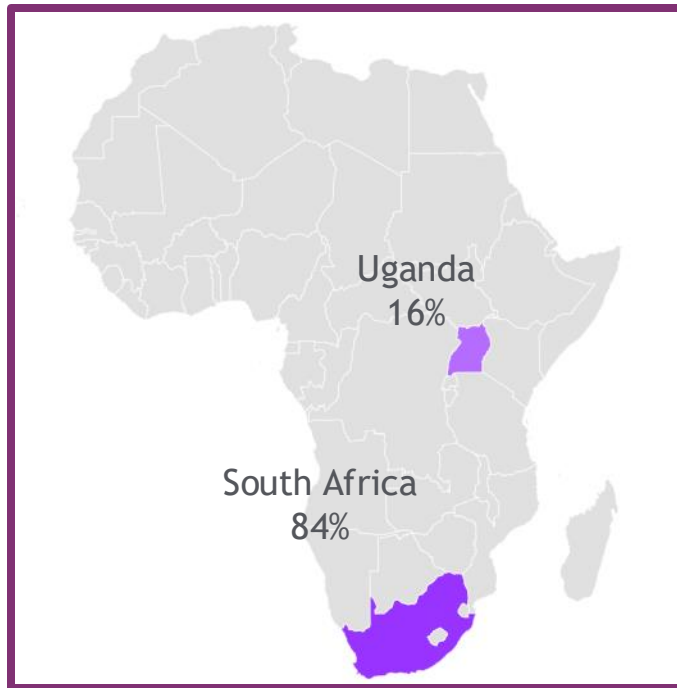


New Somerset hospital – Greenpoint, Cape Town
Oldest hospital in South Africa (1864)
First referral site for young men dying of AIDS in early 90s
First use of antiretrovirals in clinical research.

170 years later....

Lenacapavir for Prevention : Purpose

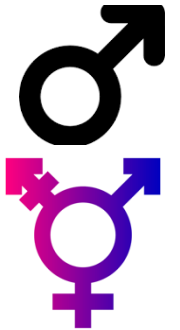
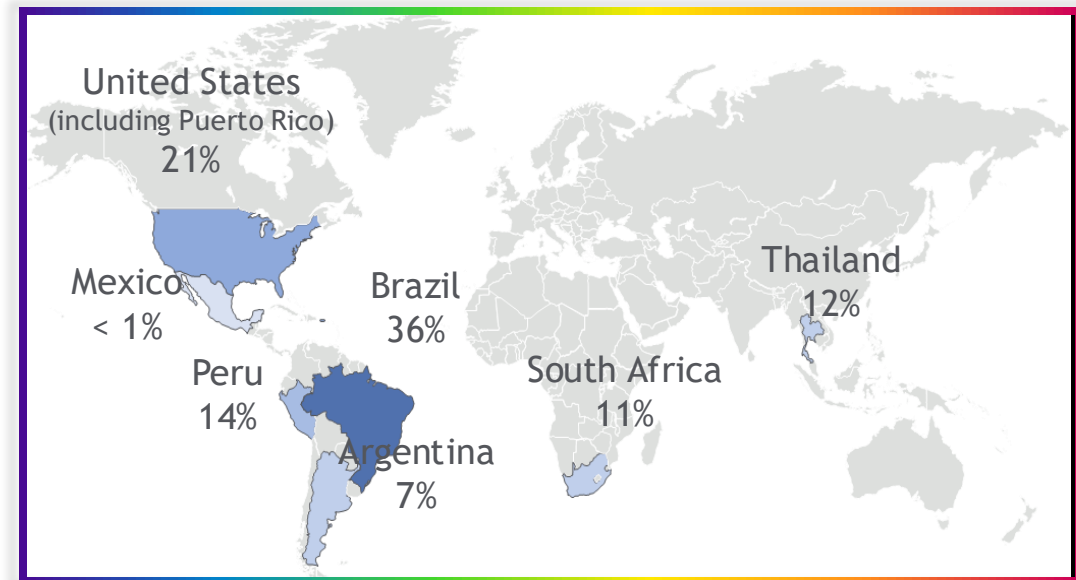
PURPOSE 1



Darker shading corresponds to a higher proportion of participants.

Young women in Africa

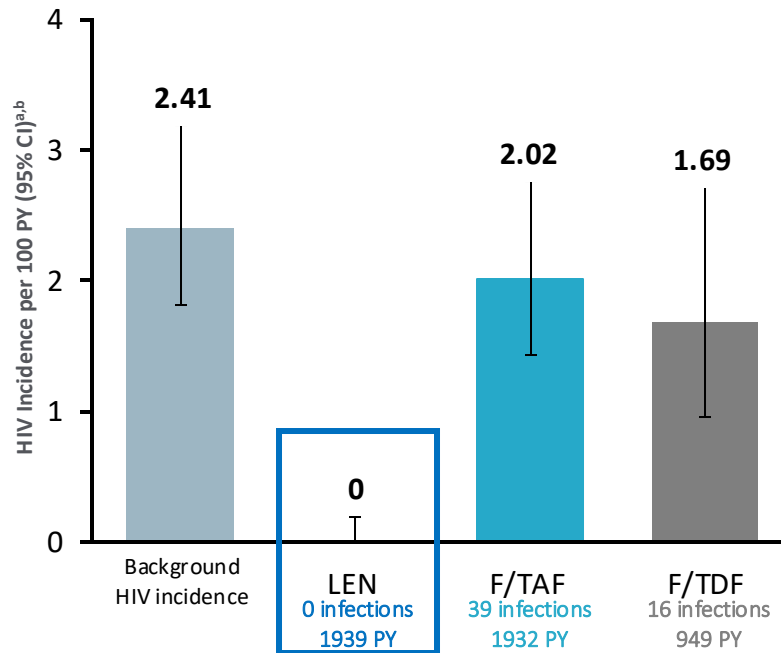
PURPOSE 2



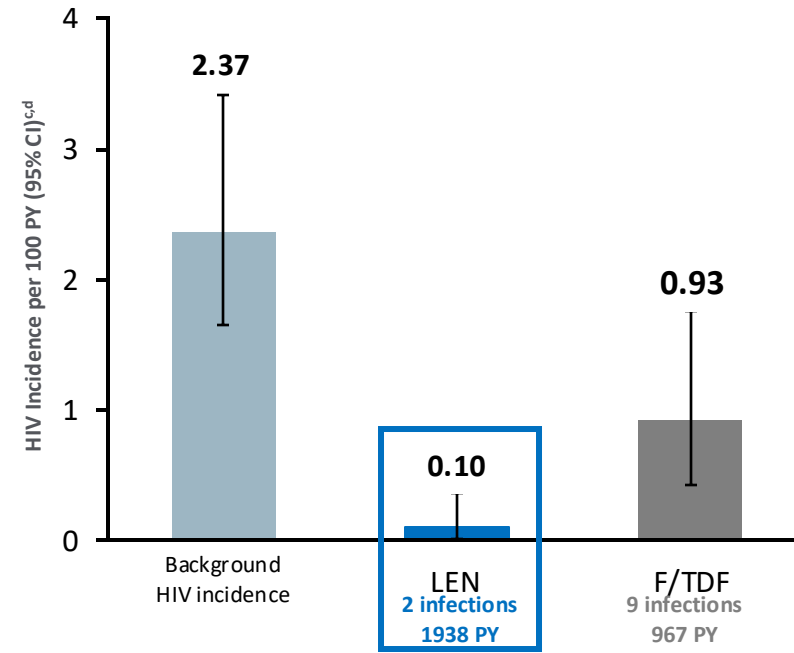
Young men, transgender women and men, non-binary people

PURPOSE 1 : Zero HIV Infections in Cisgender Women Receiving LEN

PURPOSE 2 : Two HIV Infections in Participants Receiving LEN



Median follow-up duration: 44.0 weeks



Median follow-up duration: 39.4 weeks

^aOverall n: background HIV incidence group, 8094; LEN, 2134; F/TAF, 2136; F/TDF, 1068. ^b95% 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.

^cOverall n: background HIV incidence group, 4634; LEN, 2179; F/TDF, 1086.

^d95% CIs: background HIV incidence group, 1.649-3.417; LEN, 0.012-0.373; F/TDF, 0.426-1.768.

PY, person-years.



?



BREAKING HIV NEWS

POZ

SCIENCE NEWS

Twice-Yearly Lenacapavir PrEP Is 100% Effective for Women

Advocates stress that the prevention tool must be a affordable cost to the people of the HIV world.

July 24, 2024
By Liz Highleyman

ANOTHER FEATHER

Groundbreaking HIV Prevention Option



Groundbreaking HIV prevention option is here

Will we address access barriers so that it reaches all equitably, quickly and justly?

BREAKING NEWS

Twice-Yearly Prevention by 96% and demonstrated Superiority to Daily Truvada



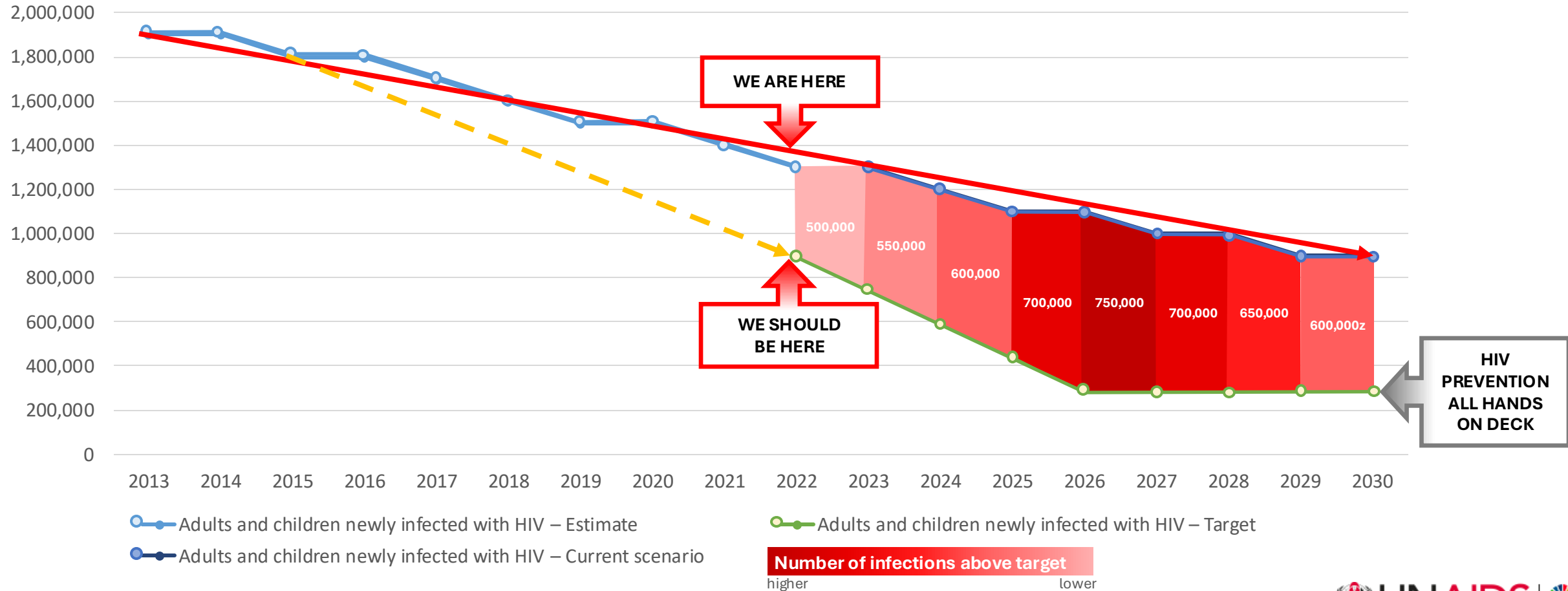
“BECAUSE ADHERENCE TO ORAL PRODUCTS CAN BE CHALLENGING FOR SOME PEOPLE, THREE-YEARLY PUNCTUATE LEMACAPAVIR FOR PREP HAS THE POTENTIAL TO BE ONE OF THE MOST IMPACTFUL INTERVENTIONS WE COULD HAVE TO DRIVE DOWN NEW INFECTIONS AND BRING US CLOSER TO ENDING THE HIV EPIDEMIC IN THE UNITED STATES.”

616 456 9063

The Red Project
Grand Rapids
redproject.org



HIV incidence – Not on track for 2030 UNAIDS targets



The need for HIV primary prevention

Adult HIV-1 incidence across 15 high-burden countries in sub-Saharan Africa from 2015 to 2019: a pooled analysis of nationally representative data



Nora E Rosenberg, Bonnie E Shook-Sa, Mincen Liu, Lynda Stranix-Chibanda, Marcel Yotebieng, Nadia A Sam-Agudu, Michael G Hudgens, Sam J Phiri, Wilbrood Mutale, Linda-Gail Bekker, Sizuku Moya, Khangelani Zuma, Manhattan E Charurat, Jessica Justman, Benjamin H Chi

HIV-1 Incidence (cases per 1,000 Person Years) by Country, Region, Age, Sex



Age group	IR (95% CI)	Difference (95% CI)
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Is HIV epidemic control by 2030 realistic?



Chris Beyrer, Georgia D Tomaras, Huub C Gelderblom, Glenda E Gray, Holly E Janes, Linda-Gail Bekker, Gregorio Millett, Giuseppe Pantaleo, Susan Buchbinder, Lawrence Corey

Rates of new HIV acquisition remain unacceptably high in most populations in low-income, middle-income, and [Lancet HIV 2024; 11: e489-94](#)

0.
2.
7.4/1,000 Southern

3.3/1,000 females
2.0/1,000 males

Other 50% of HIV acquisition in the rest of the world

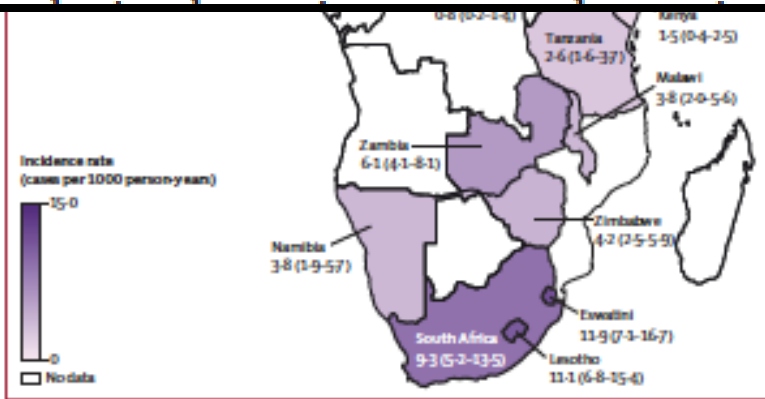


Figure 1: HIV incidence by country (cases per 1000 person-years)

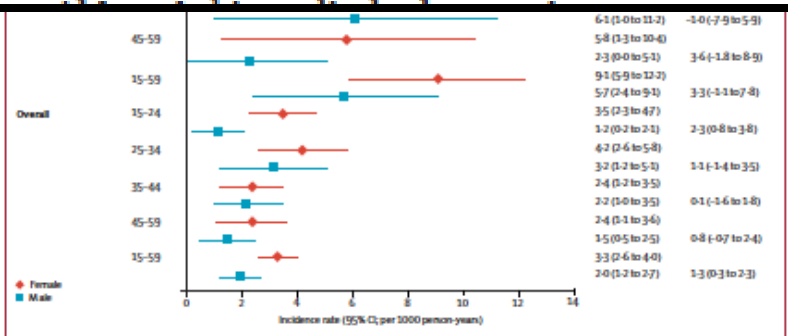


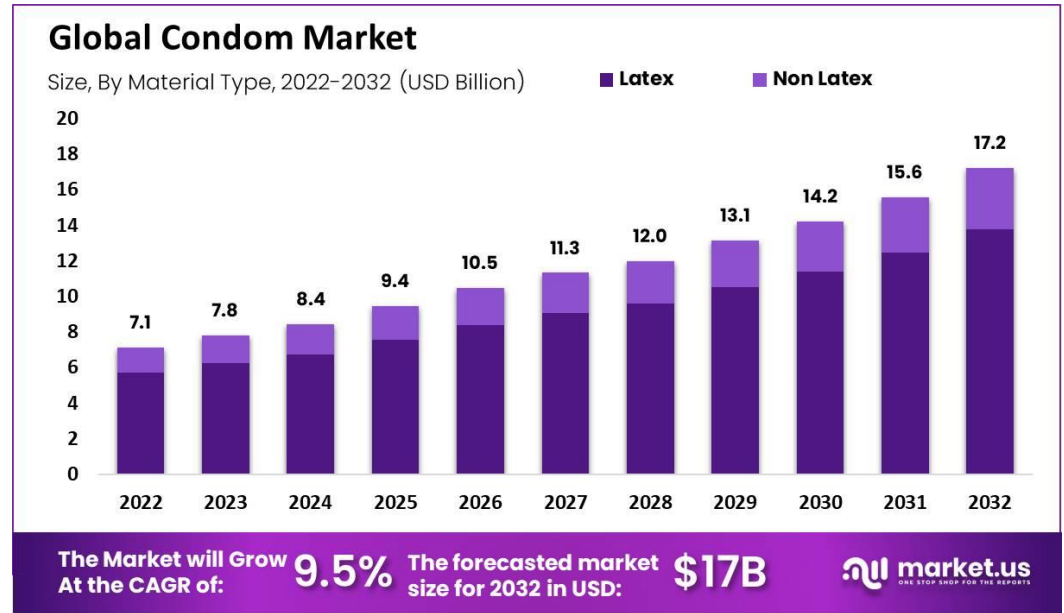
Figure 2: Pooled HIV-1 incidence rates by age, sex, and subregion



Early messaging

Male condom: 400 years and counting!

- Latex condom cornerstone of HIV prevention for 3 decades
- First (and only-so far) MPT
- Lubricant not always as available
- Female condoms not readily available



First 30 years more about treatment than prevention

Beyond ABC: Antiretroviral based biomedical prevention


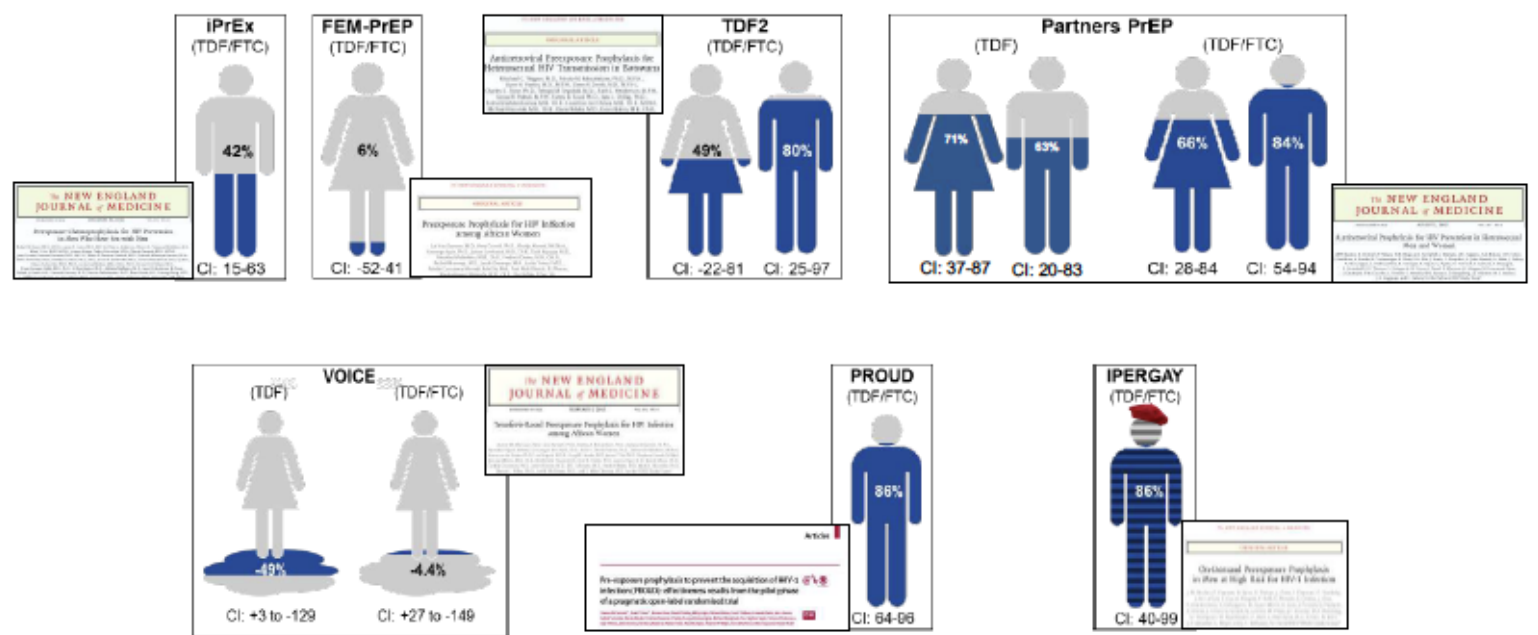
YES!!!!

CAN A PILL A DAY
PREVENT
HIV

FOR INFORMATION ON
EXCITING HIV PREVENTION

SMS "Info" at no cost to 30060 or
e-mail MCMHP@hiv-research.org.za

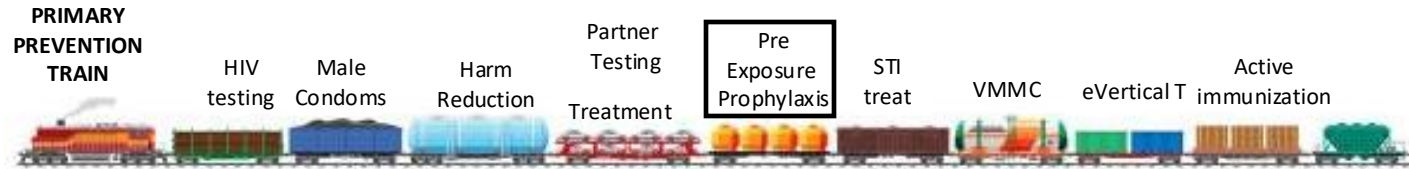
All participants will be compensated for their time.

Landovitz RJ et al. AIDS 2020, #OAXLB01



The HIV Prevention Train



1. ARV BASED PrEP

2. IMMUNE BASED PrEP (Passive immunization with monoclonal antibodies)

“bNAbs for PrEP”

[YouTube](#) [Gmail](#) [Maps](#) [IAS Profile overvie...](#) [IAS HVR4P](#) [IAS HVR4P - Cha...](#) [VAC31518COV300...](#) [2.4 Governance of...](#) [COVID-19 and chil...](#) [Oracle PeopleSoft...](#) [All Bookmarks](#)

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THE PICKY EATER
eating your way to a healthy life

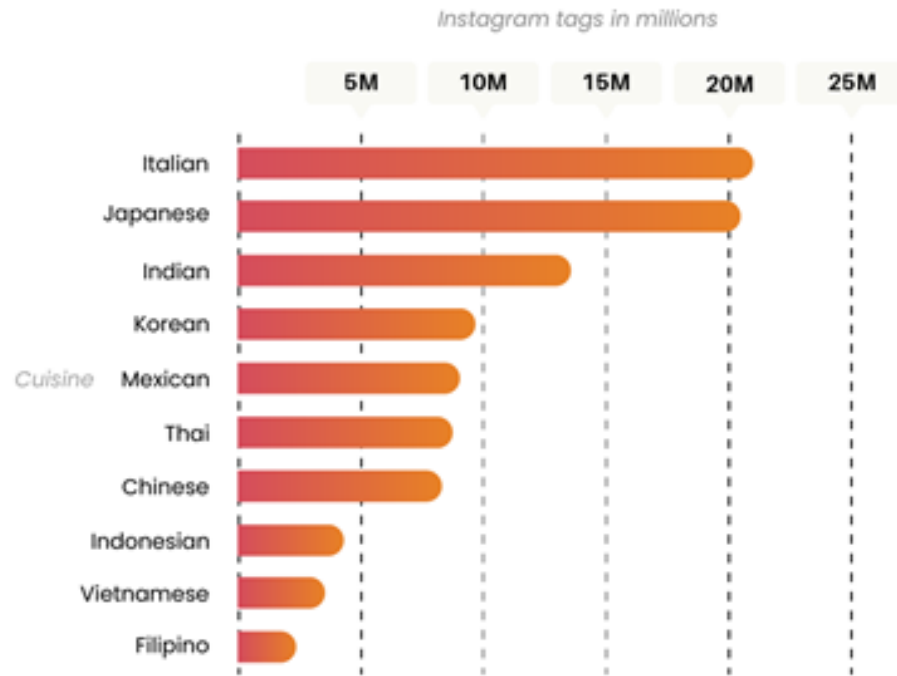
Hello! I'm Anjali. I'm a board certified health coach, author, wife, mom and food lover from the SF Bay area (now living in Seattle, WA!); with a passion for delicious food and a desire to make healthy eating easy, tasty and fun! [Learn more about me here](#) and stay for a while!



