TCA invites you
September 23, 2026
10 – 11:30 AM ET

Evolving Oral PrEP Guidance for Ciswomen

What do we know, and what will it take?

Welcome!

THE CHOICE AGENDA

HIV prevention research – a new forum for advocacy on the latest

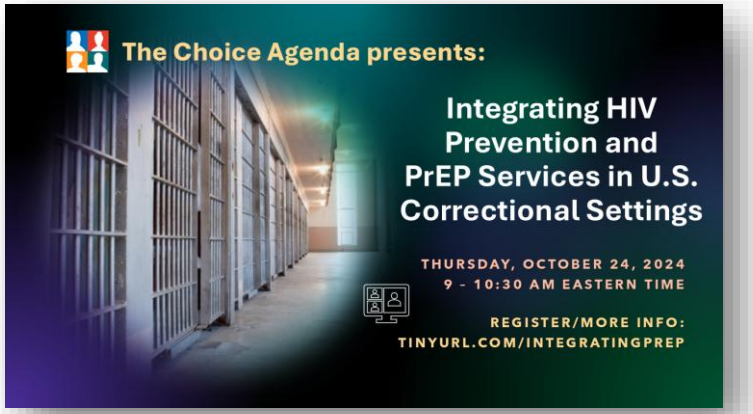
avac.org/project/choice-agenda

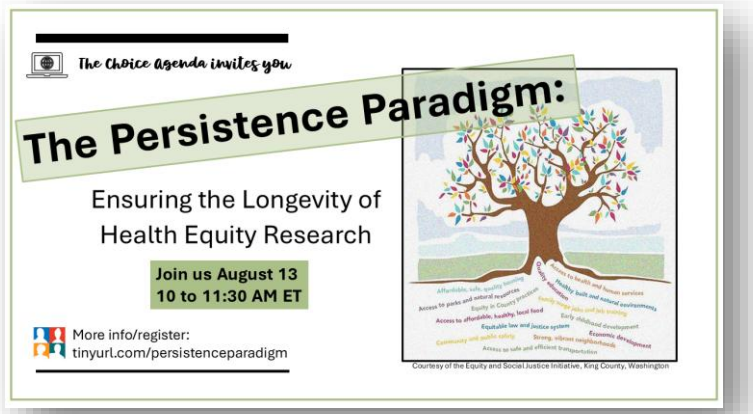

2800+ individuals from 40+ countries are subscribed to The Choice Agenda global info/discussion list. Are you?
Subscribe

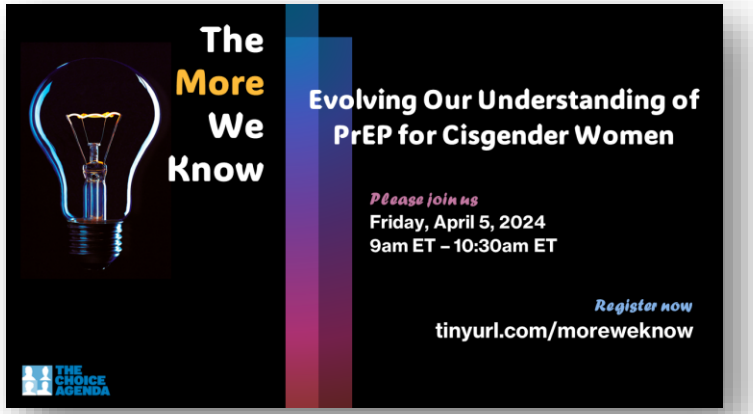
The TCA Library is Always Open

Recordings, slides, notes from all our webinars – 2022 to present

24/7/365 click tinyurl.com/tcawebinarmaterials







TCA Radio
9.23.26 playlist

the way of love
/cher

(you make me feel like) a natural woman
/aretha franklin

9 to 5
/dolly parton

finally
/cece peniston

aint no mountain high enough
/diana ross

Aftershocks Roundtable

How do we rebuild our HIV and public health infrastructure?

The Choice Agenda invites you
October 28, 9 – 10:30 AM ET

Register: tinyurl.com/aftershocksroundtable

Today's speakers

Dr. Jenell Stewart
University of Minnesota

Dr. Heather-Marie Anne Schmidt
UNAIDS

Simon Collins
HIV i-Base

Dr. Raphael Landovitz
UCLA

Evolving Guidance on Oral PrEP for Cisgender Women: What do we know?

Jenell Stewart, DO, MPH

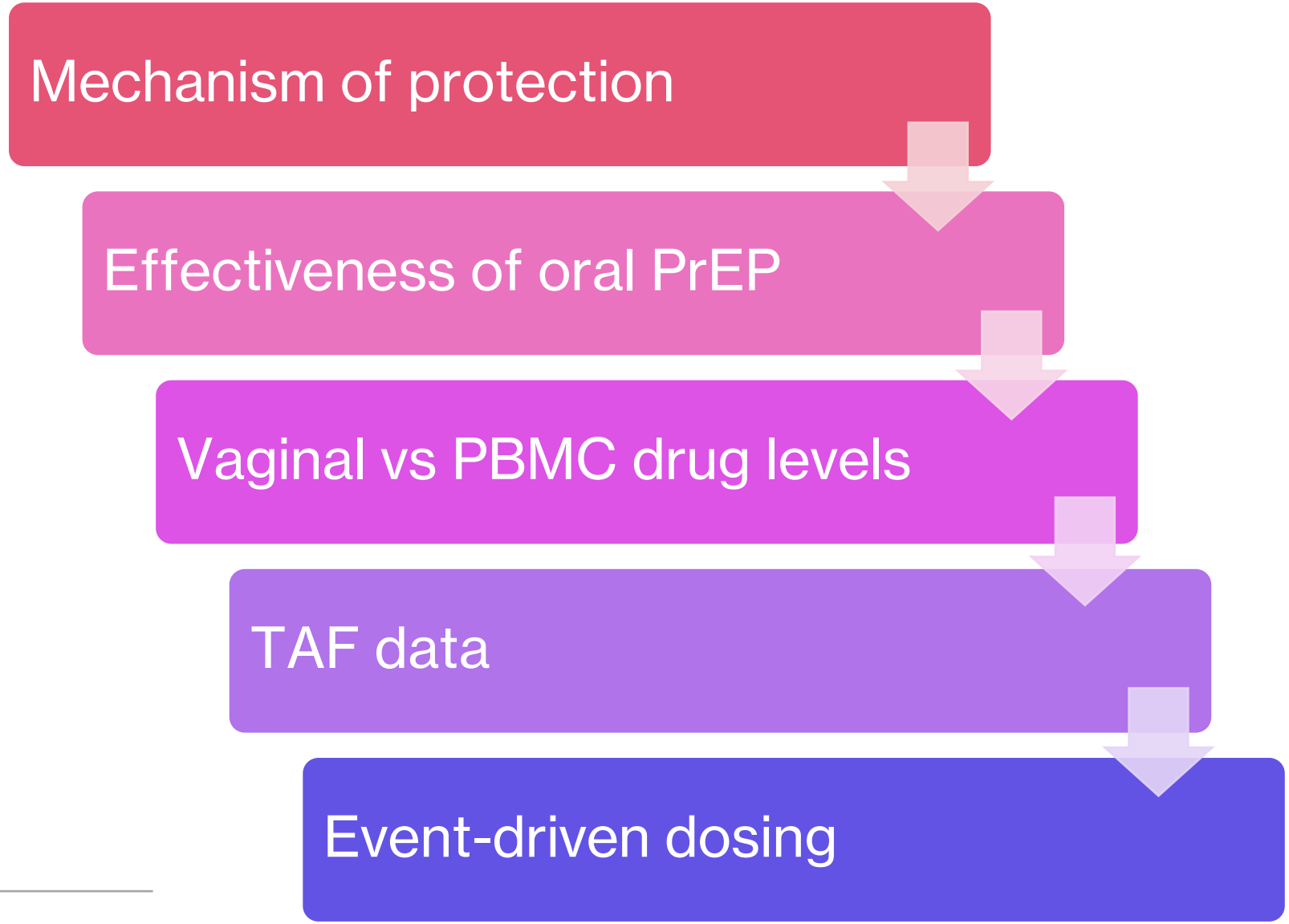
Associate Professor of Medicine, University of Minnesota

Physician-Scientist, Division of Infectious Diseases, Hennepin Healthcare Research Institute

