

HIV PrEP

Pre-Exposure Prophylaxis

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University of Kentucky College of Pharmacy



Objectives

- Review basic concepts surrounding HIV prevention.
- Discuss the efficacy of HIV Pre-exposure Prophylaxis.
- Explain the concept of U=U (undetectable equals un-transmittable).
- Review HIV post-exposure prophylaxis (PEP).

Disclosures

None to report.

**A 25 YO M presents
for a PCP visit and
requests HIV PrEP**



Eligibility

Any sexually active individual should have PrEP discussed/considered as an option.

Risk criteria & other screening tools no longer considered necessary nor appropriate.

Definitions / Acronyms

TasP

PEP

nPEP

PrEP

U=U

The Prevention Archives

Circumcision

Condoms

**Needle
Exchange**

**Perinatal
AZT**

Education

PrEP Background

99% RR (69-100%) after 5 Daily Doses
90% RR after 7 Days Following D/C
Predicated on Adherence

Most Consistently Effective
Prevention Strategy to Date

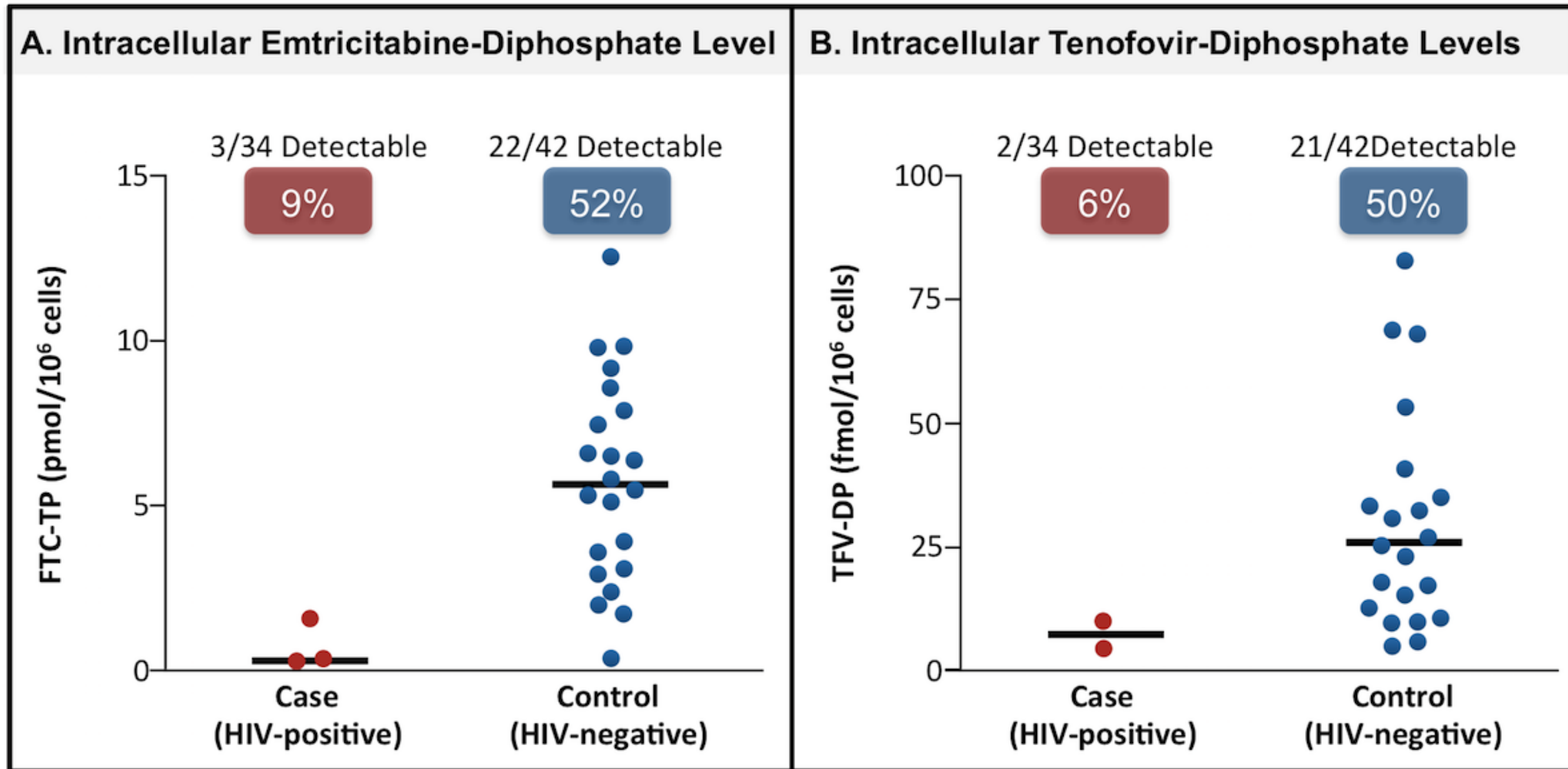
Resistance is Rare

Breakthrough Infections
Possible but Rare

Risk Compensation: Mixed
Harm Reduction

PrEP 1.0 (oral)
PrEP 2.0 (injection)
PrEP 3.0 (implants, etc.)