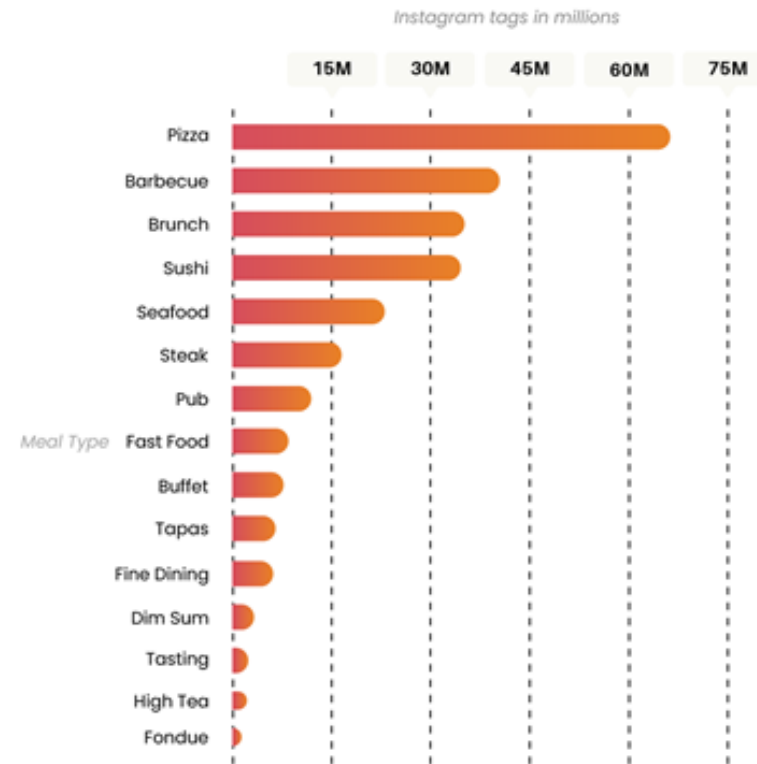
[f](#)
[t](#)
[p](#)
[i](#)

100 000 followers....

Most Popular Cuisines Around the World



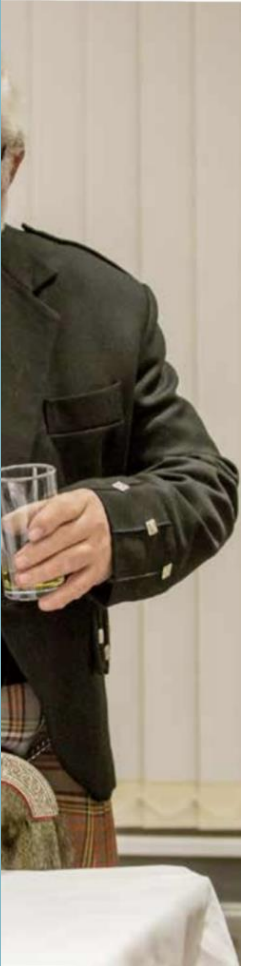
Most Popular Meal Type Around the World



W



Favourite Food??





All about spice.....Sichuan Hot Pot, China??

Only if it hits at least a million scoville units!

Most pricey – Almas Caviar
albino Iranian beluga sturgeon??



Most daring- Fugu from Japan?





Most exotic? crispy tarantula from Cambodia

Healthy? sustainable?

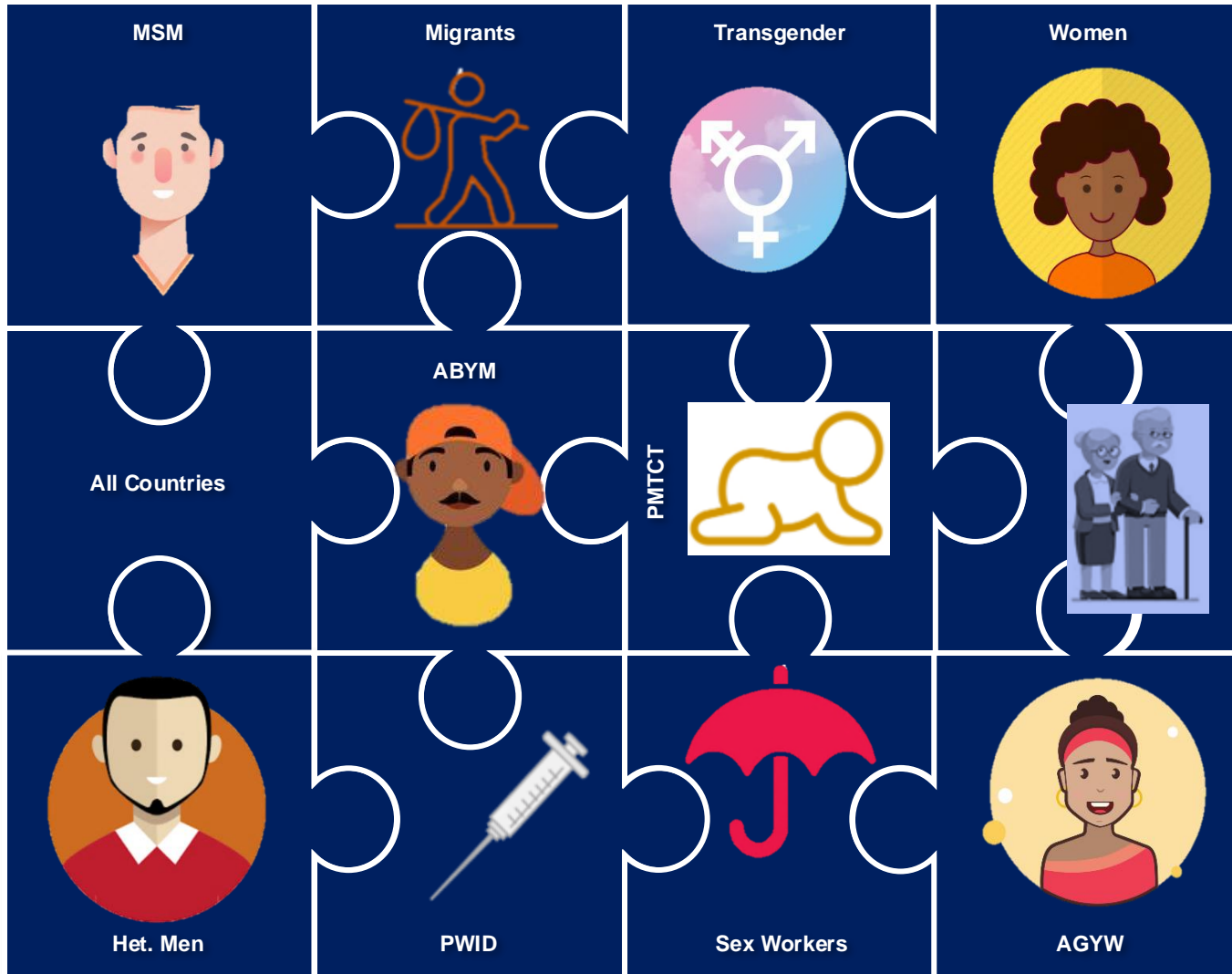


Happiest with a happy meal?

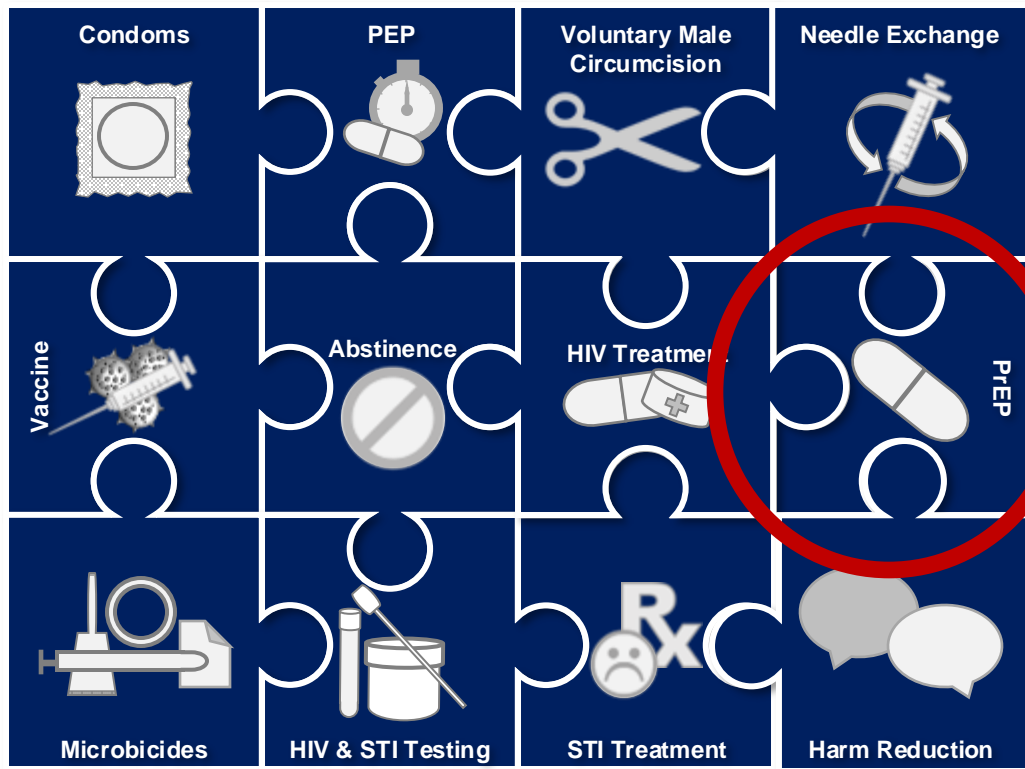
Imagine....if there was no food choice?



“Unfortunate females...”



**Humanity
Comes in many
Shapes and
Forms...**



Prevention
Should too..



Infusion
Implant
Injection
Pill
Vaginal ring
Gels
Insert
Vaginal film
Lube
Douche

With TAILORED, ACCESSIBLE services and CHOICE we may expect better coverage of all people and better coverage of all exposures!



A webinar poster with a white background. At the top left, a red box contains the word "WEBINAR" in white. The main title is "Discussing Early Results from the SEARCH Dynamic Choice Study" in a dark serif font. Below the title, it says "Join AVAC and SEARCH in conversation with Professor Moses Kamya to discuss early results from the SEARCH Dynamic Choice Study and the role choice plays in HIV prevention." To the right of this text is a small portrait of Professor Moses Kamya. At the bottom, it says "Tuesday, April 23, 10AM ET" with a right-pointing arrow. At the very bottom are the AVAC and SEARCH logos.

*“offering structured choice between CAB-LA, oral PREP and PEP with option to change over time, enrolling both women and men at risk of HIV, the SEARCH Dynamic Choice Prevention intervention increased **biomedical covered time by >5 fold to 69.7%** and reduced HIV incidence to 0% compared to 1.8% in standard-of-care.”*

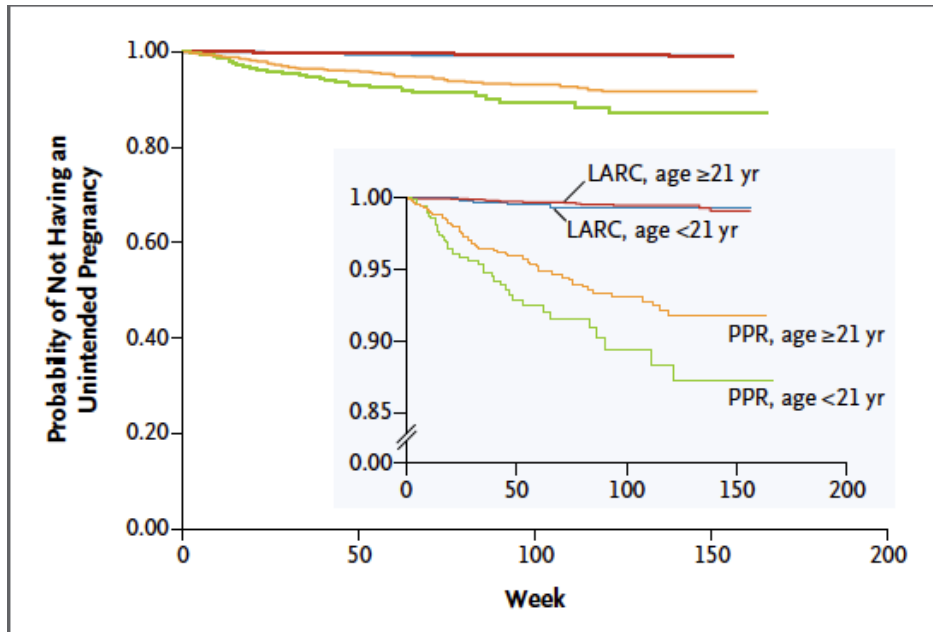
Lessons from reproductive health: LARCs

Similar adherence issues – 5% of unintended pregnancies occur amongst consistent contraception users, but **41% occur due to inconsistent use.**

- Requires no user adherence
- Gained popularity in recent years
- Lower side effects
- Greater effectiveness

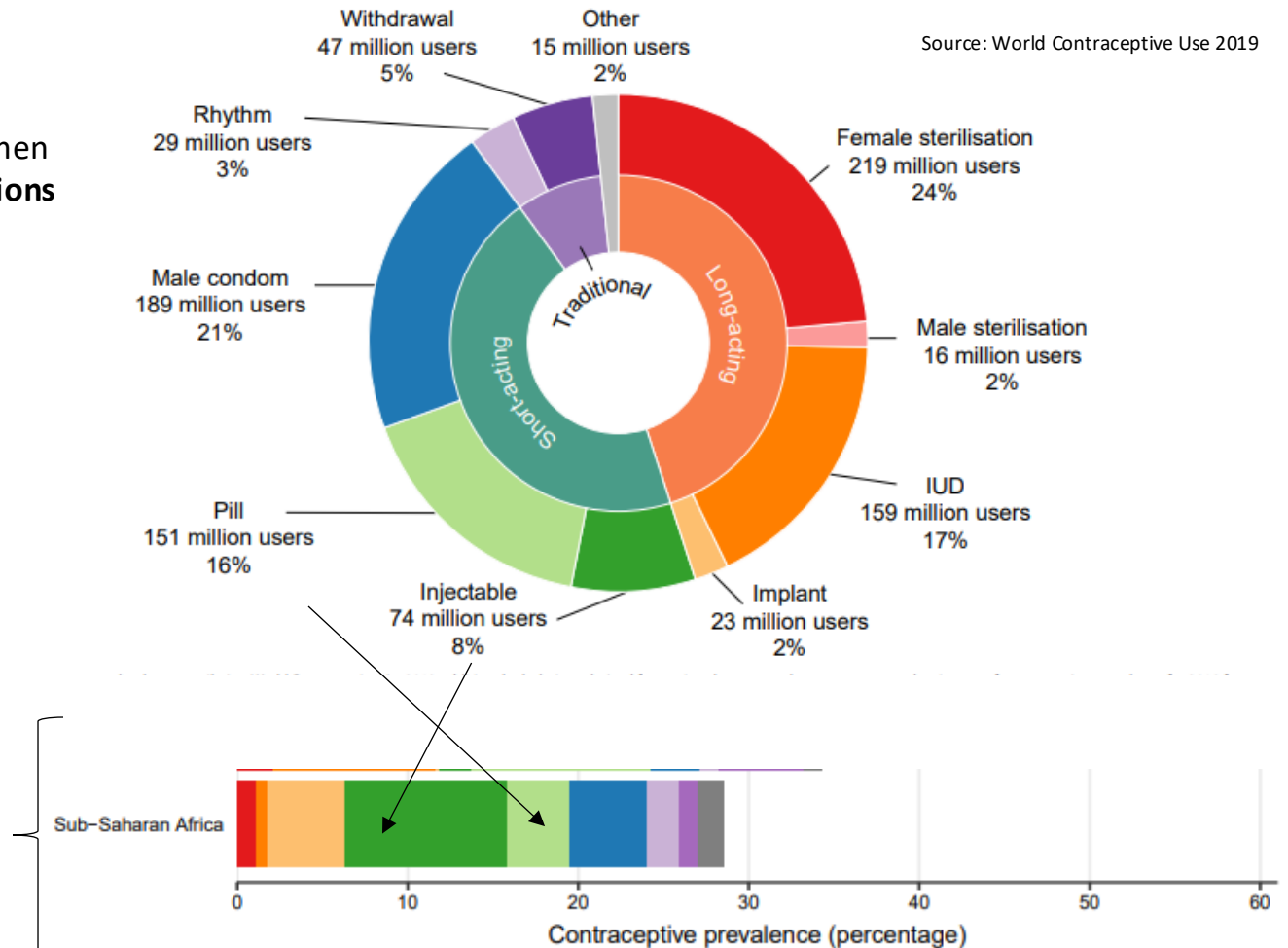


Shown to have broader acceptability among different populations of women
- higher amongst older women **but increasing amongst younger populations**



LARC= implant, IUD, injectable
PPR= PILL, PATCH, RING

Estimated numbers of women of reproductive age (15-49 years) using various contraceptive methods, worldwide, 2019

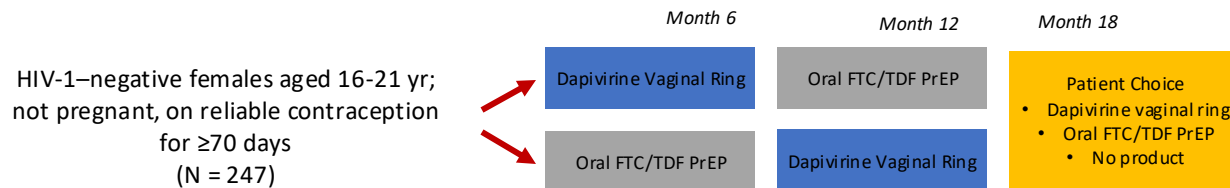


Source: World Contraceptive Use 2019

In SSA, injectable contraceptives are largely more used than the Pill

Adherence, safety, and choice of the monthly dapivirine vaginal ring or oral emtricitabine plus tenofovir disoproxil fumarate for HIV pre-exposure prophylaxis among African adolescent girls and young women: a randomised, open-label, crossover trial

Nair G, et al Lancet 2023



Non-use/little use of study product was **extremely low** throughout the first 12 months: 2.9%

Majority of participants were **highly** adherent: 54.3%

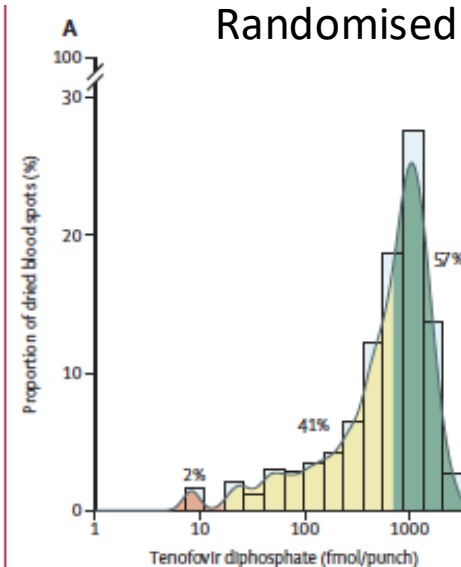


Interpretation Adherence was moderately high and similar between oral PrEP and the dapivirine ring with favourable safety and tolerability. Oral PrEP and the dapivirine ring are effective, safe, and well tolerated HIV prevention options for adolescent girls and young women who would benefit from a choice of PrEP formulations to meet their needs and preferences.

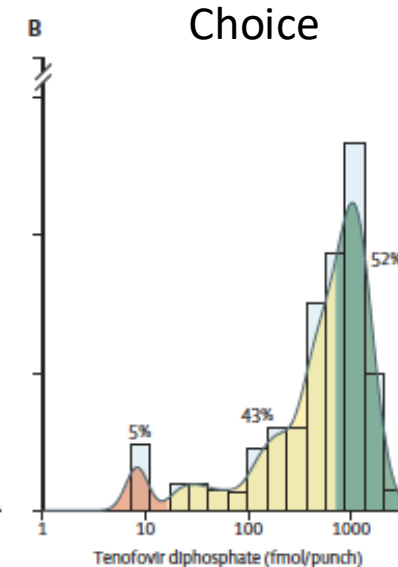


Note: Adherence support and counseling included for all patients.

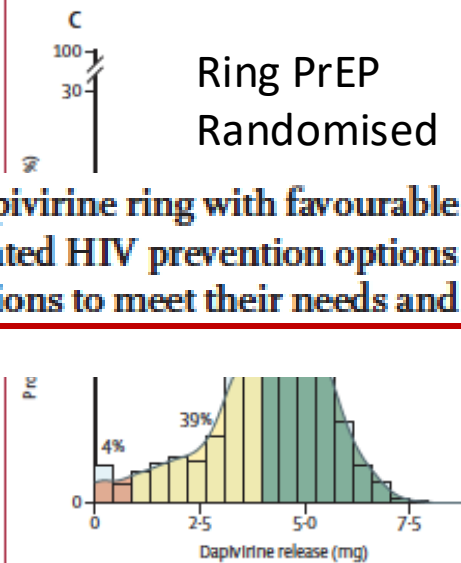
Oral PrEP
Randomised



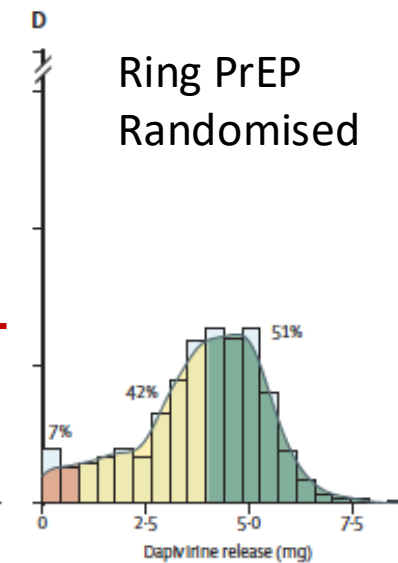
Oral PrEP
Choice



Ring PrEP
Randomised

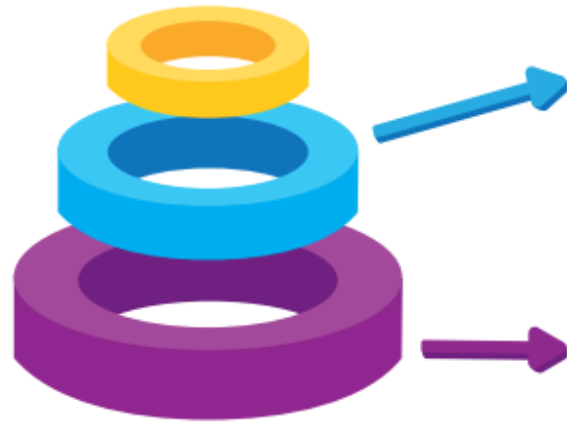


Ring PrEP
Randomised



Future PrEP is 3-Dimensional PrEP

3D PrEP



DRUG DETAILS

Characteristics of different PrEP products	
Systemic / Topical	Long / Short acting PK
Pills / Ring / Injectable	Side effects / Tolerability
Daily / Event driven pill	Nurse / Self / Peer administered
2m / 6m Injectable	
1M / SC Injectable	Viral resistance profile

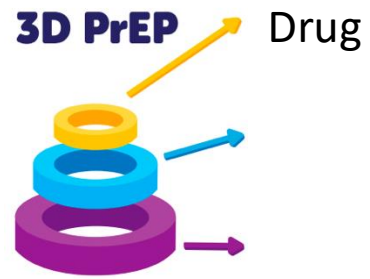
DELIVERY

Implementation delivery modalities	
Health facility	Courier / Post bank
Mobile clinic	School / Collage
Community based	Pharmacy / Mall / Other outlet
Public / Discreet	Self-testing / POC / Lab testing

DISPOSITION

Motivations, affects, attitudes, information, perceptions, and user preferences towards product details and delivery modalities
Independent / Convenience / Discreet / Introvert / Social frequent / Intermittent / Infrequent sex
Vaginal / Anal / Other sex
Sero+ / Sero-unknown partner
Regular / Shift / Irregular working
School / Tertiary / Collage





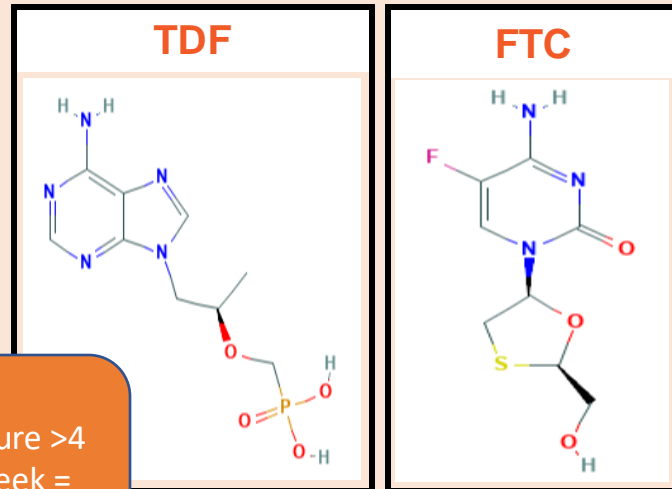
Pill options for PrEP

PrEP 1: TDF/FTC: Daily oral HIV prevention pills



Agent class:

TDF: Tenofovir and FTC: Emtricitabine are nucleotide reverse transcriptase inhibitors



PrEP Strategy: Daily oral PrEP

In anal exposure >4 doses per week = good effectiveness

When adherence is high, HIV protection is consistent and high

	% of blood samples with tenofovir detected	HIV protection efficacy in randomized comparison	HIV protection estimate with high adherence
Partners PrEP TDF/FTC arm	81%	75%	90% (tenofovir in blood)
TDF2	79%	62%	78% (prescription refill)
BTS	67%	49%	70% - 84% (tenofovir in blood / pill count)
iPrEx	51%	44%	92% (tenofovir in blood)
FEM-PrEP & VOICE	<30%	No HIV protection	N/A



Baeten et al N Engl J Med 2012; Thigpen et al N Engl J Med 2012; Choopanya et al Lancet 2013; Grant et al N Engl J Med 2010; Van Damme et al N Engl J Med 2012; Marrazzo et al CROI 2013; Lui A, et al Science Translation 2018; Marrazzo J et al Lancet HIV 2024



