AETC AIDS Education & Training Center Program Mountain West

Emerging Issues in HIV PrEP and PEP

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Disclosures

No conflicts of interest or relationships to disclose.

Only FTC/TDF (Truvada®), FTC/TAF (Descovy®), and CAB-LA (Apretude®) are approved by the U.S. Food and Drug Administration (FDA) and only for use in some, but not all, populations.

This talk will include discussion of non-FDA approved strategies for HIV prevention.

Acknowledgements
Slide credits: Joanne Stekler, Tim Menza, Hillary Liss, Raaka Kumbhakar, National HIV Curriculum

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Acknowledgment

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Objectives

- Identify areas of clinical uncertainty in HIV PrEP care
- Review considerations for viral load monitoring for PrEP
- Understand evidence for alternative PEP regimens

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Overview

- Introduction
  - Status of HIV and PrEP in the US
  - Evidence for PrEP
- Anchoring case study
  - PrEP options, including on-demand PrEP
  - Adherence and discontinuations
  - Time to protection after initiation
  - PrEP monitoring
  - Interaction with GAT
  - PEP strategies
- What's coming for PEP and PrEP

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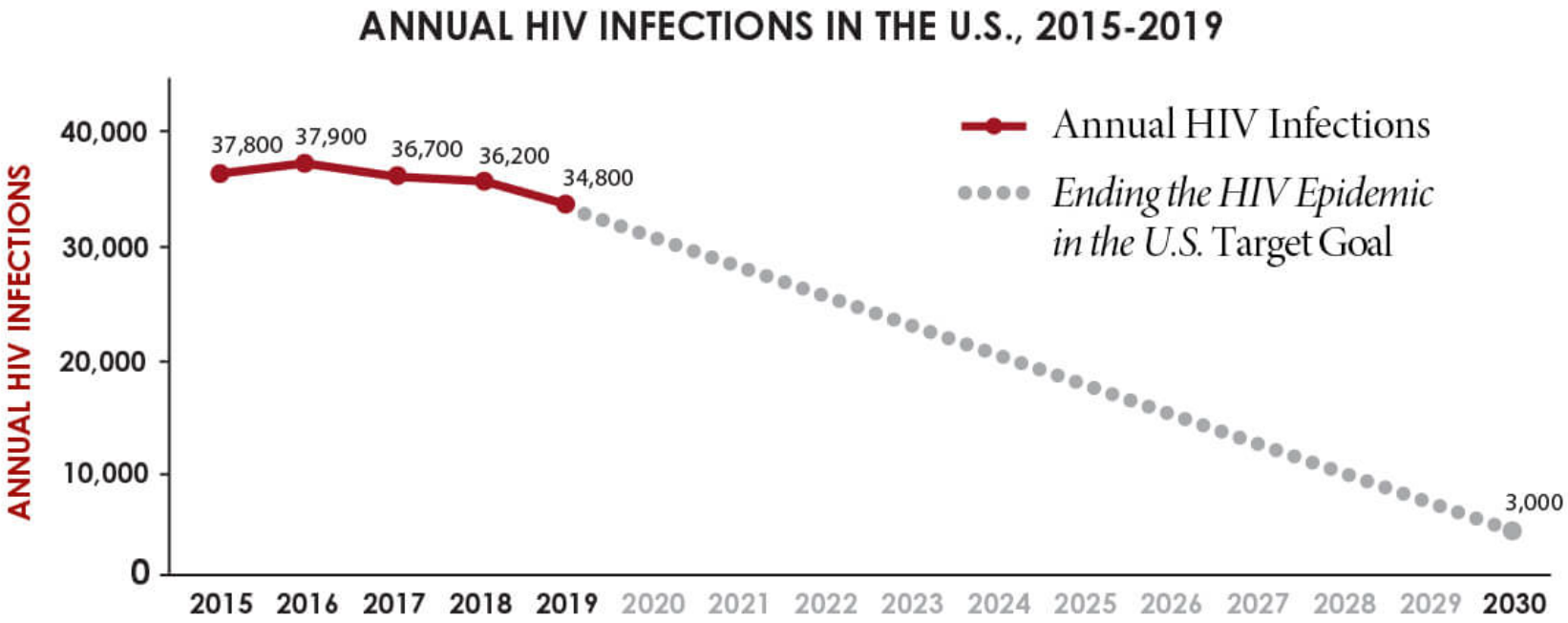
New HIV diagnoses in the US are stable to decreasing