Adherence - iPREX

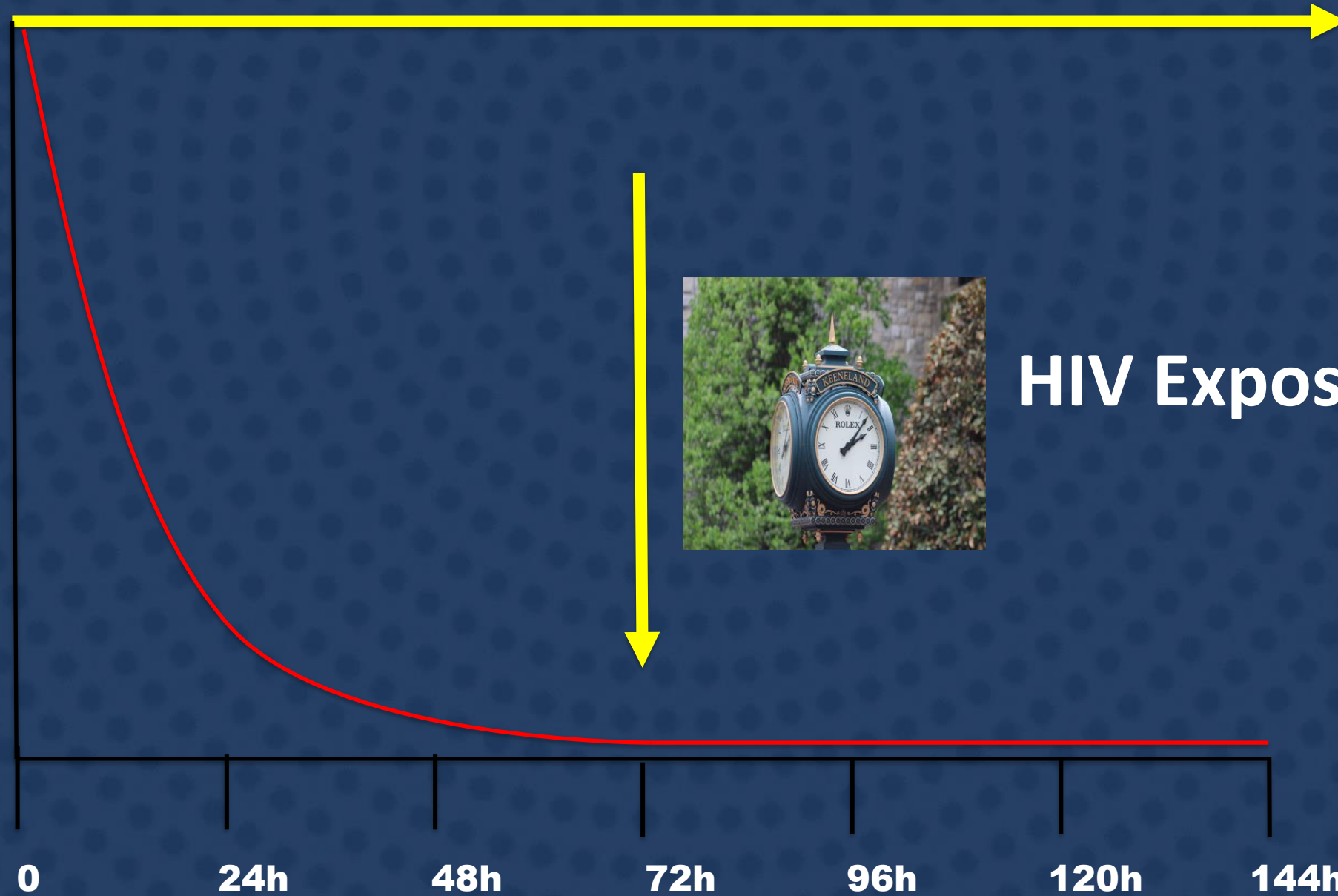


Adjusted relative risk reduction (any detectable level) = 95%

History

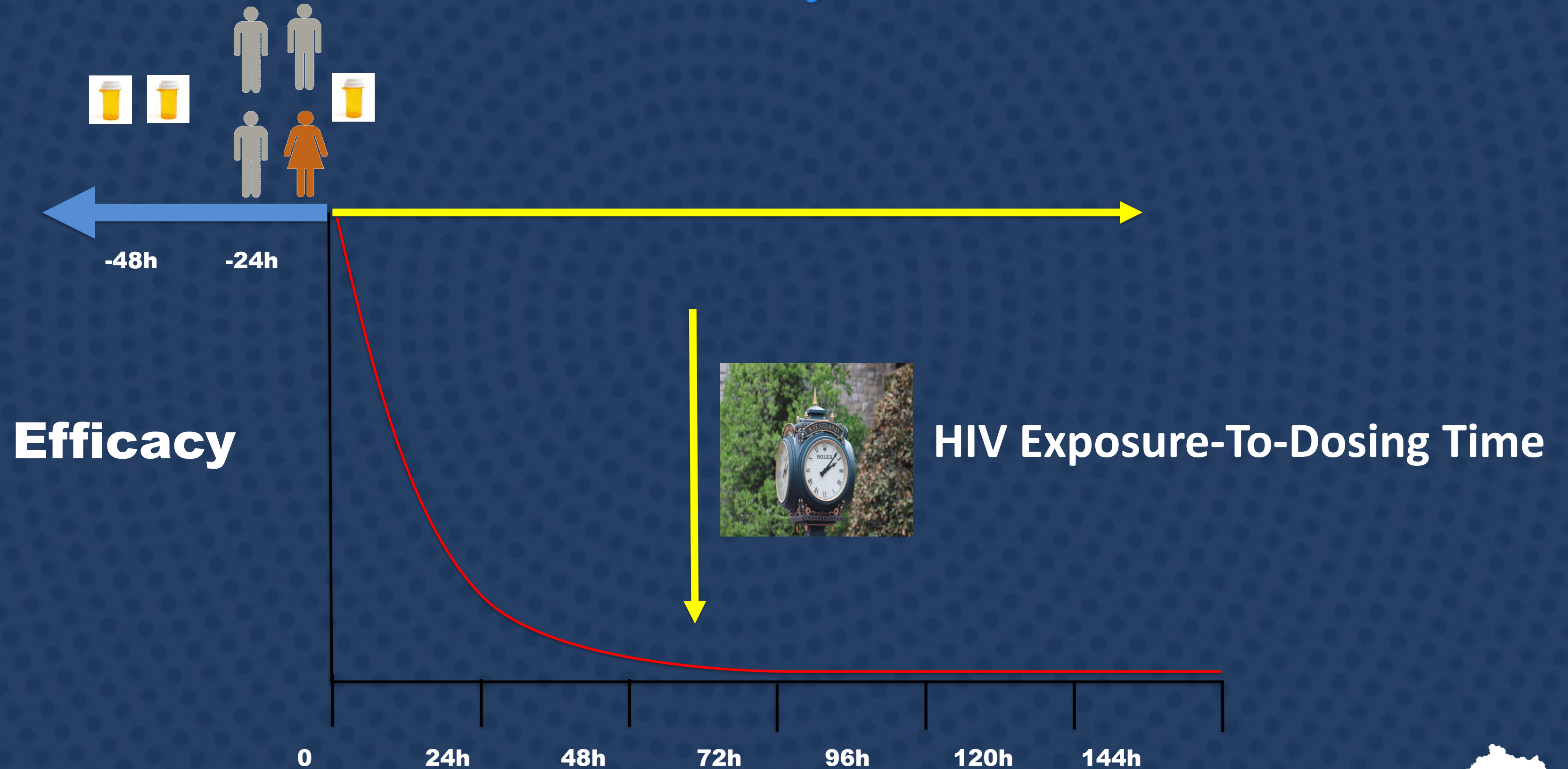


Efficacy



HIV Exposure-To-Dosing Time

History



ORAL CONTRACEPTION

FDA Approval

June 1960

Eisenstadt v. Baird

1972



PrEP 1.0



Daily TDF/FTC

- Fixed dose combo tablet
- For all populations
- Do not use if CrCl is <60 ml/min
- Test creatinine annually*
- Prescribe 90d supply at a time



2-1-1 TDF/FTC

- For MSM sexual exposure only
- 2 fixed dose combo tablets 2-24 h before sex, 1 tab 24 and 48 h later
- *Ongoing exposures, continue taking 1 tab daily until 2 d after last exposure*
- Prescribe and monitor as if being used daily