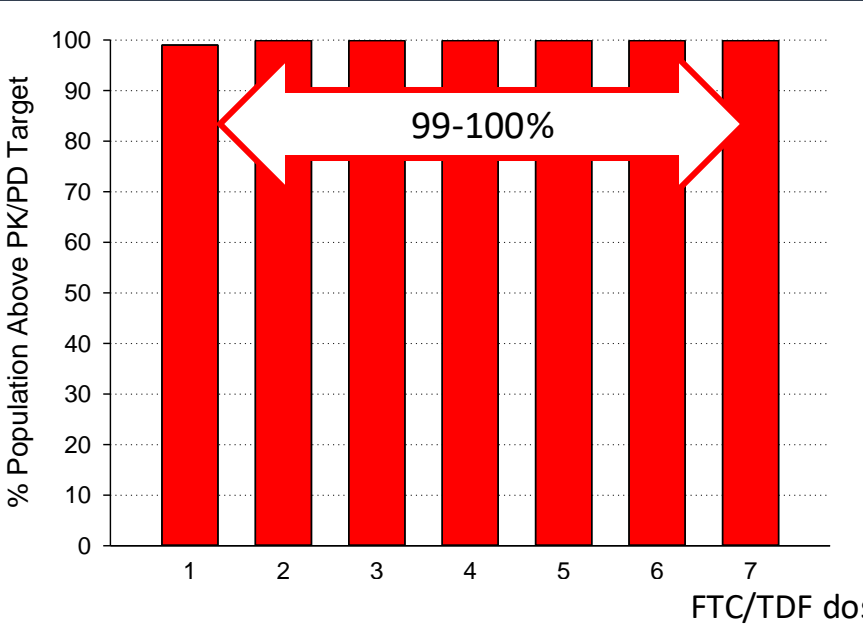
Pete Anderson with the iPrEX trial team (*Sci Transl Med* 2012;4:151)

- Took a subset of cases and matched controls with PBMC in iPrEX
- Established TFV-DP level associated with 90% protection (=EC90)
- STRAND directly observed 2x, 4x, 7x a week, took lots of samples
- Established TFV-DP level in rectal tissue, allowing for the concentration in that compartment

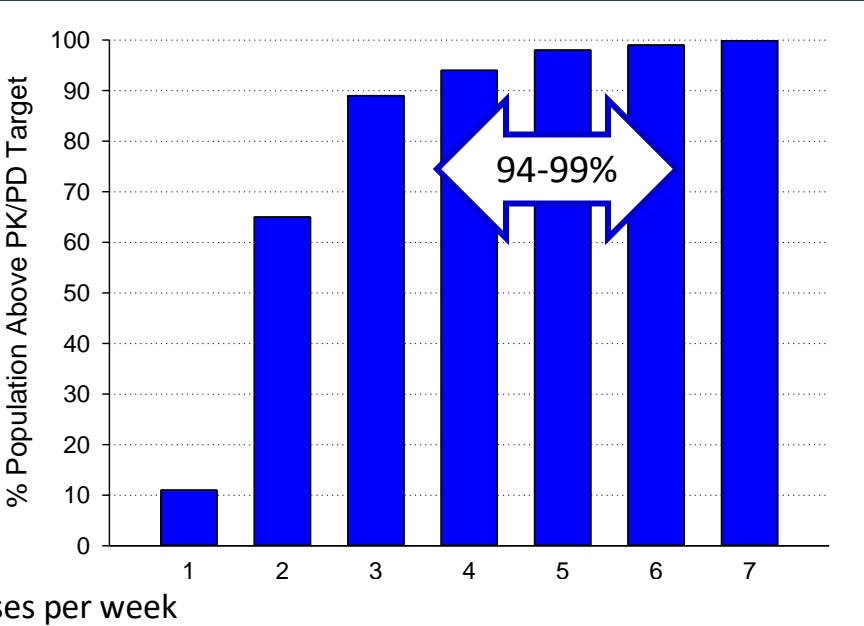
Model Predicted PrEP Effectiveness Tracks with Clinical Estimates



Rectal Tissue Simulations



FGT Tissue Simulations



Adapted from Cottrell ML et al. *J Infect Dis.* 2016 Jul 1;214(1):55-64.

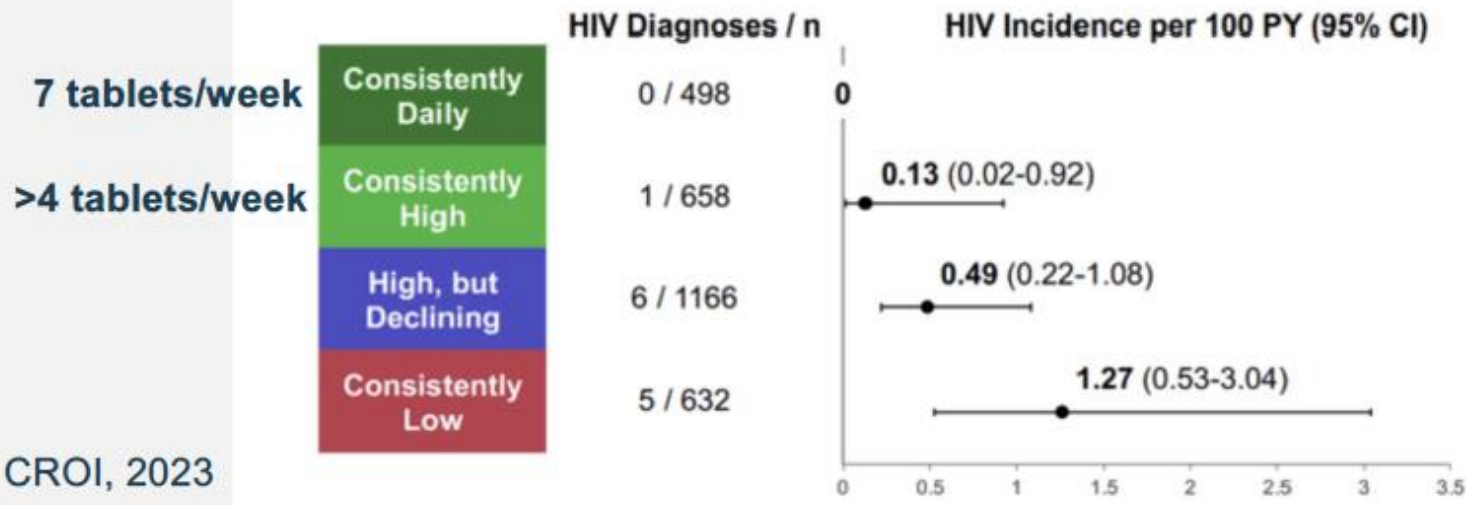
Do vaginas demand perfection?



**8+ Year Pooled Analysis:
Adherence and HIV Incidence
in >6000 Women on F/TDF for PrEP**

Jeanne Mrazzozzo,¹ Marissa Becker,² Linda-Gail Bekker,³ Connie Celum,⁴
Michael Kiragu,⁵ Ashley M. Finkelstein,⁶ Thomas F. Kelly,⁷ M. Elizabeth Hall,⁸
Melanie de Boer,⁹ Christopher...

HIV Incidence Rates Among Women with Available Adherence Data (n = 2955)



Mrazzozzo, CROI, 2023

CROI 2024

Challenges with oral PrEP so far....

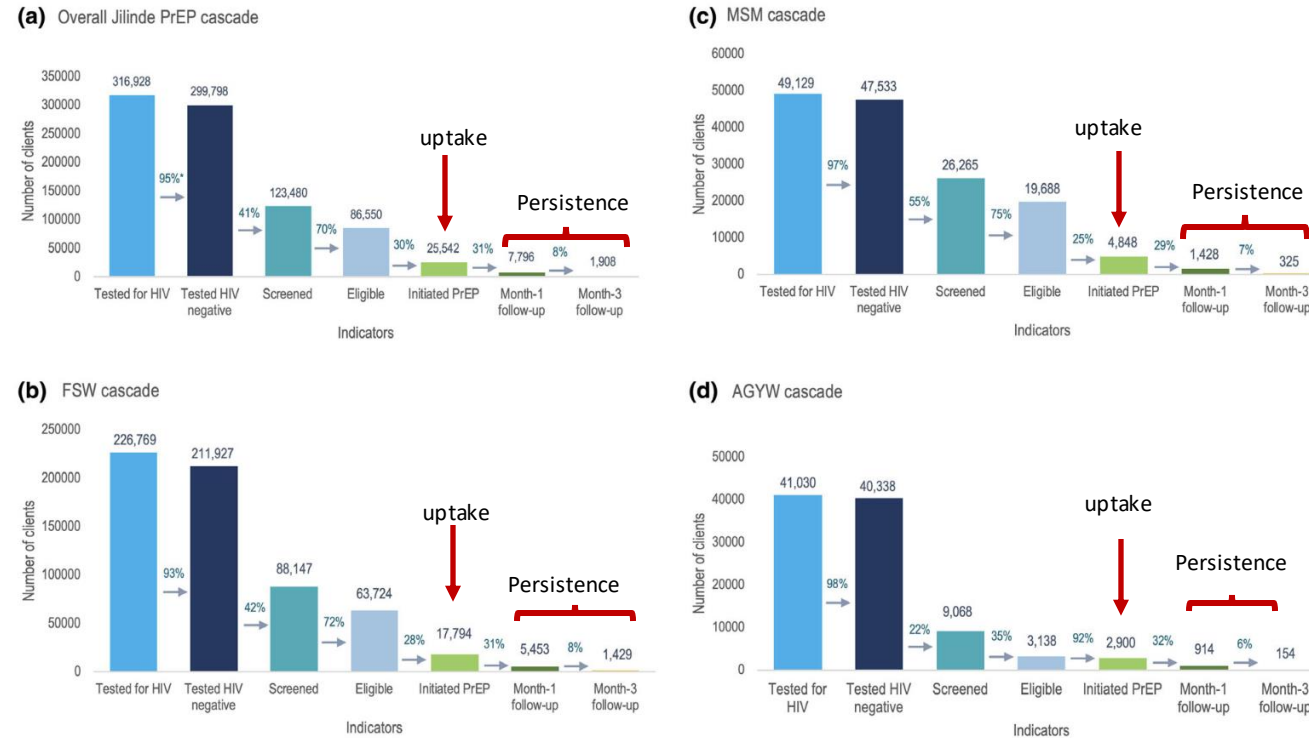


Figure 3. Overall Jilinde project (A) and population-specific (B, FSW; C, MSM; D, AGYW) PrEP cascades from February 2017 to December 2019.

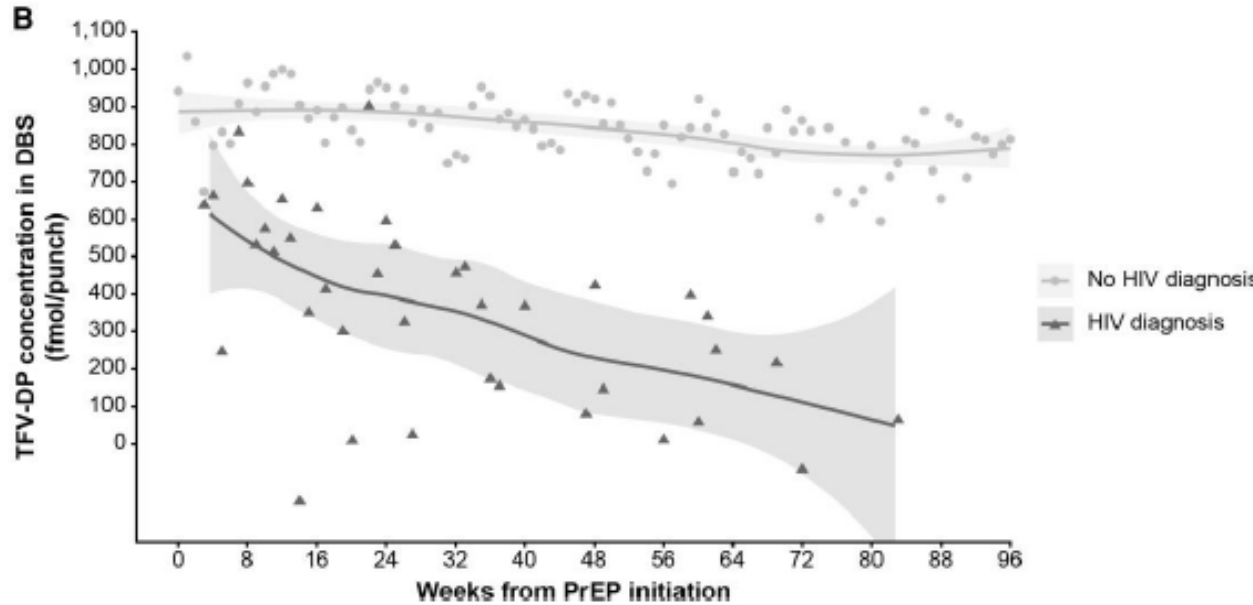
Uptake, persistence....impacting effective use.



Cohort data



>17 000 people



Type 1 Human Immunodeficiency Virus (HIV-1) Incidence, Adherence, and Drug Resistance in Individuals Taking Daily Emtricitabine/Tenofovir Disoproxil Fumarate for HIV-1 Pre-exposure Prophylaxis: Pooled Analysis From 72 Global Studies

Raphael J. Landovitz,¹ Li Tao,² Juan Yang,² Melanie de Boer,² Christoph Carter,² Moupali Das,² Jared M. Baeten,² Albert Liu,³ Karen W. Hoover,⁴ Connie Celum,⁵ Beatriz Grinsztejn,⁶ Sheldon Morris,⁷ Darrell P. Wheeler,⁸ Kenneth H. Mayer,⁹ Sarit A. Golub,¹⁰ Linda-Gail Bekker,¹¹ Souleymane Diabaté,¹² Elske Hoornenborg,¹³ Janet Myers,³ Ashley A. Leech,¹⁴ Sheena McCormack,¹⁵ Philip A. Chan,¹⁶ Michael Sweat,¹⁷ Lynn T. Matthews,¹⁸ and Robert Grant¹⁹, and the Global F/TDF PrEP Study Team^a

	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)

PrEP 1.5: TDF/FTC: Oral HIV prevention – On Demand!



Randomized Double-Blinded vs. Placebo then Open-Label Extension among MSM (TDF/FTC on demand vs placebo on demand)



Molina et al NEJM 2015;
Molina AIDS 2016
Présentation

THE NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

On-Demand Preexposure Prophylaxis in Men at High Risk for HIV-1 Infection

J.-M. Molina, C. Capitant, B. Spire, G. Pialoux, L. Cotte, I. Charreau, C. Tremblay, J.-M. Le Gall, E. Cua, A. Pasquet, F. Raffi, C. Pintado, C. Chidiac, J. Chas, P. Charbonneau, C. Delaugerre, M. Suzan-Monti, B. Loze, J. Fonsart, G. Peytavin, A. Cheret, J. Timsit, G. Girard, N. Lorente, M. Prêau, J.F. Rooney, M.A. Wainberg, D. Thompson, W. Rozenbaum, V. Doré, L. Marchand, M.-C. Simon, N. Etien, J.-P. Aboukier, L. Meyer, and J.-F. Delvaux, for the ANRS IPERGAY Study Group*

ABSTRACT

BACKGROUND
Antiretroviral preexposure prophylaxis has been shown to reduce the risk of human immunodeficiency virus type 1 (HIV-1) infection in some studies, but conflicting results have been reported among studies, probably due to challenges of adherence to a daily regimen.

METHODS
We conducted a double-blind, randomized trial of antiretroviral therapy for pre-exposure HIV-1 prophylaxis among men who have unprotected anal sex with men. Participants were randomly assigned to take a combination of tenofovir disoproxil fumarate (TDF) and emtricitabine (FTC) or placebo before and after sexual activity. All participants received risk-reduction counseling and condoms and were regularly tested for HIV-1 and HIV-2 and other sexually transmitted infections.

RESULTS
Of the 414 participants who underwent randomization, 400 who did not have HIV infection were enrolled (199 in the TDF-FTC group and 201 in the placebo group). All participants were followed for a median of 9.3 months (interquartile range, 4.9 to

*The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Molina at the Department of Infectious Diseases, Hôpital Saint-Louis, 1 Ave. Claude Vellefaux, 75475 Paris, France, or at jean-michel.molina@aphp.fr.

*A complete list of investigators in the France Recherche Nord et Sud Sida-HIV et Hépatites (ANRS) Intervention Préventive de l'Exposition aux Risques avec et pour les Gays (IPERGAY) study group is provided in the Supplementary Appendix, available at NEJM.org.

This article was published on December 1, 2015, at NEJM.org.
N Engl J Med 2015;373:2237-46.
DOI:10.1056/NEJMoa1506273
Copyright © 2015 Massachusetts Medical Society.



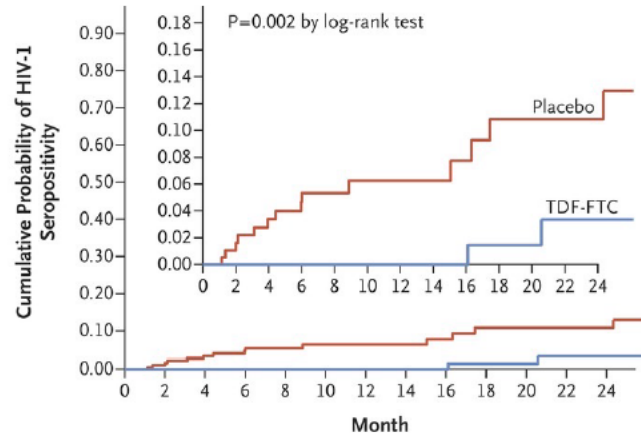
- ✓ 2 tablets (TDF/FTC or placebo) 2-24 hours before sex
- ✓ 1 tablet (TDF/FTC or placebo) 24 hours later
- ✓ 1 tablet (TDF/FTC or placebo) 48 hours after first intake



Proven efficacy in placebo-controlled RCT

ORIGINAL ARTICLE

On-Demand Preexposure Prophylaxis in Men at High Risk for HIV-1 Infection



No. at Risk	0	6	12	18	24
Placebo	201	141	74	55	42
TDF-FTC	199	141	82	58	43

400 MSM mostly in France (43 in Canada)

Median of 4 pills per week

16 HIV-1 infections: 2 assigned to event-driven PrEP - for an 86% reduction in HIV (P=0.002).

Break through infections were due to nonuse

ANRS IPERGAY
Molina et al, NEJM, 2015

CROI 2024

Many Guidelines Support Limited Use



World Health Organization

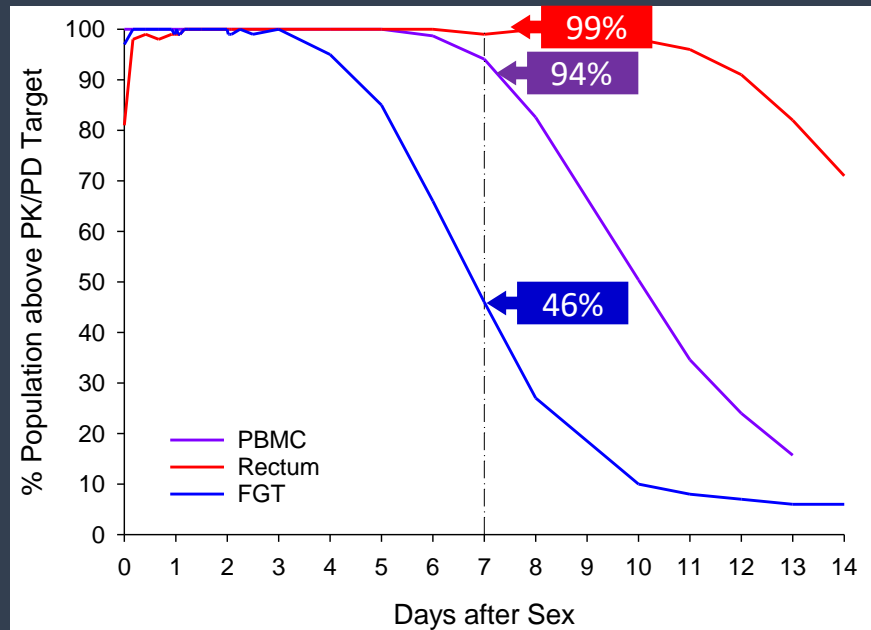
All men



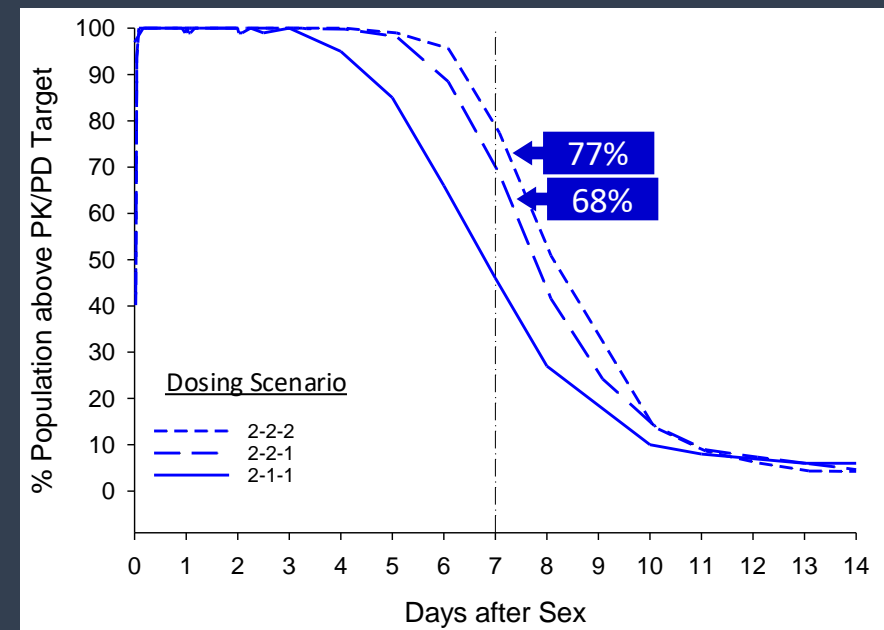
Modeling & Simulation Can be Used to Optimize On Demand PrEP for Women



Lowest 2-1-1 efficacy predicted in FGT vs blood and rectum



2-2-2 dosing increases predicted efficacy in FGT by >30%



Adapted from Cottrell ML et al. *J Infect Dis.* 2016 Jul 1;214(1):55-64 and Garrett KL et al. *J Pharmacol Exp Ther.* 2018 Nov; 367 (2):245-251.

Simulations by Dumond JB using Leung et al *CPT PSP* 2023 (12):1922-1930.

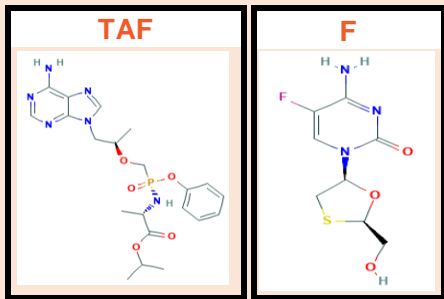
BHIVA guidelines : 2 pills pre and 1 pill for 7 days and Double up for Quick start!

PrEP 1.5: DESCOVY F/TAF: Daily/on demand Oral prevention



Agent class:

F/TAF = Emtricitabine/ Tenofovir Alafenamide are nucleotide reverse transcriptase inhibitors



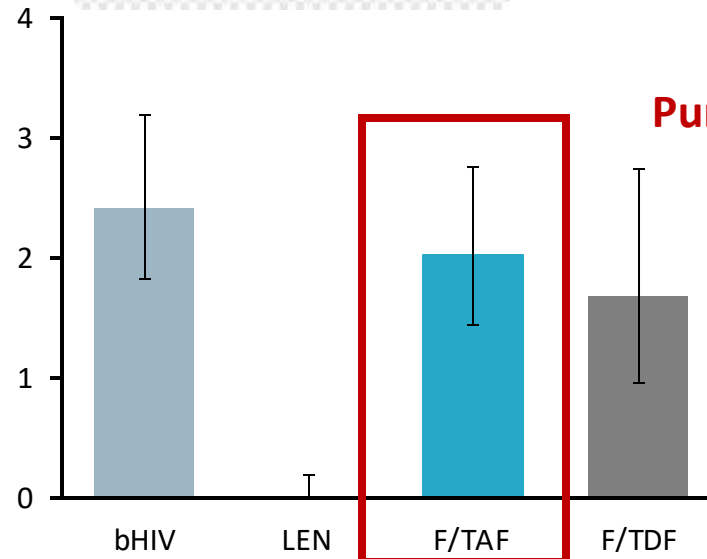
Dosing Strategy: Daily oral PrEP

Better PK and fewer side effects

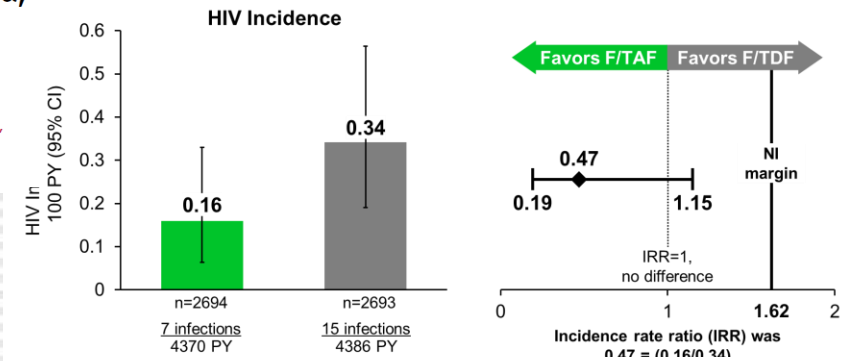


Emtricitabine and tenofovir alafenamide vs emtricitabine and tenofovir disoproxil fumarate for HIV pre-exposure prophylaxis (DISCOVER): primary results from a randomised, double-blind, multicentre, active-controlled, phase 3, non-inferiority trial

Kenneth H Mayer, Jean-Michel Molina, Melanie A Thompson, Peter L Anderson, Karam C Mounzer, Joss J De Wet, Edwin Dejesus, Heiko Jessen, Robert M Grant, Peter J Ruane, Pamela Wong, Ramin Ebrahimi, Lijie Zhong, Anita Mathias, Christian Callebaut, Sean E Collins, Moupali Das, Scott McCallister, Diana M Brainard, Cynthia Brinson, Amanda Clarke, Pep Coll, Frank A Post, C Bradley Hare



Discover Study



The NEW ENGLAND JOURNAL of MEDICINE

Purpose 1



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. Bating, 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*

Matched case-control study:
Those who took it were protected.