NEW HIV INFECTIONS FELL 8% FROM 2015 TO 2019, AFTER A PERIOD OF GENERAL STABILITY



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

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

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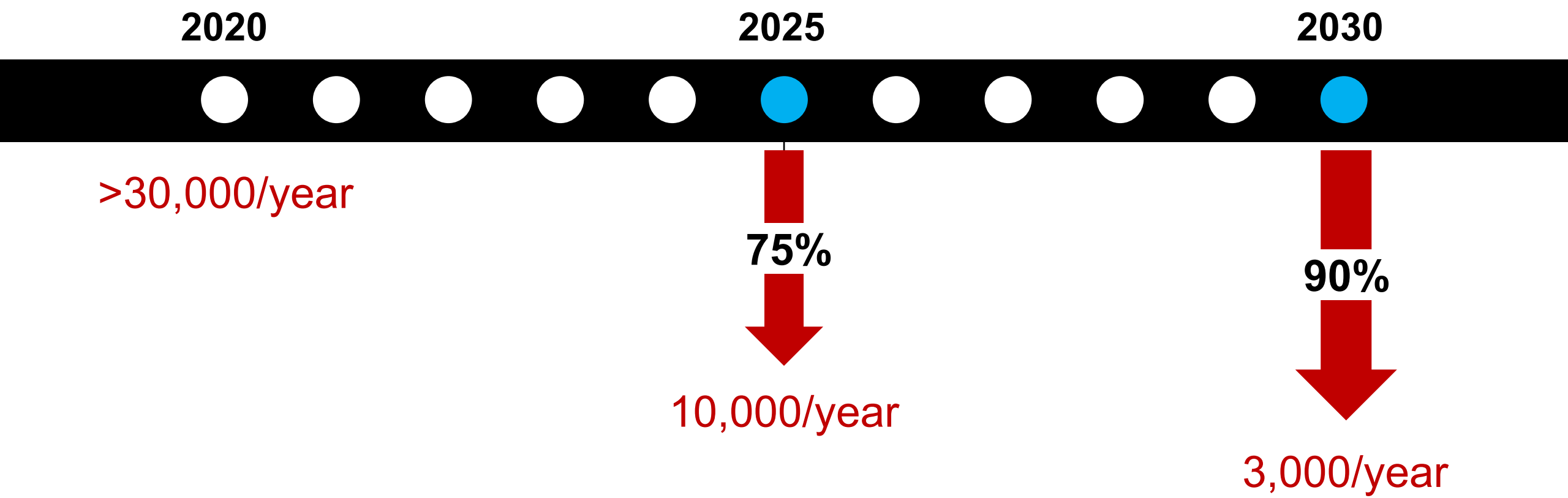
Ending HIV Epidemic (EHE) Initiative

Goals for Reducing Annual Number of New HIV Infection in U.S.



Prevention is a key pillar of the EHE initiative

What is PrEP?

Pre-Exposure Prophylaxis (PrEP): a prevention strategy in which a person without HIV takes antiretroviral medications to prevent acquiring HIV

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Is PrEP for everyone?

All people who desire PrEP should be offered PrEP

All sexually active adults and adolescents should be informed about PrEP

CDC, PrEP Clinical Practice Guidelines 2021

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3 Medications are FDA-approved for PrEP

1. Daily oral tenofovir DF-emtricitabine (F/TDF) approved 7/2012

2. Daily oral tenofovir alafenamide-emtricitabine (F/TAF) approved in 10/2019 but NOT for persons having receptive vaginal intercourse

3. Injectable cabotegravir every 2 months approved in 12/2021

4. Dapivirine vaginal ring withdrawn from FDA consideration in 12/2021

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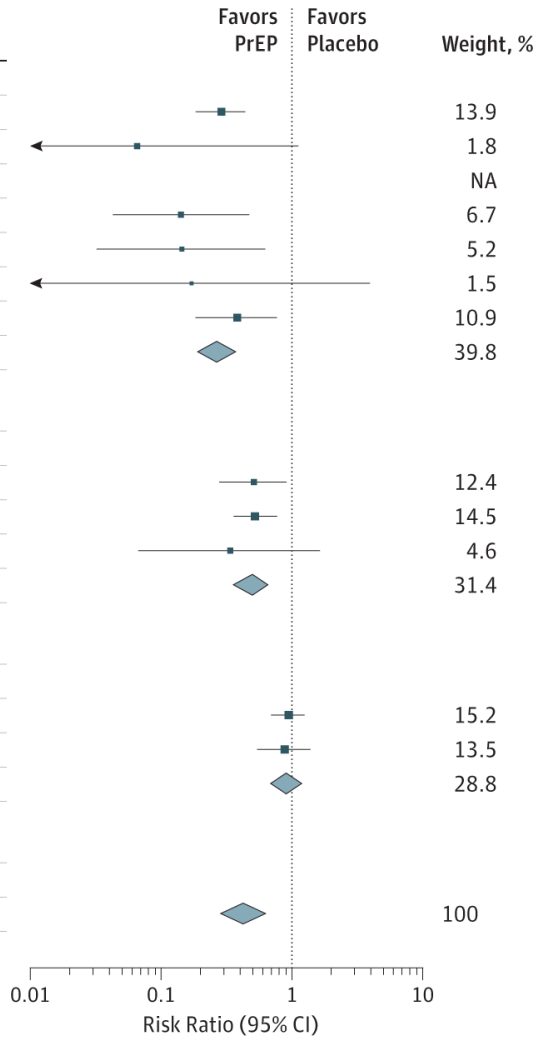
Oral PrEP is highly effective but depends on adherence