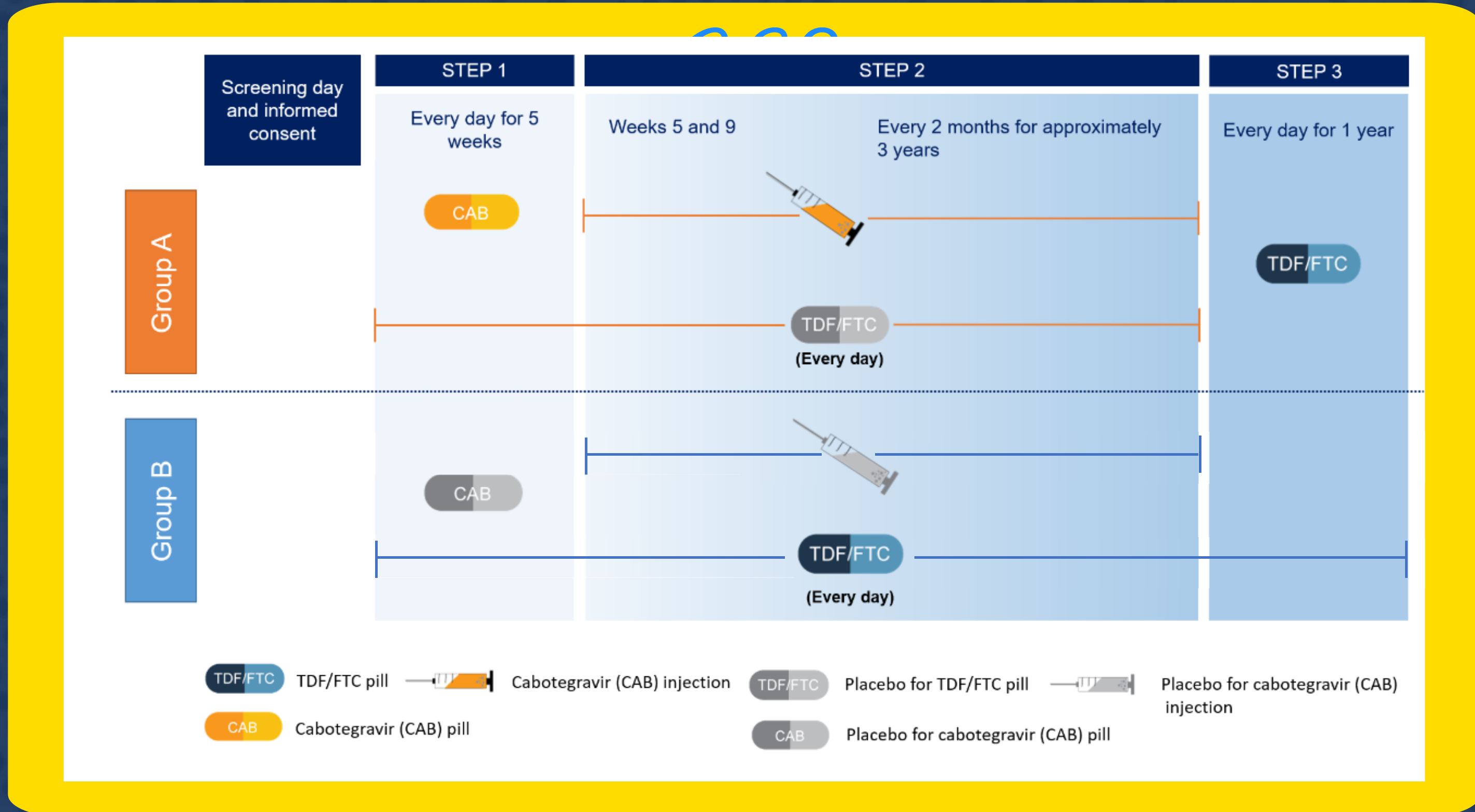


Daily TAF/FTC

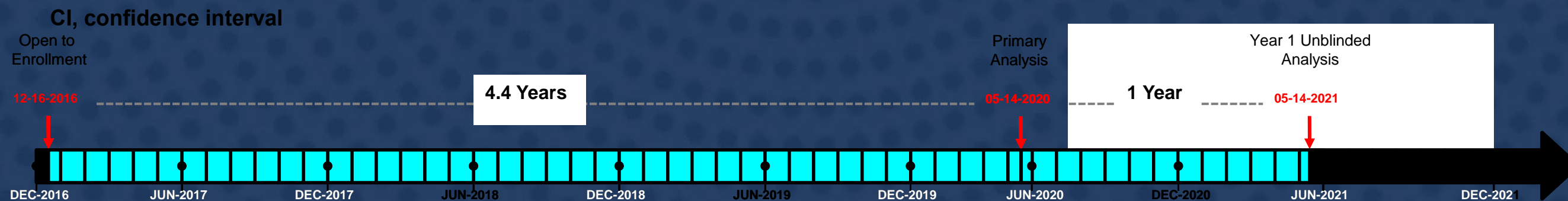
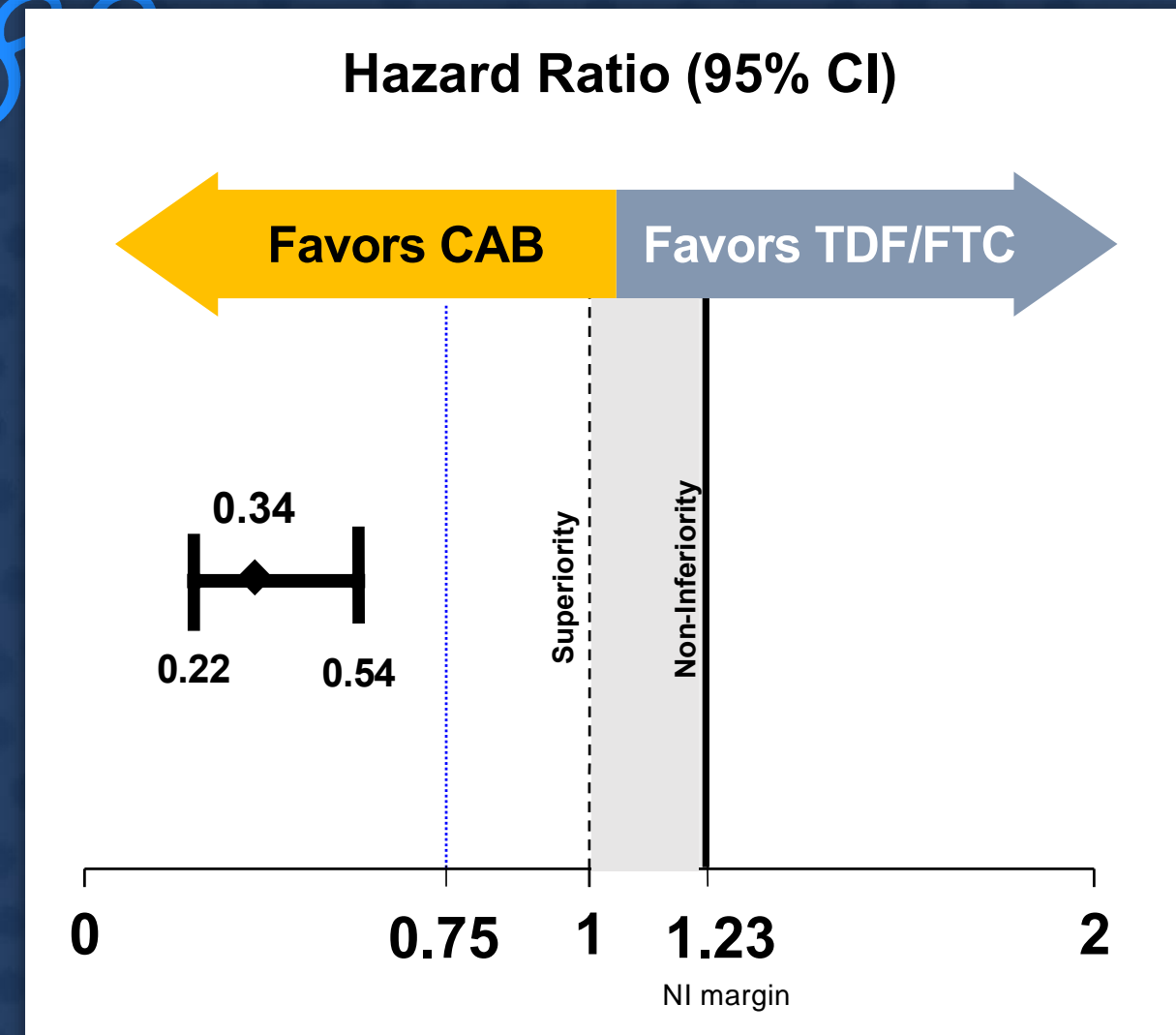
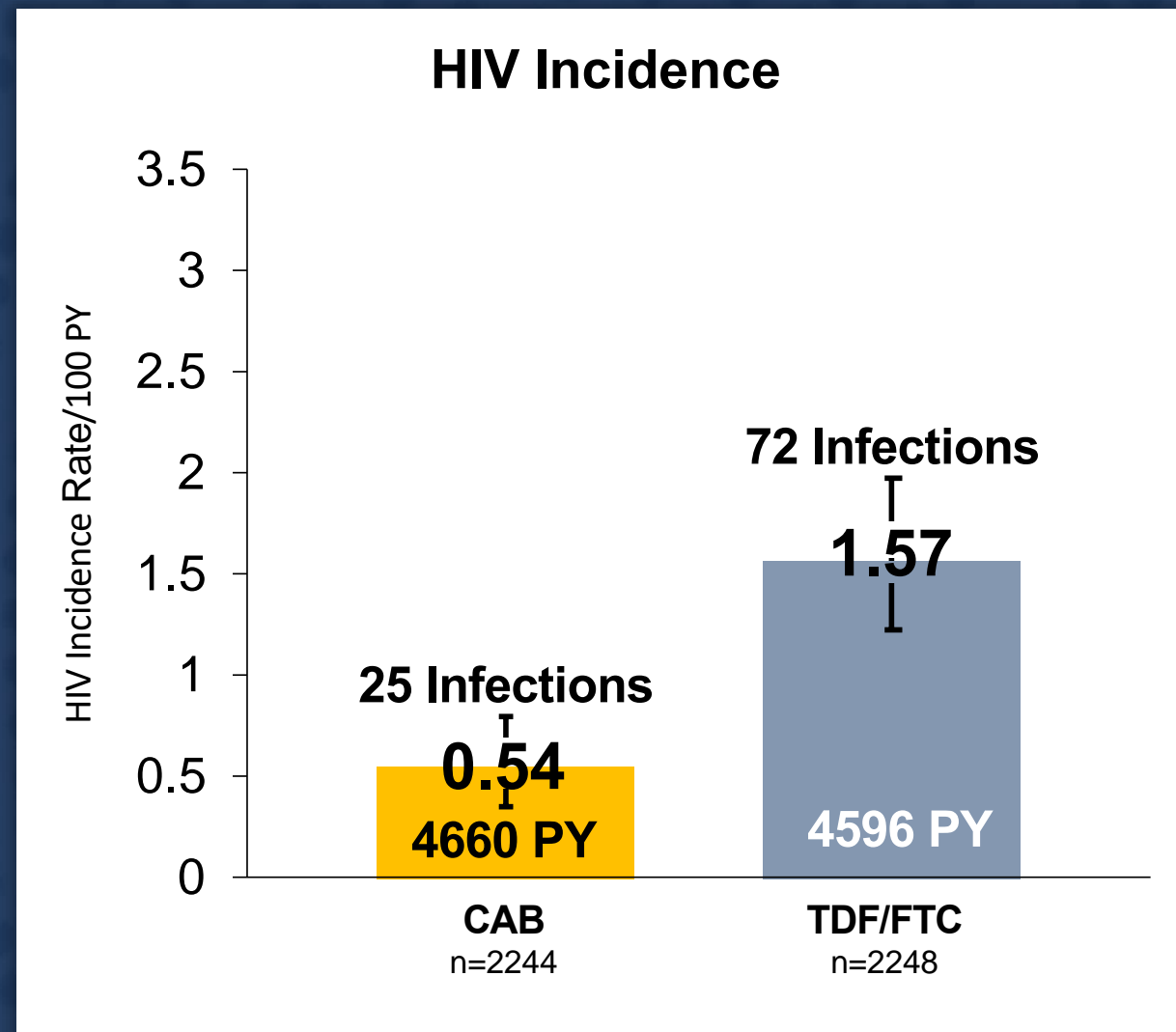
- Fixed dose combo tablet
- For MSM and TGW sexual exposure only
- Do not use if CrCl is <30 ml/min
- Test fasting lipids annually
- Test creatinine annually*
- Prescribe 90 d supply at a time