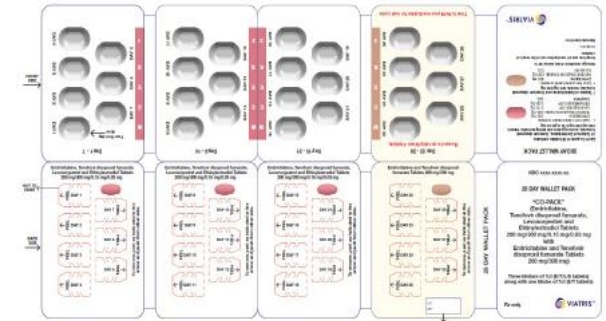
What's coming in the pill dept....

- **Multipurpose technology- Dual Prevention Pill :**
- Combines 2 already-approved products—oral PrEP (TDF/FTC) and oral contraception (ethinyl estradiol and levonorgestrel, or EE/LNG). **VIATRIS**
- **MK-8527: MONTHLY pill for HIV prevention**

Figure 1: Proposed DPP tablet colors

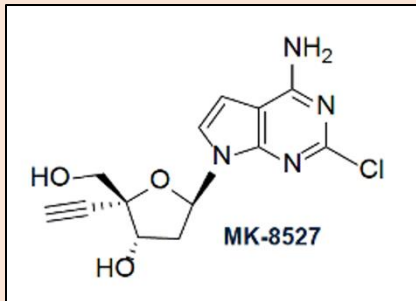


Figure 2: Illustrative mock-up of DPP packaging by Viatrix



Agent class:

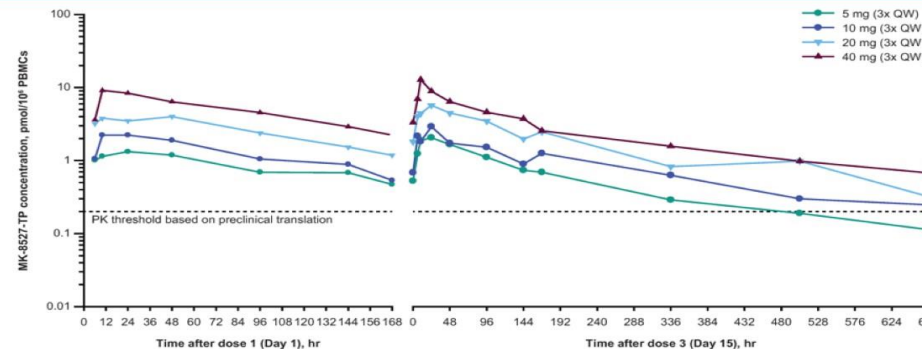
Nucleoside Reverse Transcriptase Translocation Inhibitor (NRTTI)



Long half life favours Monthly pill dosing



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



- 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_{0-168} ratios was 1.1–1.6)
- Across all dose levels, the range of MK-8527-TP apparent terminal half-life was 216–291 hours

C_{168} , concentration at 168 hours post dose.

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

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.



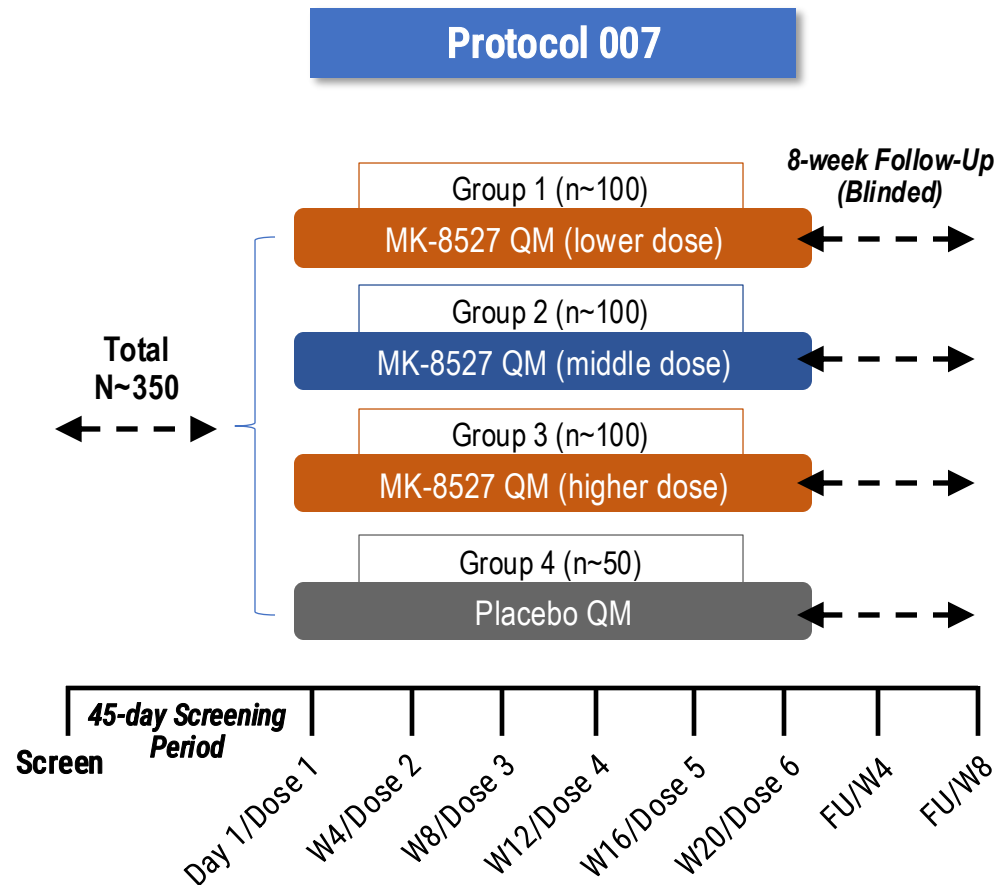
Ongoing Phase 2 Study of MK-8527 in Individuals at Low Risk of Exposure to HIV-1, Fully Enrolled

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



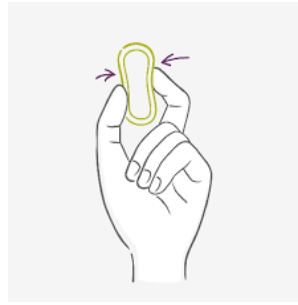
Primary Endpoints

- 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



Topical options: PrEP



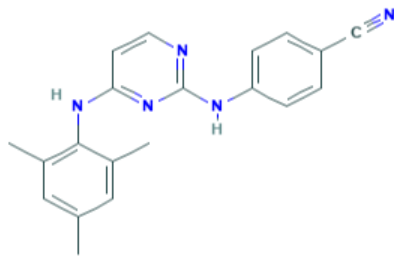
Dapivirine Ring: Use of a vaginal ring for HIV prevention



Agent class:

Non-nucleoside reverse transcriptase inhibitors (NNRTI)

DAPIVIRINE



Dosing Strategy:

Monthly dapivirine ring

2016

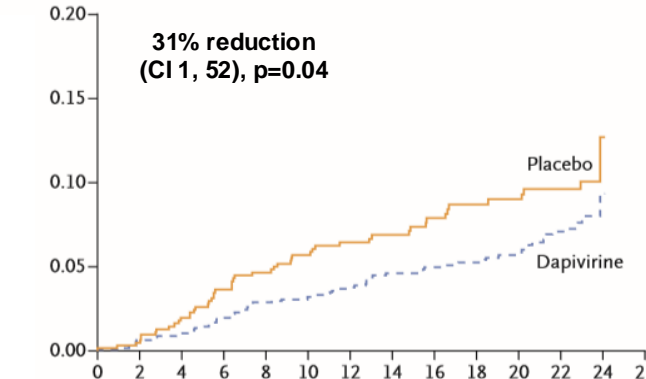
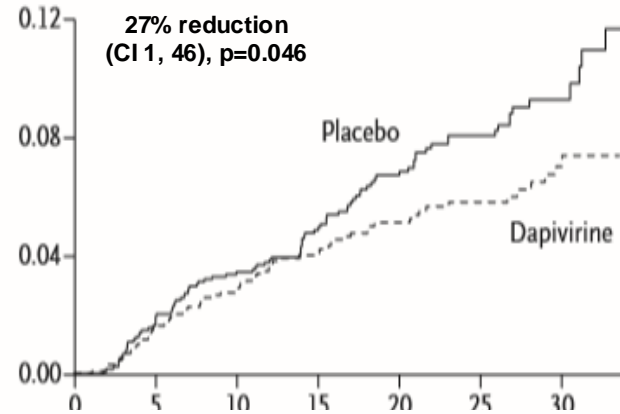
ASPIRE

A Study to Prevent Infection with a Ring for Extended Use

Trial sites in South Africa, Uganda, Zambia, Zimbabwe, Malawi



Trial sites in South Africa, Uganda



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 1, 2016 VOL. 375 NO. 22

Use of a Vaginal Ring Containing Dapivirine for HIV-1 Prevention in Women

J.M. Baeten, T. Palanee-Phillips, E.R. Brown, K. Schwartz, L.E. Soto-Torres, V. Govender, N.M. Mgodl...

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Safety and Efficacy of a Dapivirine Vaginal Ring for HIV Prevention in Women

A. Nel, N. van Niekerk, S. Kapiga, L.-G. Bekker, C. Gama, K. Gill, A. Kamali, ...

In both studies: Open label extension improved effectiveness - RR 0.50
EMA approved for section 58: (1) WHO recommendations, (2) Women in LMIC ;
Second line to PrEP.



Longer acting (3 month) DapiRing



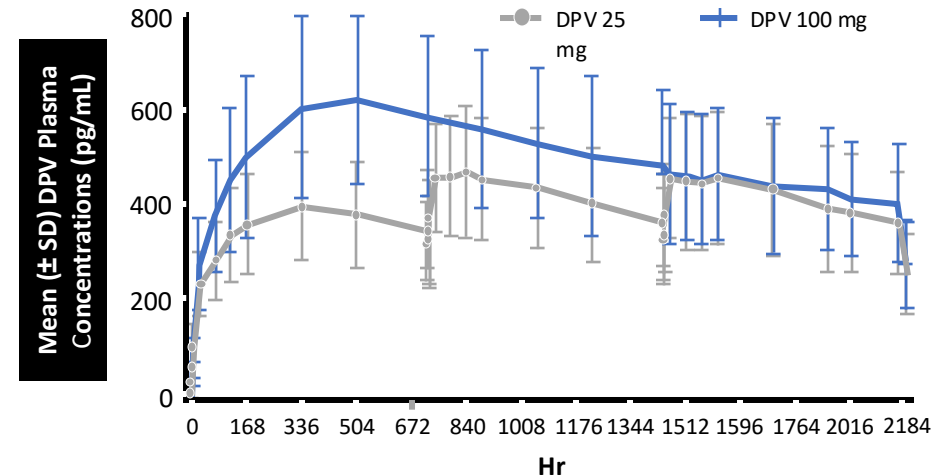
IPM 054: 1-Mo vs 3-Mo Dapivirine Vaginal Ring Pharmacokinetic Study in South Africa

Nuttal. HIVR4P 2024. Abstr OA0802LB.

shutterstock.com · 357444302

- 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)

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



- No safety concerns were found in:
 - Cohort 1 (36+ weeks/8-9 months pregnant);
 - Cohort 2 (30-35+ weeks/7-8 months pregnant);
 - Cohort 3 (12-29 weeks/3-7 months pregnant).
- Follow up for cohort 3 concluded in mid 2023, babies followed up for an additional year after birth
- Final results anticipated late 2024 or early 2025



- Favourable safety profile and previous data showing low drug transfer to breastmilk supports updates of WHO to include breastfeeding women when recommending PrEP Ring as an HIV prevention option

What's coming in topical PrEP....

MATRIX Product Pipeline Overview

Ngure K, Matrix



TAF/EVG

Fast-dissolving vaginal insert
tenofovir alafenamide & elvitegravir
NRTI & integrase inhibitor (ARVs)

TAF has also shown activity against HSV, which could be added benefit. CONRAD also evaluating the insert's rectal use.

MATRIX 001

DAPIVIRINE VAGINAL FILM

Film would slowly release drug until it completely dissolves (30 dys).

Also being developed as dual-purpose product

MATRIX 002

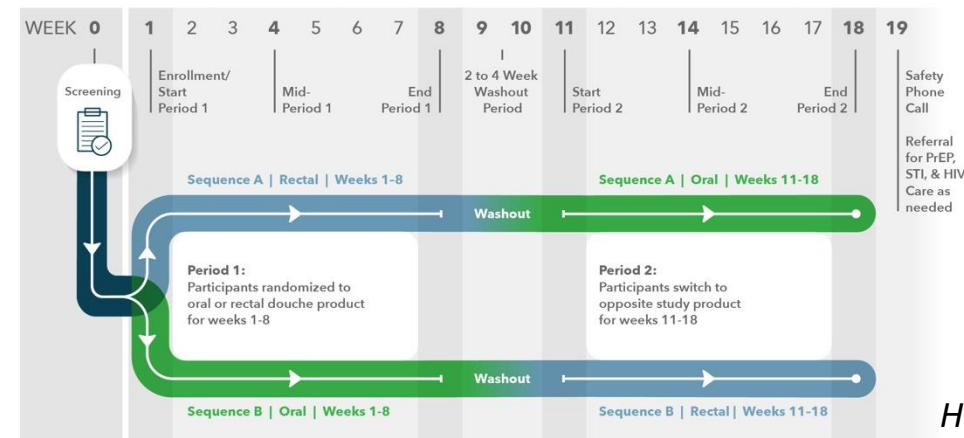
OneRing:
Antiviral peptide (non-ARV)
(protein fragment)

Non-hormonal contraceptive
A soluble Adenylate Cyclase (sAC) inhibitor; affects sperm's ability to move, fertilize eggs

Oak Crest Institute of Science
Matrix 003



Phase 2: Rectal douche vs. Oral PrEP (HPTN 106)



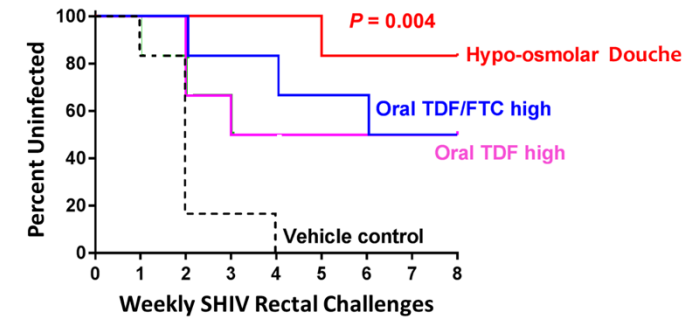
Rectal vs. Oral Use of On-demand PrEP

Hendrix C, HPTN

Rectal Douche program

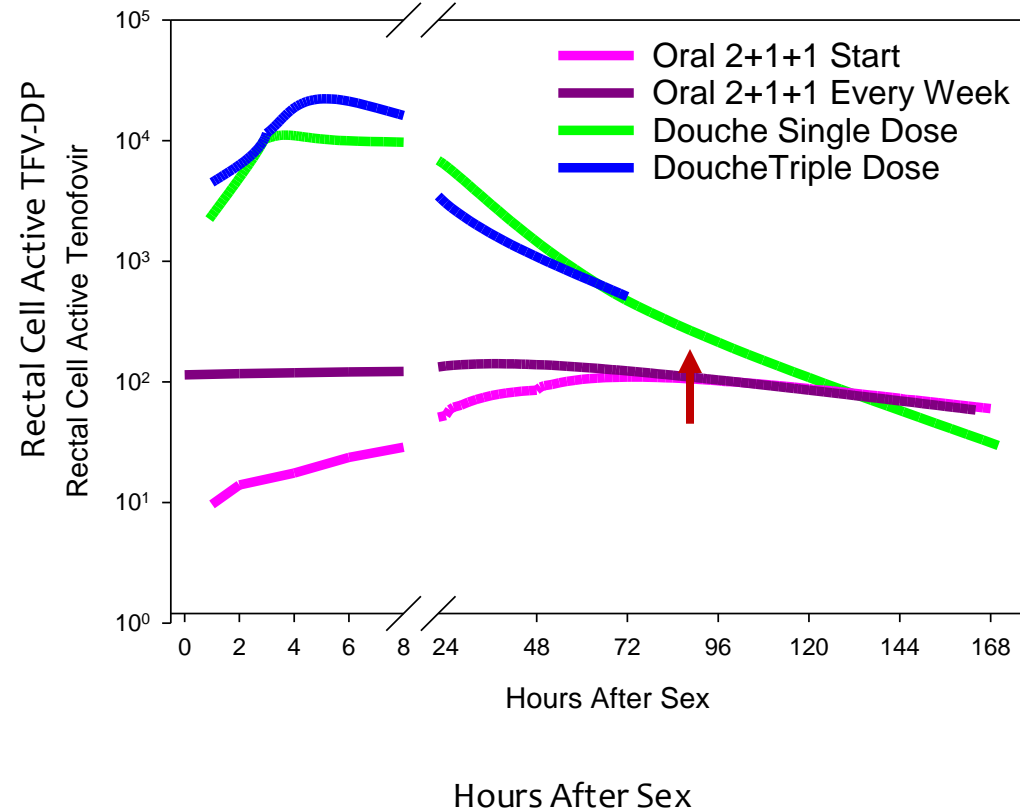
TFV Douche Weekly
- 5 of 6 protected

Truvada™ Oral Daily
- 3 of 6 protected



5 Phase I Studies Completed: Safety, Acceptability, PK/PD targets achieved

- Douche Triple Dose
- Douche Single Dose
- Oral 2+1+1 Weekly
- Oral 2+1+1 Start

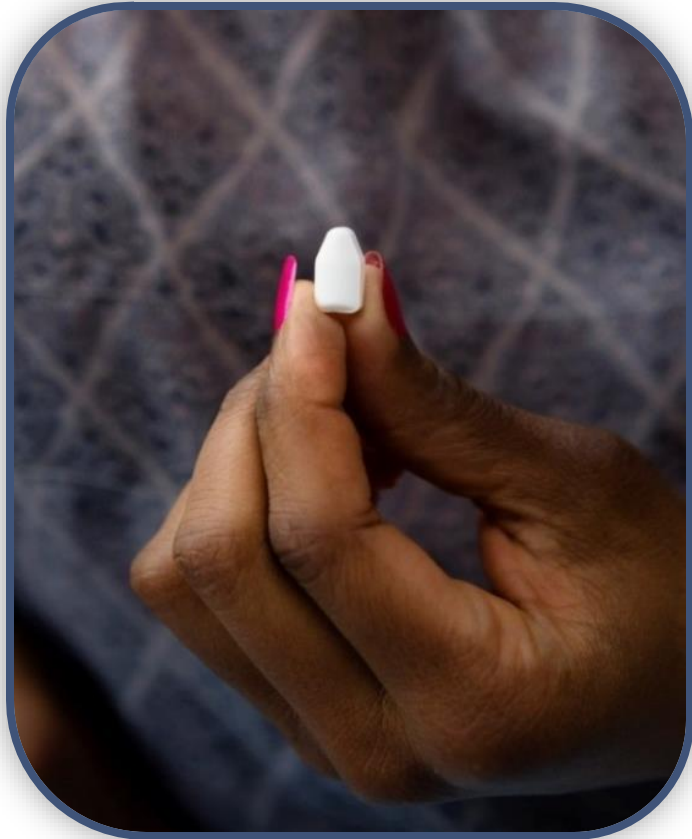


Douche Advantage:

- Cleansing action as desired
- 20-1,000 times higher throughout first day
- Stays higher for 5-6 days
- Far lower blood conc'n

TAF/Elvitegravir Topical Inserts

On-Demand (PrEP or PEP) Dual-Compartment MPT for HIV & HSV Prophylaxis



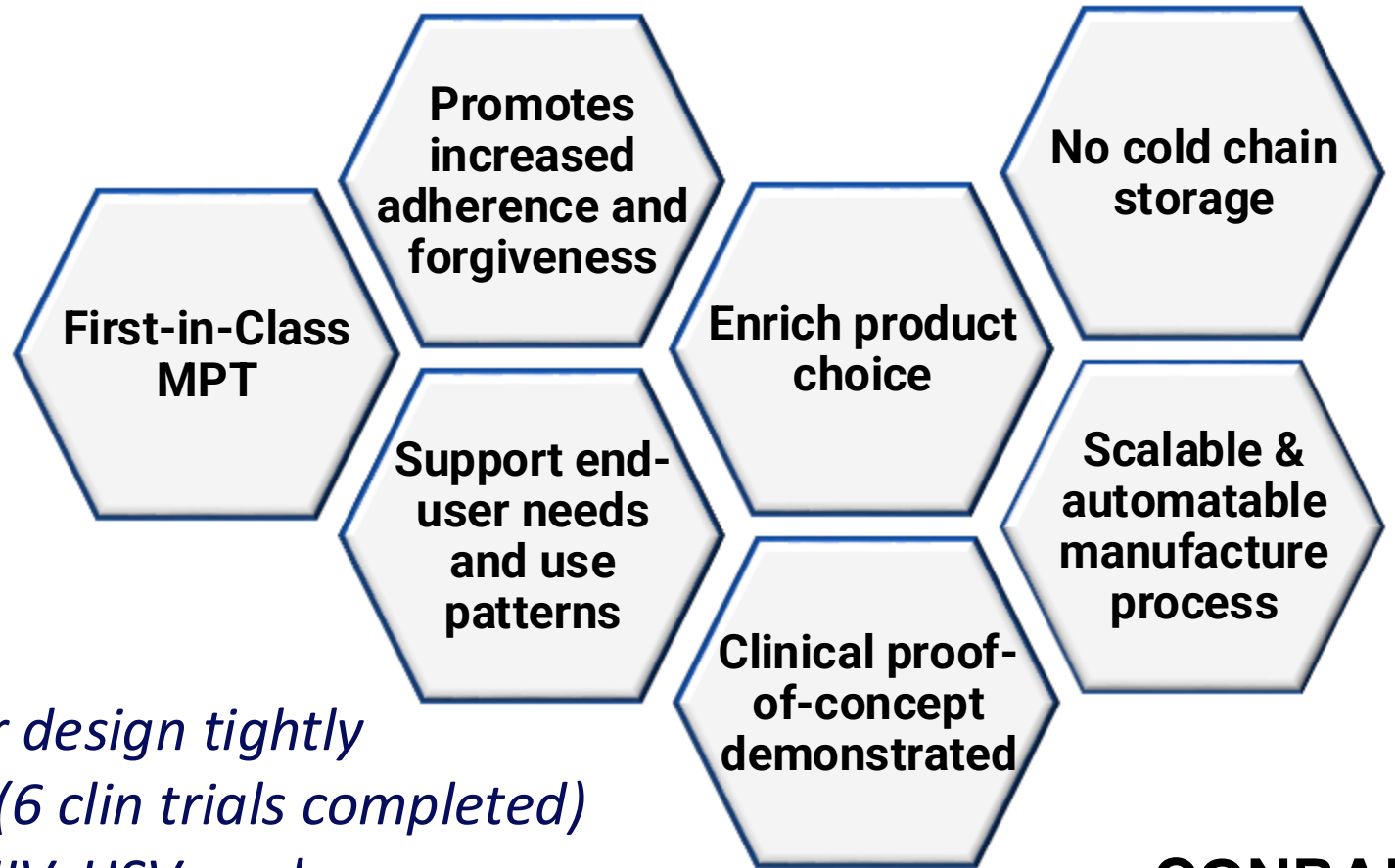
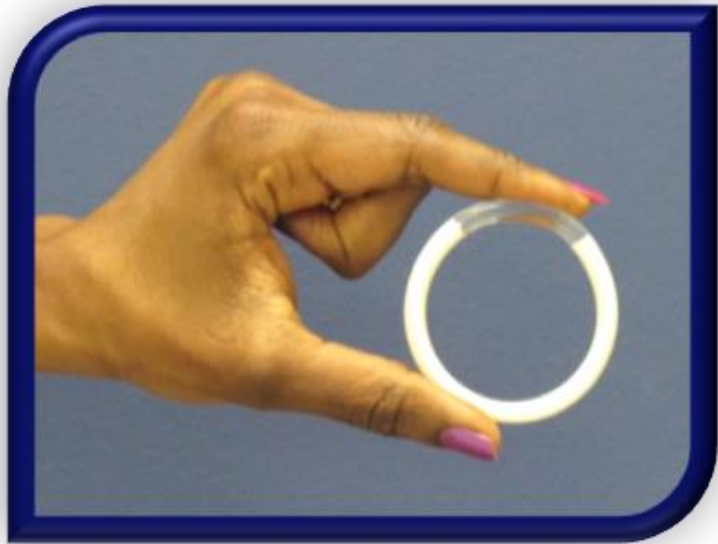
- ❖ **Fills important unmet need in HIV & MPT method mix**
 - Flexible on-demand, PrEP or PEP
 - For vaginal or rectal use
 - Low systemic drug exposure
 - Economical; easy to manufacture
 - Discreet, highly portable, easy to self-administer
- ❖ **Preclinical & Clinical Proof-of-Concept demonstrated**
 - NHP SHIV challenge (vaginal PEP/PrEP, rectal PrEP) ¹
 - CONRAD-146 (*FIH vaginal PK/PD, single dose*) ²
 - MTN-039 (*FIH rectal PK/PD, single and double dose*) ³
- ❖ **Expanded Phase I studies ongoing** (*MATRIX-001, RITE-PREP*)

