THE FENWAY INSTITUTE

Prevention Update from IAS 2021

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HOPE Conference

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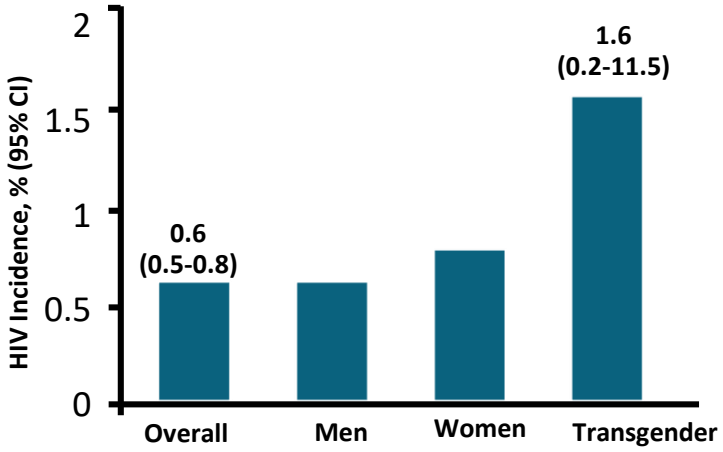
thefenwayinstitute.org

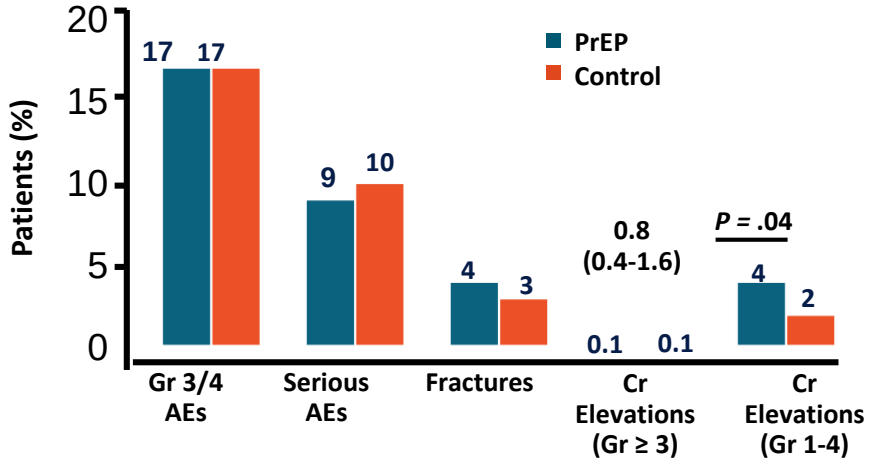
IAS 2021
18 – 21 July

Real-World Efficacy and Clinical Trial Safety of PrEP

- **46 PrEP demonstration projects [1]**
  - Overall incident HIV infections: n = 91[1]
  - Occurred > 30 days after last PrEP dose: n = 27
  - Occurred < 3 mos after starting PrEP: n = 17
  - Comparable to HIV incidence in active arms of clinical trials



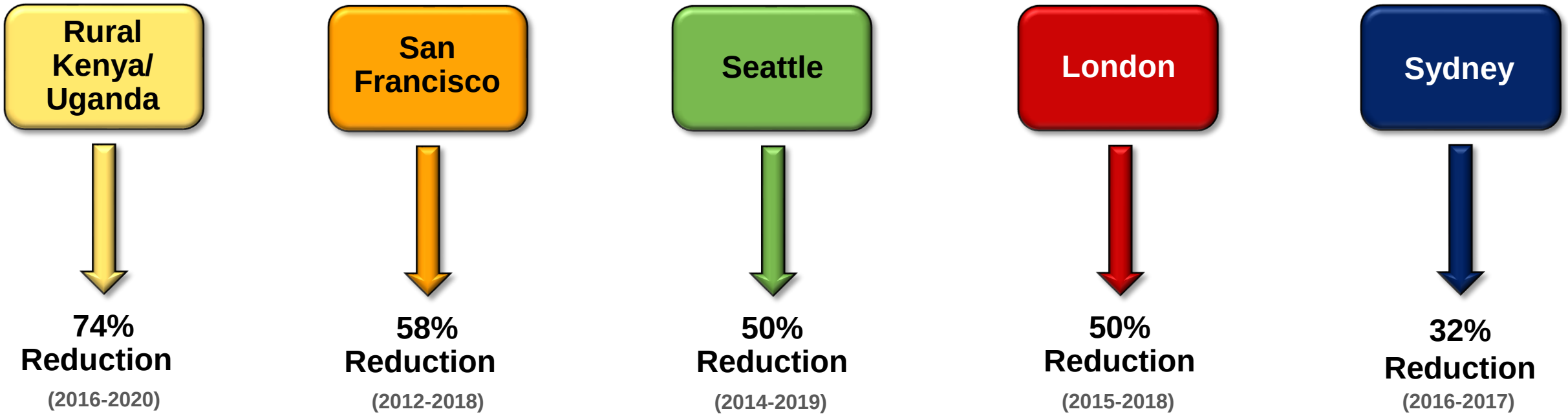
Meta-Analysis of 13 Randomized Daily Oral PrEP Trials (n = 15,678)[2]



1. Baeten. AIDS Res Hum Retroviruses. 2018;34(suppl 1):121. 2. Pilkington. J Virus Erad. 2018;4:215.

The Power of Targeted PrEP Implementation

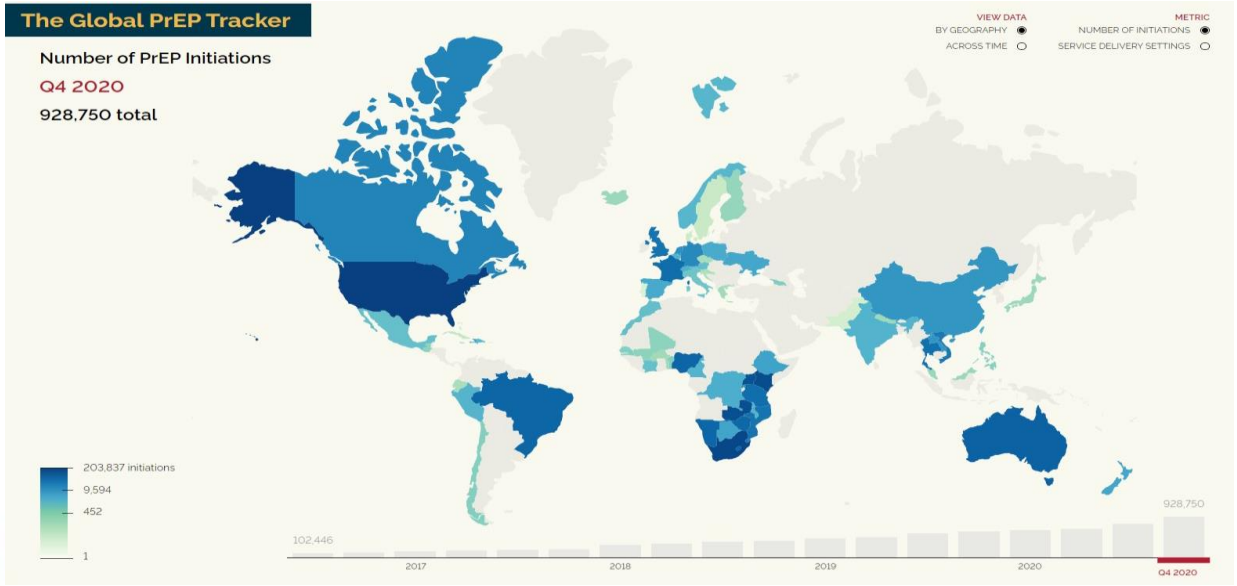
Scaling Up PrEP Access in Major Cities Has Resulted in Population-Level Reductions in HIV Risk, among PrEP Users and Non-Users Combined



Koss C, et al. *PLoS Med*. 2021;18(2):e1003492.
Buchbinder SP, et al. *J Acquir Immune Defic Syndr*. 2019;82(suppl 3):S176-S182.
Seattle & King County and the Infectious Disease Assessment Unit. HIV/AIDS Epidemiology Report 2020, Volume 89.
Public Health England. Health Protection Report. 2019;13(31).
Grulich A, et al. *Lancet HIV*. 2018;5:e629-e637.

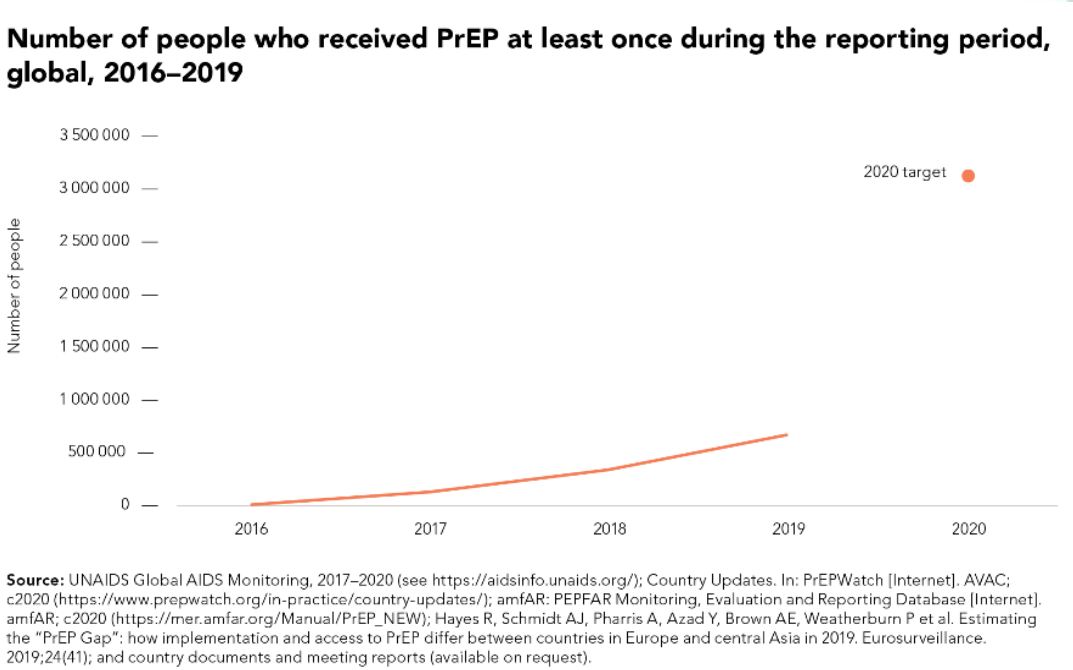
Tracking global PrEP access

By Q4 2020, oral PrEP
Included in >70 country programmes
928,750 people on PrEP world wide