ORAL OPTIONS

PrEP 2.0 - HTPN

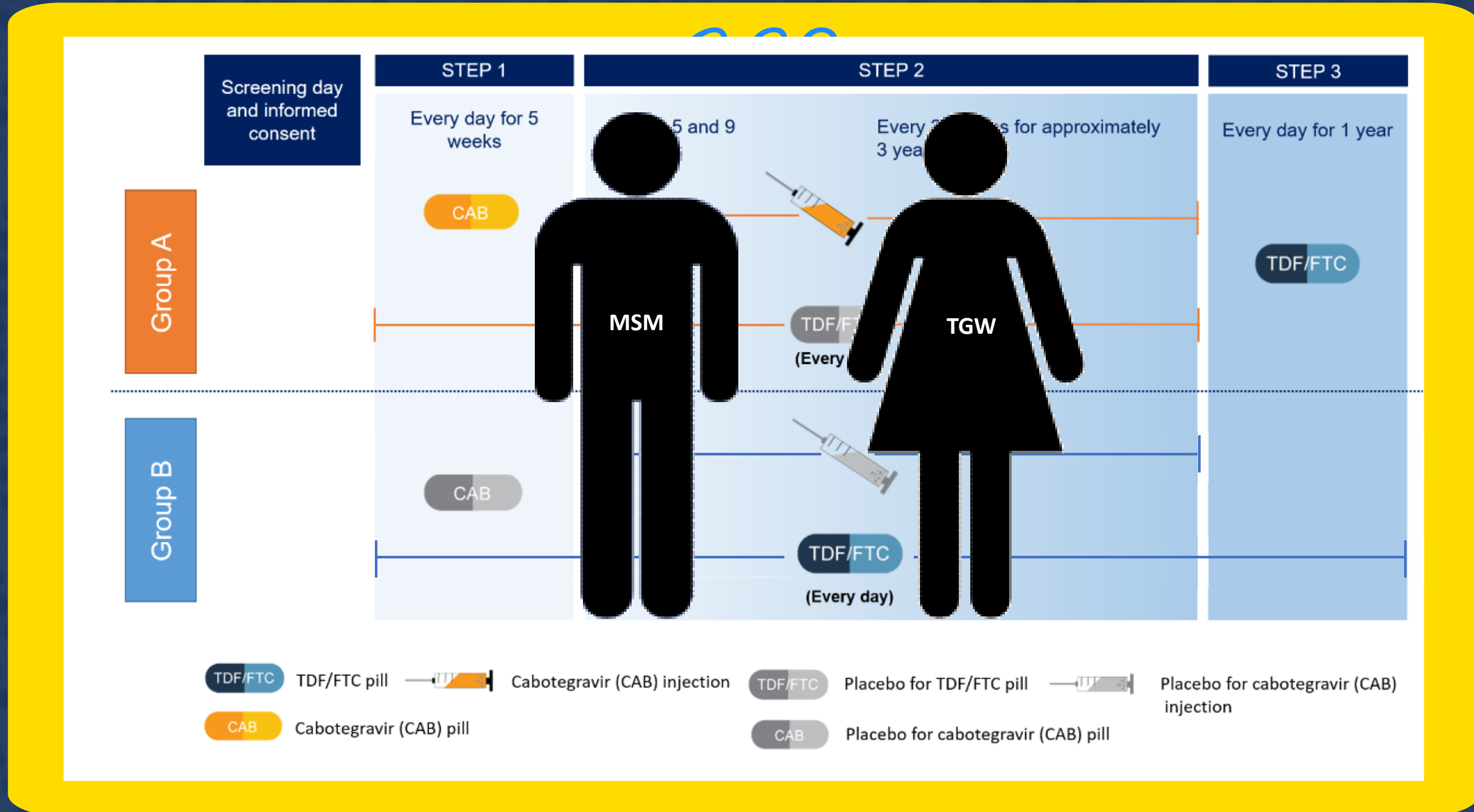


PrEP 2.0 - HTPN



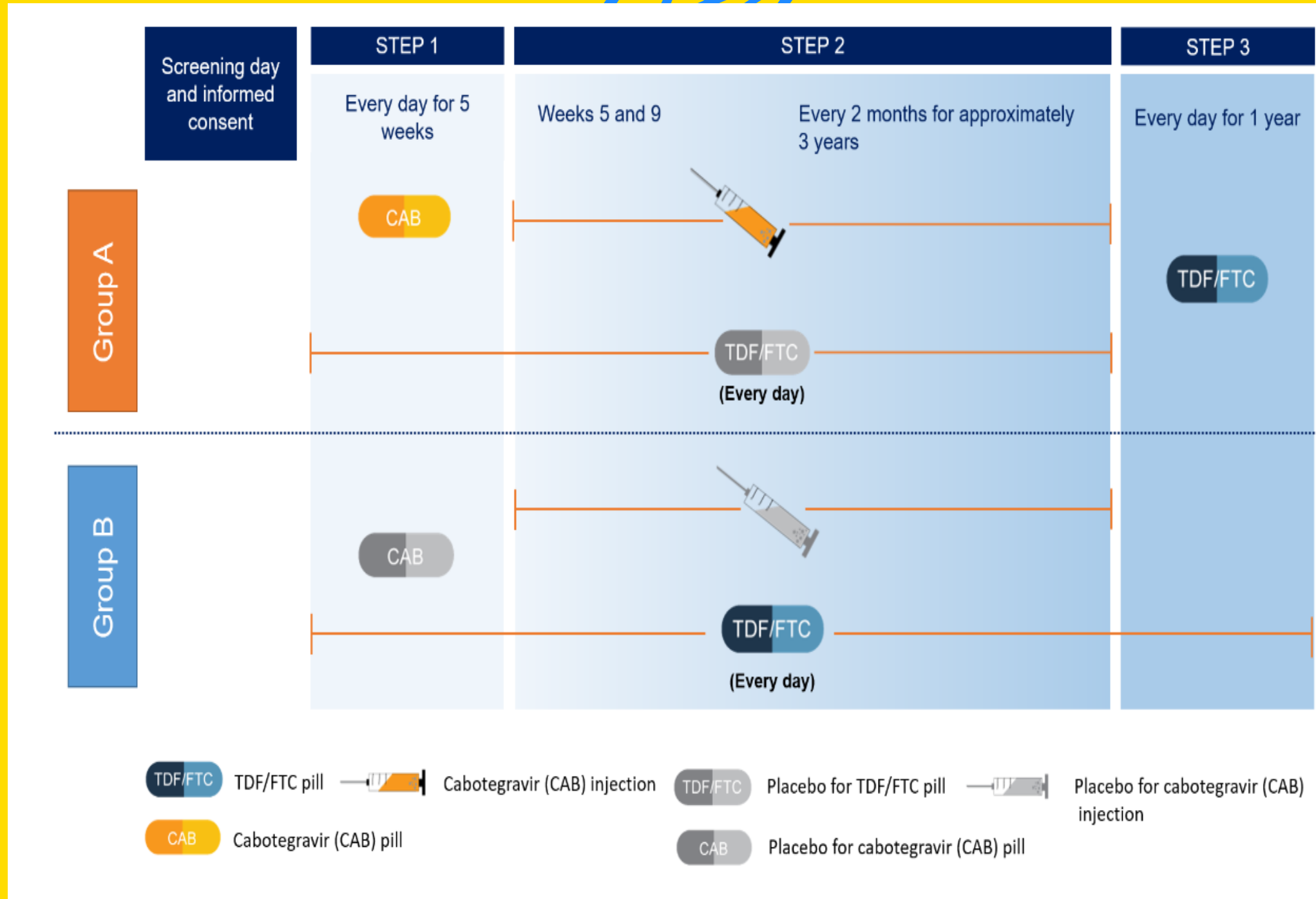
PARENTERAL OPTIONS

PrEP 2.0 - HTPN



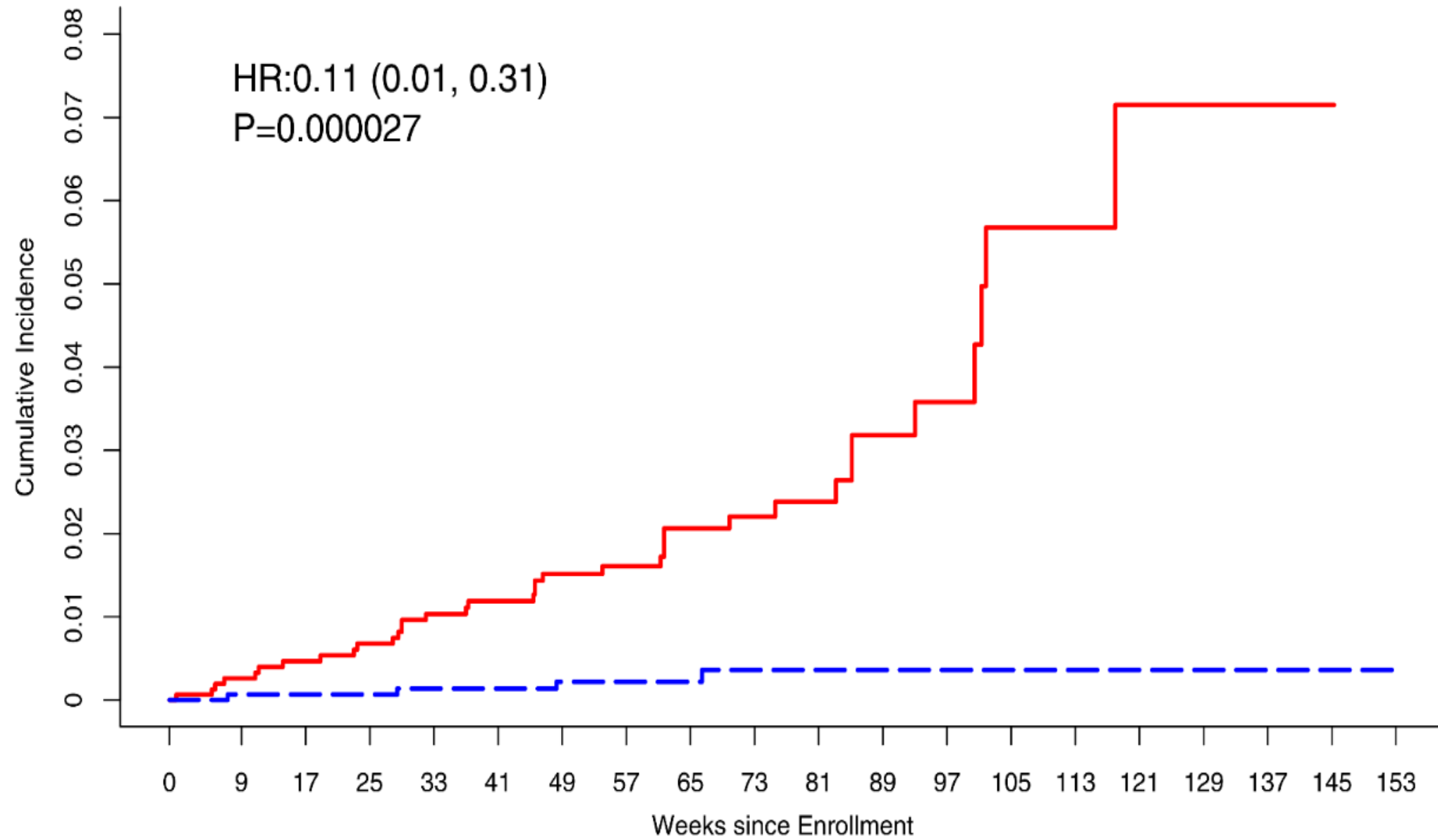
PrEP 2.0 - HTPN

094



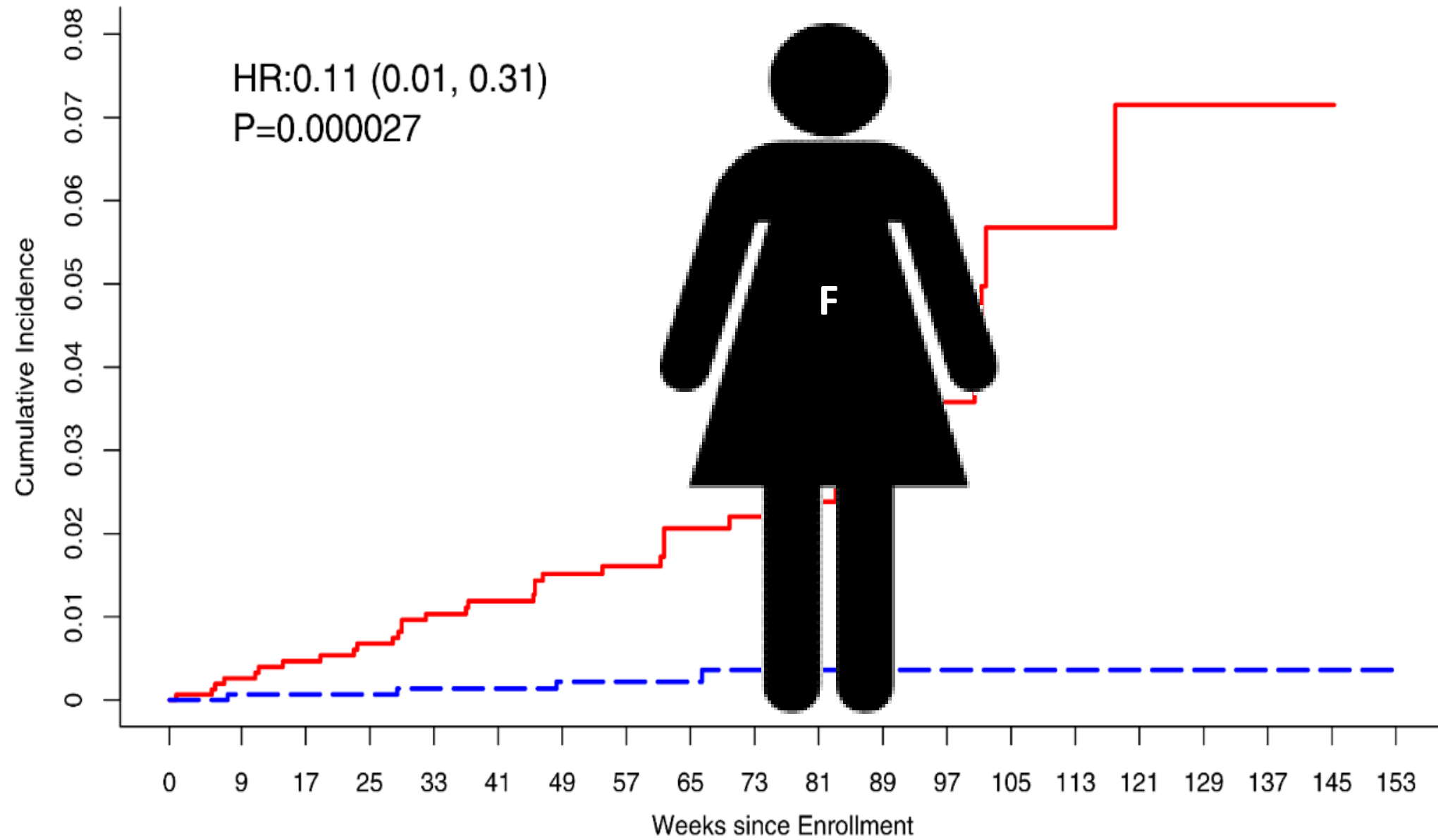
PrEP 2.0 - HTPN

0.84



PrEP 2.0 - HTPN

084
































PrEP 2.0 - HTPN

	HPTN 083	HPTN 084
Active Products	Long-acting injectable cabotegravir (CAB LA), oral cabotegravir (CAB), oral FTC/TDF	Long-acting injectable cabotegravir (CAB LA), oral cabotegravir (CAB), oral FTC/TDF
Populations	4,570 cisgender men and transgender women who have sex with men	3,200 (projected) cisgender women
Locations	Argentina, Brazil, Peru, South Africa, Thailand, U.S., Vietnam	Botswana, Eswatini, Kenya, Malawi, South Africa, Uganda, Zimbabwe
Start Date	December 2016	November 2017
Study Design	Non-Inferiority of CAB LA to FTC/TDF A non-inferiority study tests whether one drug works about the same as, but not worse than, another drug	Superiority of CAB LA to FTC/TDF A superiority study tests whether one drug works better than another drug