CONRAD

¹ Dobard et al., 2022; Makarova et al., 2022, Makarova et al., 2023; ² Thurman et al. 2023; ³ Riddler et al. 2024

Tenofovir/Levonorgestrel Intravaginal Ring

Value Added Long-Acting Contraceptive MPT (cMPT)



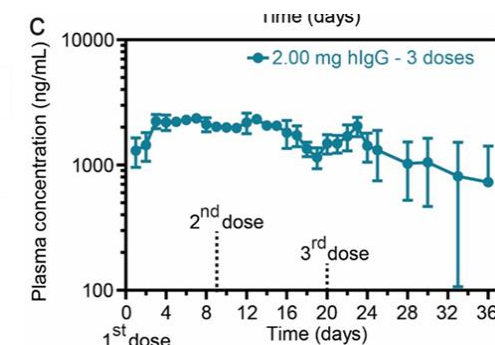
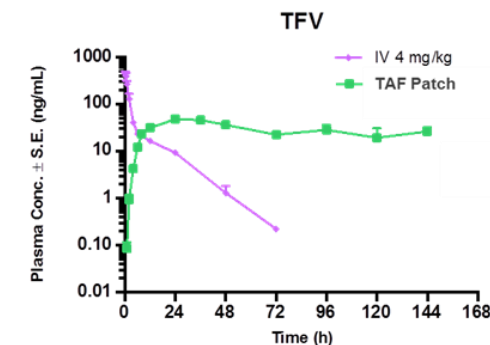
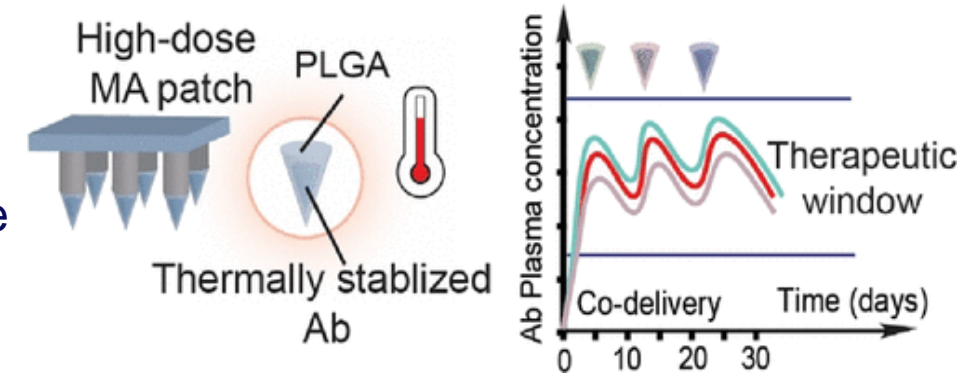
*Innovative polyurethane reservoir design tightly
Most advanced cMPT in the field (6 clin trials completed)
Designed for protection against HIV, HSV, and pregnancy*

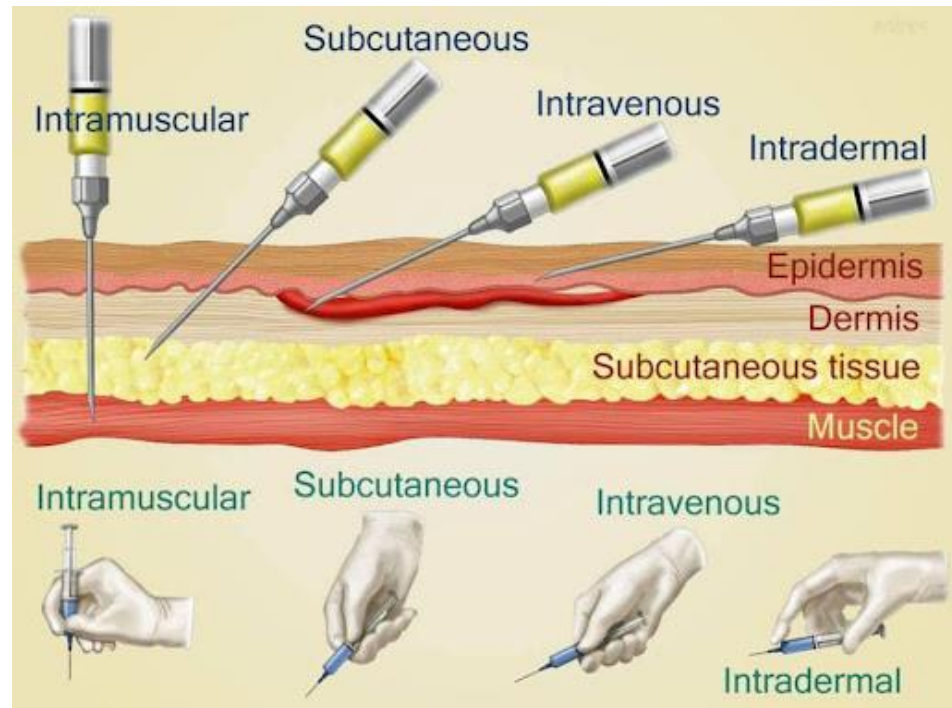
CONRAD

Transdermal MA Patch for Long-term ARV or Antibody (bnAb) Release

PreClinical

- + Minimally invasive, self-administrable
- + Benefits to supply chain, storage & distribution
- + Powder-filling drug loading method
- + High drug loading & tightly controlled, long-term release capability
- + PLGA-based core-only or core-shell microarrays
- + Sustained release of ARV via MA patch
- + Antibody stabilization via combination of excipients
- + Highly-controlled immediate or time-delayed release of ARVs and/or bnAbs for long-term prevention or treatment





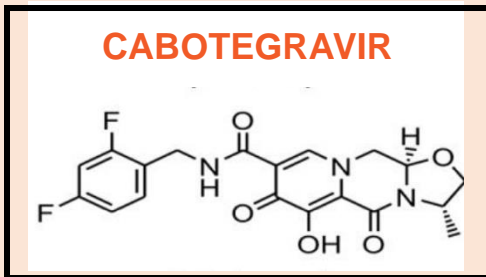
Injectable PrEP

Cabotegravir LA: Long-acting suspension for delivery via IM injection



Agent class:
Strand-transfer integrase inhibitor

Trials:
HPTN 084 & 083



Half-life:
Oral: 40 hours
Injectable: 40-65 days

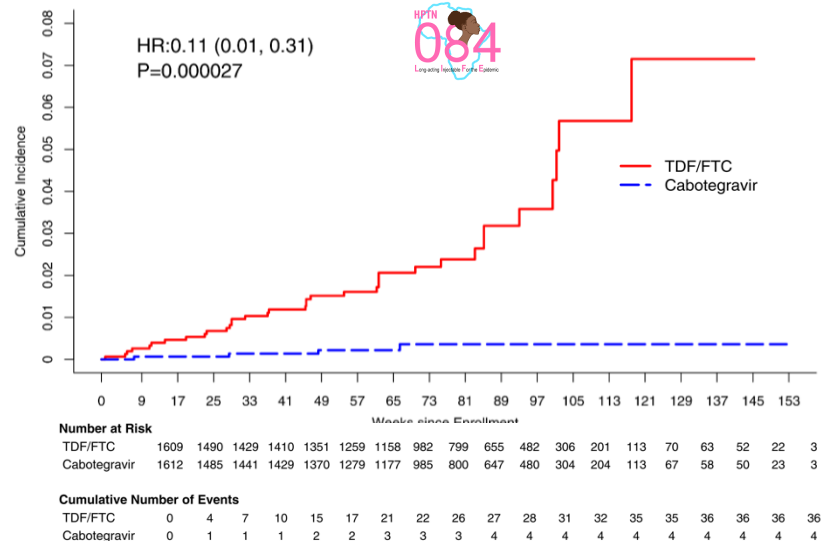
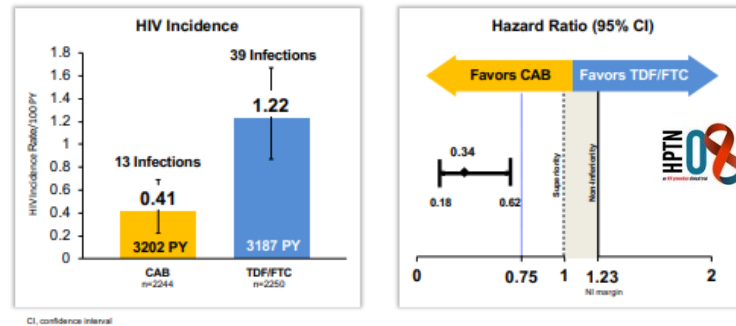
Dosing Strategy:
Single injection every 8 weeks

2 monthly IM



HPTN 083: superiority of CAB over daily oral TDF/FTC among cisgender men and transgender women who have sex with men.

Landovitz, 2020, AIDS 2020 Virtual



HPTN 084: LA CAB is safe and superior to TDF/FTC amongst cisgender African women

Women in the CAB group had an **89% lower risk of HIV infection**, compared to TDF/FTC group

- As safe and well-tolerated as TDF/FTC
- Pregnancy incidence in the study was 1.5 per 100 person-years in the CAB group, with **no congenital abnormalities** reported
- STI incidence (CT and NG) was similar in both arms

New: Ultra Long Acting CAB



Ongoing, open-label, single-dose, dose-escalation, phase 1 study (NCT05418868) evaluating CAB200 SC + rHuPH20 and CAB-ULA^a SC or IM without rHuPH20

- Inclusion criteria**
- Aged 18-55 years
 - HIV-negative
 - Body weight ≥40 kg
 - BMI 18-32 kg/m²

Part A	CAB200 dose (+ rHuPH20 10,000 IU)	Route	N
A1	800 mg (4 mL)	SC ^b	10
A2	1600 mg (8 mL)	SC ^b	10
A3	3200 mg (16 mL)	SC ^b	2
Part B Not conducted – candidate formulation not progressed			
Part C	CAB-ULA dose	Route	N
C1	800 mg (2 mL)	SC ^b	8
C2	800 mg (2 mL)	IM ^c	8
C3	1200 mg (3 mL)	SC ^b	8
C4	1200 mg (3 mL)	IM ^c	8
C5	1600 mg (3 mL)	IM ^c	16

- Monitoring of**
- PK parameters
 - Adverse events, including ISRs
 - Vital signs
 - Clinical laboratory values
- To evaluate potential CAB-ULA dosing regimens, CAB PK profiles were simulated using an established CAB200 IM population PK model modified based on observed PK data in Part C

Day 1 rHuPH20 = recombinant human hyaluronidase Week 52^d

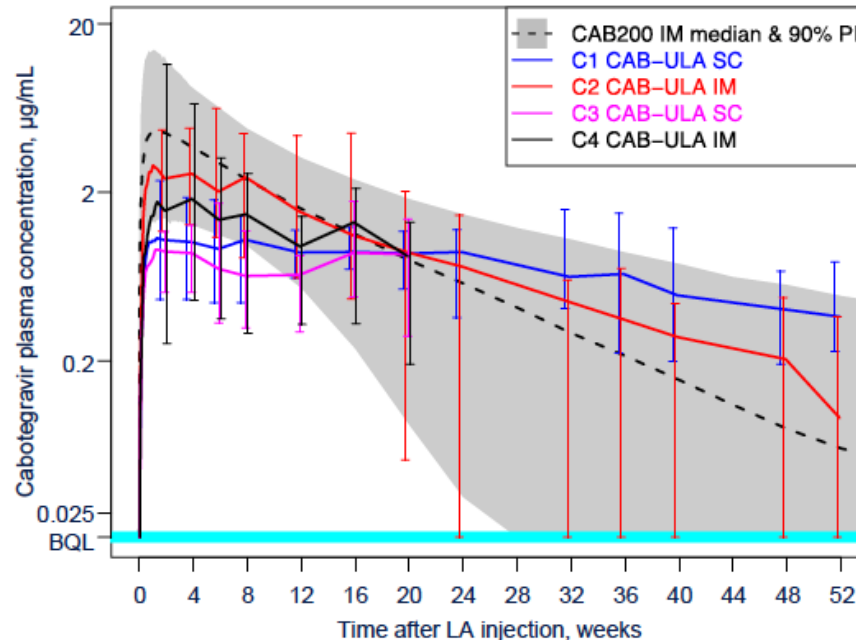
Part C: CAB-ULA

Parameter, geometric mean (%CVb)	SC		IM	
	C1 800 mg (2 mL) (n=8)	C3 1200 mg (3 mL) (n=8)	C2 800 mg (2 mL) (n=8)	C4 1200 mg (3 mL) (n=8)
C _{max} , µg/mL	0.7 (35.5)	0.8 (39.0)	1.8 (53.5)	1.8 (148)
t _{max} , hours	570 (158)	349 (147)	298 (136)	383 (107)

CAB-ULA has slower absorption and longer t_{1/2} than CAB200 IM

- PK profiles were flatter than CAB200 IM
- CAB-ULA C_{max} was lower with SC than IM; both were lower than CAB200 IM¹
- t_{max} was longer than CAB200 IM¹
- CAB-ULA t_{1/2} for SC and IM was predicted to be >6x and >2x the t_{1/2} of CAB200 IM, respectively^{1,a}

Observed median and range (error bar) dose-normalized to 1600 mg^b



CAB-ULA IM Q4M is progressing into upcoming late-stage HIV-1 PrEP and treatment studies

The potential benefits of long-acting injectable cabotegravir in pregnant and breastfeeding women and their infants

AIDS 2024

Leigh F. Johnson^a, Landon Myer^b, Lise Jamieson^{c,d,e},
Gesine Meyer-Rath^{c,e,f}, Sinead Delany-Moretlwe^g
and Dvora Joseph Davey^{b,h}



Updates from HPTN 084

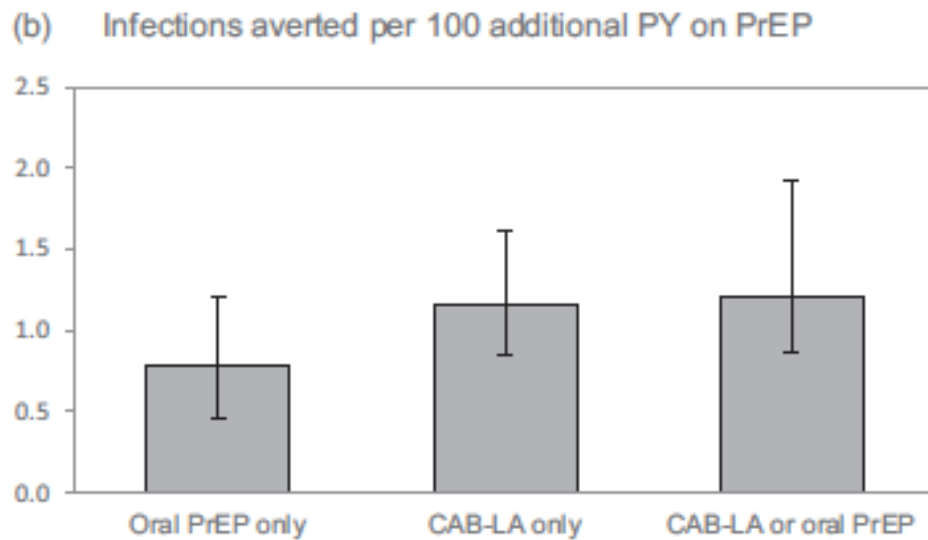
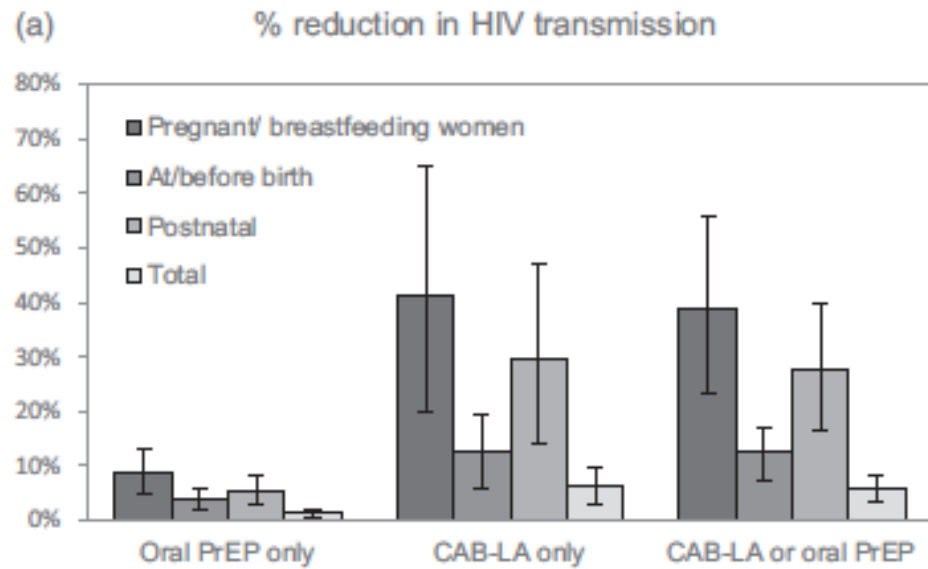


Fig. 1. Impact and efficiency of promoting preexposure prophylaxis to pregnant and breastfeeding women. Bars

The HPTN 084 OLE : CAB LA for PrEP maternal and pregnancy outcomes were consistent across CAB LA and FTC/TDF exposure groups and with expected background rates.

None of the women who became pregnant acquired HIV during pregnancy.

The sub-study PK analysis of the HPTN 084 OLE: 50 participants who continued to receive cabotegravir LA for PrEP prior to and during pregnancy. The study found that concentrations of cabotegravir were comparable between the pre-pregnant, pregnant and post-partum.

Delany-Moretlwe S, et al R4P 2014

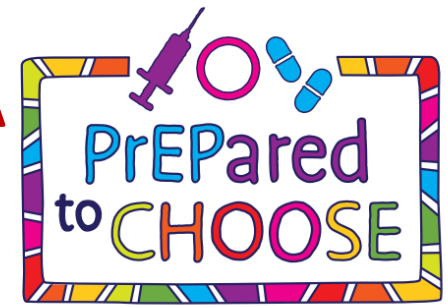
**HIVR4P
2024**



6-10 October, Lima, Peru



PrEPared to Choose: 77% chose Cab-LA (of which 62% were PrEP naïve at initiation)



	Oral PrEP	DVR	CAB-LA	Total
N (%)	125 (22.4%)	5 (0.9%)	429 (76.7%)	559 (100.0%)
Age m(IQR)	23(20-28)	23(22- 24)	24(21-28)	24 (20-28)
Weight (kg)	70(58-83)	67.4(63- 70)	71.2(60.5 86)	71 (60-86)
Gender				
Male	49 (39.2%)	0 (0.0%)	136 (31.7%)	185 (33.1%)
Female	73 (58.4%)	5 (100.0%)	289 (67.4%)	367 (65.7%)
MSM	3 (2.4%)	0 (0.0%)	4 (0.9%)	7 (1.3%)
PrEP experienced				
No	102 (81.6%)	2 (40.0%)	267 (62.2%)	371 (66.4%)
Yes	23 (18.4%)	3 (60.0%)	162 (37.8%)	188 (33.6%)

Commenced
February 2024

862 started CAB-LA;



Cab-LA roll-out highly feasible at public facilities and mobiles with Cab-LA being most popular choice

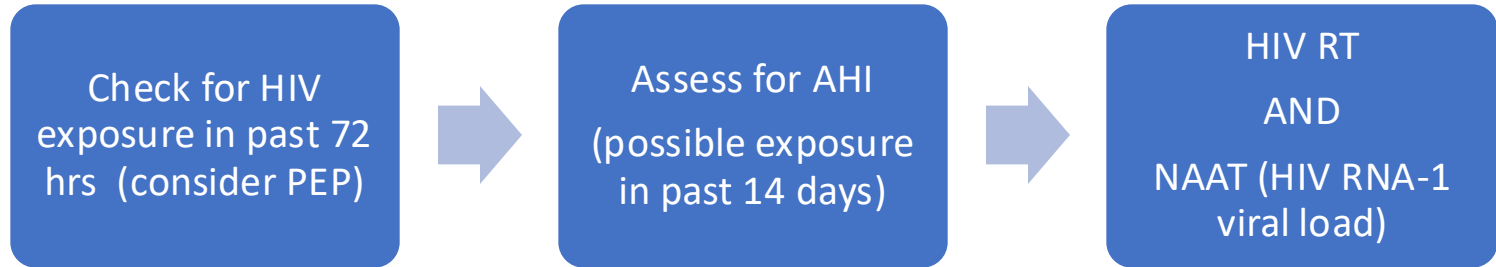
	mobile truck	Vuyani Clinic	Total
N (%)	402* (71.9%)	157 (28.1%)	559 (100.0%)
PrEP Products at baseline			
Oral PrEP	98 (24.4%)	27 (17.2%)	125 (22.4%)
DVR	5 (1.2%)	0 (0.0%)	5 (0.9%)
CAB-LA	299 (74.4%)	130 (82.8%)	429 (76.7%)

PrEP persistence at M1: 59% for Cab-LA compared to 21% for oral PrEP

Oral PrEP (attended/due)	DVR (attended/due)	CAB-LA (attended/due)
15/70 (21%)	0/2 (0%)	125/209 (59%)

*attended within 7 days of scheduled visit as per ViiV protocol

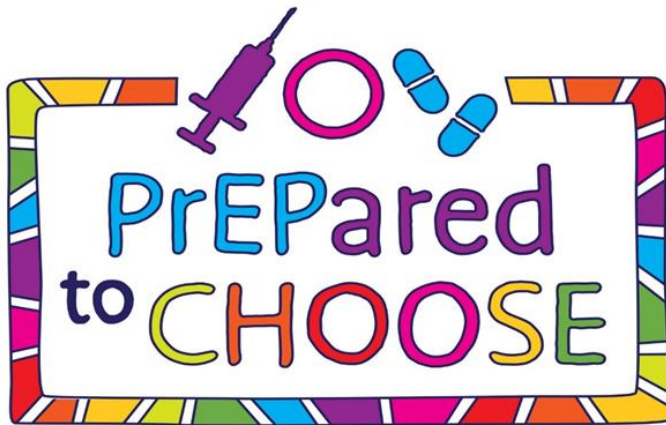
Testing to start CAB LA for PrEP



- A total of **3/862 (0.35%)** had a **discrepant detectable VL** at CAB-LA initiation:
 - 4th Gen HIV Ag/Ab RT: 1/588 (0.17%)
 - 3rd Gen HIV Ab RT: 2/666 (0.30%)

Participants with detectable VLs, were recalled for additional testing, including HIV confirmatory testing (Lab ELISA), and HIV-Drug Resistance testing.

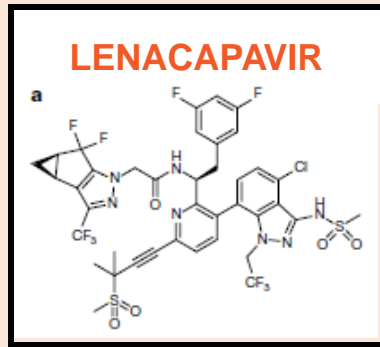
All 3 participants were started on standard 1st line ART Tenofovir/Lamivudine/Dolutegravir (TLD), within 5 days of CAB-LA initiation.





Lenacapavir : LA (6 monthly) Injectable for HIV Prevention

Agent class:
HIV-1 capsid inhibitor



Dosing Strategy: One injection every 6 months (ARVs that you only need to take twice a year!)