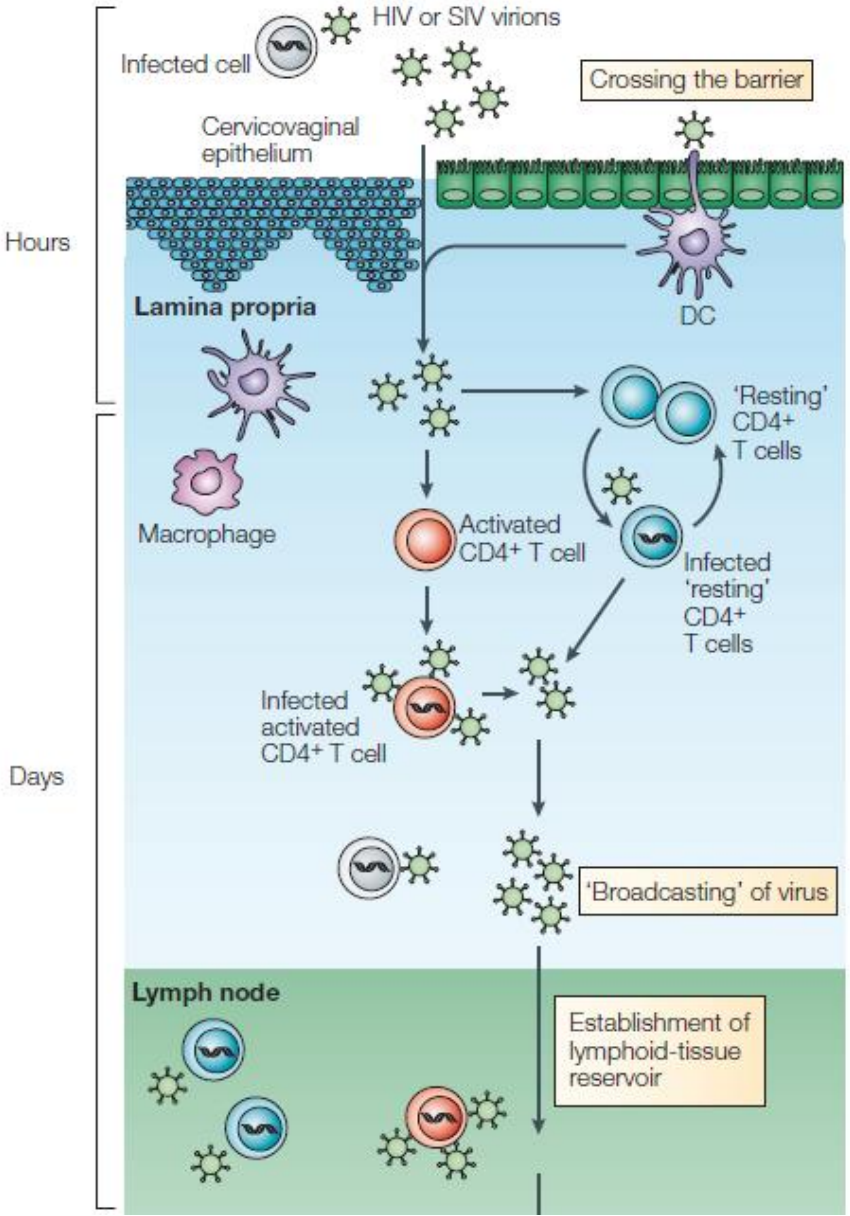
Medical Director, Hennepin County Red Door Sexual Health Clinic

Disclosures: None

Overview


Mechanism of protection
Effectiveness of oral PrEP
Vaginal vs PBMC drug levels
TAF data
Event-driven dosing

HIV Prevention with TDF/FTC is in CD4 cells



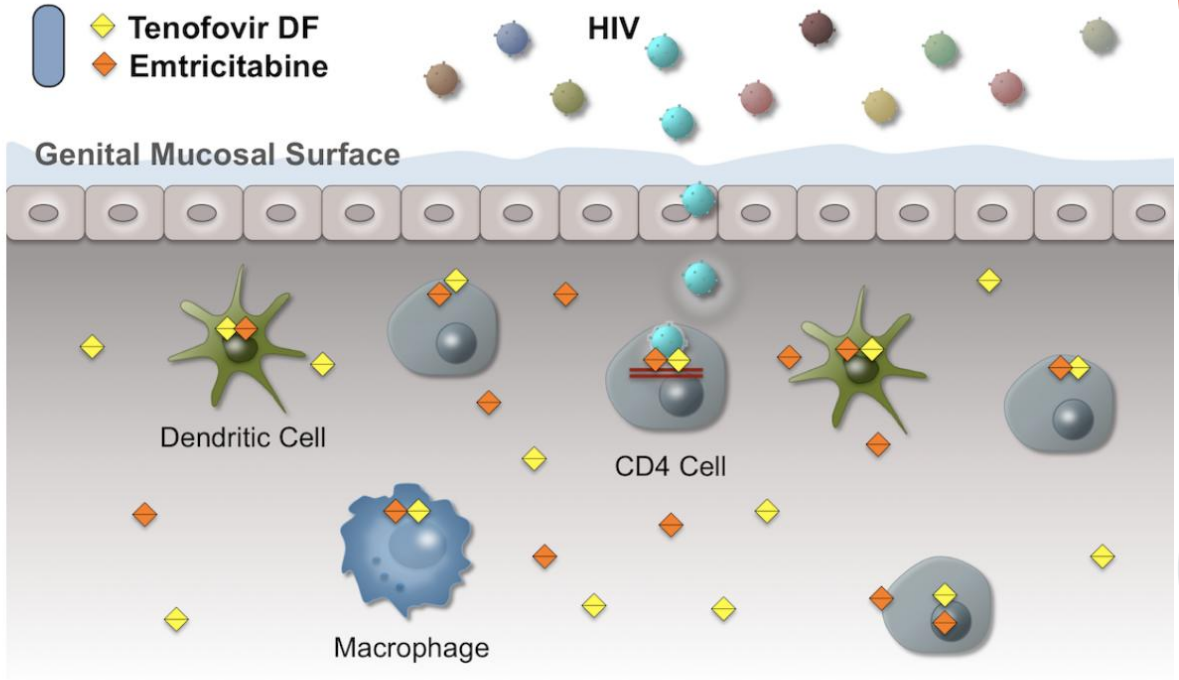


Figure 2 (Image Series) - HIV PrEP for Sexual Transmission of HIV
C. Tenofovir and Emtricitabine Blocking HIV Replication
In an individual taking PrEP who has high intracellular levels of tenofovir diphosphate and emtricitabine triphosphate, HIV infection of submucosal cells results in a dead end, since the medications block HIV reverse transcription. Thus, in this situation, HIV transmission is blocked since HIV cannot replicate and spread to other cells.

Illustration by David H. Spach, MD

Haase, Nat Rev, 2005
National HIV Curriculum

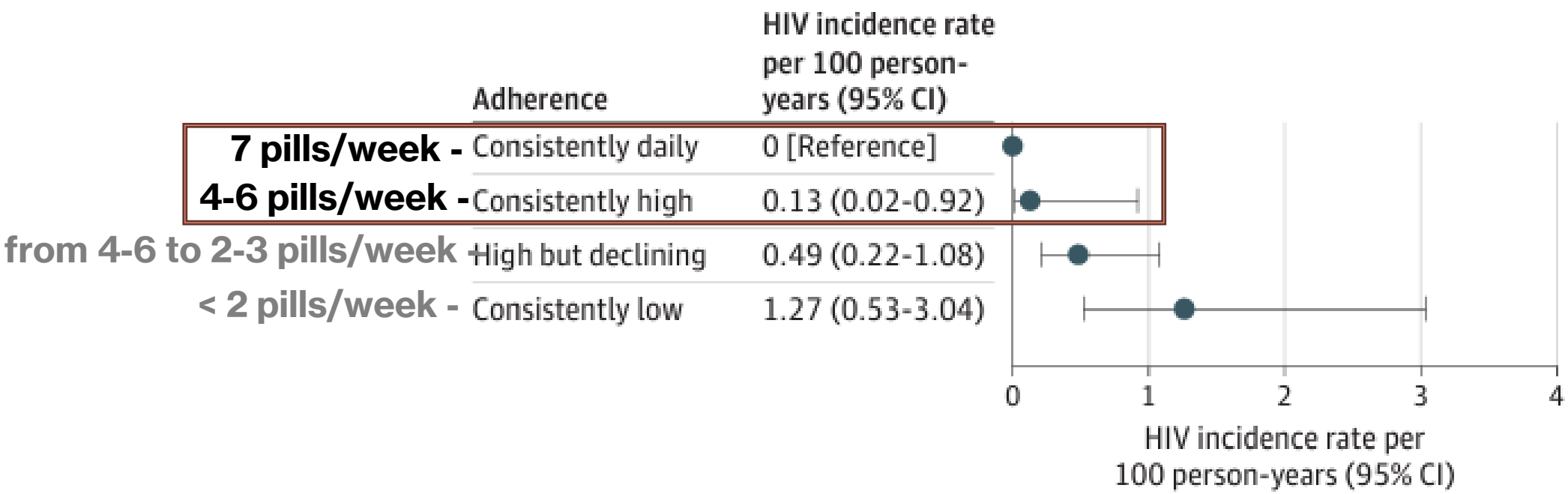
PrEP Efficacy Data Comparing Adherence Patterns among Cisgender Women