Study Steps	<p>STEP 1 5 weeks of 2 daily oral pills – 1 active and 1 placebo</p> <p>STEP 2 Injections every 8 weeks and daily pills for up to 3 years</p> <p>STEP 3 Daily oral pills for 48 weeks</p>	<p>STEP 1 5 weeks of 2 daily oral pills – 1 active and 1 placebo</p> <p>STEP 2 Injections every 8 weeks and daily pills for up to 3 years</p> <p>STEP 3 Daily oral pills for 48 weeks</p>
Study Results	<p>The study showed superiority of CAB LA over oral FTC/TDF, meaning CAB LA worked better to prevent HIV infection in the population than oral FTC/TDF.</p> <p>There was a 66% reduction in HIV infections in study participants provided CAB compared to FTC/TDF.</p>	<p>The study showed superiority of CAB LA over oral FTC/TDF, meaning CAB LA worked better to prevent HIV infection in the population than oral FTC/TDF.</p> <p>There was a 89% reduction in HIV infections in study participants provided CAB compared to FTC/TDF.</p>





























■ = placebo


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PrEP 1.0 versus PrEP 2.0

Both CAB and TDF/FTC highly effective.

CAB-LA superior to TDF/FTC in both HTPN 083 & 084.

CAB-LA well tolerated despite some injection site reactions.

Breakthrough infections possible for both TDF/FTC and CAB-LA.