- 6 monthly injectable
- Subcutaneous
- Novel mechanism of action
- Excellent for prevention

PURPOSE 1 and 2 Data Summary

PURPOSE 1

PURPOSE 2



Study population

Baseline demographics and clinical characteristics

Efficacy

Safety

Cisgender women

Balanced across randomized groups

LEN HIV prevention efficacy was **superior** to both background HIV incidence and daily oral F/TDF

Zero HIV infections among 2134 participants receiving LEN

LEN reduced HIV infections by **100%** compared with bHIV incidence and daily oral F/TDF

LEN and F/TAF were **safe and well tolerated**

Most common ISRs: SC nodules, injection-site pain, and **swelling**
ISR frequency and grade diminished with subsequent injections (also observed in other studies¹⁻³)

Adherence to F/TDF was too low to impact eGFR

CGBMSM, TGW, TGM, and GNB people who have sex with partners assigned male sex at birth

Balanced across randomized groups

LEN HIV prevention efficacy was **superior** to both background HIV incidence and daily oral F/TDF

Two HIV infections among 2179 participants receiving LEN

LEN reduced HIV infections by **96%** compared with bHIV incidence and by **89%** compared with daily oral F/TDF

LEN and F/TDF were **safe and well tolerated**

Most common ISRs: SC nodules, injection-site pain, and **erythema**
ISR frequency and grade diminished with subsequent injections (also observed in other studies¹⁻⁴)

LEN increased eGFR while F/TDF decreased eGFR; this **difference was more pronounced** in PURPOSE 2 vs PURPOSE 1

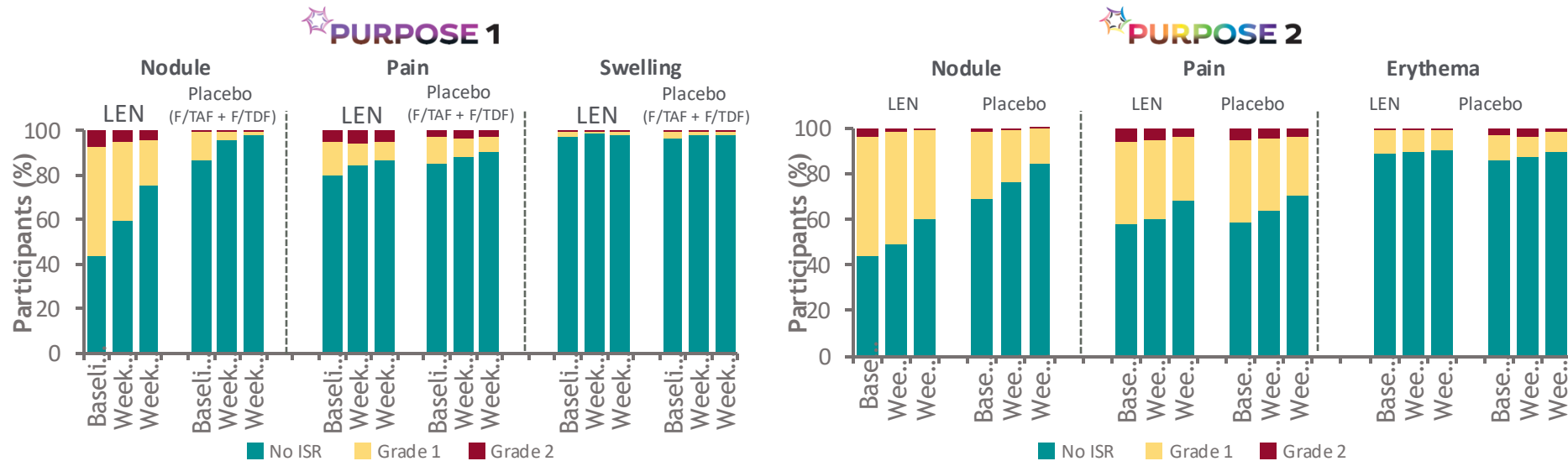
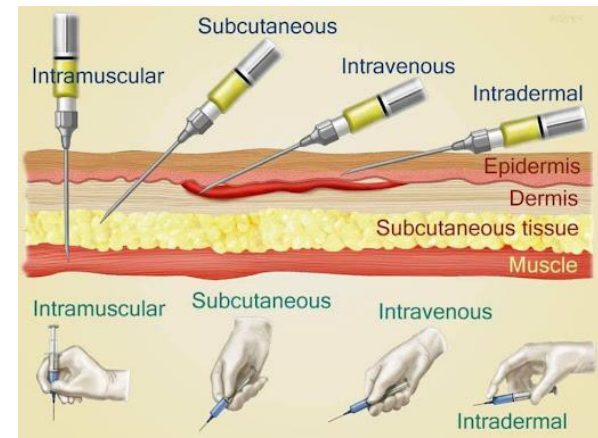
Safe in adolescents, pregnancy and lactation

1. Segal-Maurer S, et al. *N Engl J Med.* 2022;386:1793-1803. 2. Landovitz RJ, *N Engl J Med.* 2021; 385(7):595-608. 3. Delany-Moretlwe S, et al. *Lancet.* 2022; 399:1779-1789. 4. Bekker L-G, et al. *N Engl J Med.* 2024;391:1179-92.

Injection-Site Reaction: Frequency and Grade

LEN is injected into the SC space and forms a drug depot that may be palpable under the skin but may not be visible. As the drug elutes over time, the depot gets smaller, and the nodules resolve or reduce in size prior to the next injection.

The frequency of ISRs, including nodules, decreased with subsequent doses (also observed with HIV treatment¹).



In PURPOSE 1, among 25,329 LEN/placebo injections, only 4 ISRs led to discontinuation (all LEN)
 In PURPOSE 2, among 15,239 LEN/placebo injections, only 29 ISRs led to discontinuation (LEN, 26; F/TDF, 3)

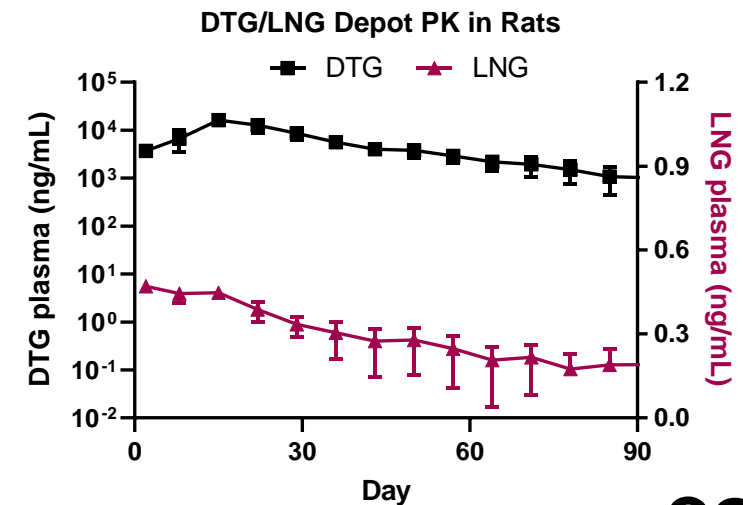
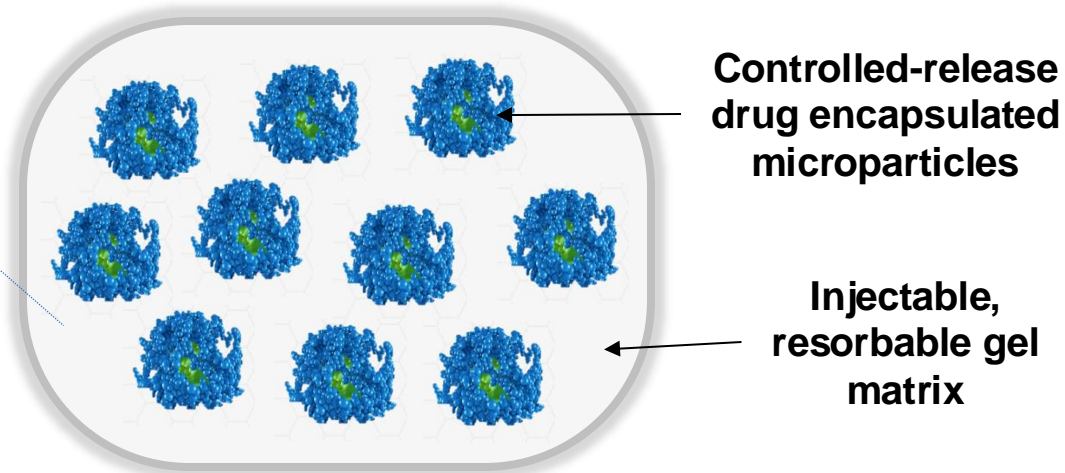
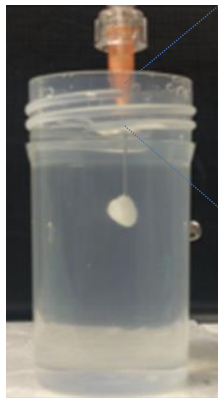
AEs coded according to Medical Dictionary for Regulatory Activities, Version 27.0. Grade 1 and 2 ISRs are shown. In PURPOSE 1: LEN n: baseline, 2138; Week 26, 1930; Week 52, 862. Placebo (F/TAF + F/TDF) n: baseline, 3206; Week 26, 2883; Week 52, 1274; SC nodules, injection-site pain, and swelling were the most commonly reported ISRs, occurring in 63.8%, 31.2%, and 4.4% of participants in the LEN group, respectively, vs 16.6%, 23.7%, and 5.4% of participants given placebo injections; Grade 3 ISRs in the LEN group: n = 1 nodule; F/TDF group: n = 1 pain. In PURPOSE 2, LEN n: baseline, 2183; Week 26, 1859; Week 52, 744; Placebo n: baseline, 1088; Week 26, 946; Week 52, 379; SC nodules, injection-site pain, and erythema were the most commonly reported ISRs; over the period of study, they occurred in 63.4%, 56.4%, and 17.3% of participants in the LEN group, respectively, vs 39.2%, 53.4%, and 19.4% of participants given placebo injections; Grade 3 ISRs in the LEN group: n = 4 pain, n = 3 erythema; F/TDF group: n = 1 pain. 1. Kumar P, et al. Abstract EPB184 presented at the 24th International AIDS Conference, July 29 to August 2, 2022; Montreal, Canada.

Whats coming in injectables?:

Long-Acting Injectable Hydrogel Depot

In situ gel forming depot platform

- Natural, FDA-recognized GRAS material
- Thixotropic gel is injectable & fully biodegradable
- Drug release tuned by controlling depot erosion
- Uses small gauge needle (~25 G) & smaller volume (1-2 mL)
- Can accommodate controlled-release of at least two ARVs or MPTs

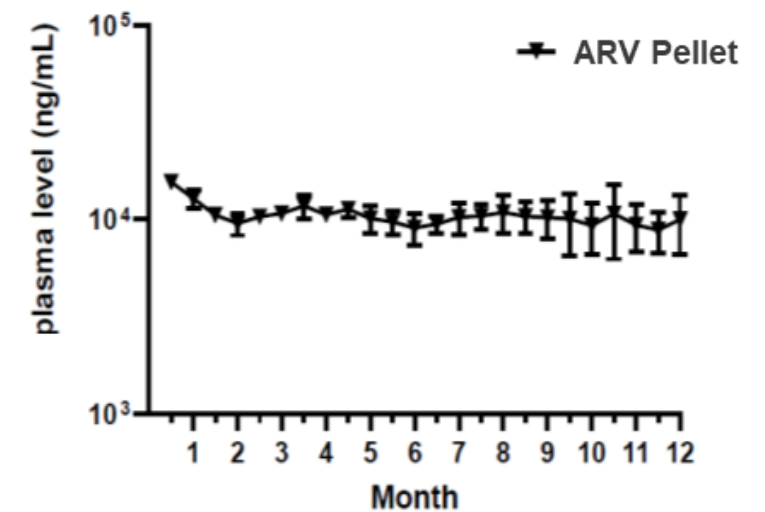
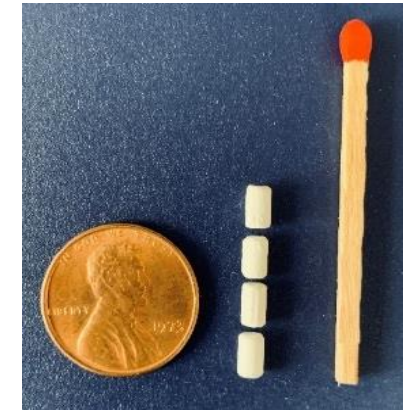


PreClinical

CONRAD

Resorbable ARV Pellet-Type Implants

- ❖ Uses simple, readily scalable & low cost manufacturing process
- ❖ Single subdermal insertion of multiple pellets, *akin to injectable depot*
- ❖ Provides sustained & controlled release for at least 12 months
- ❖ Flexible dose adjustment
- ❖ No need for removal
- ❖ Highly suitable DDS for long-acting ARV delivery, alone or in combination with other potent ARV or contraceptive (MPT)



Librela
(polysulfated glycosaminoglycan)

About Librela Discussing OA With Your Clients Resources for Your Practice Prescribing Info Buy Now

Or call 1-888-963-8471 to order

Give Dogs More Days of Play

See what pet owners and veterinarians are saying about Librela!

[See Success Stories](#)

The First and Only Monthly Injectable Anti-NGF Monoclonal Antibody Therapy for the Control of Canine Osteoarthritis (OA) Pain

This site is intended for US Animal Healthcare Professionals. [Visit Pet Owner Site](#)

Overview Librela Mechanism of Action Efficacy Safety Dosing & Storage

LIBRELA OVERVIEW

Librela is the First and Only Monthly Injectable Monoclonal Antibody Therapy for Dogs With OA Pain

- Approved as safe and effective and provides long-term canine OA pain control^{1,2}
- A monthly subcutaneous injection, administered at the clinic by veterinary professionals
- Reduced canine OA pain, which led to increased activity and improved quality of life^{3,4}



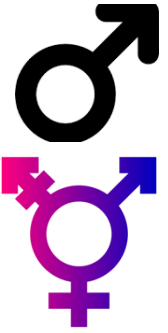
Infusible PrEP

“We can manufacture and market bNAbs for oasteoarthritis in our cats and dogs, shouldn’t we be able to do this to prevent life-long HIV in people”

Huub Gelderblom, HVTN 2024.

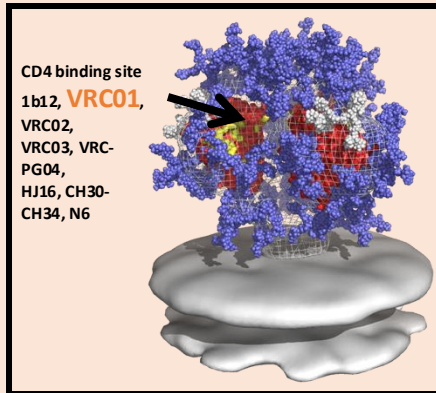


BNABs: Broad-neutralizing antibodies, VRC01



Agent class:

Broad-neutralizing antibodies



Dosing Strategy (AMP Trial)

VRC01 mAb (IV), given on 8 weekly schedule

VRC01 Efficacy in Preventing HIV-1 Infection Dependent on Viral Neutralization Sensitivity

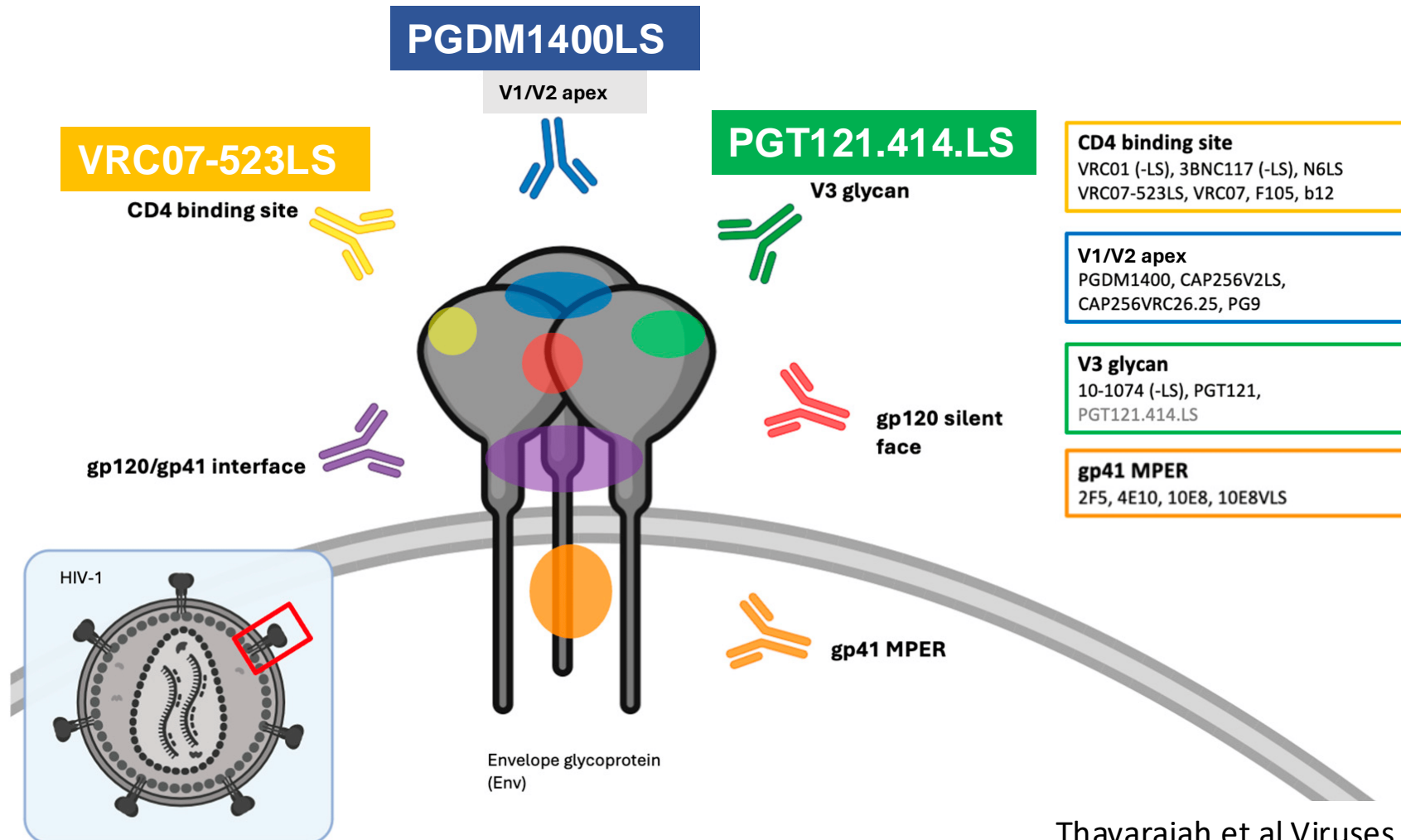
Corey L, et al NEJM 2021

In vitro viral susceptibility to VRC01 predicts prevention efficacy in vivo; **only effective against viruses to be neutralization sensitive (< 1 mg/mL)**

In overall data, no significant difference seen in HIV-1 acquisition between treatment arms
Only 30% of circulating strains in control group were susceptible in vivo to the antibody (IC₈₀ < 1 mg/mL), giving study low power to detect overall efficacy

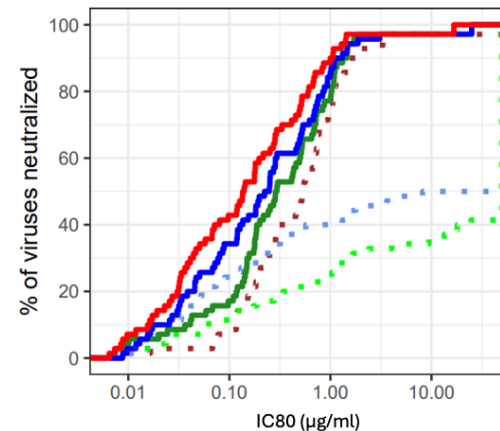
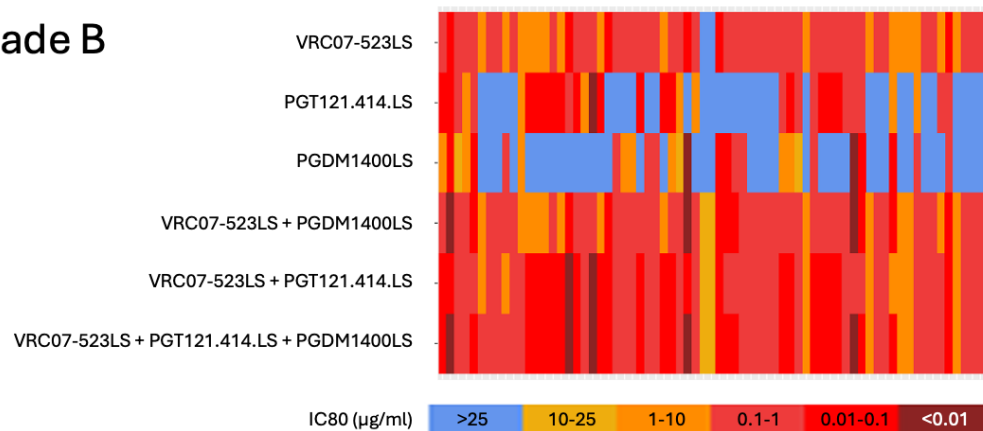
HIV-1 Cases by Treatment Arm (Pooled Studies), n (%)	Sensitive (< 0.3 mg/mL)	Moderately Sensitive (0.3-1 mg/mL)	Intermediate (1-3 mg/mL)	Moderately Resistant (3-10 mg/mL)	Resistant (> 10 mg/mL)	Total
Control	4 (6)	15 (23)	10 (16)	18 (28)	17 (27)	64 (100)
VRC01 10 mg/kg	0	4 (7)	13 (24)	18 (33)	19 (35)	54 (100)
VRC01 30 mg/kg	0	5 (11)	6 (14)	15 (34)	18 (41)	44 (100)

HVTN 206 / HPTN 114 Study bnAbs

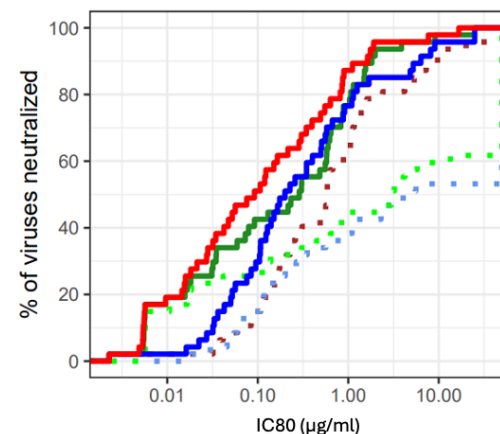
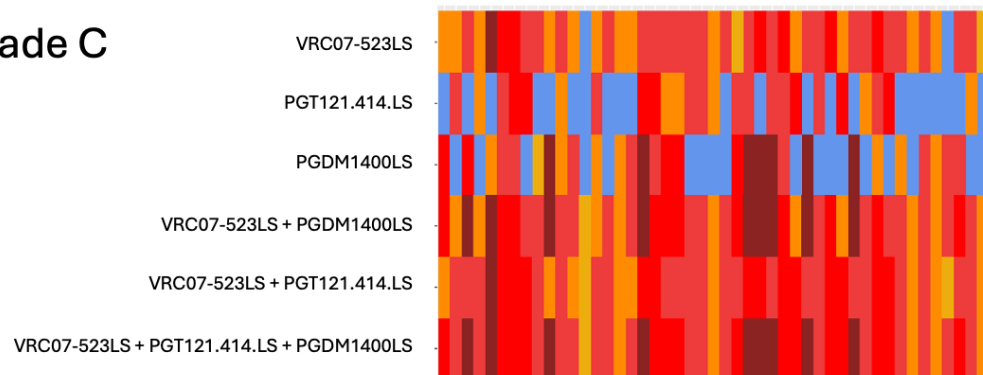


Proposed Combination of 3 bnAbs gives the most potent and broadest neutralization

HIV-1 clade B



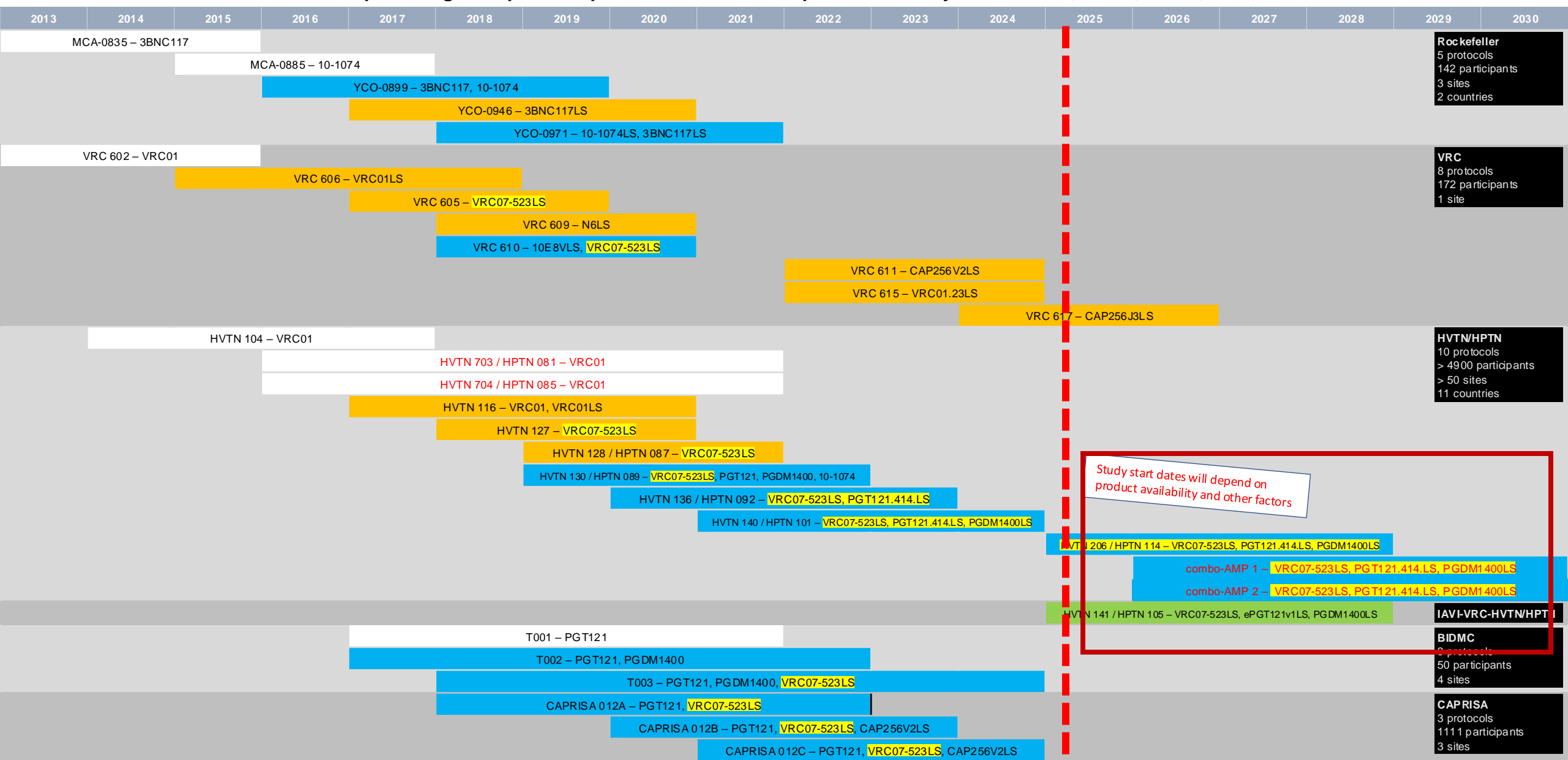
HIV-1 clade C



- VRC07-523LS
- PGT121.414.LS
- PGDM1400LS
- VRC07-523LS+PGDM1400LS
- VRC07-523LS+PGT121.414.LS
- VRC07-523LS+PGT121.414.LS+PGDM1400LS