	Efficacy data source	Adherence or PK data source	Adherence patterns			
			<2 doses/ week	2-3 doses/ week	4-6 doses/ week	daily
Anderson et al, Sci Transl Med, 2021	iPrEX	PBMC adherence bands determined from directly observed dosing (STRAND)		76 (95%CI 56-96)	96 (95%CI 90->99)	99 (95%CI 96->99)
Anderson et al, CID, 2023	HPTN 083/084	DBS adherence bands determined from directly observed therapy	16 (95%CI 0-60)	80 (95%CI 32-97)	88 (95%CI 43-99)	99 (95%CI 0-99)
Cottrell et al , JID, 2016	In vitro EC_{90} in CD4+ T cells	Population PK study built from directly observed dosing study	10% population >EC_{90}	65% population >EC_{90}	99% population >EC_{90}	100% population >EC_{90}
Moore et al, Nat Med, 2023	FEM-PrEP VOICE Partners PrEP	TFV plasma used to impute TFVdp and estimate adherence bands from HPTN 082		59 (95%CI 30-96)	84 (95%CI 52-100)	96 (95%CI 73-100)
Zhang et al, Nat Med, 2023	Molecular mechanism modeling	Simulated PBMC concentrations from population PK models	74 (95%CI 10-99)	96 (95%CI 58-99)	>99 (95%CI 96->99)	>99 (95%CI 99 ->99)
		Simulated tissue concentrations from population PK models	37 (95%CI 3-75)	64 (95%CI 25-84)	74 (95%CI 44-88)	78 (95%CI 52-89)

(Irie W et al., Lancet HIV, 2025)

Does vaginal sex demand perfection?

Figure 4. HIV Incidence Rates Among Cisgender Women by Adherence Trajectory (n = 2954)

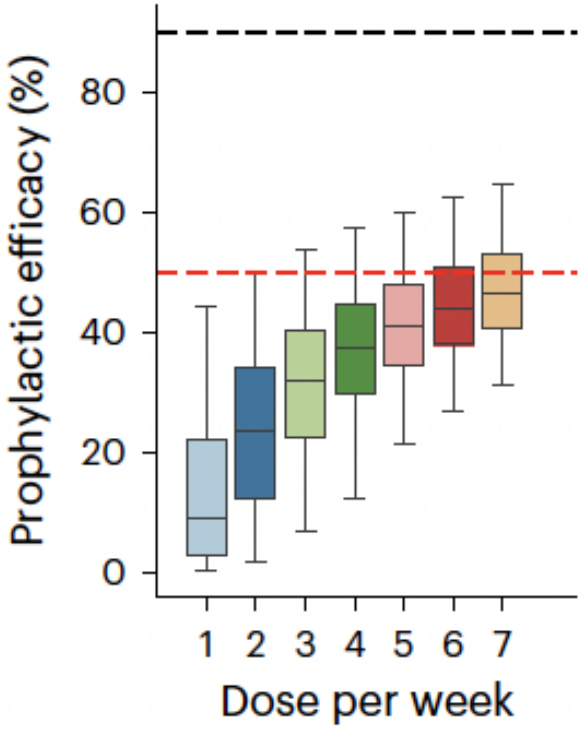


Pooled data from 11 F/TDF PrEP studies among cisgender women in 6 countries [2012 to 2020]

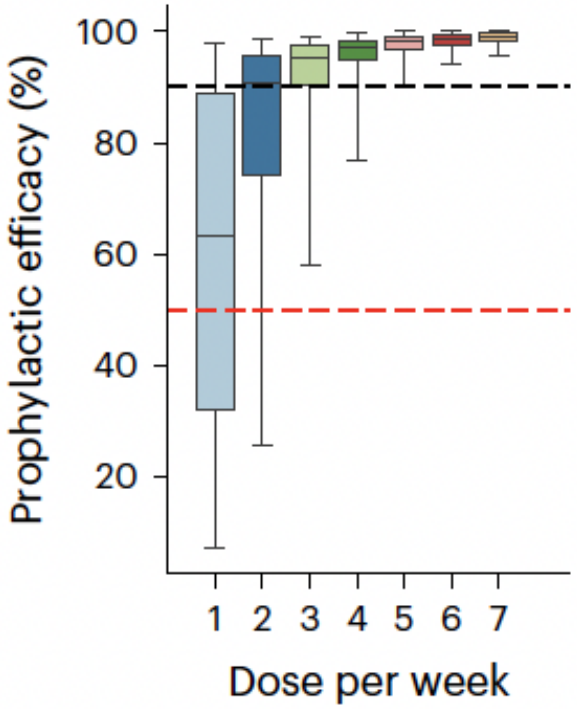
Marrazzo et al, JAMA, March 1, 2024

Clinical data incongruent with vaginal drug levels

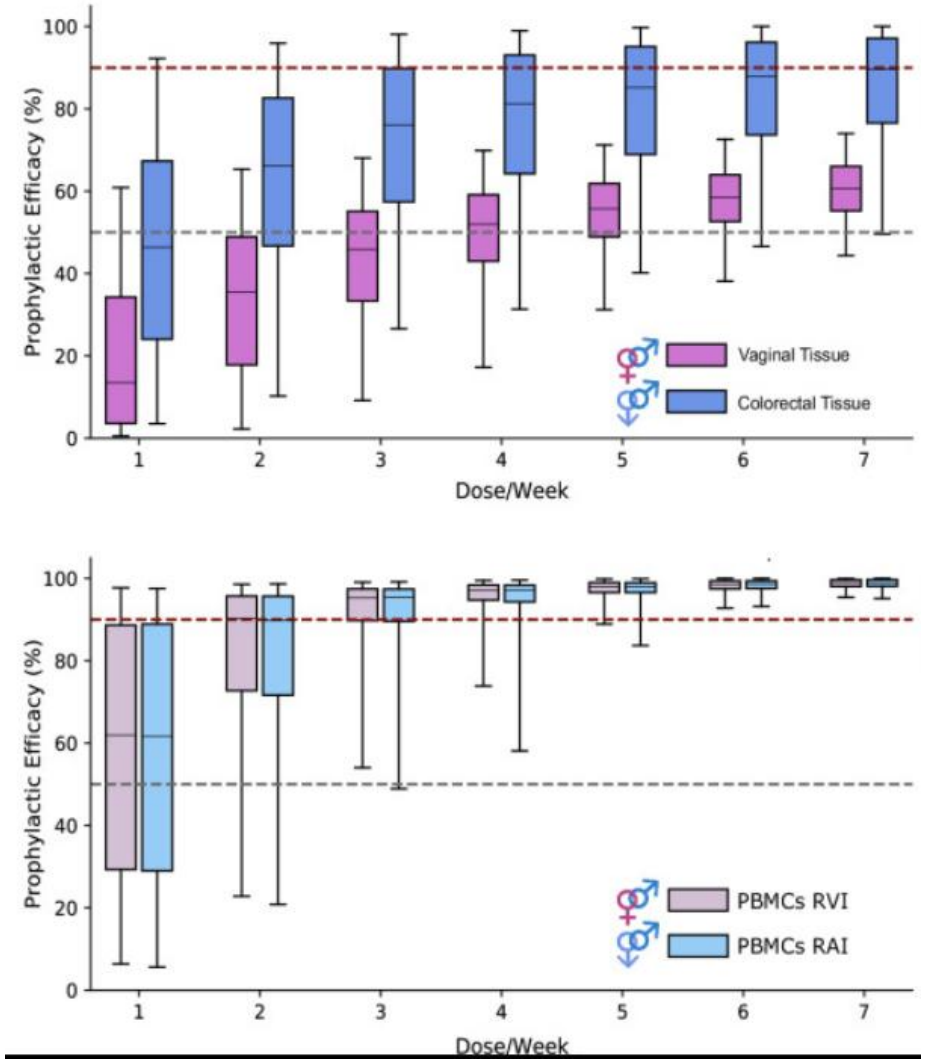
Dose-dependent effectiveness, vaginal PK data