USA, South Africa, Kenya, top 3 countries for PrEP initiations

Expanded PrEP access associated with reductions in HIV incidence in MSM in in Australia, USA, and UK

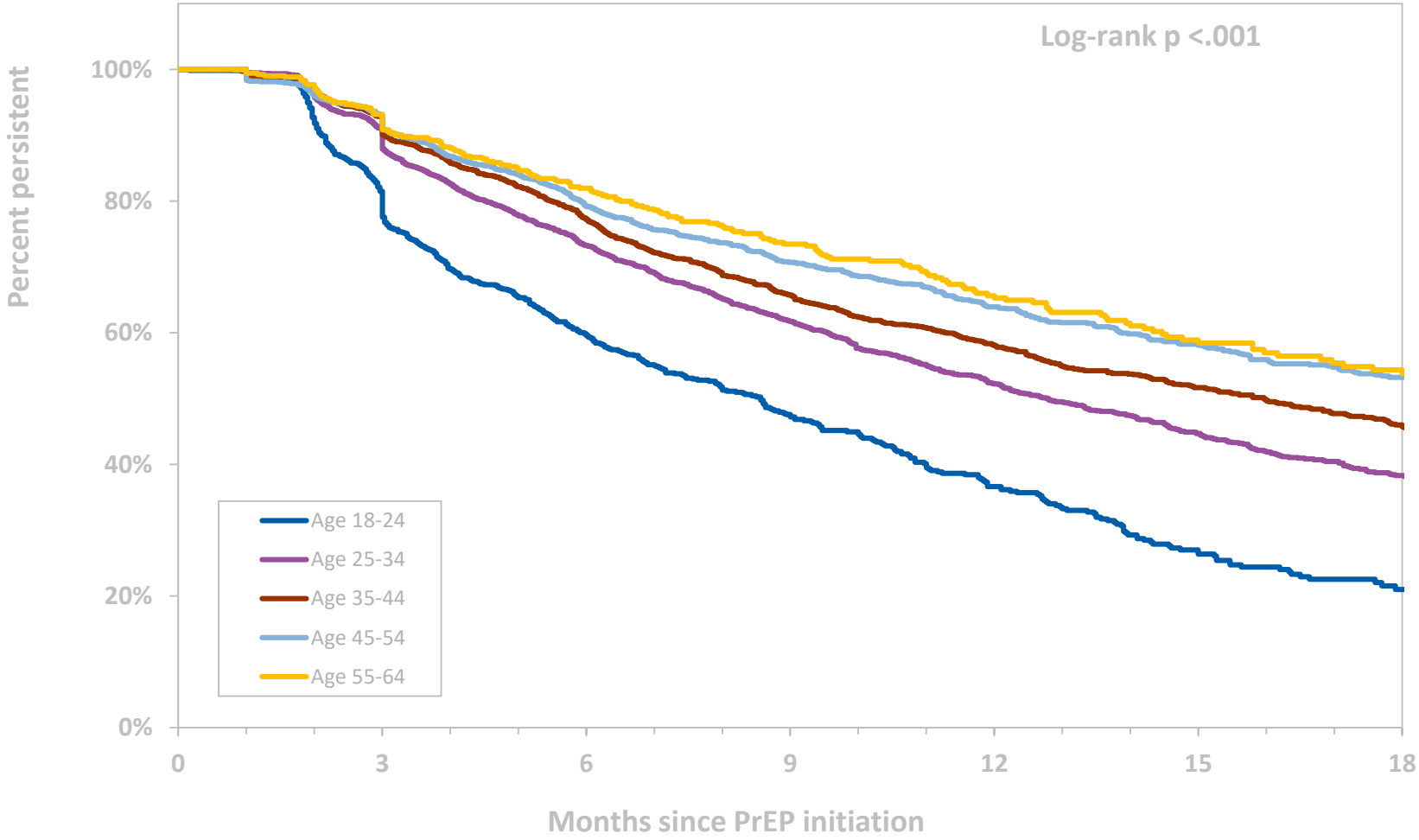


Source: UNAIDS Global AIDS Monitoring, 2017–2020 (see https://aidsinfo.unaids.org/); Country Updates. In: PrEPWatch [Internet]. AVAC; c2020 (https://www.prepwatch.org/in-practice/country-updates/); amfAR: PEPFAR Monitoring, Evaluation and Reporting Database [Internet]. amfAR; c2020 (https://mer.amfar.org/Manual/PrEP_NEW); Hayes R, Schmidt AJ, Pharris A, Azad Y, Brown AE, Weatherburn P et al. Estimating the "PrEP Gap": how implementation and access to PrEP differ between countries in Europe and central Asia in 2019. Eurosurveillance. 2019;24(41); and country documents and meeting reports (available on request).

Goal: 3 million on PrEP by 2020
Still had 1.7 million new HIV infections in 2020

www.prepwatch.org; www.unaids.org

Among commercially insured PrEP users, persistence declined significantly over time, especially in younger pts



Huang CROI 2019 #106

Real-World HIV Seroconversions in MSM on Daily PrEP

Location	Time Between PrEP Initiation and HIV Diagnosis (months)	Major Resistance Mutations	Inferred Resistance	Likely Cause of PrEP Failure (per study authors)
Toronto	24	NRTI (M41L, D67G, T69D, K70R, M184V, Y215E); NNRTI (Y181C); PI (L10I); INSTI (H51Y, E92Q)	FTC resistance TDF low-level resistance	Transmitted FTC/TDF resistance
New York City	5	NRTI (K65R, M184V) NNRTI (K103S, E138Q, Y188L)	FTC/TDF resistance	Transmitted FTC/TDF resistance
Amsterdam	8	None	None	High inoculum effect with multiple exposures and concomitant lymphogranuloma infection
Charlotte, NC	14	NRTI (M184V, K70T, K65R) NNRTI (K103N)	FTC/TDF resistance	Transmitted FTC/TDF resistance or HIV acquisition during period of low adherence
Pattaya	2	NRTI (M184V) NNRTI (A98G, K103N)	FTC resistance	Transmitted FTC or HIV acquisition very proximate to PrEP initiation
San Francisco	13	NRTI (L74V, M184V) NNRTI (L100I, K103N)	FTC resistance	Unknown

Knox DC, et al. *N Engl J Med*. 2017;376:501-502.
Markowitz M, et al. *JAIDS.* 2017;76:e104-e106.
Hoornenborg E, et al. *Lancet HIV*. 2017;4:e522-e528.
Thaden JT, et al. *AIDS*. 2018;32:F1-F4.
Colby DJ, et al. *Clin Infect Dis.* 2018;67:962-964.
Cohen SE, et al. *Lancet HIV*. 2018;Nov 29. [Epub ahead of print].

GEMS: Characteristics of Patients Who Seroconverted on PrEP

- Referrals from several large African PrEP implementation projects
- 229 reported seroconversions of >104,000 pts on PrEP between December 2017 and June 2021
- 208 (91%) patients provided a sample
  - South Africa: 79 (38%)
  - Kenya: 65 (31%)
  - Zimbabwe: 36 (17%)
  - Eswatini: 28 (13%)

Characteristic	Patients (N = 208)
Female sex, n (%)	155 (75)
Age category at seroconversion, n (%)	
▪ 16-24	108 (52)
▪ ≥25	95 (46)
▪ Unknown	5 (2)
Population, n (%)	
▪ Adolescent girl/young woman	87 (42)
▪ Serodifferent couple	50 (23)
▪ Female sex worker	20 (10)
▪ Men who have sex with men	15 (7)
▪ Transgender woman	12 (6)
▪ Pregnant or lactating	8 (4)
▪ Incarcerated	1 (<1)

Parikh. IAS 2021. Abstr OALC01LB02.