HIV bnAb clinical trials in adults without HIV

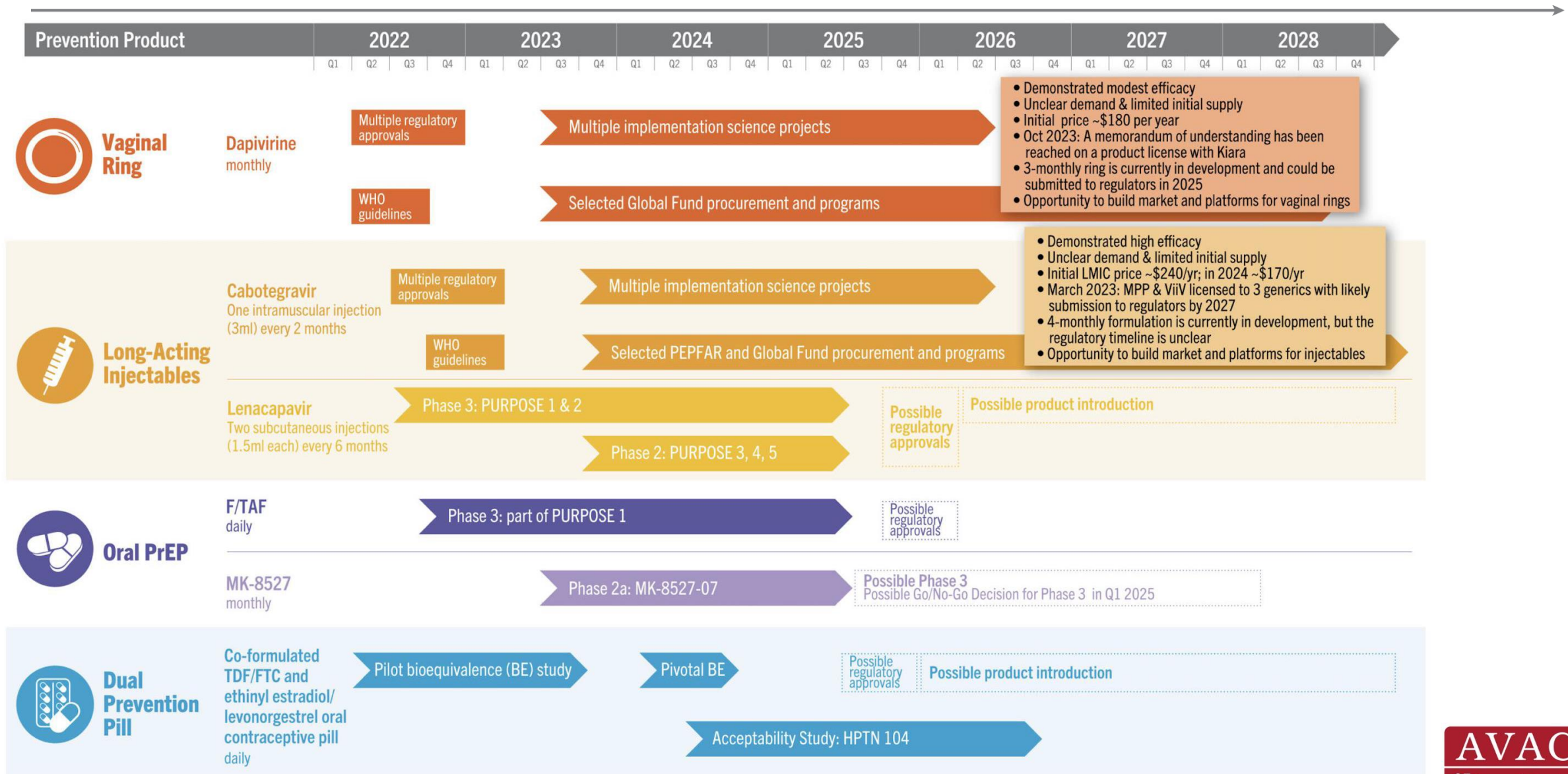
Partnership to bring the optimal triple bnAb cocktail into phase 2 efficacy trials: HVTN, HPTN, NIAID, VRC, IAVI



Study start dates will depend on product availability and other factors

Legend
 Single antibodies (White)
 Single antibodies, LS versions (Yellow)
 Antibody combinations (Blue)
 Next-generation ebnAbs (Green)
 combo-AMP antibodies (Cyan)
 Phase 1 = black font
 Phase 2-3 efficacy = red font

Updated PrEP Pipeline

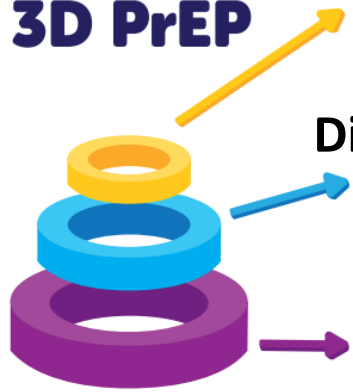


Pros and Cons for PrEP types and modalities



Product	frequency	administration	Integration	No NAT testing	Infrequent dosing	DDI	Pregnancy safe	Cost	Load	Tail
Oral PrEP		(self/peer)						LMIC		
CAB LA		(nurse)				TB drugs				
Oral Mnthly		(self/peer)				?	?	?		
Len LA		(nurse/self)				TB drugs				
Implants		(nurse)		?		?	?	?		
bNAbs		nurse								
Vaginal Ring		(nurse/self)					+?			

Will the new agents lead to re-medicalization??



Disposition



Segmentation of PrEP-users



The “Convenient PrEP-user”

CHARACTERISTICS

- Platforms at easily accessible locations
- One-stop integrated SRH services
- Platforms that utilize minimum resources (time and money)

PrEP DELIVERY PLATFORM PREFERENCE



The “Social PrEP-user”

CHARACTERISTICS

- Prefers PrEP pick-up in shared peer spaces
- Needs affirmation and social support for continued PrEP use

PrEP DELIVERY PLATFORM PREFERENCE



The “Independent PrEP-user”

CHARACTERISTICS

- Seeks PrEP delivery outside of traditional medical environments
- Requires minimal PrEP adherence support
- Prefers HIVST to assess HIV status without having to talk to counselor/nurse about lifestyle

PrEP DELIVERY PLATFORM PREFERENCE



The “Discreet PrEP-user”

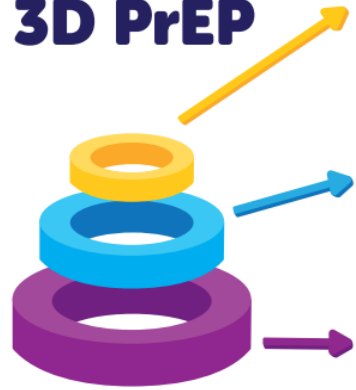
CHARACTERISTICS

- Actively avoid PrEP delivery options that include groups of people waiting for a service
- Fear unintentional PrEP use disclosure
- Frequently report controlling sex partners

PrEP DELIVERY PLATFORM PREFERENCE



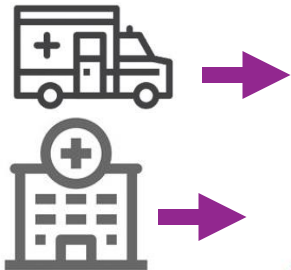
3D PrEP



Delivery



Initiation



DTHF: Fast-PrEP (like Fast food!)

Implementation science project to evaluate uptake, coverage and effectiveness of a youth-focused, decentralized district-wide PrEP program: Walkable hub and spokes approach in Cape Town

BMGF funded

In a single health subdistrict of 1 million people in Cape Town

PEER NAVIGATION

Follow-up



Roll out to 25 000 people in 3 years

- Contraception
- PoC STI screening and Treatment
- HIV testing
- PrEP
- ART
- mental health support

- Target pop:
- AGYW (15-29yrs)
 - PBFW (15-29yrs)
 - MSM (15-29yrs)
 - Male Partners (18yrs & older)

HUB-and-SPOKES Approach

Rousseau E, et al FastPrEP



Increased

- FastPrEP introduced multiphased approach between
- In this analysis we included
- 2648 people (2276 men)
 - Median age 23 (IQR 18-28)
 - 1625 (61.4%) were young

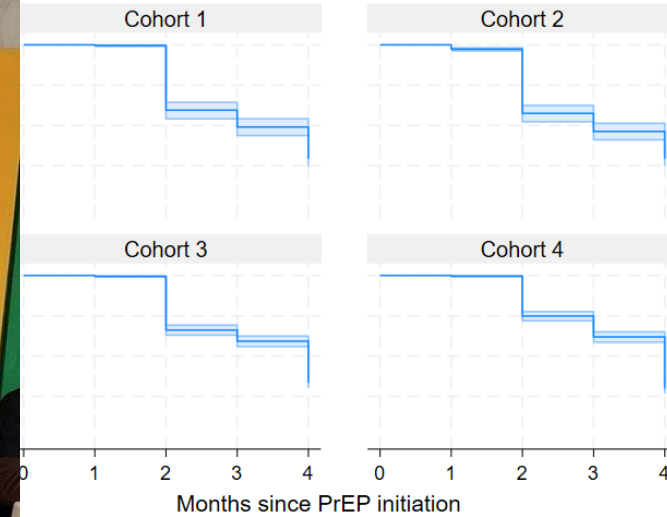
1	A
2	D
3	A
4	A



crease in PrEP



Kaplan–Meier survival estimates
If month 1 attended



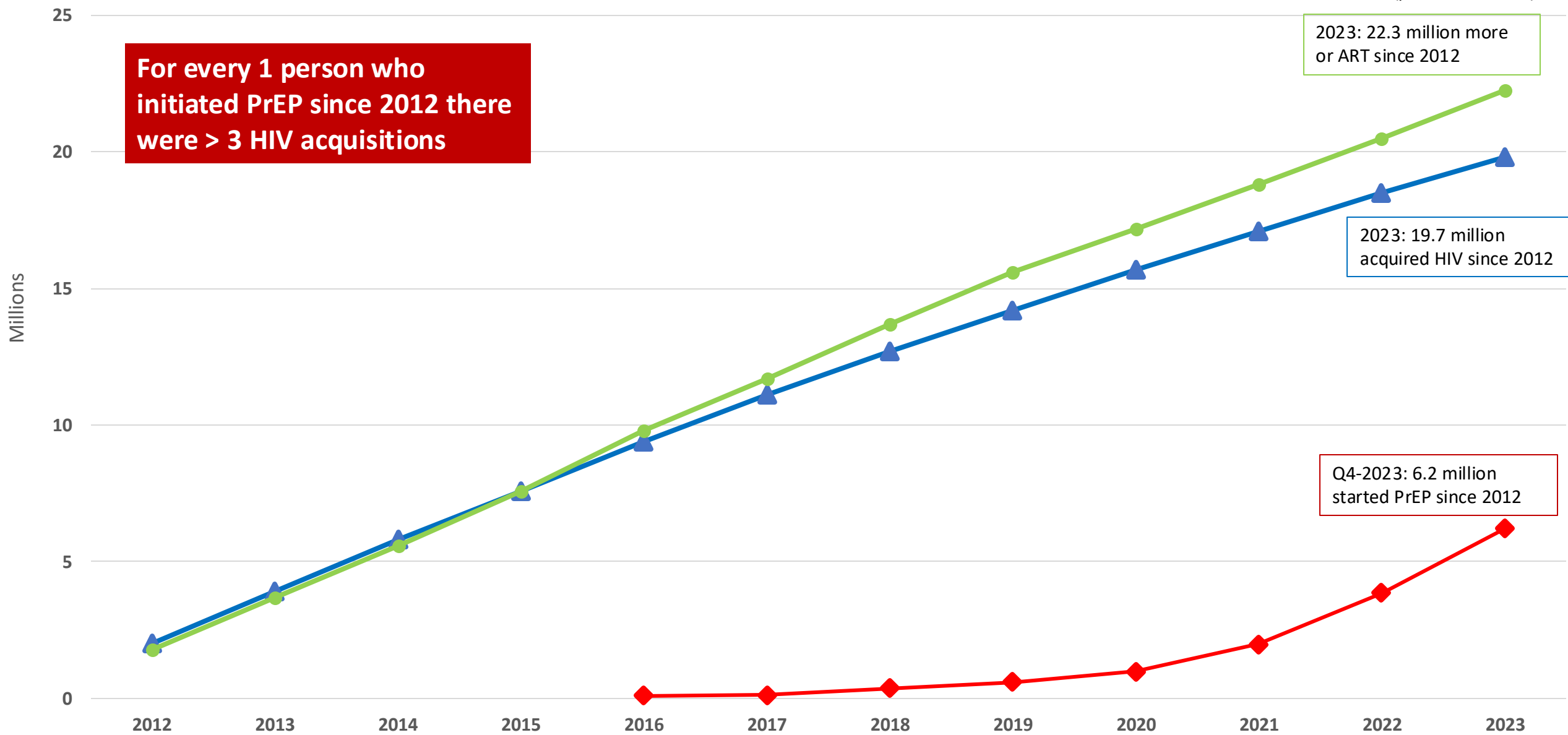
PrEP Persistence at month 3

49.9% (95% CI: 44.5%-55.1%)
48.1% (95% CI: 42.6%-53.3%)
59.7% (95% CI: 56.3%-62.9%)
62.5% (95% CI: 59.1%-65.6%)

er accessibility

HIV/AIDS Key Numbers 2012-2023 – Global

Huub Gelderblom, HVTN (personal comms)



HIV/AIDS Key Numbers 2012-2023 – Peru

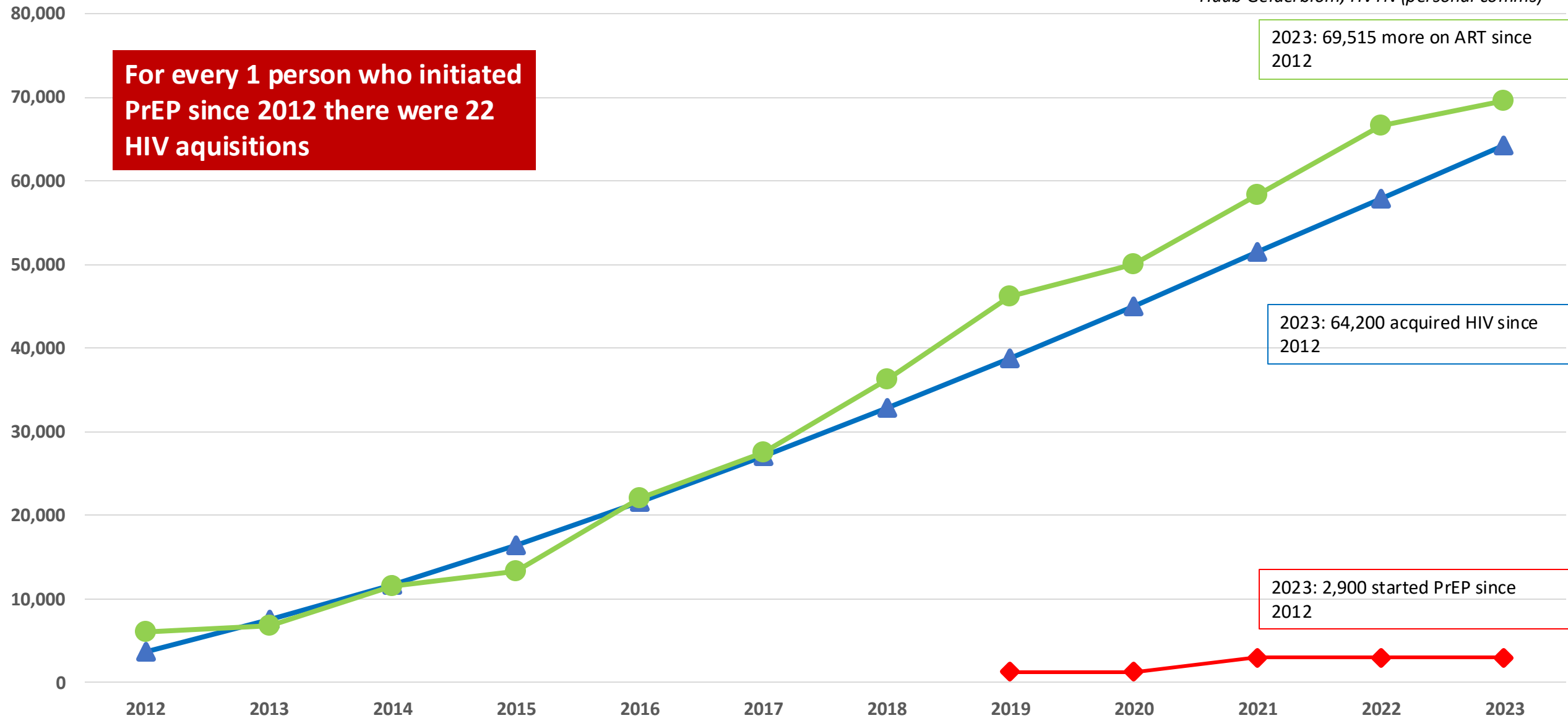
Huub Gelderblom, HVTN (personal comms)

For every 1 person who initiated PrEP since 2012 there were 22 HIV acquisitions

2023: 69,515 more on ART since 2012

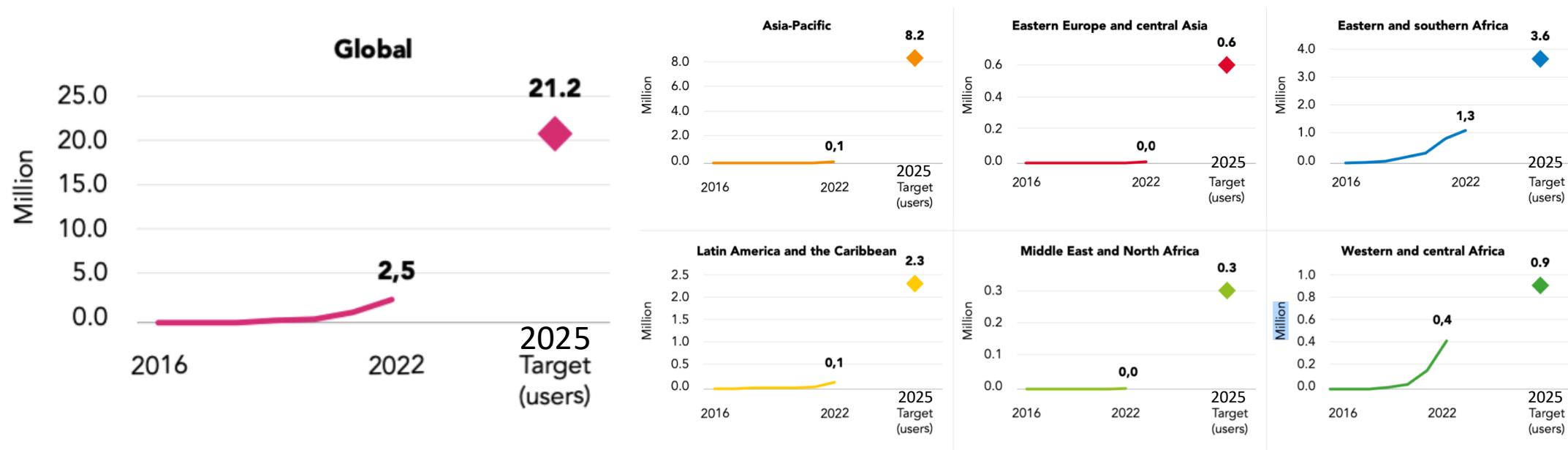
2023: 64,200 acquired HIV since 2012

2023: 2,900 started PrEP since 2012



People need access to options so they can use what works for them

Number of people using HIV PrEP, relative to 2025 targets



1. We need to increase the number of people accessing HIV PrEP
AND
2. We need more HIV PrEP options – so that people can choose what works for them

PrEP4Prevention 1.3 Million 2023

PrEP in 26 million to avert ¼ million

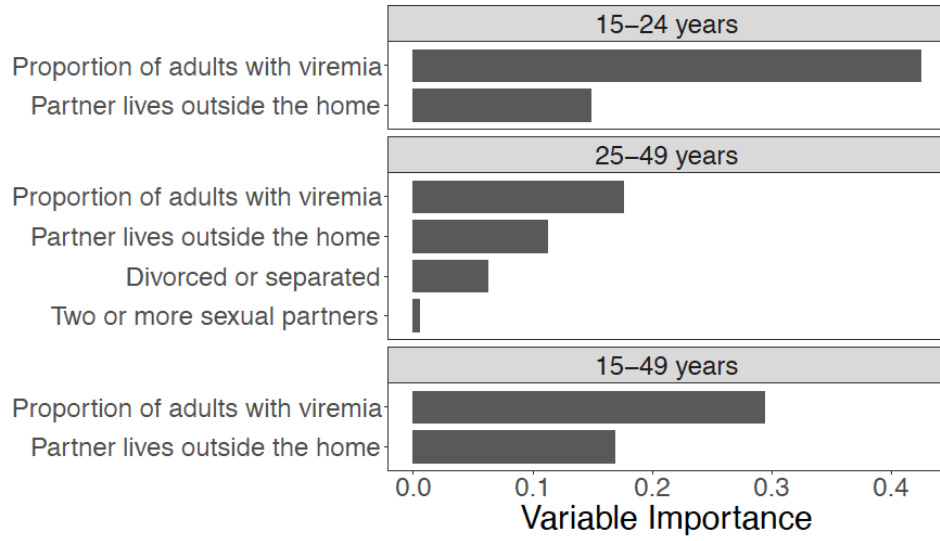
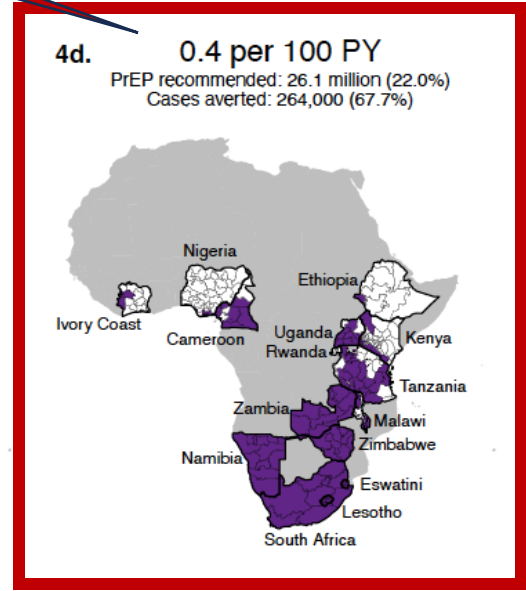
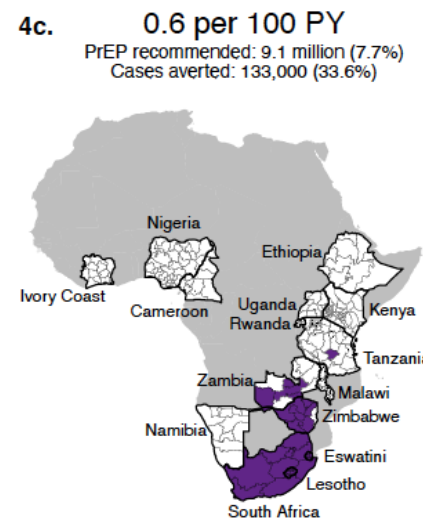
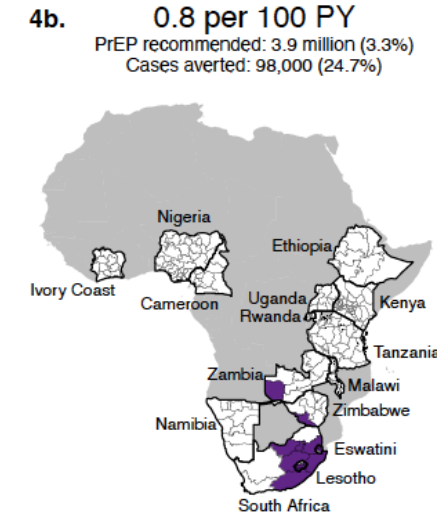
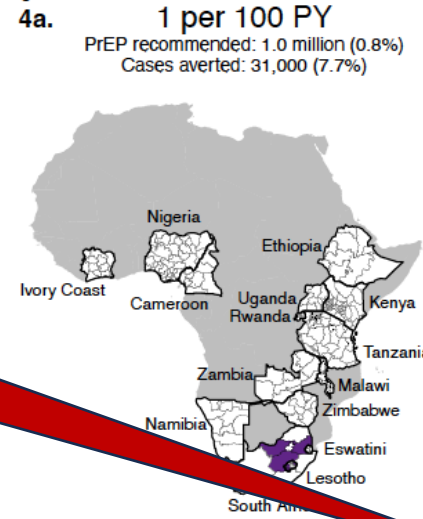
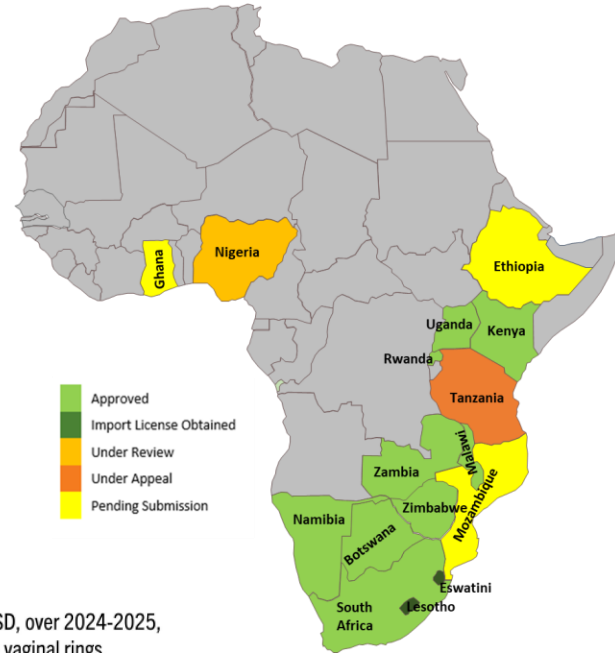


Figure 4

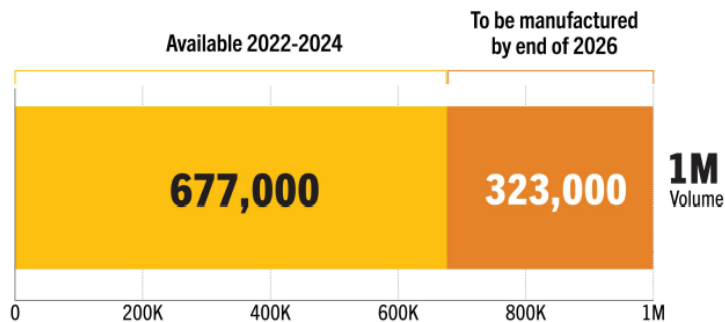


PrEP Recommended No Yes

Dapi Ring: Regulatory and availability



CIFF and the Global Fund have committed up to \$2 million USD, over 2024-2025, for the purchase of approximately 150,000 dapivirine vaginal rings.