Dose-dependent effectiveness, PBMC PK data



Comparative rectal and vaginal effectiveness, PK data



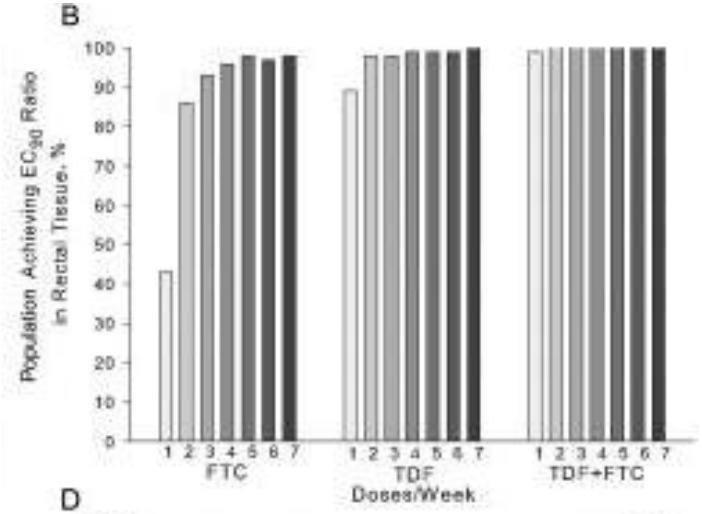
Zhang et al, *Nature Medicine*, 2023

Ianuzzi et al, *Nature Comm*, 2026

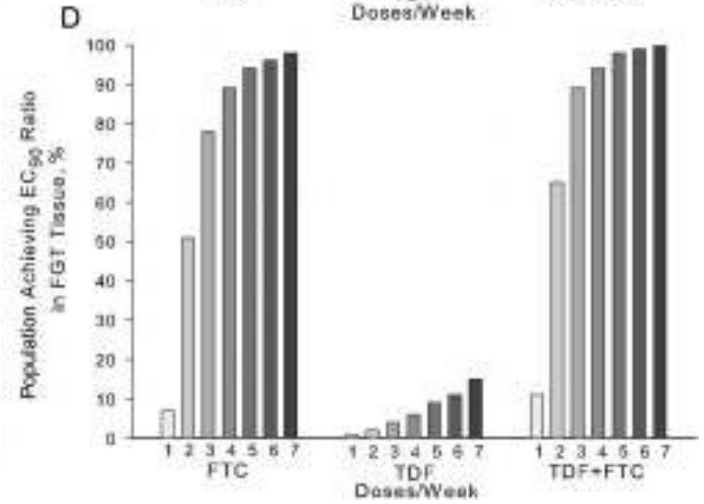
TDF drug levels are higher in rectum than vagina

47 cisgender women given TDF/FTC to predict time to protective EC90

Rectal Tissue



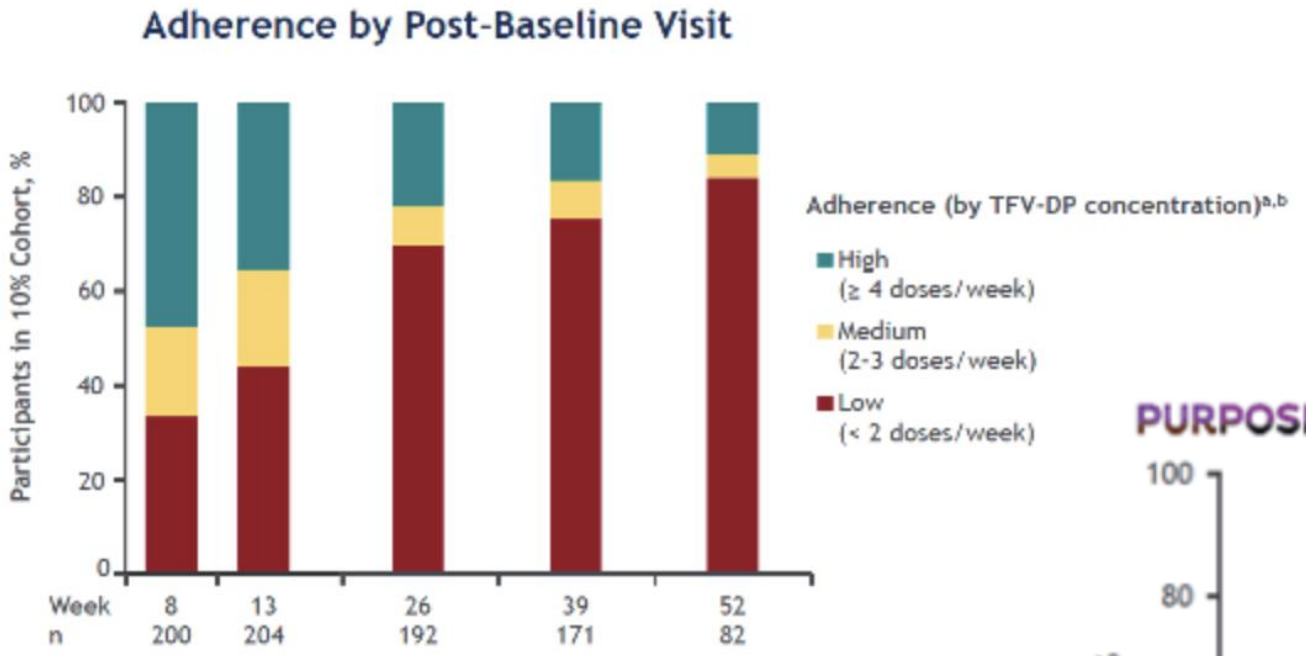
Vaginal Tissue



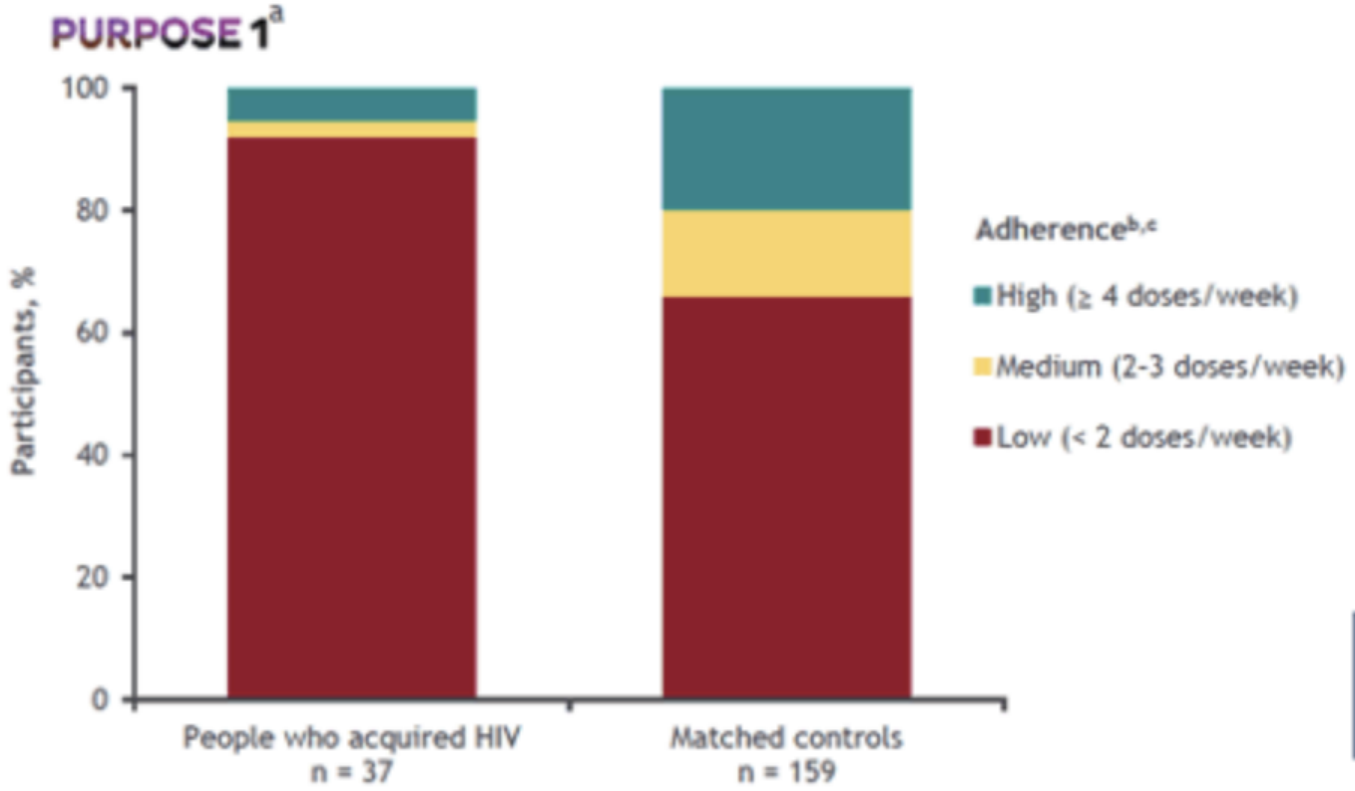
Daily TDF/FTC is proven to be protective for vaginal/front sex