Source	No. of Events/Total PrEP	Placebo	Risk Ratio (95% CI)	Weight, %
Adherence ≥70%				
Baeten et al,[12] 2012	30/3140	52/1586	0.29 (0.19-0.45)	13.9
Grohskopf et al,[18] 2013[a,b]	0/201	7/199	0.07 (0.00-1.15)	1.8
Kibengo et al,[21] 2013[b]	0/48	0/24	NA[c]	NA
McCormack et al,[31] 2016[a,d]	3/268	20/255	0.14 (0.04-0.47)	6.7
Molina et al,[33] 2015[a]	2/199	14/201	0.14 (0.03-0.63)	5.2
Mutua et al,[39] 2012[a,b]	0/48	1/24	0.17 (0.01-4.03)	1.5
Thigpen et al,[42] 2012[e]	10/601	26/606	0.39 (0.19-0.80)	10.9
Subtotal	45/4505	120/2895	0.27 (0.19-0.39)	39.8
$I^2=0\%$; $\chi^2_5=3.98$ for heterogeneity, $P=.55$; $\tau^2=0.00$ Overall effect: $z=7.33$, $P<.001$				
Adherence >40% to <70%				
Choopanya et al,[14] 2013	17/1204	33/1207	0.52 (0.29-0.92)	12.4
Grant et al,[17] 2010	38/1251	72/1248	0.53 (0.36-0.77)	14.5
Peterson et al,[40] 2007	2/427	6/432	0.34 (0.07-1.66)	4.6
Subtotal	57/2882	111/2887	0.51 (0.38-0.70)	31.4
$I^2=0\%$; $\chi^2_2=0.28$ for heterogeneity, $P=.87$; $\tau^2=0.00$ Overall effect: $z=4.14$, $P<.001$				
Adherence ≤40%				
Marrazzo et al,[27] 2015	113/2010	60/1009	0.95 (0.70-1.28)	15.2
Van Damme et al,[43] 2012	31/1024	35/1032	0.89 (0.55-1.44)	13.5
Subtotal	144/3034	95/2041	0.93 (0.72-1.20)	28.8
$I^2=0\%$; $\chi^2_1=0.04$ for heterogeneity, $P=.84$; $\tau^2=0.00$ Overall effect: $z=0.56$, $P=.58$				
Overall				
Subtotal	246/10421	326/7823	0.44 (0.29-0.65)	100
$I^2=72\%$; $\chi^2_{10}=36.11$ for heterogeneity, $P<.001$; $\tau^2=0.25$ Overall effect: $z=4.04$, $P<.001$ Subgroup differences: $I^2=93.7\%$; $\chi^2_2=31.59$ for heterogeneity, $P<.001$				

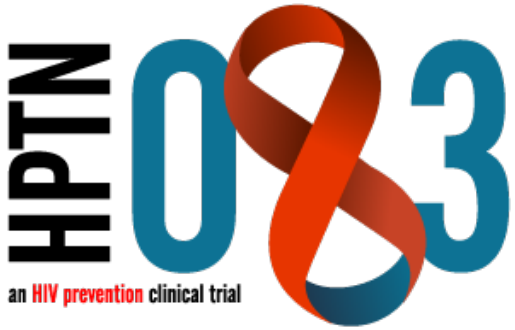


Population, by adherence	PrEP effectiveness (% protection rate)	GRADE of evidence
MSM (all RCTs)	75%	++++ High
MSM (≥80% vs <80%)	86% vs 45%	++++ High
Heterosexual (≥80% vs <80%)	80% vs not effective	++++ High +++ Moderate
PWID (1 RCT)	49%	+++ Moderate

Chou R, et al. *JAMA* 2019; Table adapted from Murchu EO, et al. *BMJ Open* 2022

Injectable cabotegravir (CAB)

Superior to oral F/TDF



HPTN 083 (4570 cisgender men and transgender women)

- 13 infections in the CAB arm (incidence rate 0.41%)
- 39 infections in the FTC/TDF arm (incidence rate 1.22%)
- Hazard ratio for CAB versus FTC/TDF was **0.34 (95% CI 0.18-0.62)**