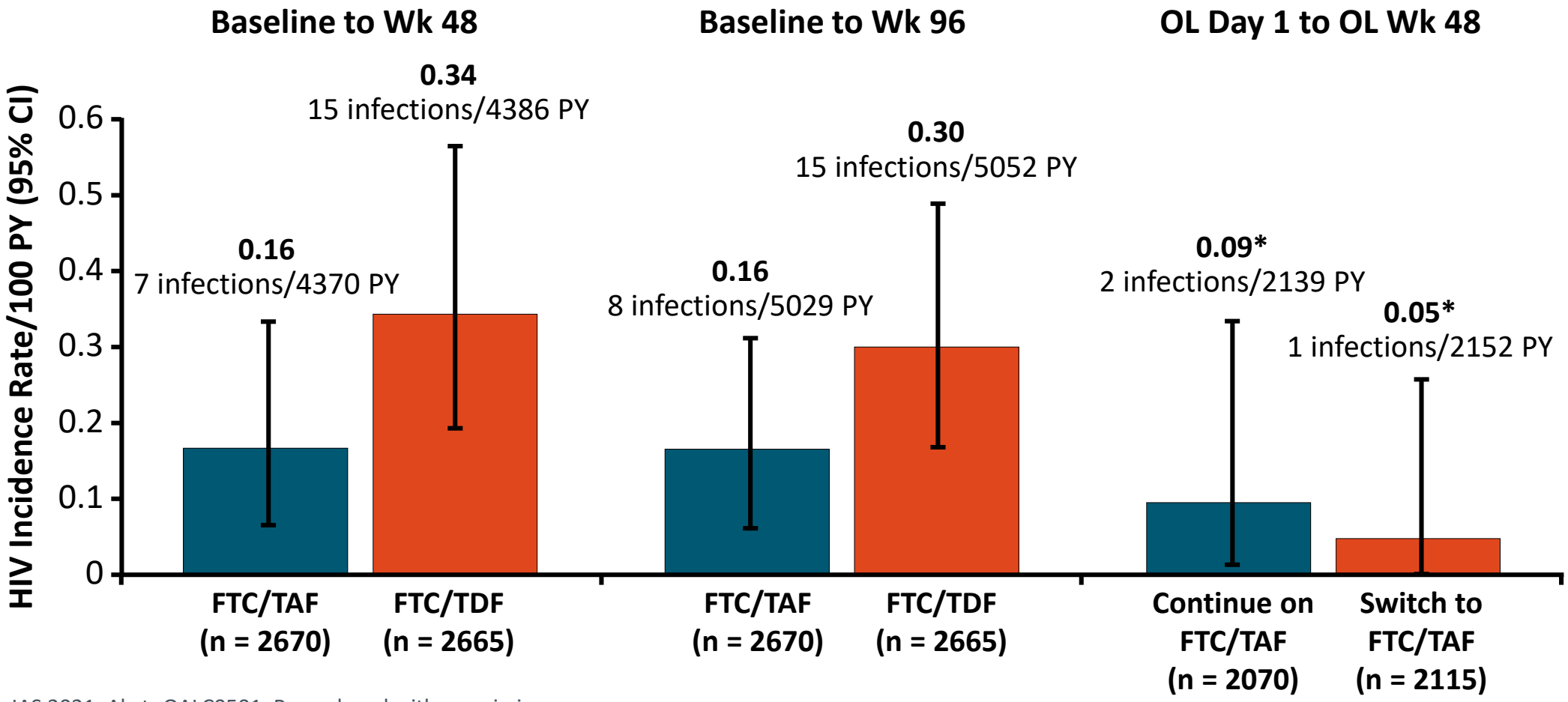
GEMS: Conclusions

- Number of reported HIV infections in patients on PrEP in Sub-Saharan Africa extremely small (229 out of >104,000 estimated to be on PrEP), but ART resistance frequency in these patients with breakthrough infections was high
- Of the 118 patients with breakthrough infections and successfully sequenced samples:
  - 22% had NNRTI mutations only, signifying background transmitted resistance
  - 23% had PrEP-associated mutations, the majority of which had TFV-DP levels that correlated with high rates of adherence (c/w transmitted resistance)
- Authors conclude that accurately diagnosing acute HIV infection prior to PrEP initiation, and monitoring for HIV drug resistance on PrEP, is essential to preserve ART options for treatment and prevention

Parikh. IAS 2021. Abstr OALC01LB02.

DISCOVER: HIV Incidence Through Open-Label Wk 48

- Switch to FTC/TAF associated with low HIV infection rate



Spinner. IAS 2021. Abstr OALC0501. Reproduced with permission.

DISCOVER Open-Label Phase: Changes in Metabolic Indicators, Renal Biomarkers From Baseline to Wk 48

- Prior to switch, participants receiving FTC/TDF had significantly lower eGFR, HDL, LDL, and weight and numerically lower bone mineral density in hip and spine vs those who received FTC/TAF

Median Δ From OL Baseline to Wk 48	Continue on FTC/TAF (n = 2070)	Switch to FTC/TAF (n = 2115)	*P* Value
Bone mineral density, %	(n = 111)	(n = 106)	
▪ Hip	0.20	0.86	.03
▪ Spine	-0.06	1.18	.0012
Renal function			
▪ eGFR, mL/min	-2.8	0.3	<.0001
▪ β2M:Cr, %	-7.3	-30.8	<.0001
▪ RBP:Cr, %	-9.9	-26.8	<.0001

Median Δ From OL Baseline to Wk 48	Continue on FTC/TAF (n = 2070)	Switch to FTC/TAF (n = 2115)	*P* Value
Fasting lipids, mg/dL			
▪ Total cholesterol	9	22	<.01
▪ LDL	7	13	<.01
▪ HDL	0	3	<.01
▪ Triglycerides	8	16	<.01
Fasting glucose, mg/dL	2	1	0.86
Weight, kg	1.2	2.0	<.01

- Switch to TAF associated with improvements in renal function and BMD and lipid increases, but also modest changes in lipids and weight

Spinner. IAS 2021. Abstr OALC0501.

On Demand PrEP (2.1.1)

- IPERGAY: double-blind, randomized, placebo-controlled study showed on-demand FTC/TDF PrEP (taken before and after sex) highly effective in preventing HIV infection among MSM[1]
  - Relative reduction in HIV incidence with on-demand FTC/TDF vs placebo: 86% (95% CI: 40-98; *P* = .002)
  - Relative reduction in HIV incidence during open-label extension phase: 97% (95% CI: 81-100)[2]
- Prevenir study of at risk Parisian MSM evaluated open label on-demand vs. daily FTC/TDF PrEP, finding HIV incidence of 0.12% in each group[3] About half of the pts picked either strategy, and about ¼ switched over time.

1. Molina. NEJM. 2015;373:2237. 2. Molina. Lancet HIV. 2017;4:e402. 3. Molina. CROI 2021. Abstr 148.

PREVENIR/Sapris-Sero Substudy: Incidence of SARS-CoV-2 in People Using TDF/FTC-Based PrEP

- Lower risk of COVID-19 and COVID-19–related hospitalization observed among cohort of 77,590 PWH receiving TDF/FTC vs other HIV therapies[1]
- Matched-cohort analysis compared seroprevalence of SARS-CoV-2 IgG in[2]:
  - **Exposed group:** Men enrolled on PREVENIR study receiving on-demand or daily TDF/FTC PrEP and with an available HIV-1 RNA sample between May and October 2020
  - **Matched control group:** Men included in Paris region of Sapris-Sero survey of SARS-CoV-2 antibody prevalence in general population of France
  - Participants matched based on age (± 5 yr), socio-occupational category, and sample date (± 1 mo); when all 3 not possible, matched by age + occupation, then age + sampling date, then age alone
- Primary objective: proportion of patients with positive* SARS-CoV-2 anti-spike IgG

*Low positive/undetermined considered as negative.

1. del Amo. Ann Intern Med. 2020;173:536. 2. Delaugerre. IAS HIV Science 2021. Abstr OAC0201.

PREVENIR/Sapris-Sero Substudy: IgG Spike Seroprevalence

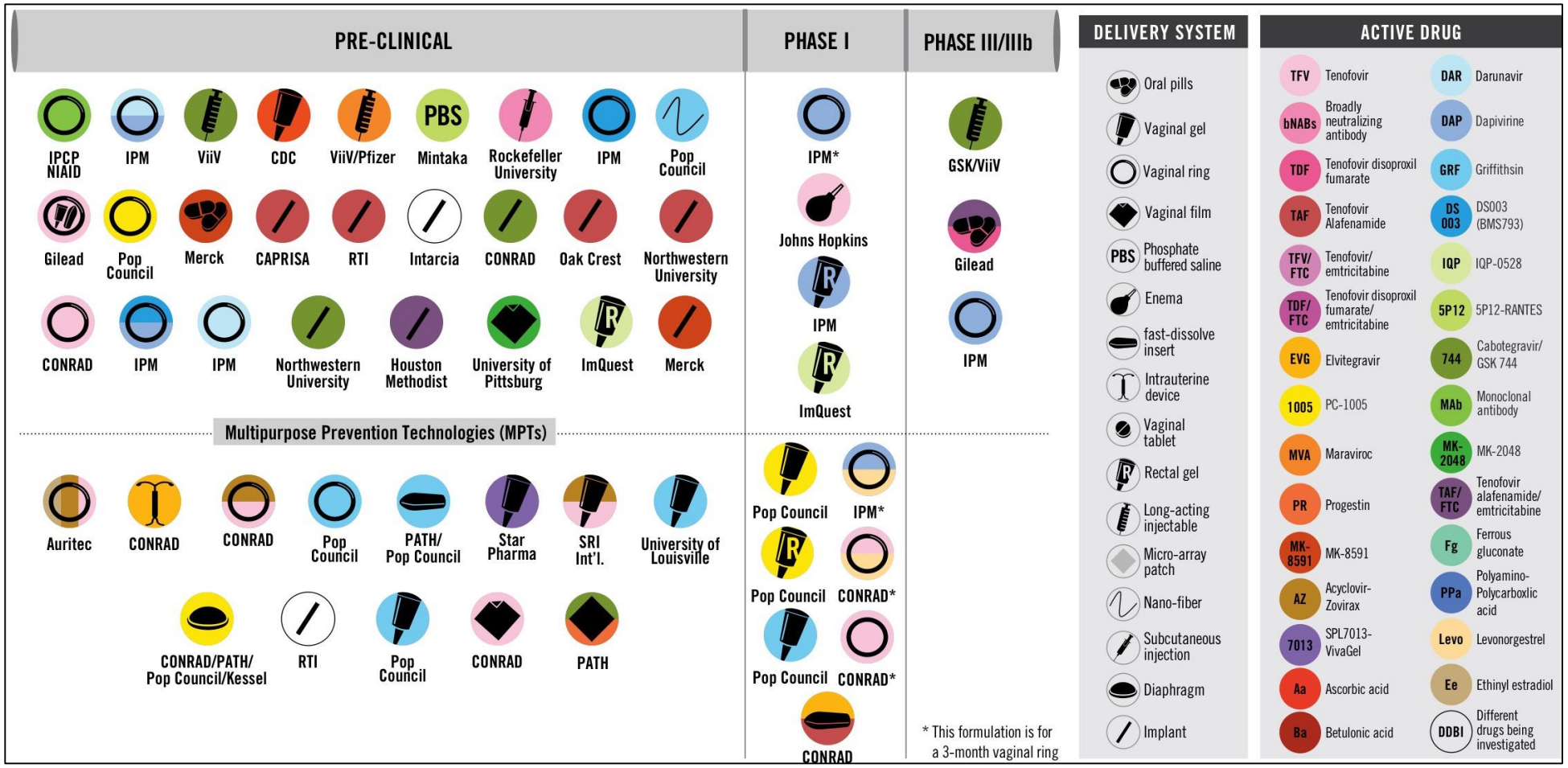
Serology Outcome, n (%)	PrEP Exposed	Unexposed	*P* Value
Whole population (n = 844)			
▪ Limit/weak positive	4 (0.5)	28 (3.3)	
▪ Negative	753 (89.2)	738 (87.4)	
▪ Positive	87 (10.3)	78 (9.2)	.4700
Full matched population (all 3 criteria, n = 730)			
▪ Limit/weak positive	4 (0.5)	22 (3.0)	
▪ Negative	652 (89.3)	642 (88.0)	
▪ Positive	74 (10.1)	66 (9.0)	.1876