Cottrell et al, JID, 2016

TAF has potential for AFAB

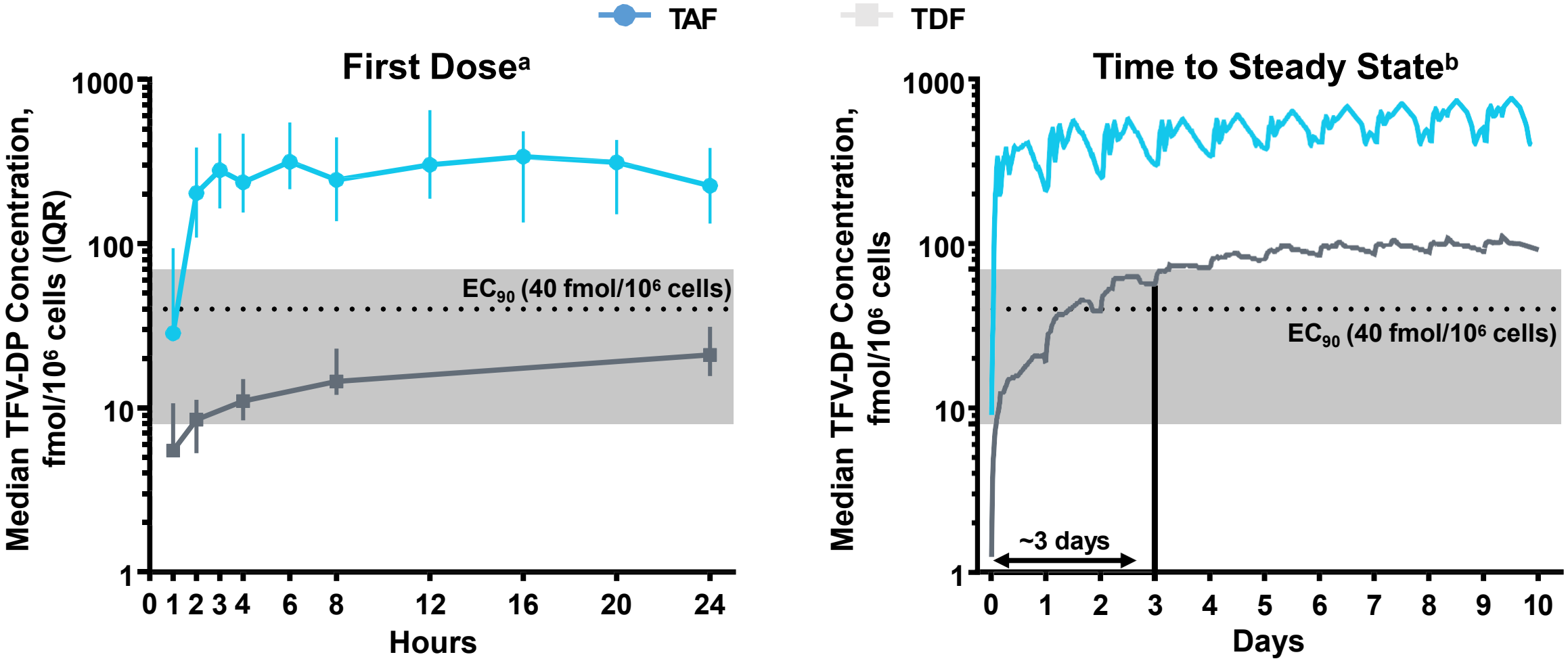


Odds of HIV acquisition were 89% lower among cisgender women who took ≥ 2 pills/week
(OR 0.11; 95% CI: 0.012-0.49; P = 0.0006)



Kiweewa et al, CROI, 2025

TDF and TAF drug levels in PBMCs

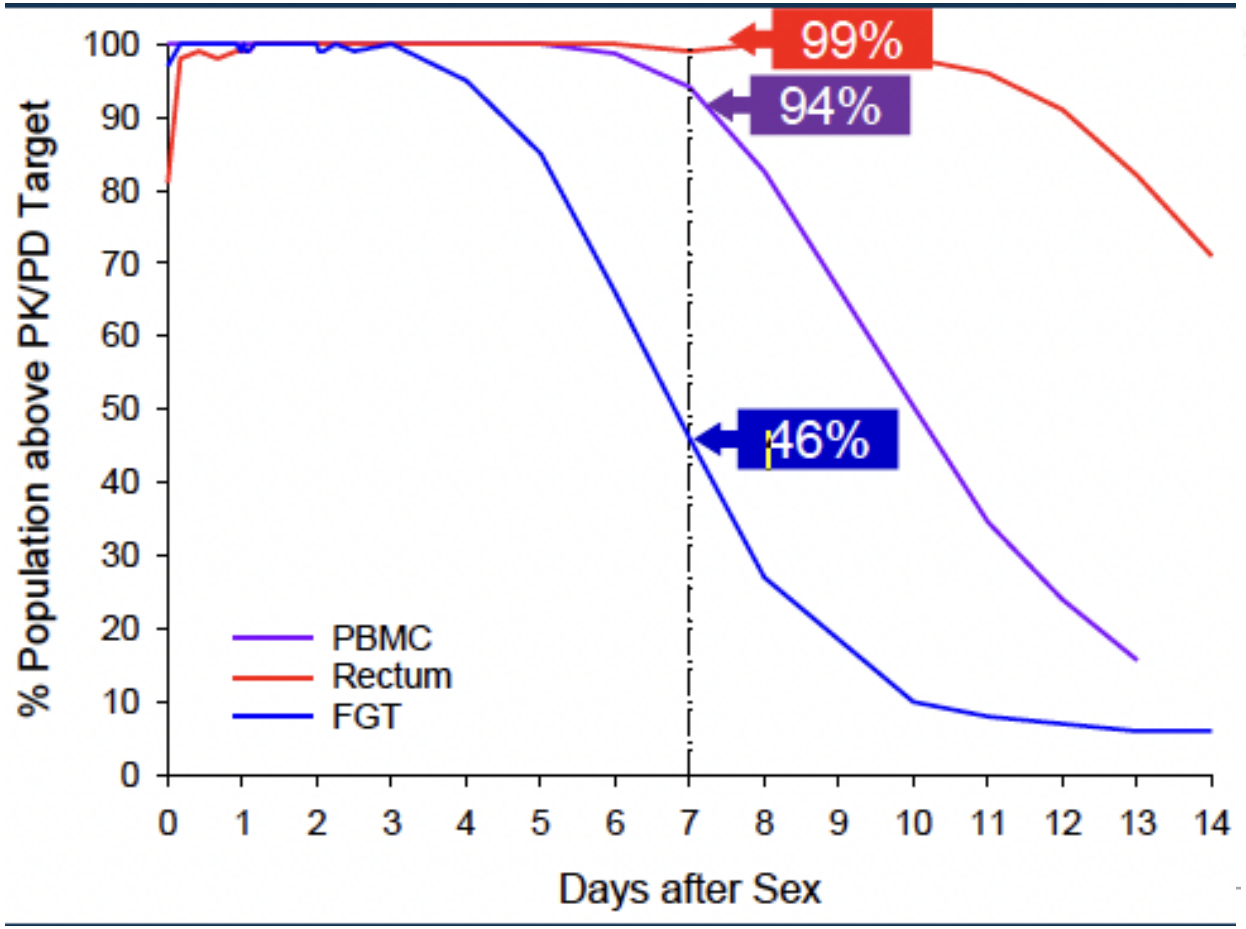


EC_{90}=90% effective concentration (40 fmol/10^6 cells, Anderson PL, et al. CROI 2012); IQR=interquartile range.
a. DVY data from bictegravir/F/TAF 50/200/25 mg in volunteers (N=26) and TVD data from Schwartz JL, et al. HIV Research for Prevention 2018 (n=25), Cottrell 2017; b. Mean simulated time to steady state.