**A 25 YO M presents
for a PCP visit and
requests HIV PrEP**



HIV Screening

If the patient has not taken oral PrEP or PEP medication in the past 3 months
AND
has not received a cabotegravir injection in the past 12 months

HIV antibody/antigen plasma test laboratory (preferred) with reflex confirmation
OR blood rapid test

Nonreactive
(negative)

Indeterminate
Differentiation Assay

Reactive
(positive)

HIV+ (if laboratory test)

(pending supplemental confirmatory testing, if non-laboratory rapid test)

Reported HIV exposure-prone event in prior 4 weeks
AND
Signs/symptoms of acute HIV infection any time in prior 4 weeks

HIV-

No

Yes

Send plasma for HIV
antibody/antigen assay

Reactive
(positive)

HIV+

Nonreactive
(negative)

HIV-

±

Send plasma for quantitative
or qualitative HIV-1 RNA assay

HIV-1 RNA ≥ 200 copies/mL

HIV+

HIV-1 RNA detectable but
<200 copies/mL

Draw new plasma specimen
Defer PrEP decision until
false positive ruled out

HIV-1 RNA < level of detection
no signs/symptoms on day of blood draw

HIV-

HIV-1 RNA < level of detection with
signs/symptoms on day of blood draw
Retest in 2-4 weeks
Defer PrEP decision, consider nPEP

Legend

HIV-
Eligible for PrEP

HIV+
Not eligible for PrEP

HIV status unclear
Defer PrEP decision

HIV Screening

If the patient has not taken oral PrEP or PEP medication in the past 3 months
AND
has not received a cabotegravir injection in the past 12 months

HIV antibody/antigen plasma test laboratory (preferred) with reflex confirmation
OR blood rapid test

Nonreactive (negative) Indeterminate Differentiation Assay Reactive (positive)

Reported HIV exposure-prone event in prior 4 weeks
AND
Signs/symptoms of acute HIV infection any time in prior 4 weeks

HIV- No Yes

Send plasma for HIV antibody/antigen assay

Reactive (positive) HIV+

±
Send plasma for quantitative or qualitative HIV-1 RNA assay

HIV-1 RNA ≥200 copies/mL HIV+

HIV-1 RNA detectable but <200 copies/mL

Draw new plasma specimen
Defer PrEP decision until false positive ruled out

HIV-1 RNA < level of detection no signs/symptoms on day of blood draw HIV-

HIV-1 RNA < level of detection with signs/symptoms on day of blood draw
Retest in 2-4 weeks
Defer PrEP decision, consider nPEP

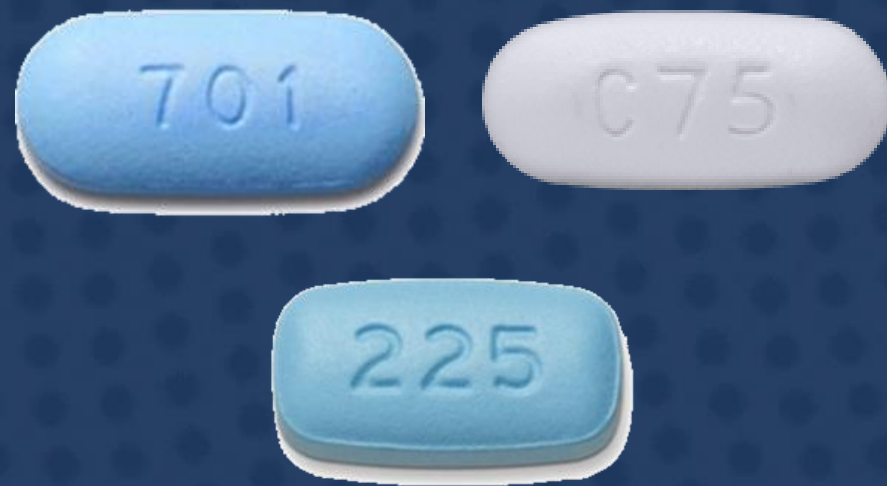
U = U
Undetectable means Untransmittable

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Legend

- HIV- Eligible for PrEP
- HIV+ Not eligible for PrEP
- HIV status unclear Defer PrEP decision

Prescribing PrEP



ORAL

IM



Prescribing PrEP



Prescribing PrEP

ORAL

Which medication should I prescribe for daily PrEP?

TDF/FTC (Truvada)

FDA approval: 2012



19 mm



EFFECTIVENESS

- ✓ for multiple populations

SAFETY

- Small ↓ in eGFR and BMD

COST

- \$1,845/month in 2019
- Generic in 2020



TAF/FTC (Descovy)

FDA approval: 2019



12.5 mm

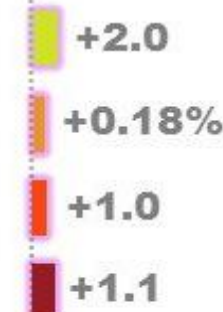


EFFECTIVENESS*

MSM & TRANS WOMEN
HETEROSEXUALS
PWID

SAFETY / 48 WKS

eGFR (mL/min)
HIP BMD
LDL (mg/dL)
BODY WEIGHT (kg)



EFFECTIVENESS

- ✓ for MSM and transwomen
- ? for other populations

SAFETY

- Small ↑ in LDL and weight

COST

- \$1,845/month in 2019



*No data available for trans men. Sources: [fda.gov/media/129607/download](https://www.fda.gov/media/129607/download); [fda.gov/media/129609/download](https://www.fda.gov/media/129609/download); [cdc.gov/hiv/risk/estimates/preventionstrategies.html](https://www.cdc.gov/hiv/risk/estimates/preventionstrategies.html) Created by: @JuliaLMarcus

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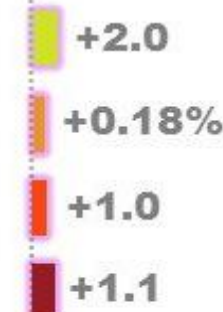
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EFFECTIVENESS*

- MSM & TRANS WOMEN
- HETEROSEXUALS
- PWID

SAFETY / 48 WKS

- eGFR (mL/min)
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Prescribing PrEP

ORAL - Laboratory Testing

Pre-Start

HIV Ag/Ab

HIV RNA (CDC)

SCr

HepA Ab

HepB SAb&Ag, HepBCAb

HepCAb

Rectal, Urinary, Pharyngeal GC/CT

RPR

Quarterly

HIV Ag/Ab

HIV RNA (CDC)

Rectal, Urinary, Pharyngeal GC/CT

RPR

Prescribing PrEP

Injectable

Week 1

Optional Oral Lead

30 mg x 30 days



WEEK 4

CAB (Apretude®)

600 mg (3 ml) gluteal



WEEK 8

CAB (Apretude®)

600 mg (3 ml) gluteal



Prescribing PrEP

Injectable

Week 1

Optional Oral Lead

30 mg x 30 days



WEEK 4

CAB (Apretude®)

600 mg (3 ml) gluteal



WEEK 8

CAB (Apretude®)

600 mg (3 ml) gluteal



> 4 weeks lag = reload

Every 2 Months +/- 7 d

Prescribing PrEP

Injectable - Laboratory Testing

Pre-Start

HIV Ag/Ab
HIV RNA (CDC)
CMP
HepA Ab
HepB SAb&Ag
HepCAb

Rectal, Urinary, Pharyngeal GC/CT
RPR

Pre-Injection

HIV Ag/Ab
HIV RNA

Every 4 Months

Rectal, Urinary, Pharyngeal GC/CT
RPR

CABIM

Breakthrough Infections

Difficult to detect

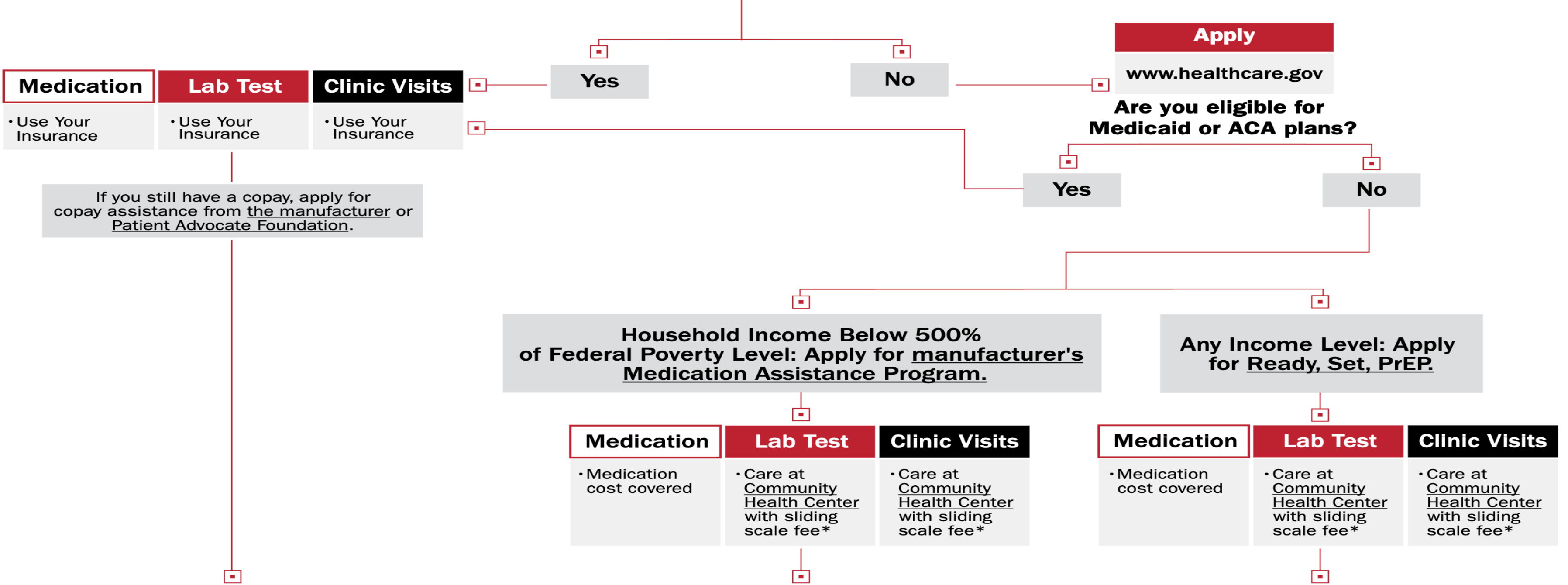
↑ Index of suspicion

Long drug tail

Expert consultation

How do I Pay for Pre-Exposure Prophylaxis (PrEP)?