- Results same when considering weak positive as positive
- PrEP regimen (daily vs on-demand) did not affect SARS-CoV-2 seroprevalence (positive rate 9.2% in those receiving daily TDF/FTC vs 11.5% in those receiving on demand; *P* = .28)
- **Investigators suggest TDF/FTC PrEP does not reduce risk of SARS-CoV-2 infection**

Delaugerre. IAS HIV Science 2021. Abstr OAC0201.

Slide credit: clinicaloptions.com

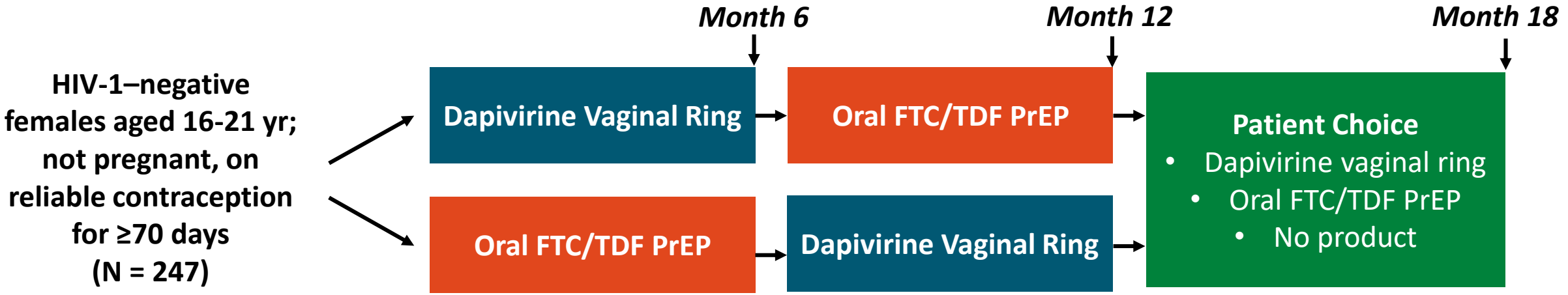
Next Generation PrEP



www.avac.org

REACH: Dapivirine Intravaginal Ring Phase IV Study

- Randomized, open-label, phase IIa crossover study



Note: Adherence support and counseling included for all patients.

- Endpoints: safety (AEs ≥ grade 2), adherence, acceptability, preference

Adherence	DPV (Rate Based on No. Returned Rings)	FTC/TDF (Measured via Dried Blood Spots)
High	≥0.1071 mg/day	≥4 doses/wk (>500 fmol/punch at Wk 4, >700 fmol/punch at Wk 8)
Medium	0.0321- <0.1071 mg/day	~1-3 doses/wk (16.6-499 fmol/punch at Wk 4, 16.6-699 fmol/punch at Wk 8)
Low	≤0.0321 mg/day	No drug detected (<16.6 fmol/punch)

Nair. IAS 2021. Abstr OALC01LB01.

REACH: Adherence, Compliance, Acceptability, and Key Outcomes Through Month 12

Outcome, %	Dapivirine Vaginal Ring	Oral PrEP
Adherence		
▪ High	50.2	58.6
▪ Medium	45.4	39.9
▪ Low/none	4.4	1.5
Compliance*		
▪ Full compliance	50.2	22.4
▪ Below full compliance	49.8	77.6
Acceptable		
▪ Yes	88.5	63.9
▪ No	11.5	36.1

* Full compliance to ring defined as leaving the ring in place a full month; full compliance to oral PrEP defined as 6+ doses per week.

- HIV-1 incidence: 0.5/100 woman-yr (1/247)
- Pregnancy incidence: 1.8/100 woman-yr (4/247)

Nair. IAS 2021. Abstr OALC01LB01.

REACH: Conclusions

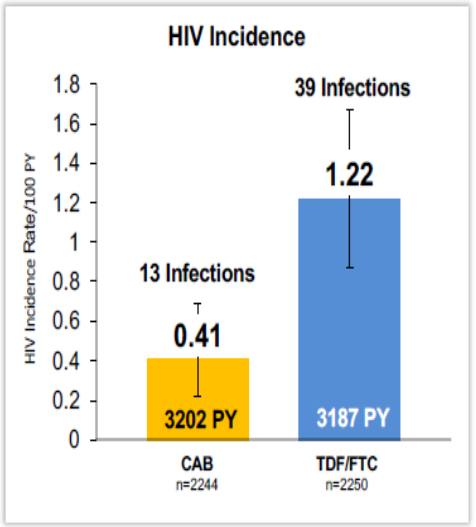
- In this open-label crossover study, adherence to the dapivirine vaginal ring and oral PrEP was higher than anticipated among adolescent girls and young women in Africa at 50% and 59%, respectively
- Both options well tolerated and rated as highly acceptable by participants
- Investigators conclude that the dapivirine vaginal ring is a promising new option for HIV-1 prevention, and they stress that adherence to both the vaginal ring and oral PrEP can be achieved with tailored adherence support
- EMA and a few African countries have approved its use. US FDA application is under review.

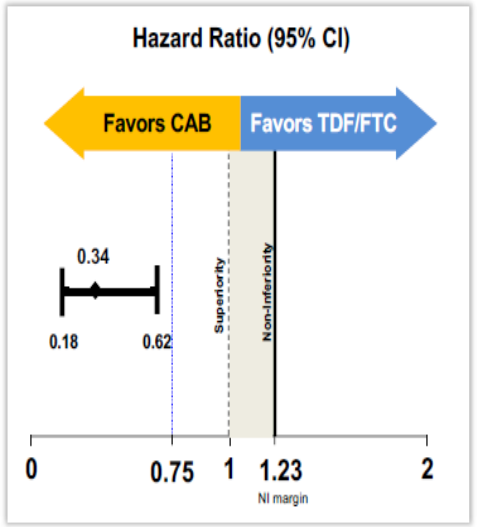
Nair. IAS 2021. Abstr OALC01LB01.

Injectable Cabotegravir

HIV Incidence
CAB vs. TDF/FTC

52 HIV infections in 6389 PY of follow-up
1.4 (IQR 0.8-1.9) years median per-participant follow-up
Pooled incidence 0.81 (95%CI 0.61-1.07) per 100 PY





CI, confidence interval

Landovitz RJ et al. AIDS 2020, #OAXLB01

HPTN HIV Prevention Trials Network

Primary outcome: HIV incidence

40 infections over 3892 person-years
Pooled HIV incidence 1.03 (0.73, 1.4) per 100 person-years

	CAB	TDF/FTC
HIV infections	4	36
Person-years	1,953	1,939
HIV incidence (95% CI)	0.2 (0.06, 0.52)	1.86 (1.3, 2.57)

Wald test z statistic – 4.20, efficacy stopping bound (z scale) – 3.61

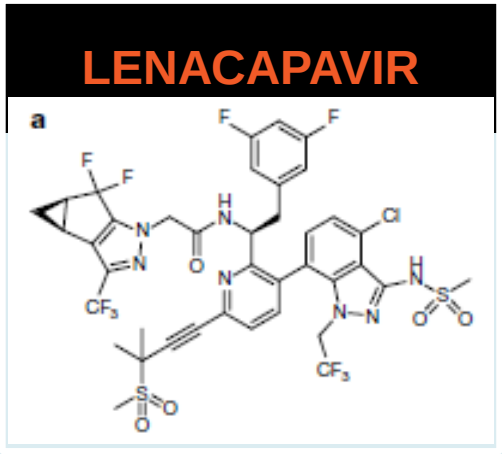
- **Pooled incidence in both trials lower than previously observed in the community**
- **Both trials showed superiority of CAB-LA against a highly effective TDF/FTC control**
- **CAB-LA well tolerated despite injection site reactions**