	IPM Submission Date	Status
South Africa	Final Submission via USB 26-Mar-2021	Product Registration 08-March-2022
Zimbabwe	03-February-2021	Product Registration 06-July-2021
Rwanda	11-February-2021	Approved by RFDA 10 Feb 2023
Uganda	17-February-2021	Product Registration 05-October-2021
Malawi	22-February-2021	Product Registration 10-May-2021
Tanzania	11-March-2021	IPM was notified on 12-April-2022 that TMDA has rejected the registration of DapiRing. IPM submitted an appeal.
Zambia	05-March-2021	Product Registration 10-May-2021
Kenya	23-March-2021	Product Registration 16-July-2021
Namibia	01-September-2021	Product Registration (insert date)
Botswana	08-September-2021	Product Registration 21 December 2022
Nigeria	18-August-2023	Under Review
Mozambique	TBD	
Ethiopia	TBD	
Ghana	TBD	

DapiRing Access:

- Only one large buyer for DVR at present: **The Global Fund**
 - **PEPFAR only buying DVR for discrete pilot projects**
- FDA re-submission strategy; DVR extension products
- Dec 2023: Announcement of Pop Council's intention to license product to African based company to reduce production costs and expand access



Current \$13 per ring

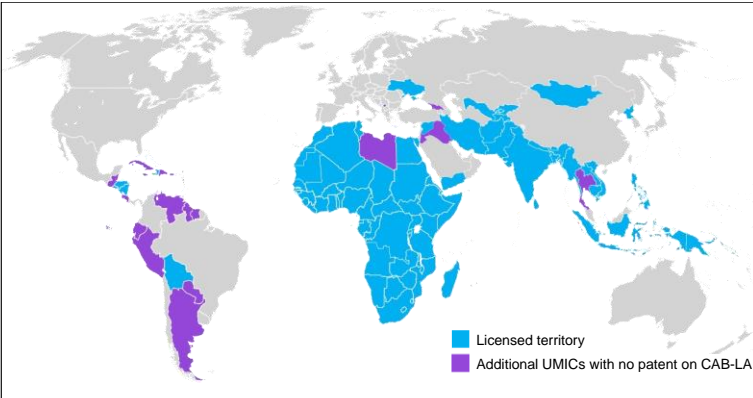
Finalize agreement with
Kiara Health for
Manufacturing and
Distribution

Explore Volume
Guarantees and Price
refinement with current
manufacturer

Advance Development
of the Three-month DVR

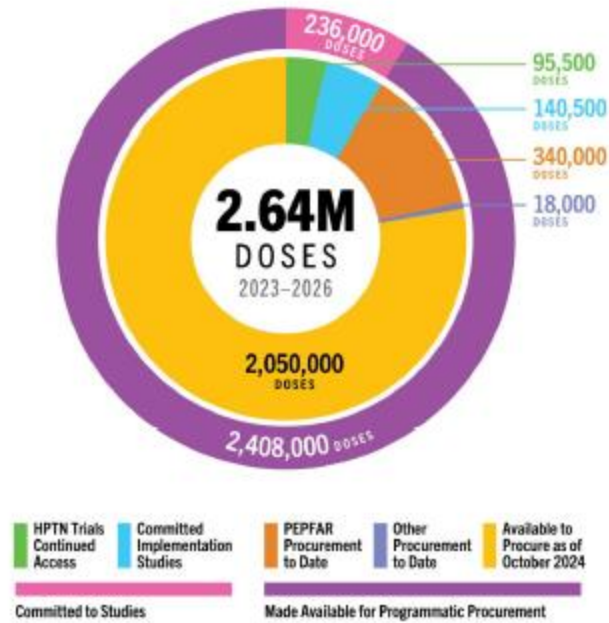
Medicines Patent Pool signs sublicences with Aurobindo, Cipla and Viartis to produce generic versions of ViiV Healthcare’s innovative long-acting HIV prevention medicine

30 March 2023

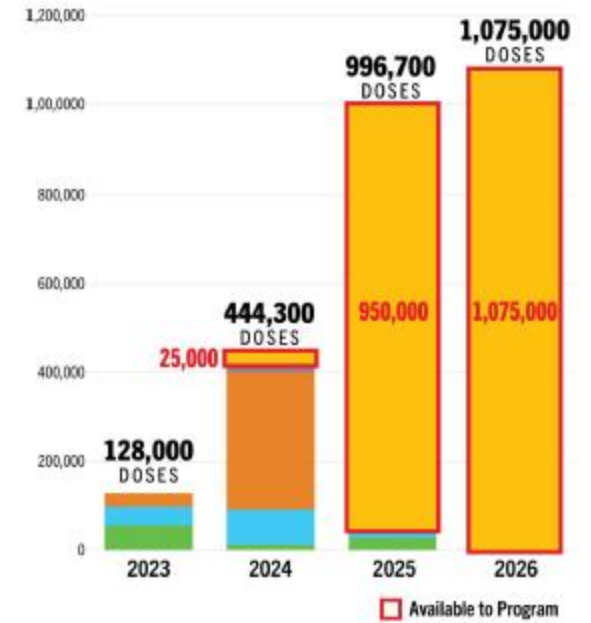


Source: Beatriz Grinsztejn, Long-acting PrEP implementation: Fostering access and equity, AIDS 2022

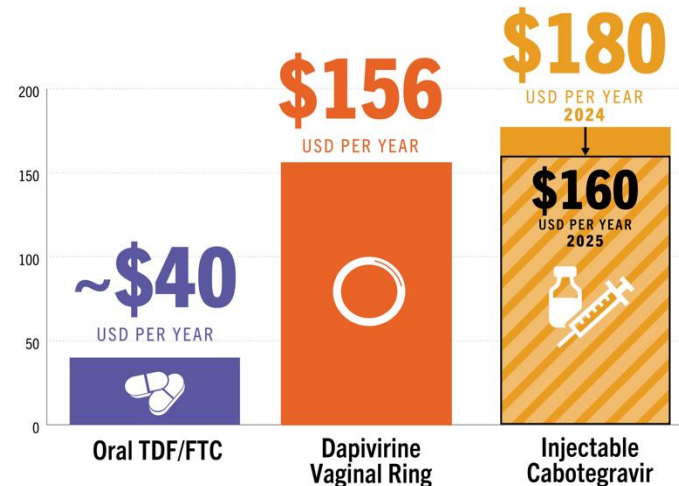
Allocation of Non-Commercial CAB for PrEP Supply in Low- and Middle-Income Countries, 2023-2026, as of October 2024 — BY CATEGORY



Allocation of Non-Commercial CAB for PrEP Supply in Low- and Middle-Income Countries, 2023-2026, as of October 2024 — BY YEAR



PrEP Price Comparison, 2024



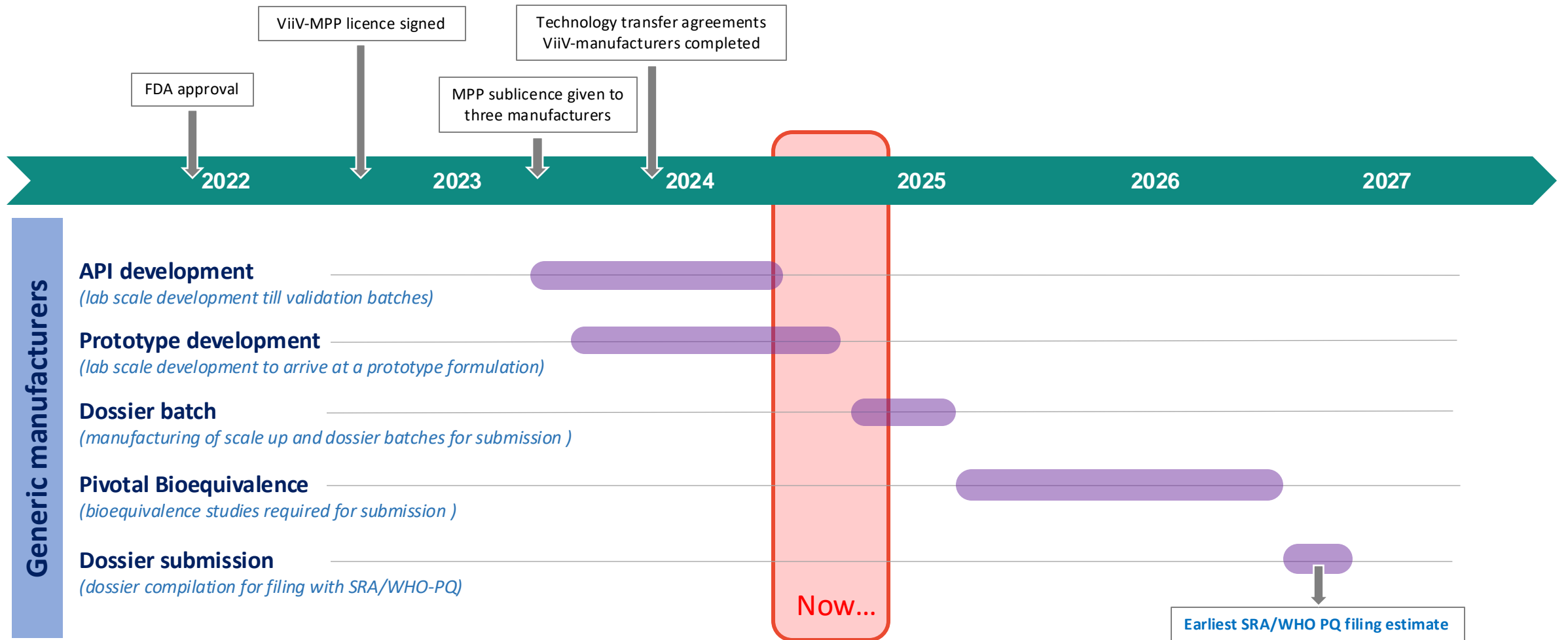
DETAILED REPORT
Tracking Progress to Market of New Long-Acting HIV PrEP Products

A quarterly update from Coalition for Access to Long-Acting PrEP

QUARTER 1 2024

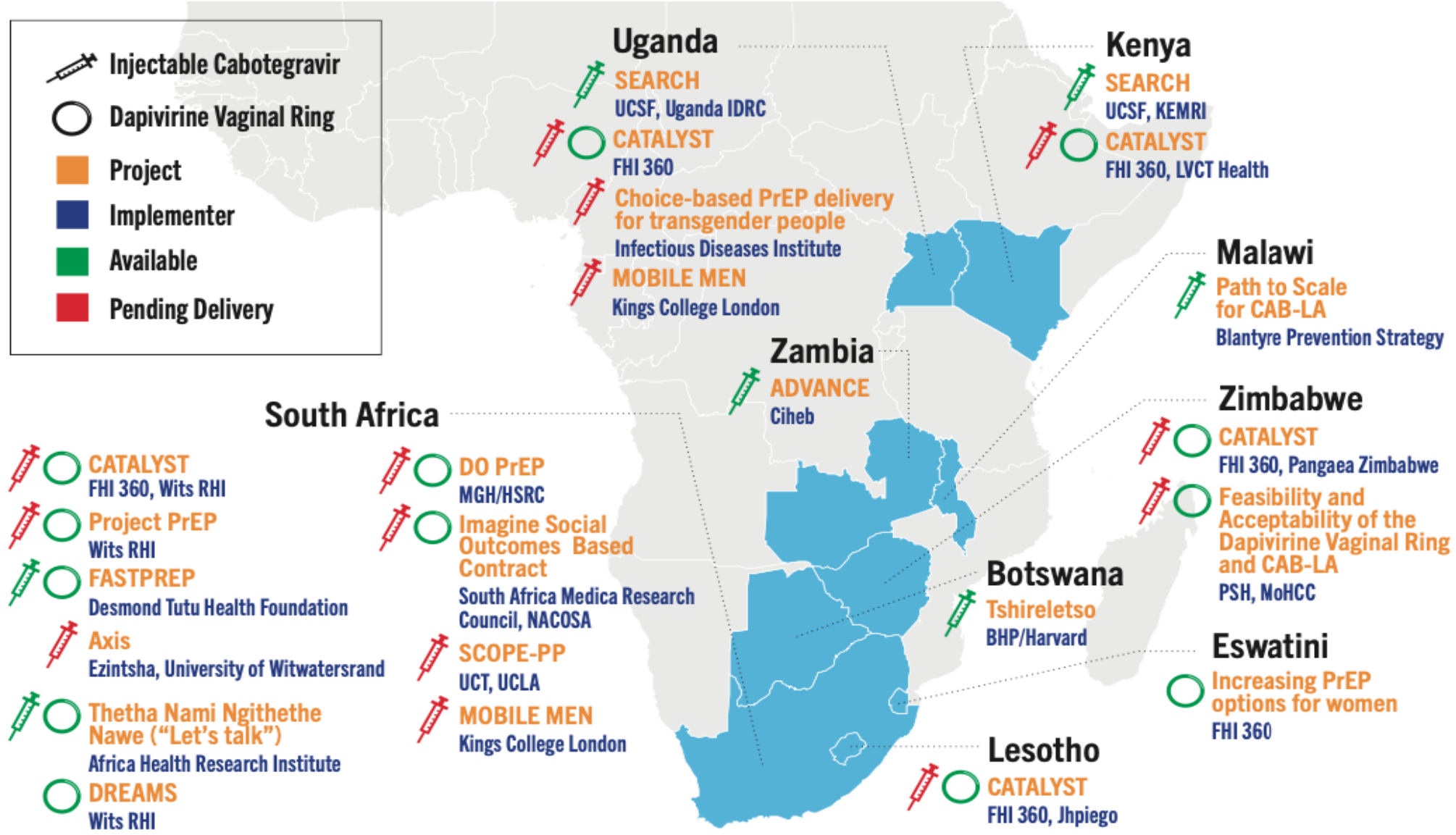
Coalition to Accelerate Access to Long-Acting PrEP

Generic CAB-LA for PrEP: Tentative development timeline



- These timelines are not specific to any generic company; these are averages of the timelines required for different activities as shared by MPP licensees.
- The earliest possible timelines for filing is **H2 2026** based on the current estimation by MPP.
- Due to the uncertainty associated with product development, especially for such long-acting products, the timelines quoted here are tentative and can change during development of the product.

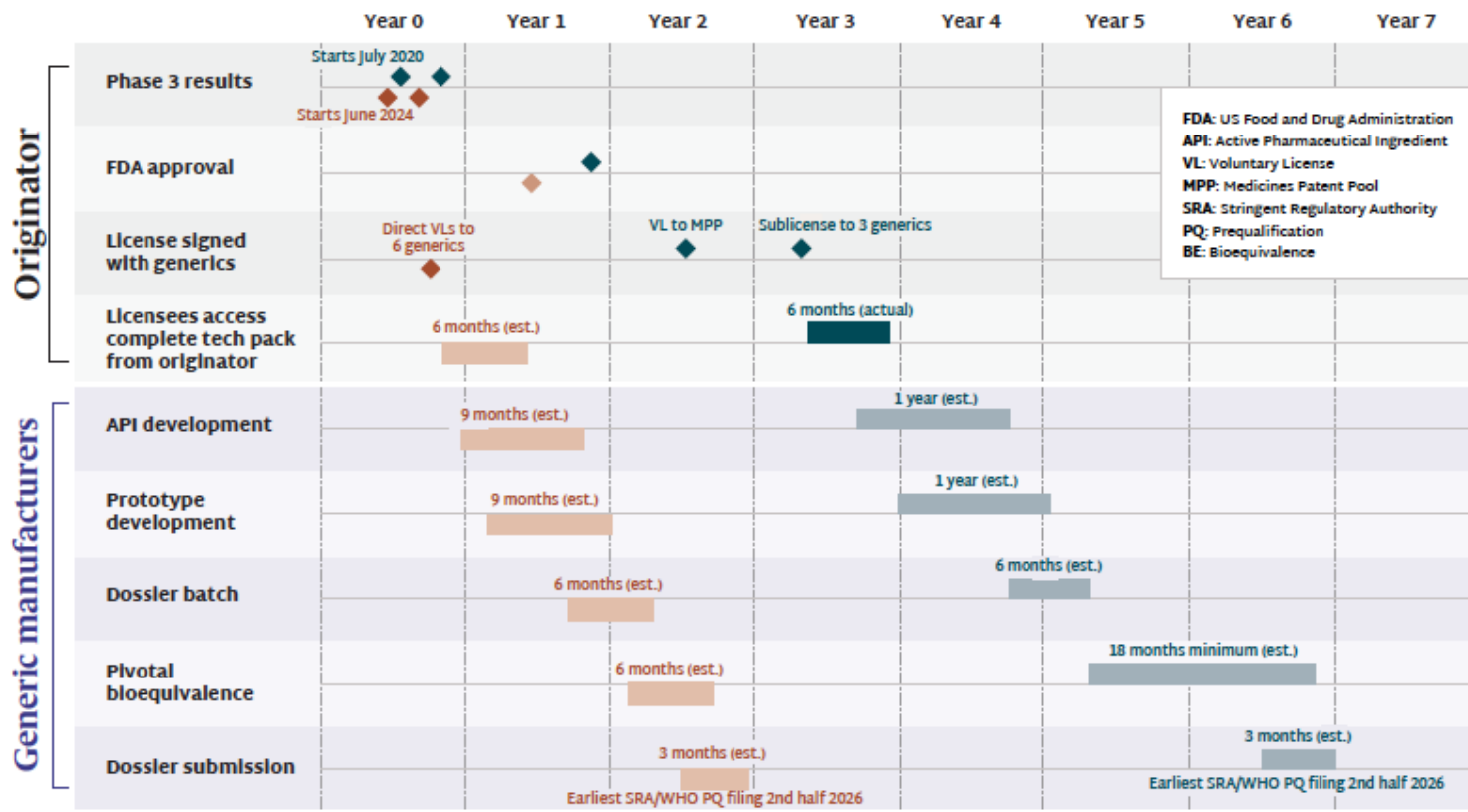
Real World Research and (some) roll out



Len for PrEP access



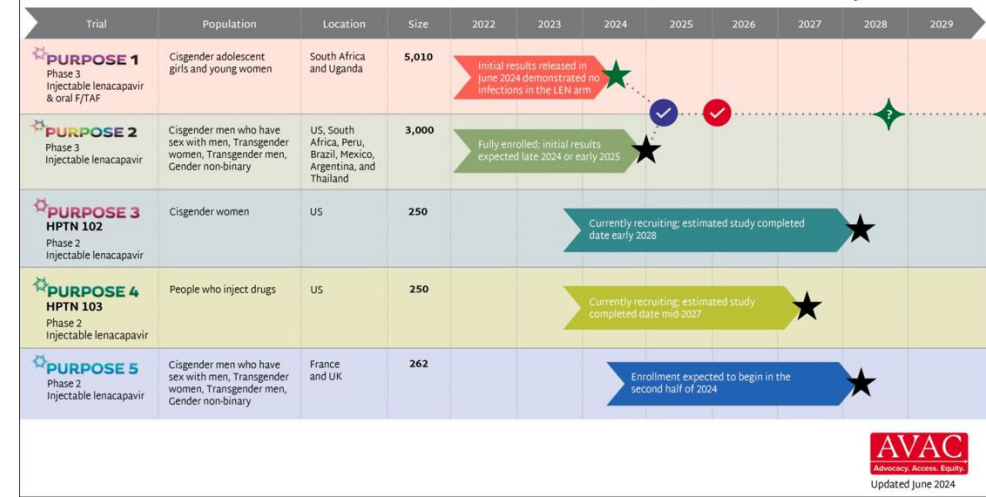
LEN generics may submit for regulatory approval around the same time as CAB generics (Q3-4 2026), primarily because LEN has been licensed even before regulatory submission / approval, is already moving towards tech transfer to generic manufacturers (as of Q4 2024) and because BE timelines are expected to be much shorter for LEN than for CAB.



This graphic aims to exhibit average timelines, but it is important to acknowledge that each generic manufacturer will move at different timelines and that unanticipated delays can happen at any step of the processes shown below. This graphic therefore aims to estimate timelines but should be used as a guideline rather than taken as 100%-definitive.

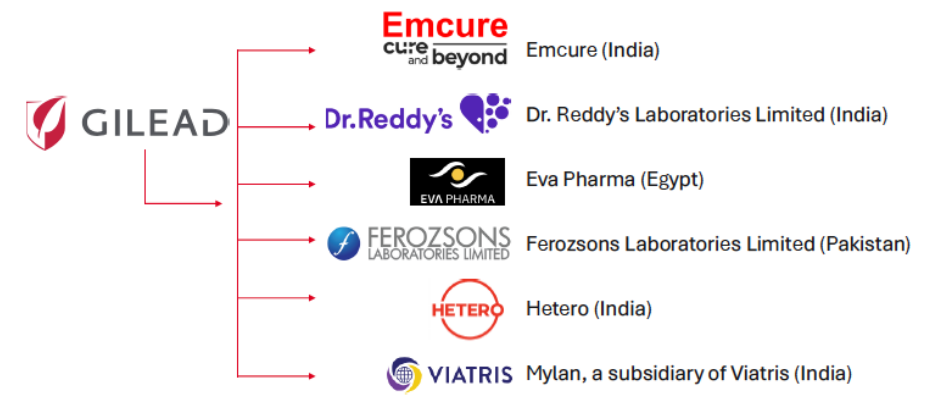
Overview of Lenacapavir (LEN) for PrEP Trials

- ★ Initial data
- ★ Possible data
- ★ Possible earliest regulatory submissions
- ★ Possible earliest regulatory approval and market entry with product from Gilead
- ★ Possible earliest generic manufacturer(s)



Purpose 1 and 2 participants have/are transitioning to open label “choice” PrEP
 Originator Len will be made available until generics come on board

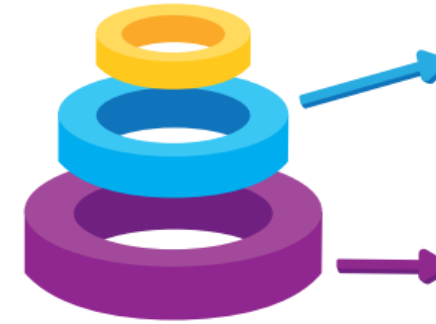
In October, Gilead announced voluntary licenses to six generic manufacturers



Precision Prevention: 3-Dimensional PrEP

- **Drug/ Modality**
 - duration of action, modality of administration
- **Disposition/season/personality**
 - cruising, discordant, holidaying
- **Delivery**
 - Courier, postal, pharmacy, clinic, self administration

3D PrEP



DRUG DETAILS

Characteristics of different PrEP products	
Systemic / Topical	Long / Short acting PK
Pills / Ring / Injectable	Side effects / Tolerability
Daily / Event driven pill	Nurse / Self / Peer administered
2m / 6m Injectable	
1M / SC Injectable	Viral resistance profile

DELIVERY

Implementation delivery modalities	
Health facility	Courier / Post bank
Mobile clinic	School / Collage
Community based	Pharmacy / Mall / Other outlet
Public / Discreet	Self-testing / POC / Lab testing

DISPOSITION

Motivations, affects, attitudes, information, perceptions, and user preferences towards product details and delivery modalities
Independent / Convenience / Discreet / Introvert / Social frequent / Intermittent / Infrequent sex
Vaginal / Anal / Other sex
Sero+ / Sero-unknown partner
Regular / Shift / Irregular working
School / Tertiary / Collage



Affordability + Availability + Demand creation + Access = IMPACT

Thank you!

Co-chairs and OC, Glasgow for this honour
Mitchell Warren and AVAC
Raphy and HPTN 083 teams
Sinead and HPTN 084 teams
Gusatvo and CONRAD
Craig Hendrix, HPTN
McKenzie Cottrell
Jenell Stewart
Huub Gelderblom, HVTN
Moupali , Jared and Purpose Teams
Kenneth Ngure and Matrix
Jeanne Marrazzo
Nora Rosenberg
Lulu and REACH
Rebeca and Merck team
Jean-Michel Molina and Ipergay Team
Elzette, Pippa, Carey and FastPrEP team



*Best Buddies
Keith Haring 1990*

Pay tribute to the YWAG and other young people who teach me EVERYDAY!!