Slide adapted from Jean-Michel Molina

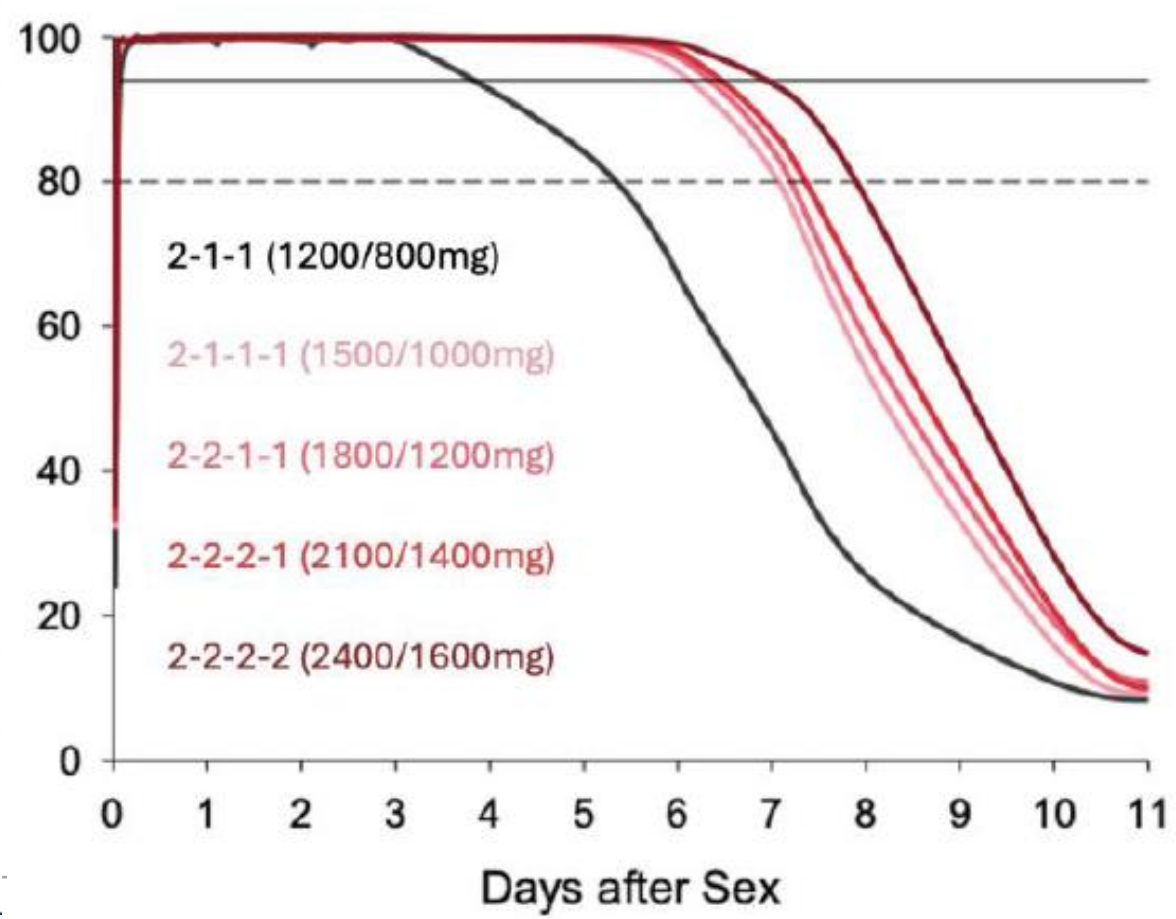
Modeling Event-Driven PrEP dosing for AFAB

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



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

2-1-1-1 dosing increases predicted efficacy in FGT by >40%



Engel et al, *J Infect Dis*, 2026 Feb;233:257-258.

Slide adapted from Cottrell

Conclusion

Adherence-effectiveness

- Efficacy trials of oral PrEP highlight adherence barriers and effective prevention when taken

Vaginal drug levels are not the whole story

- Low vaginal tenofovir levels are not the same thing as low vaginal sex protection levels.

Guidance based on nonRCT data

- RCTs are increasingly infeasible and unethical so updating guidelines will need to rely on PK, modeling, and animal data.

Choice increases impact

- Choice is trauma-informed care, and some PrEP is better than no PrEP.

Thank you

Jenell.Stewart@hcmed.org

Oral PrEP dosing for women*:
current guidance and key questions

Dr Heather-Marie Schmidt
Advisor HIV Prevention Programme Implementation
UNAIDS and the Global HIV Prevention Coalition Secretariat

Schmidth@unaids.org

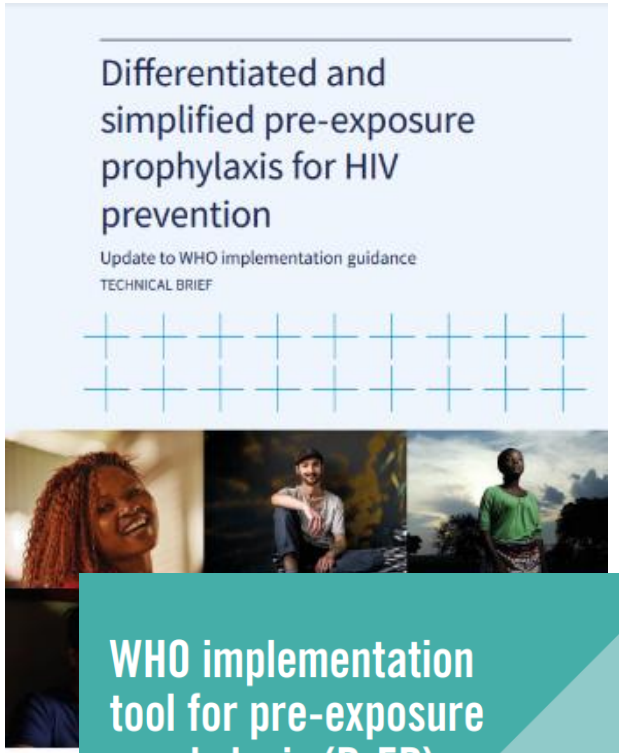
On behalf of the WHO PrEP team: Michelle Rodolph, Heather Ingold, and Erica Spielman

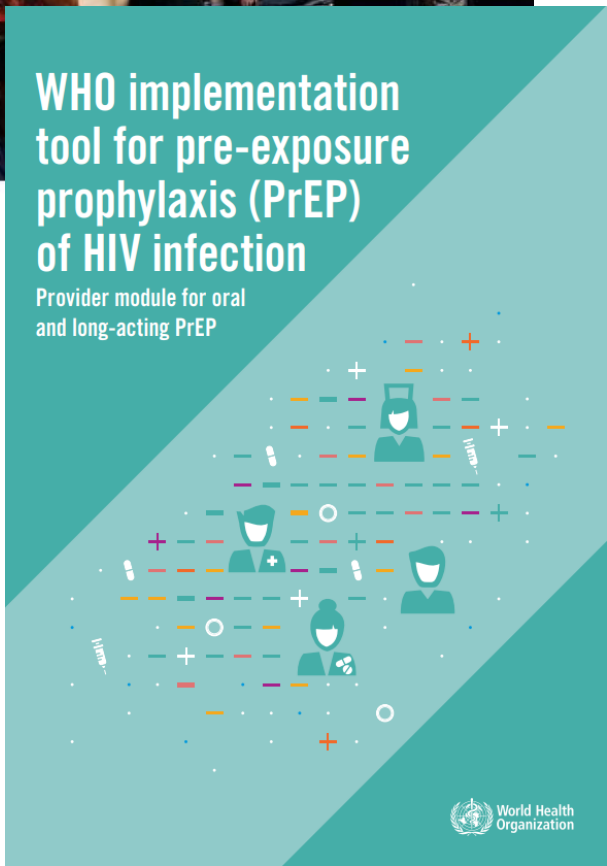
World Health Organization

UNAIDS

WHO guidance on oral PrEP

- 2015 WHO recommendation: oral PrEP containing tenofovir for people at substantial risk of HIV as part of combination HIV prevention approaches
  - Daily dosing
- 2019 WHO guidance: 2+1+1 dosing for MSM
- 2022 (& 2024) WHO guidance: two simplified dosing regimens depending on the individual's characteristics, circumstances and route of exposure
- Note: TDF/FTC and TDF/3TC considered interchangeable for oral PrEP
- Note: For the purposes of this presentation, the focus for dosing will be on:
  - cisgender women and adolescent girls
  - transgender men and other individuals assigned female at birth
  - transgender women using gender affirming hormones