HPTN 083

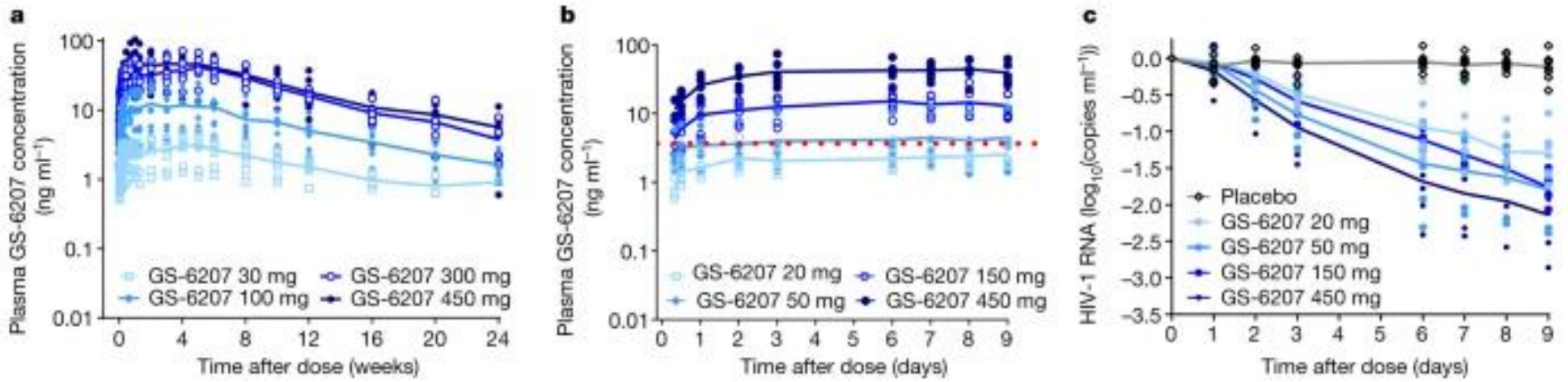
- 2.2% discontinued injections because of discomfort
- Of 12 incident HIV infections in CAB arm, 8 were in pts who were either acutely HIV infected, or non-adherent; 4 observed in participants with on-time injections: under further study (at least 2 were early, raising questions about adherence during one month oral lead in period)
- Detection of HIV infection using standard testing algorithms delayed in patients receiving CAB LA (good reason to check HIV RNA prior to initiation)
- INSTI resistance: rare, but prompt diagnosis and initiation of ART are important to avoid resistance with CAB LA
- Mild weight gain in CAB arm
- Suboptimal adherence observed in 37/39 incident infections in FTC/TDF arm

Lenacapavir (GS-6207):

Agent class:
HIV-1 capsid inhibitor



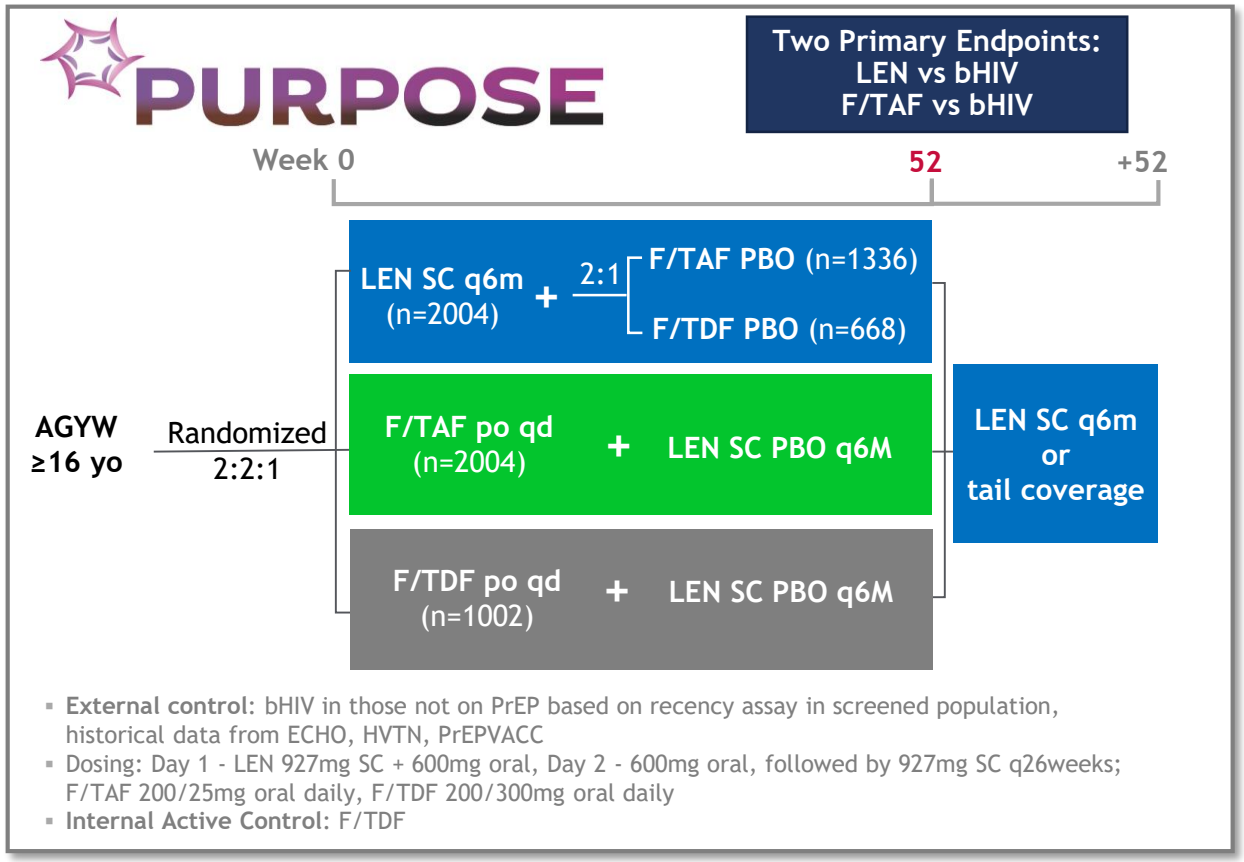
Dosing Strategy:
One injection every 6 months (ARVs that you only need to take twice a year!)



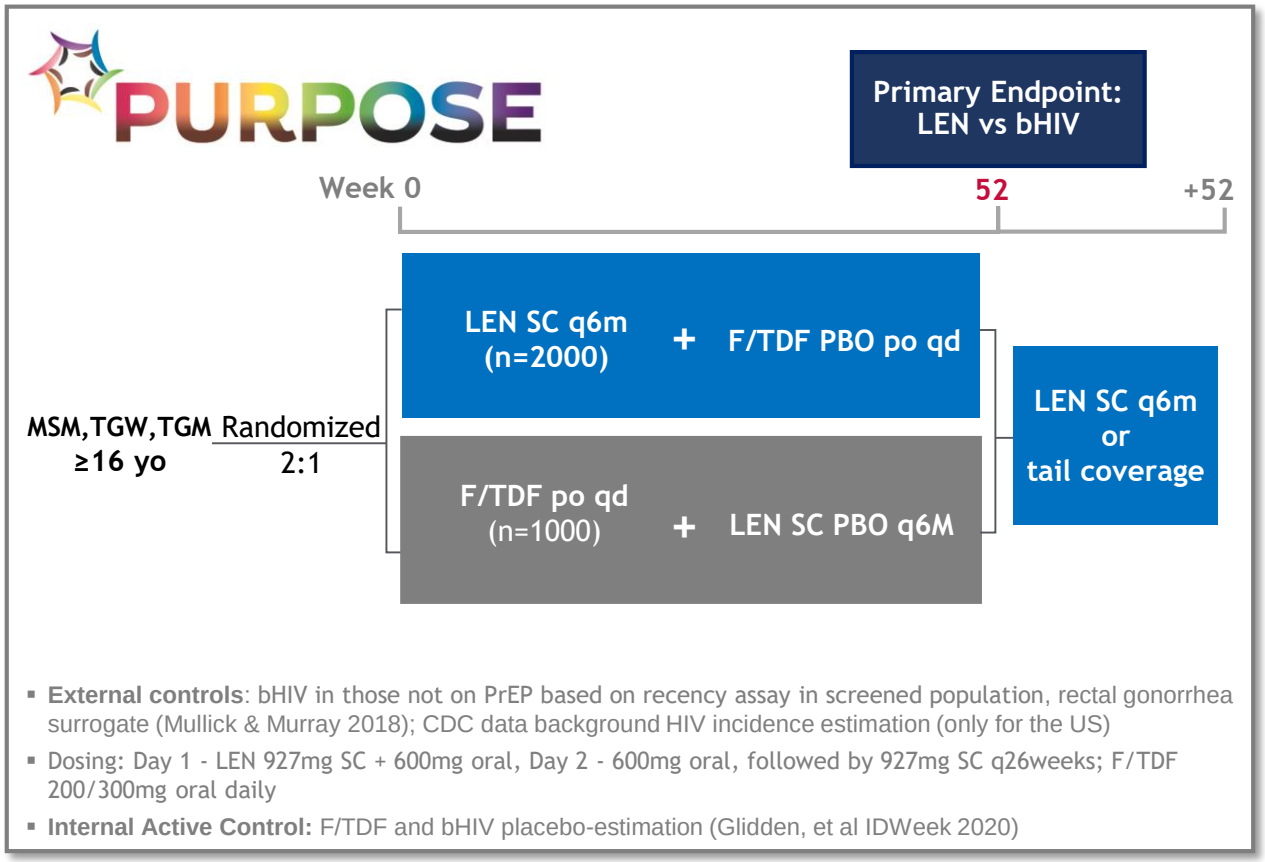
Mean plasma concentration-time profiles of Lenacapavir after a single injection to individuals uninfected with HIV (Graph A, n=8) and individuals living with HIV (Graph B, n=6).