Do you have health insurance?



Check to see if your state provides PrEP assistance. Costs for lab tests and clinic visits may be reduced or eliminated. Check your state PrEP Assistance Program at: www.nastad.org/prepcost-resources/prep-assistance-programs

* To find a Community Health Center: findahealthcenter.hrsa.gov



Ending the HIV Epidemic

PrEP

Other Notes

**Risk Reduction
Counseling**

nPEP to PrEP

**Racial & Gender
Disparities**

Stigma

PrEP 3.0

AVAC

Global Advocacy for HIV Prevention

The Future of ARV-Based Prevention and More (October 2022)

The pipeline of non-vaccine HIV prevention products includes oral pills, vaginal rings, vaginal and rectal gels, vaginal films, long-acting injectable antiretrovirals and more. Also pictured are the range of multipurpose prevention technologies in development that aim to reduce the risk of HIV and STIs and/or provide effective contraception for women. (Visit www.avac.org/hvad for vaccine and broadly neutralizing antibody pipelines.)

PRE-CLINICAL			PHASE I			PHASE II			PHASE III/IIIb/IV			DELIVERY SYSTEM		ACTIVE DRUG	
TAF	CONRAD		MAVR TNFV	Nigerian Institute for Medical Research	CAB	ViiV	ELVG TAF	CONRAD	DS03	Pop Council	F/TAF	Gilead Daily		5P12	5P12-RANTES
CAB	CONRAD		CAB	PATH/ Queens University Belfast	MAVR	ViiV/Pfizer	TNFV	Johns Hopkins	DPVR	Pop Council ¹ 3-monthly	LEN	Gilead 6-monthly		ACZX	Acyclovir-Zovirax
CAB	CONRAD		DS03	Queen's University Belfast	ISL	Merck ³	MK20	University of Pittsburgh	CAB	ViiV-GSK ² 2-monthly	ISL	Merck ³ 1-monthly		AMPR	Amphora
TNFV	Gilead		BNAB	Rockefeller University	TAF	Oak Crest /CAPRISA	GRFS	University of Pittsburgh	ISL	Merck ³ 1-monthly	DPVR	Pop Council 1-monthly		BNAB	Broadly neutralizing antibody
F/TAF	Houston Methodist		TAF	RTI	OB2H	Orion								CAB	Cabotegravir/ GSK 744
5P12	Mintaka		DPVR	University of Pittsburgh										CRGN	Carrageenan
Multipurpose Prevention Technologies (MPTs)															
ETED ACZX TNFV	Auritec	PC05	PATH /Pop Council /Kessel	F/TDF MAB	UMass and Planet Biotechnology /Oak Crest /MassBiologics	TAF ELVG	CONRAD	TNFV	CONRAD	F/TAF ETED LVGR	Pop Council /Medicines360 ⁴		ETED	Ethinylestradiol	
ACZX TNFV	CONRAD	CAB PRGT	PATH/Queens University Belfast	DPVR PRTV LVGR	University of North Carolina	DPVR LVGR	Pop Council	TNFV LVGR	CONRAD	F/TDF ETED LVGR	Viatrix ⁴		ETGS	Etonogestrel	
CAB LVGR	CONRAD	ETGS GRFS ETED	Pop Council	ETGS ISL ETED	University of North Carolina	DPVR LVGR PRTV	University of North Carolina						GRFS	Griffithsin	
TNFV EFAV	i3S/University of Porto	CRGN GRFS	Pop Council /Evofem Biosciences	DPVR LVGR PRTV	University of North Carolina								ISL	Islatravir	
PRGT ISL	Magee-Women's Research Institute /University of Pittsburgh	RTI ⁵		ISL	University of North Carolina								LVGR	Levonorgestrel	
F/TDF MAB	Oak Crest /University of North Carolina			PPCM	Yaso Therapeutics								MAVR	Maraviroc	

¹ This is a Bioequivalency trial with the monthly DVR.
² Dec. 2021 Approved by the FDA; Aug. 2022 Approved by the Australian regulatory agency
³ Discontinued in Sept. 2022
⁴ These two dual pill products are undergoing bioequivalency trials. The drug components are approved, but not in their combination. Therefore, it does not follow the traditional R&D pathway.
⁵ Non-specific to any drug; for development of a long-acting biodegradable implant suitable for an MPT use to protect against pregnancy and HIV. See SCHIELD Implant for more information.

PrEP 3.0

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CAB	CONRAD	CAB	PATH/ Queens University Belfast	MAVR	ViiV/Pfizer	TNFV	Johns Hopkins	DPVR	Pop Council ¹ 3-monthly	LEN	Gilead 6-monthly	Enema	ACZX	Acyclovir-Zovirax
CAB	CONRAD	DS03	Queen's University Belfast	ISL	Merck ³	MK20	University of Pittsburgh	CAB	ViiV-GSK ² 2-monthly	ISL	Merck ³ 1-monthly	Intramuscular injection	CA...	Cabotegravir/ GSK 744
TNFV	Gilead	BNAB	Rockefeller University	TAF	Oak Crest /CAPRISA	GRFS	University of Pittsburgh	ISL	Merck ³ 1-monthly	DPVR	Pop Council 1-monthly	Implant	CRG1	Carrageenan
F/TAF	Houston Methodist	TAF	RTI	OB2H	Orion							Micro-array patch	DPV1	Dapivirine
5P12	Mintaka	DPVR	University of Pittsburgh									Non-specific mucosal insert	F/TAF	Descovy
Multipurpose Prevention Technologies (MPTs)														
ETED ACZX TNFV	Auritec	PC05	PATH /Pop Council /Kessel	F/TDF MAB	UMass and Planet Biotechnology /Oak Crest /MassBiologics	TAF ELVG	CONRAD	TNFV	CONRAD	F/TAF ETED LVGR	Pop Council /Medicines 360 ⁴	Oral pills	DLGR	Dolutegravir
ACZX TNFV	CONRAD	CAB PRGT	PATH/Queens University Belfast	DPVR PRTV LVGR	University of North Carolina	DPVR LVGR	Pop Council	TNFV LVGR	CONRAD	F/TDF ETED LVGR	Viatrix ⁴	Subcutaneous injection	DS03	DS003 (BMS793)
CAB LVGR	CONRAD	ETGS GRFS ETED	Pop Council	ETGS ISL ETED	University of North Carolina	DPVR LVGR	Pop Council					Vaginal film	EFAV	Efavirenz
TNFV EFAV	i3S/University of Porto	CRGN GRFS	Pop Council /Evofem Biosciences	DPVR PRTV	University of North Carolina							Vaginal insert	ELVG	Elvitegravir
PRGT ISL	Magee-Women's Research Institute /University of Pittsburgh	RTI ⁵		ISL	University of North Carolina							Vaginal ring	ETED	Ethinylestradiol
F/TDF MAB	Oak Crest /University of North Carolina	PPCM	Yaso Therapeutics										ETGS	Etonogestrel

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⁵ Non-specific to any drug; for development of a long-acting biodegradable implant suitable for an MPT use to protect against pregnancy and HIV. See SCHIELD Implant for more information.

PrEP 3.0

AVAC

Global Advocacy for HIV Prevention

The Future of ARV-Based Prevention and More (October 2022)

The pipeline of non-vaccine HIV prevention products includes oral pills, vaginal rings, vaginal and rectal gels, vaginal films, long-acting injectable antiretrovirals and more. Also pictured are the range of multipurpose prevention technologies in development that aim to reduce the risk of HIV and STIs and/or provide effective contraception for women. (Visit www.avac.org/hvad for vaccine and broadly neutralizing antibody pipelines.)