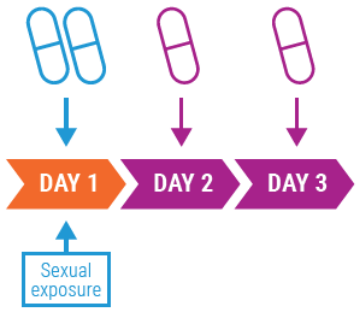
Oral PrEP containing TDF: Dosing regimen for people assigned male at birth with sexual exposure and who are not taking GAH

Whether for a single event, a short timeframe or a long time,

- Start with 2 doses 2-24 hours prior to the first exposure
- Continue with 1 dose per day for as long as oral PrEP use is desired
- Stop by taking 1 dose per day for at least 2 days after the last potential exposure
- Note on effective use: maintain **at least 4 pills per week**

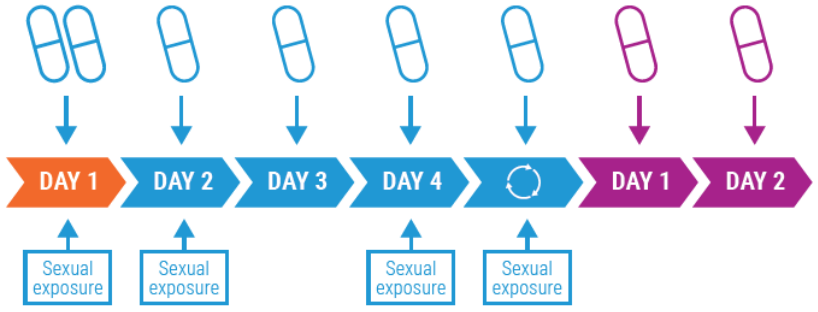
For example, cisgender men and transgender women and other gender diverse people assigned male at birth **not** taking exogenous gender affirming hormones

PrEP for a single event e.g. sex on 1 day



No longer using the term ED-PrEP to describe the dosing regimen

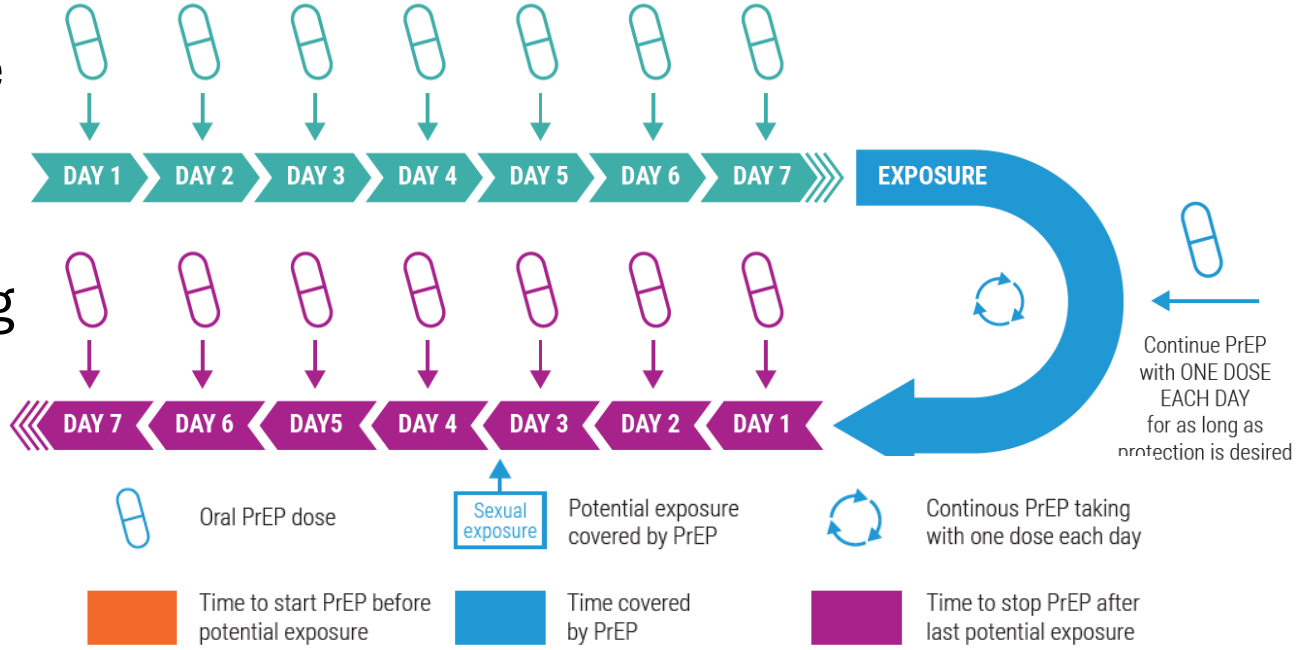
PrEP for multiple events or daily



Continue PrEP with
ONE DOSE EACH DAY
for as long as protection is desired

Oral PrEP containing TDF: Dosing regimen for most groups of people with sexual or injecting exposure

- Start with 1 dose per day for 7 days (use alternative HIV prevention options during that time)
- Continue with 1 dose per day for as long as oral PrEP use is desired
- Stop by taking 1 dose per day for at least 7 days after the last potential exposure



- NOTE on effective use: this group should maintain **6-7 pills per week** during periods of exposure for high levels of protection.

For example, cisgender women, trans and other gender diverse people assigned female at birth, transgender women and other gender diverse people assigned male at birth taking exogenous gender affirming hormones, people who inject drugs

Have other guidelines adopted alternative dosing regimens for women?

- **EACS 2025**
  - **Starting with a double dose** (2 tablets loading dose) 2-24 hours prior to exposure, **followed by 1 tablet daily** and **stopping by taking PrEP daily for 7 days** after the last exposure
  - Low adherence is defined by <4 pills per week, regardless of the distribution
- **Britain (BASHH/BHIVA) 2025**
  - If the risk of acquisition is through receptive vaginal / neovaginal sex, PrEP can be **started** with **a double dose (2 pills) 2-24 hours** before risk and **stopped with a single dose daily for 7 days** after the last risk (2:7 event-based dosing) (Grade1C receptive vaginal, Gade1D receptive neovaginal)
  - When daily dosing is continuous (i.e. when four or more doses have been taken in the week prior to an exposure), four doses per week in subsequent weeks are likely to provide good protection for all types of risk exposure.

British Association for Sexual Health and HIV/British HIV Association guidelines on the use of HIV pre-exposure prophylaxis (PrEP) 2025

WHO Guidance: can we make oral PrEP easier and more flexible for women*?

Do we have sufficient evidence for:

1. A double-dose reducing the time to protection to 2-24 hours?
2. ≥4 pills per week sufficient for a high level of protection for women?
3. Reducing the time to stop to less than 7 days?
4. And if yes, could sufficient protection be achieved with more than one of these options? E.g. 2+1+1 dosing achieve sufficient protection?