Graph C: Mean log10 transformed change in plasma HIV-1 RNA in individuals with untreated HIV-1 infection (drug, n = 6 and placebo, n=2)

LEN for Pre-Exposure Prophylaxis (PrEP): The PURPOSE Studies



- **External control:** bHIV in those not on PrEP based on recency assay in screened population, historical data from ECHO, HVTN, PrEPVACC
- Dosing: Day 1 - LEN 927mg SC + 600mg oral, Day 2 - 600mg oral, followed by 927mg SC q26weeks; F/TAF 200/25mg oral daily, F/TDF 200/300mg oral daily
- **Internal Active Control:** F/TDF



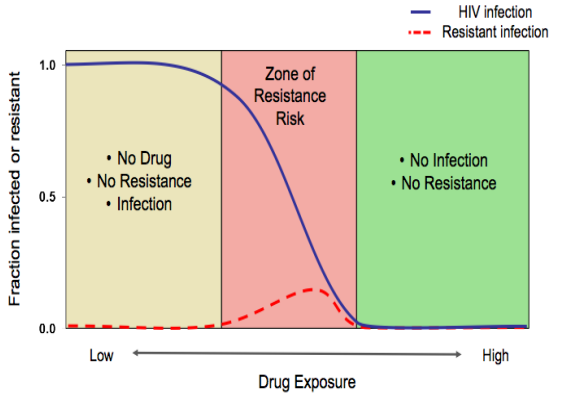
- **External controls**: bHIV in those not on PrEP based on recency assay in screened population, rectal gonorrhea surrogate (Mullick & Murray 2018); CDC data background HIV incidence estimation (only for the US)
- Dosing: Day 1 - LEN 927mg SC + 600mg oral, Day 2 - 600mg oral, followed by 927mg SC q26weeks; F/TDF 200/300mg oral daily
- **Internal Active Control:** F/TDF and bHIV placebo-estimation (Glidden, et al IDWeek 2020)

These proposed studies will use a counterfactual analysis to determine efficacy

AGYW, adolescent girls and young women; bHIV, background HIV incidence; LEN, lenacapavir; PBO, placebo; SC, subcutaneous
Data on file, Gilead Sciences

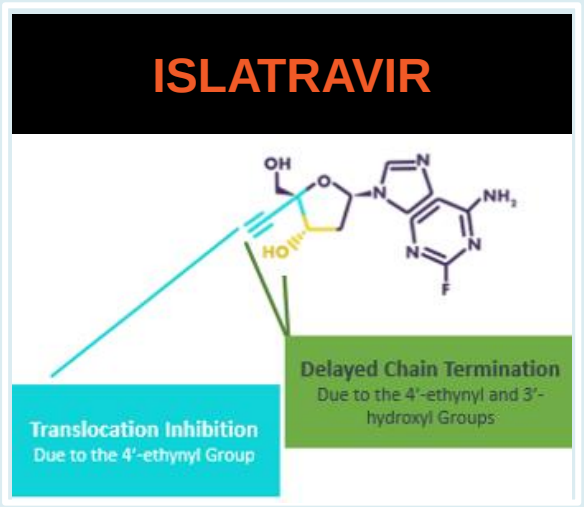
LA injectables PrEP: Pros and Cons

YES!	More thought needed
Improved adherence	Understanding the “long tail” implications
Less frequent reminding	Access when travelling or away from home base
potentially healthcare visits	Accredited administrators – trained individuals to administer
Discreet – easier to keep private than pills	Still need to consider intimacy & other SRH needs, eg timing with LARC



Islatravir (ISL, MK-8591):

Nucleoside Reverse Transcriptase Translocation Inhibitor (NRTTI)

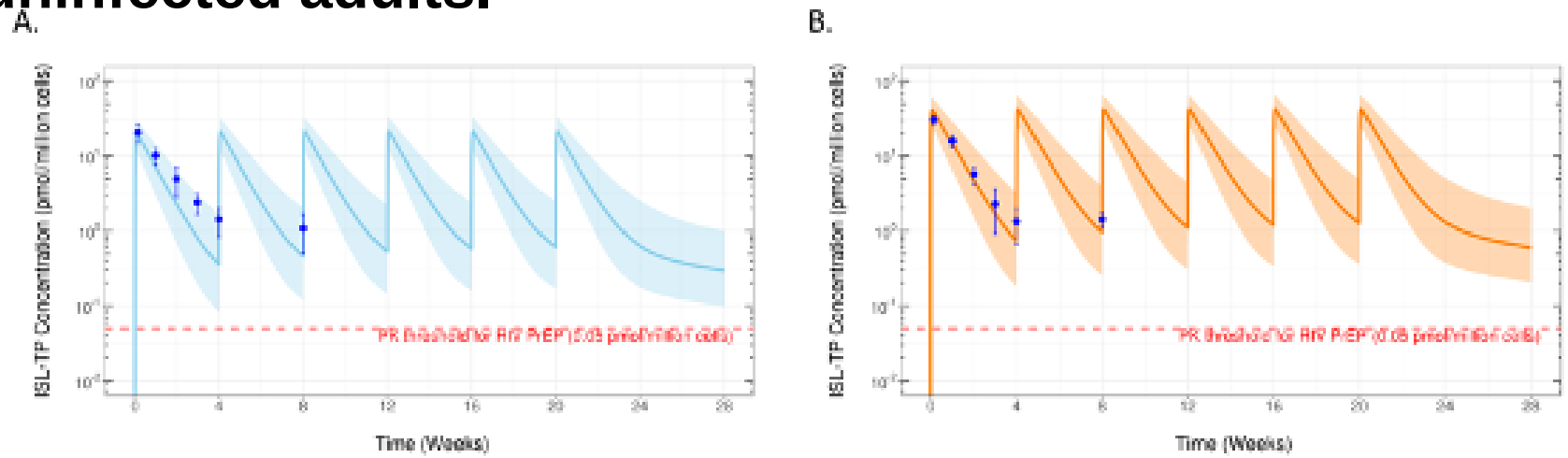


Novel mechanism of action, being developed as a monthly pill and an implant for prevention

Demographics, blinded safety and pharmacokinetics (PK) data from a phase 2a trial of Islatravir once monthly (QM) for HIV PrEP

HIV VIRTUAL AN IAS CONFERENCE

Half-life in PBMCs approximately 190 hrs after oral dose in uninfected adults.



Shaded area represent 95% Prediction Interval (N=1000 simulations); Solid lines represent the pop PK model predicted median concentration; Blue filled circles represent mean of P016 interim observed data; Blue error bars represent standard deviation of P016 interim observed data

Interim analysis suggests that monthlyISL 60 mg and 120 mg achieved pre-specified efficacious PrEP PK threshold. Blinded safety data indicate that ISL was well tolerated.

ISL QM Oral Prep – Ongoing Clinical Development Program

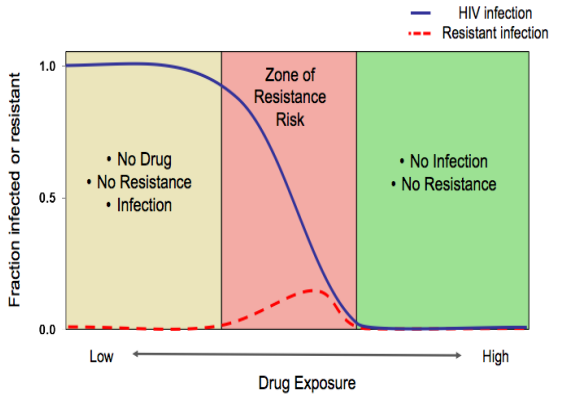
	Trial name (protocol number)	Population	Active comparator	ClinicalTrials.gov
Phase 3	IMPOWER-022	Cisgender women at high risk of HIV-1 infection	FTC/TDF	NCT04644029
	IMPOWER-024	Men and transgender women who have sex with men and are at high risk for HIV-1 infection	FTC/TDF or FTC/TAF	NCT04652700

IMPOWER 022 will be done in collaboration with the Bill & Melinda Gates Foundation which intends to provide grant funding to the International Clinical Research Center (ICRC) at the University of Washington Department of Global Health who will be working together with MSD to conduct the trial

Hillier S, IAS 2021: ISL q monthly was found to be safe and well-tolerated in Phase II study

Less frequent and alternative dosing

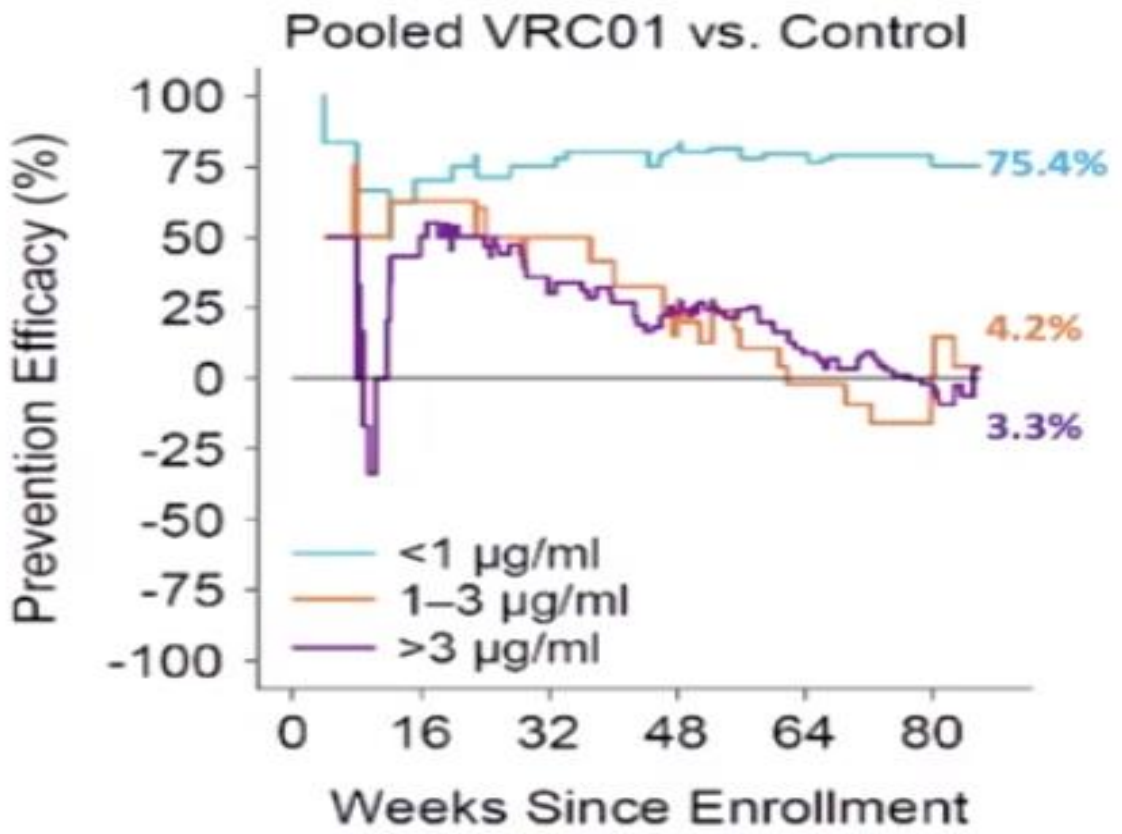
YES!	More thought needed
Improved adherence	Understanding PK and stopping and starting
Less frequent reminding	Managing frequency and place of clinic visits
Fewer healthcare visits	Service distribution models and service providers
Discretion	Still need to consider intimacy & other SRH needs, eg timing with LARC



Broadly neutralising antibodies

Key messages from AMP trials

- **Biological success against viruses with IC80 of1μg/ml, not clinically relevant as these were only 30% circulating strains**
- **Very acceptable to trial participants, but have to be realistic about service delivery**
- **Critical to work on formulations that can be stored and administered at home (SC) or last for longer (6-12m)**
- **Cannot ignore cost and differential spend on prevention compared to treatment**



HIV-Specific Neutralizing Antibodies by Target

This graphic depicts HIV's spike protein—or envelope (Env) protein—and broadly neutralizing antibodies that target key regions that play a role in infection of human (host) cells. Antibodies listed in color are those that have been through any phase of clinical testing.

gp41 MPER

Helps disrupt viral membrane during fusion of HIV with host cell.