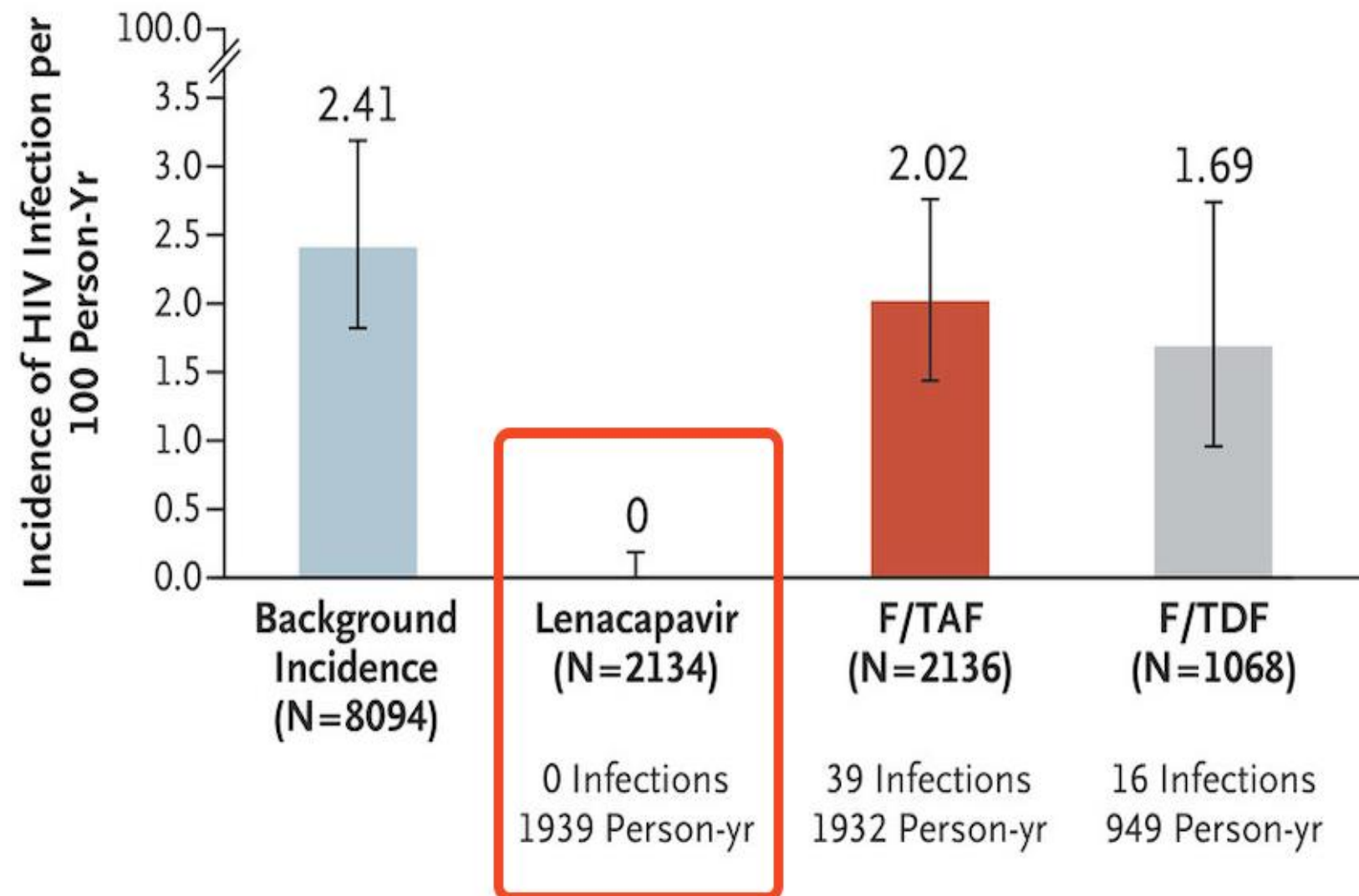
PRE-CLINICAL			PHASE I		PHASE II		PHASE III/IIIb/IV		DELIVERY SYSTEM	ACTIVE DRUG	
TAF	CONRAD	MAVR TNFV	Nigerian Institute for Medical Research	CAB	ViiV	ELVG TAF	CONRAD	DS03	Pop Council	Diaphragm	5P12 5P12-RANTES
CAB	CONRAD	CAB	PATH/ Queens University Belfast	MAVR	ViiV/Pfizer	TNFV	Johns Hopkins	DPVR	Pop Council ¹ 3-monthly	Enema	ACZX Acyclovir-Zovirax
CAB	CONRAD	DS03	Queen's University Belfast	ISL	Merck ³	MK20	University of Pittsburgh	CAB	ViiV-GSK ² 2-monthly	Intramuscular injection	AMPR Amphora
TNFV	Gilead	BNAB	Rockefeller University	TAF	Oak Crest /CAPRISA	GRFS	University of Pittsburgh	ISL	Merck ³ 1-monthly	Implant	BAAB Broadly neutralizing antibody
F/TAF	Houston Methodist	TAF	RTI	OB2H	Orion			DPVR	Pop Council 1-monthly	Micro-array patch	CAB Cabotegravir/ GSK 744
5P12	Mintaka	DPVR	University of Pittsburgh							Non-specific mucosal insert	CRG1 Carrageenan
Multipurpose Prevention Technologies (MPTs)											
ETED ACZX TNFV	Auritec	PC05	PATH /Pop Council /Kessel	F/TDF MAB	UMass and Planet Biotechnology /Oak Crest /MassBiologics	TAF ELVG	CONRAD	TNFV	CONRAD	F/TAF	Pop Council
ACZX TNFV	CONRAD	CAB PRGT	PATH/Queens University Belfast	DPVR PRTV LVGR	University of North Carolina	DPVR LVGR	Pop Council	TNFV LVGR	CONRAD	F/TDF ETED LVGR	Viatis ⁴
CAB LVGR	CONRAD	ETGS GRFS ETED	Pop Council	ETGS ISL ETED	University of North Carolina	DPVR LVGR	Pop Council				
TNFV EFAV	i3S/University of Porto	CRGN GRFS	Pop Council /Evofem Biosciences	DPVR LVGR PRTV	University of North Carolina						
PRGT ISL	Magee-Women's Research Institute /University of Pittsburgh	RTI ⁵		ISL	University of North Carolina						
F/TDF MAB	Oak Crest /University of North Carolina	PPCM	Yaso Therapeutics								
										Subcutaneous injection	LEN Lenacapavir
										Vaginal ring	LVGR Levonorgestrel
										Vaginal gel	MAVR Maraviroc
										Vaginal insert	MAAB Monoclonal antibody
										Vaginal ring	OB2H OB-002H
											PC05 PC-1005
											PPCM PPCM polyanionic microbicide
											RTV Pritelivir
											PRGT Progestin
											TNFV Tenofovir
											TAF Tenofovir Alafenamide
											F/TDF Truvada

¹ This is a Bioequivalency trial with the monthly DVR.
² Dec. 2021 Approved by the FDA; Aug. 2022 Approved by the Australian regulatory agency
³ Discontinued in Sept. 2022
⁴ These two dual pill products are undergoing bioequivalency trials. The drug components are approved, but not in their combination. Therefore, it does not follow the traditional R&D pathway.
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Purpose-1

***Twice-yearly Injection Fully Protects Women from HIV
New Drug Provides Total Protection From HIV in Trial of Young African Women
Lenacapavir Shows 100% Efficacy and Zero Infections in HIV Prevention
Beginning of End of HIV Epidemic?***

A Background HIV Incidence and HIV Incidence in Lenacapavir, F/TAF, and F/TDF Groups



- Enrollees were from a high incidence population.
- 20% had an active STI at enrollment.
- Blinded.
- 927 mg SQ in (2) 1.5 ml injections.
- LEN superior to no PrEP and TDF/FTC.
- Adherence to oral therapy was sub-optimal.
- Preg/breast-feeding participants remained enrolled.
- Injection site reactions and HA (13%).
- Approval and implementation (HPTN 084).

Purpose-2

MSM

2,180 LEN & 1,020 TDF/FTC. (2:1 randomization)

Cisgender M, transgender M, transgender W.

All participants report sex with persons assigned M at birth.

Argentina, Brazil, Mexico, Peru, South Africa, Thailand, US.

Blinded cohort of the Phase III trial halted.

99.9% of participants in L protected with 2 incident cases.

Superior to TDF/FTC.

Swift Approval?

Dec 2025

Cost?

Purpose-3
Cis-Gender US Women

Purpose-4
Injection Drug Users



Lenacapvir (Sunlenca®)

- US Approval: Dec 2022
- Gilead
- Capsid Inhibitor
- Resistant and failing therapy
- Drug eluting depot
- \$40K annual cost

AETC Program

National Centers and National HIV Curriculum

National Coordinating Resource Center serves as the central web-based repository for AETC Program training and capacity building resources; its website includes a free virtual library with training and technical assistance materials, a program directory, and a calendar of trainings and other events.

Learn more: <https://aidsetc.org>

National Clinician Consultation Center provides free, peer to peer, expert advice for health professionals on HIV prevention, care, and treatment and related topics. Learn more: <https://nccc.ucsf.edu>

National HIV Curriculum provides ongoing, up to date HIV training and information for health professionals through a free, web-based curriculum; also provides free CME credits, CNE contact hours, CE contact hours, and maintenance of certification credits. Learn more: www.hiv.uw.edu