Note: this is focused on standalone PrEP – options for the the dual prevention pill (DPP) may be more limited due to the OCC dosing requirements

Types of evidence that can support guidance updates

- Direct and indirect evidence including:
  - Sub-analyses of existing RCTs, observational studies etc.
  - PK/PD data
  - Animal model data
  - In vitro data
  - Modelling data
  - Values and preferences
- Triangulation from multiple data types, sources, studies etc. adds extra weight

WHO's global work on PrEP:
https://www.who.int/teams/global-hiv-hepatitis-and-stis-programmes/hiv/prevention/pre-exposure-prophylaxis

WHO Global PrEP Network webinars:
https://www.who.int/groups/global-prep-network

WHO technical brief on PrEP implementation guidance:
https://www.who.int/publications/i/item/9789240053694

WHO guidelines on CAB-LA:
https://www.who.int/publications/i/item/9789240054097

WHO consolidated key population guidelines:
https://www.who.int/publications/i/item/9789240052390

WHO consolidated HIV guidelines:
https://www.who.int/publications/i/item/9789240096394

WHO PrEP Implementation Tool:
https://www.who.int/tools/prep-implementation-tool

Updated PEP Guideline in 2024
https://www.who.int/publications/i/item/9789240095137

Global Prevention Coalition Resource Hub:
https://hivpreventioncoalition.unaids.org/

Thank you!

Thank you to the PrEP experts, advocates and users all over the globe – you are making PrEP happen!

Thanks to the **WHO HIV PrEP** team: Michelle Rodolph, Erica Spielman, Heather Ingold

Evolving Oral PrEP Guidance for Cis Women: panel discussion

THE CHOICE AGENDA

HIV prevention research – a new forum for advocacy on the latest

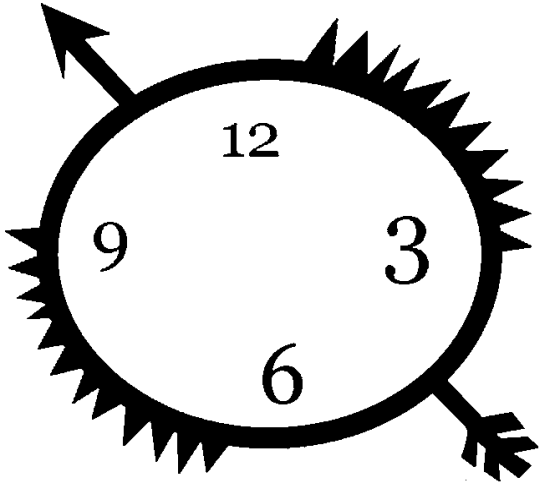
[i-base]

Community background

23 September 2026

Simon Collins, i-Base.info

A community perspective



TIME = how many people become positive.

>1 million HIV cases every year (1.2m in 2025).

<4 million people access PrEP – vs 20 million target.

<5% of people using PrEP in the EU are women.

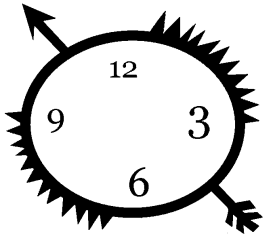
Daily oral PrEP isn't popular in many settings but might be the only option for many women – easier dosing might help.

STIGMA and politics delayed both research and access.

EU approval and indication to use with condoms.

No RCTs of on-demand dosing in cis women, delay for F/TAF

PrEP: an activist timeline



1994

TDF works as PrEP in animals - 32 years ago [1]

2010 – 2012

iPrEX inc [2]

~14% TGW. US FDA approval.

2013 – 2015

iPrEX PK; TGW; WHO guidelines, IPERGAY (2:1:1 in MSM &TGW [3, 4, 5]

2016

Oral TDF/FTC approved in Europe (2020 in the UK).

2019

Oral F/TAF – better PK - approved in MSM/TGW in US.

Never in EU. [6]

2021

CAB-LA PrEP in US FDA.

2025

LEN PrEP in US

Why are there no data on PrEP efficacy in transgender men?

1. Tsai et al. Science (1995). 2. Grant RM et al, NEJM (2010). 3. Anderson PL et al. NEJM (2013). 4. Deutsch MB et al. Lancet HIV (2015). 5. Molina J-M et al. NEJM (2015). 6. Mayer KH, Lancet 2020.

A new understanding of PrEP

Early theory based on drug levels in vaginal/rectal tissue.

Recently, efficacy now explained by drug levels in cells. [1, 2]

"the insights into PK/PD in PBMCs and large observational datasets … [means] … we may soon be seeing recommendations to harmonise 2:1:1 dosing across populations." [3]

>> Drug levels in cells (PBMCs) are not affected by sex or gender – or route of exposure – ie systemic not just local protection.

Zhang L et al. Nat Med 2023. Sara Iannuzzi S et al. Nat Commun 2026. 3. Raphael Landovitz, AIDS 2026

Examples adherence and levels in cells?

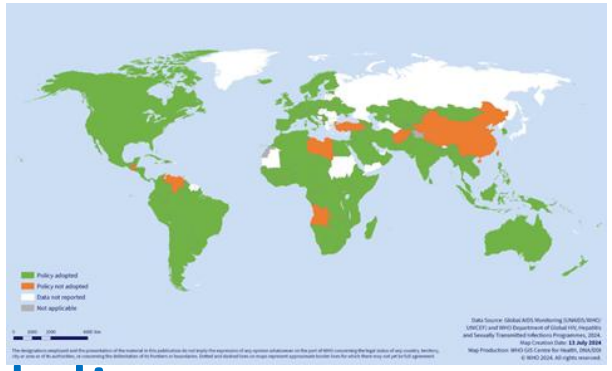
- Partners PrEP: 71% efficacy of oral TDF alone in women despite negligible TDF levels in tissue predicting zero protection. [1]
- PURPOSE 1: high levels of protection from F/TAF in young women if only two or more daily doses were taken in a week. [2]
- Ongoing French/Thai SimpPrEP study uses 1:1 dosing of F/TAF in MSM and TWG – results in 2027. [3]

TAF has 4-7 x higher active levels in cells (PBMCs) than in rectal tissue, 90% lower levels in blood. [4]

Do any studies disprove PBMC/adherence hypothesis?

1. Baeten JM. NEJM (2012). 2. Bekker L-G AIDS 2024. 3. NCT05813964. 4. Thurman AR eClinMed (2021)

Challenges for guidelines *

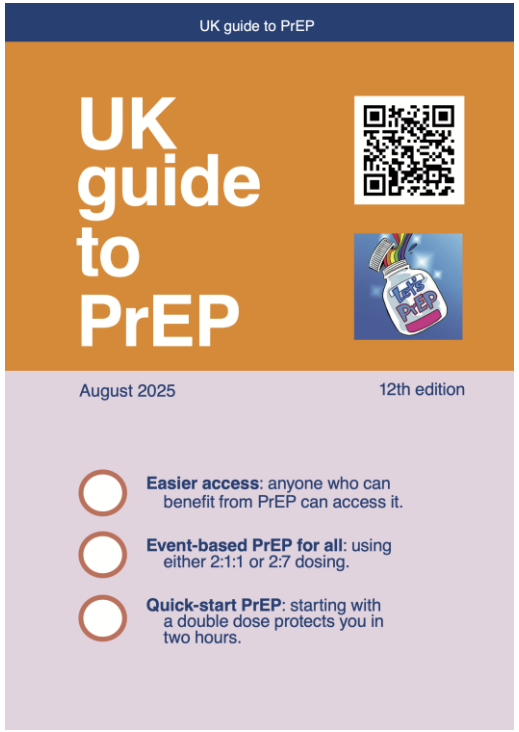


- Acceptable evidence without new RCTs?

  WHO PEP guidelines and trans men in PrEP guidelines.
- PK/PD/adherence data proves ACTUAL efficacy. *ie iPrEX efficacy increased from 44% to >99% based on drug levels – even though still an indirect marker – (assumes adherence at diagnosis is the same as when exposed).*
- Include easier PrEP - rapid protection & less strict adherence.
- Limited access to injectable PrEP. Window for alimatravir?

* EBD is currently included in UK and EACS guidelines but not in US or WHO.

Thank you


UK guide to PrEP
UK guide to PrEP
August 2025
12th edition
Easier access: anyone who can benefit from PrEP can access it.
Event-based PrEP for all: using either 2:1:1 or 2:7 dosing.
Quick-start PrEP: starting with a double dose protects you in two hours.

The current block: based on vaginal/rectal tissue

On demand – 2:1:1 dosing	Daily for cisgender women
Rapid protection within 2 hours	Daily PrEP for 7 days *
High cover with 4 doses a week	Minimum 6-7 doses a week
Stop after 2 x daily doses	Stop after 7 x daily doses