MPER: Membrane-proximal external region

2F5 4E10 10E8VLS 10E8.4

Fusion peptide

Inserts into and disrupts host cell membrane, allowing HIV to release genetic material into the cell.

ACS202 VRC34.01

gp120-41 interface

Where gp120 and gp41 meet; involved in structural changes to the Env protein during entry into the host cell.

35022 LN02 SANC 195
8ANC195 PGT151

V3-glycan

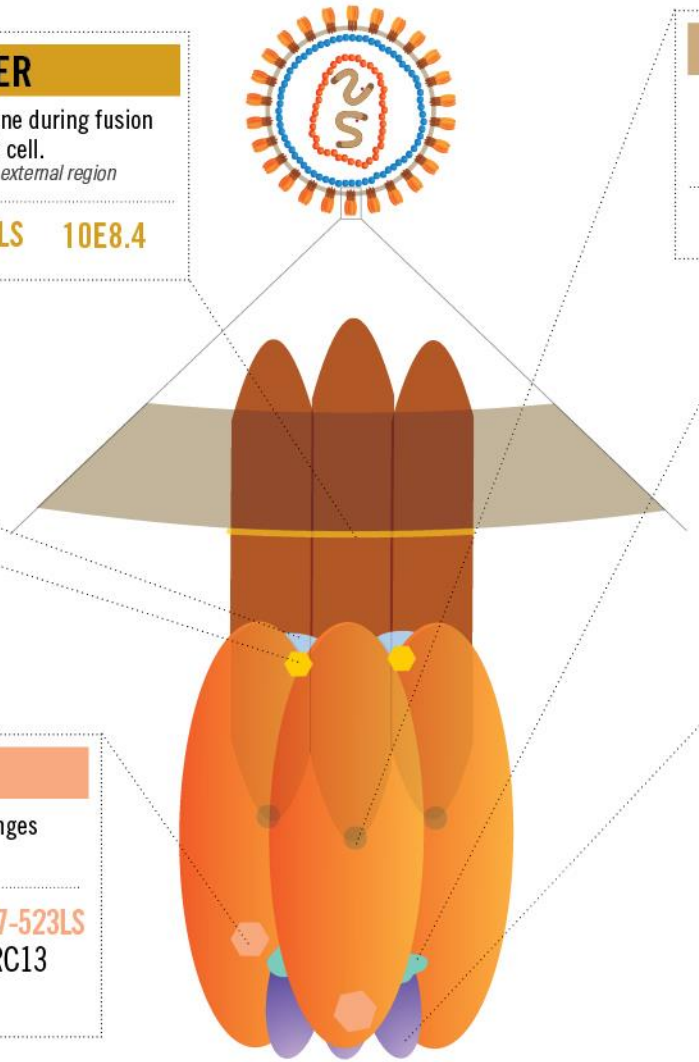
Involved in the initial interaction and resulting fusion between the Env protein and a coreceptor in the host cell membrane.

10-1074 DH270 PGT121.414.LS
10-1074LS PGT121 PGT128
10-1074LSJ PGT121LS PGT135

gp120 Silent face

A region of the Env protein that is heavily sugar-coated and has little functional role in virus entry.

SF12 VRC-PG05



V1/V2-glycan

Involved in a structural change to the Env protein enabling HIV to fuse and infect the host cell.

CAP256V2LS CH01-04 PG9 PG16 PGDM1400 PGDM1400LS PGT141-145

CD4 binding site

Binds to the CD4 receptor on the surface of the host cell, causing structural changes that allow the gp120 protein to bind to the host cell membrane.

3BNC117 3BNC117LS 3BNC117LSJ 12A12 BANC131 CH103 CH235.12 CH31 N49P7 N6LS NIH 45i PG04 VRC01 VRC01LS VRC07 VRC07-523LS VRC13

AVAC 25 Years and Counting www.avac.org January 2021

MPTs in Clinical Trials

Product Candidate	Development Stage	Prevention Indications
IVRs		
Dapivirine + levonorgestrel IVR	Phase I	HIV, pregnancy
Tenofovir IVR	Phase II	HIV, HSV-2
Vaginal and Rectal Gels		
MIV-150 (investigational NNRTI) + zinc acetate in carrageenan gel (PC-1005)	Phase II	HIV, HPV, HSV-2
EVO100 gel (modulates vaginal pH)	Phase III	Chlamydia, gonorrhea, pregnancy
Fast-Dissolving Vaginal Insert		
Tenofovir alafenamide/elvitegravir topical insert	Phase I	HIV, pregnancy
Vaginal Film		
MB66 film (contains mAbs against HIV-1 and HSV-1 and -2)	Phase I	HIV, HSV-2
Oral Tablet		
Dual prevention pill (containing oral PrEP and oral contraception)	Phase IV	HIV, pregnancy

Palanee-Phillips. HIVR4P 2021. Abstr S10.04.

New PrEP Product Preferences

- **Data Source: American Men's Internet Survey**
  - **Large annual, cross-sectional online survey since 2013**
  - **n=10,000 cisgender men**
  - **Ages 15+**
  - **Identify as gay, bisexual, and/or reported sex with men**
  - **US & territories**

- **Discrete-Choice Experiment (DCE)**

American Men's Internet Survey

- **Preference heterogeneity: variation in what users will value & will avoid**
  - **➔ Audience segmentation**
  - **➔ Tailor messaging & approaches to implementation**

Cost Conscious Class	Side Effects Adverse Class	Stigma-Conscious Class
Public & private insurance coverage **Subsidies & Lower costs** **Messaging: "Free!"**	**Reassure clients: "some pain at the injection site"** **Messaging: Report actual side effects to assuage misconceptions & fears**	**Emphasize privacy & confidentiality** **Decrease frequency of injections (future formulations)** **Messaging: Normalize & de- stigmatize PrEP use**

PrEP use among MSM is associated with high rates of bacterial STIs

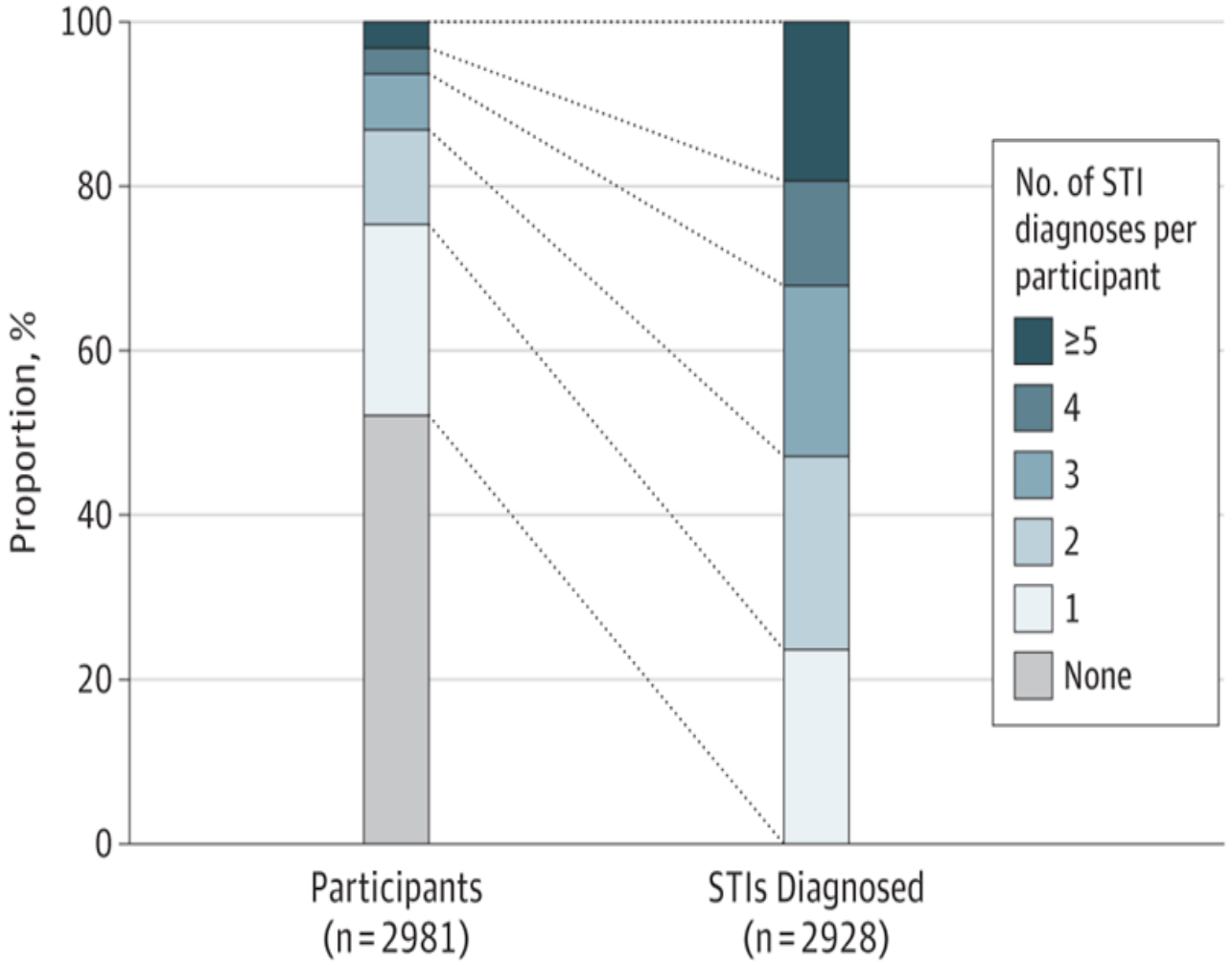
PrEPX: open-label study in Victoria, Australia (n=4275 MSM)

STI incidence: 91.9 per 100 py

25% participants accounting for 76% of all STIs

STI incidence increased by 12% after adjusting for increased testing

Frequent STI screening is important

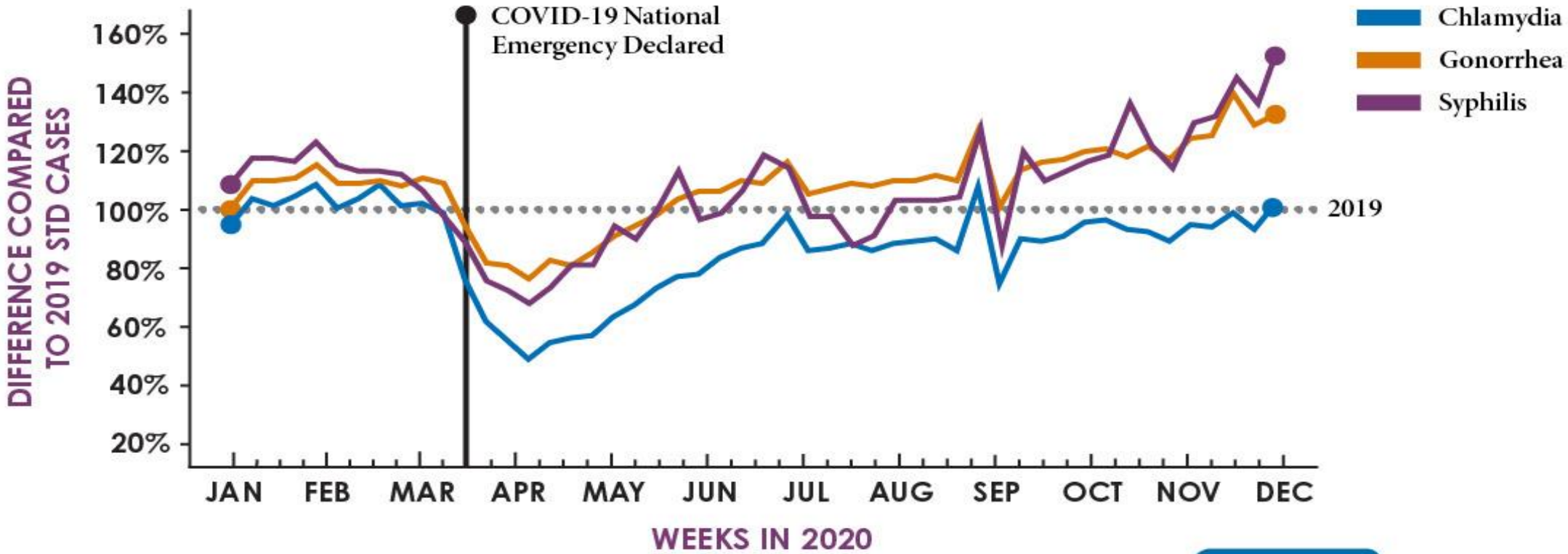


Traeger M et al, JAMA, 2019

WEEKLY REPORTED U.S. STD CASES: 2020 VS. 2019

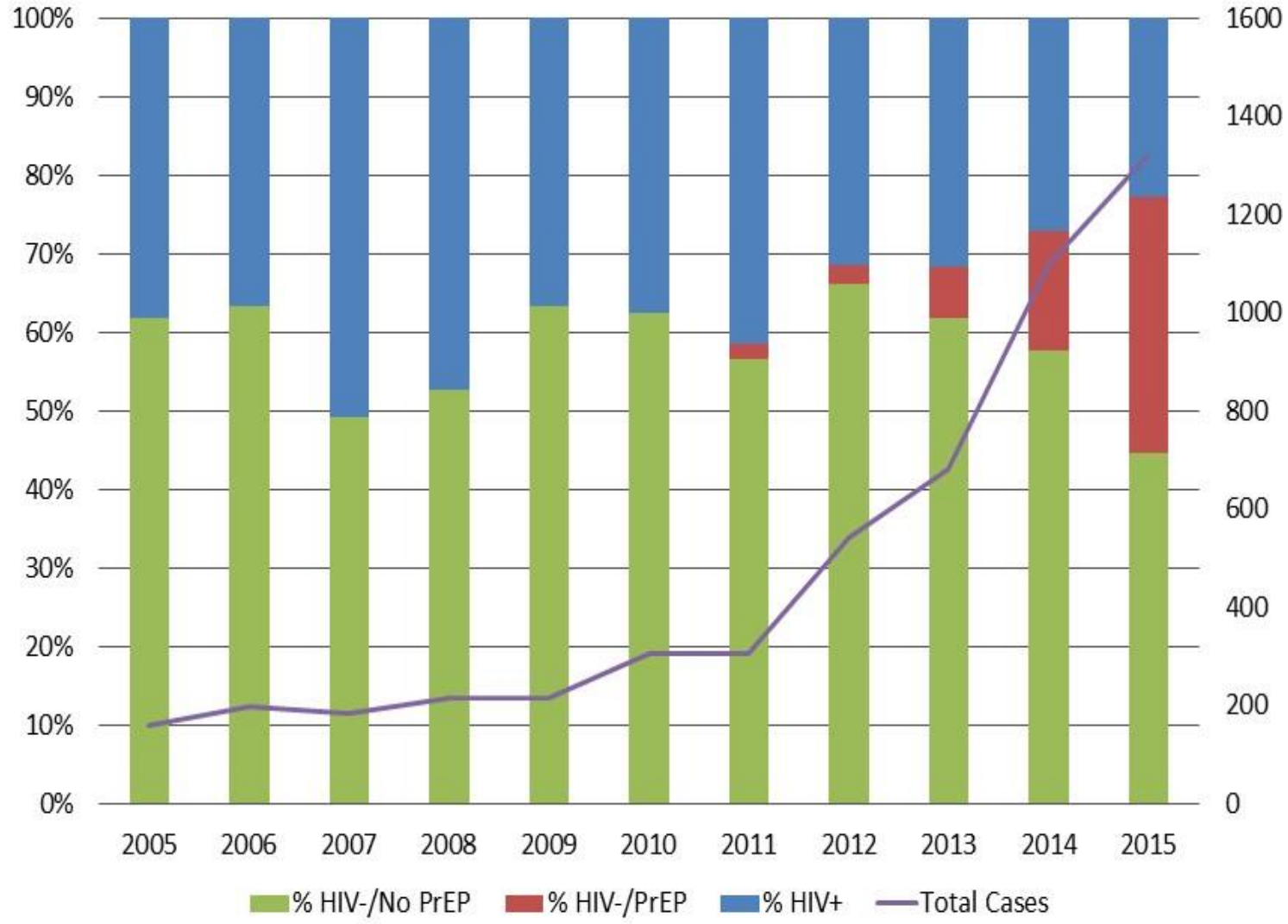
AFTER COVID-19 STAY-AT-HOME ORDERS, WEEKLY STD CASES DROPPED▼
to 50% (chlamydia), 71% (gonorrhea), and 64% (syphilis) compared to their 2019 levels.

AT THE END OF 2020, REPORTED STD CASES RESURGED▲



For more information, visit
cdc.gov/nchhstp/newsroom

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention



More than U=U and PrEP

- **Social media**
- **Sex Networking sites**
- **In US, ACA**
- **Extragenital Screening**

Schillinger, CROI, 2018

PrEP as a gateway to care: Fenway Health

Primary care utilization by PrEP users and non-users– Fenway Health, 2012-2016 (N=5,857)	
Flu vaccination	**1.57 (1.47-1.67)**
Tobacco screening	**1.13 (1.09-1.16)**
Depression screening	**1.18 (1.15-1.22)**
Hemoglobin A1c or glucose testing	**1.83 (1.75-1.92)**
Hemoglobin A1c testing	0.89 (0.79-1.01)
Glucose testing	**2.03 (1.93-2.14)**

Prevalence ratios obtained from Poisson models with generalized estimating equations. Adjusted models included age, gender, race/ethnicity, insurance type, and year, with diabetes, hypertension, and overweight/obesity additionally included in models for hemoglobin A1c and glucose testing.

Marcus et al.; AJPH, 2018

Conclusions

- The uptake of PrEP biobehavioral HIV prevention modalities has been suboptimal to date.
- The development of new approaches will offer opportunities for less frequent dosing, culturally congruent modes of delivery, and the possibility of MPTs.
- Future prevention may include antibody “cocktails” and vaccines, but for the time being antiretrovirals are the mainstay.
- Insufficient adherence and decreased rates of uptake are not exclusively due to dislike of daily pill taking
- For PrEP to achieve its promise, social/structural and individual behavioral issues (ranging from poverty, violence/victimization, to depression and substance use) must be addressed.