HPTN 084 (3223 cisgender women)

- 4 infections in the CAB arm (incidence rate 0.2%)
- 36 infections in the FTC/TDF arm (incidence rate 1.85%)
- Hazard ratio for CAB versus FTC/TDF was **0.12 (95% CI 0.05-0.31)**

Images: hptn.org/research/studies

Landovitz R, et al. *NEJM* 2021; Delany-Moretlwe S, et al. *Lancet* 2022

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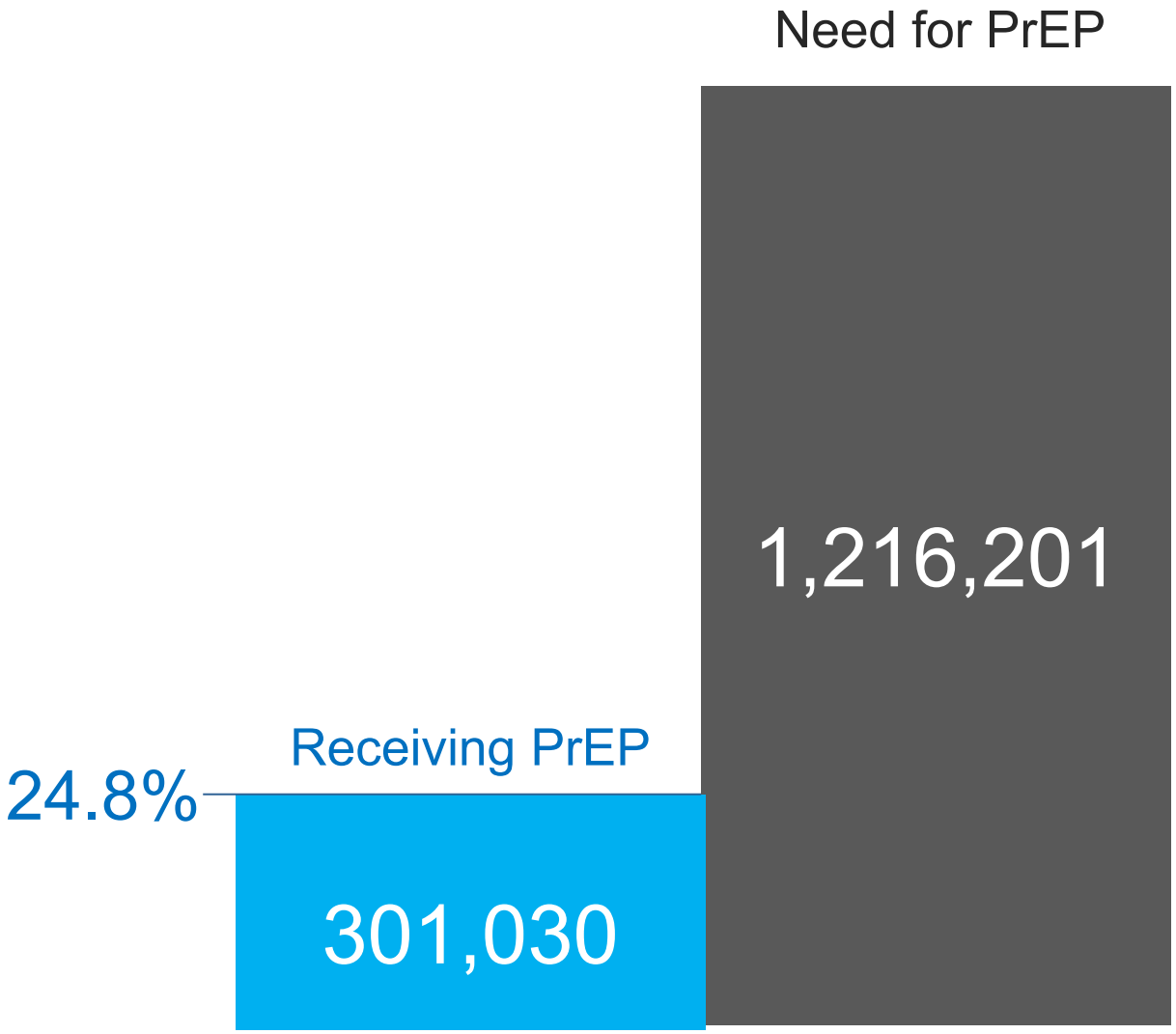
Estimated number of persons with need for PrEP in United States (US)

Source: CDC. HIV Surveillance Supplemental Report. 2021;26(No. 1). May 2021

National HIV Curriculum

Proportion of persons receiving PrEP versus need for PrEP



Source: CDC. HIV Surveillance Supplemental Report. 2021;26(No. 1). May 2021

PrEP is underutilized in the US

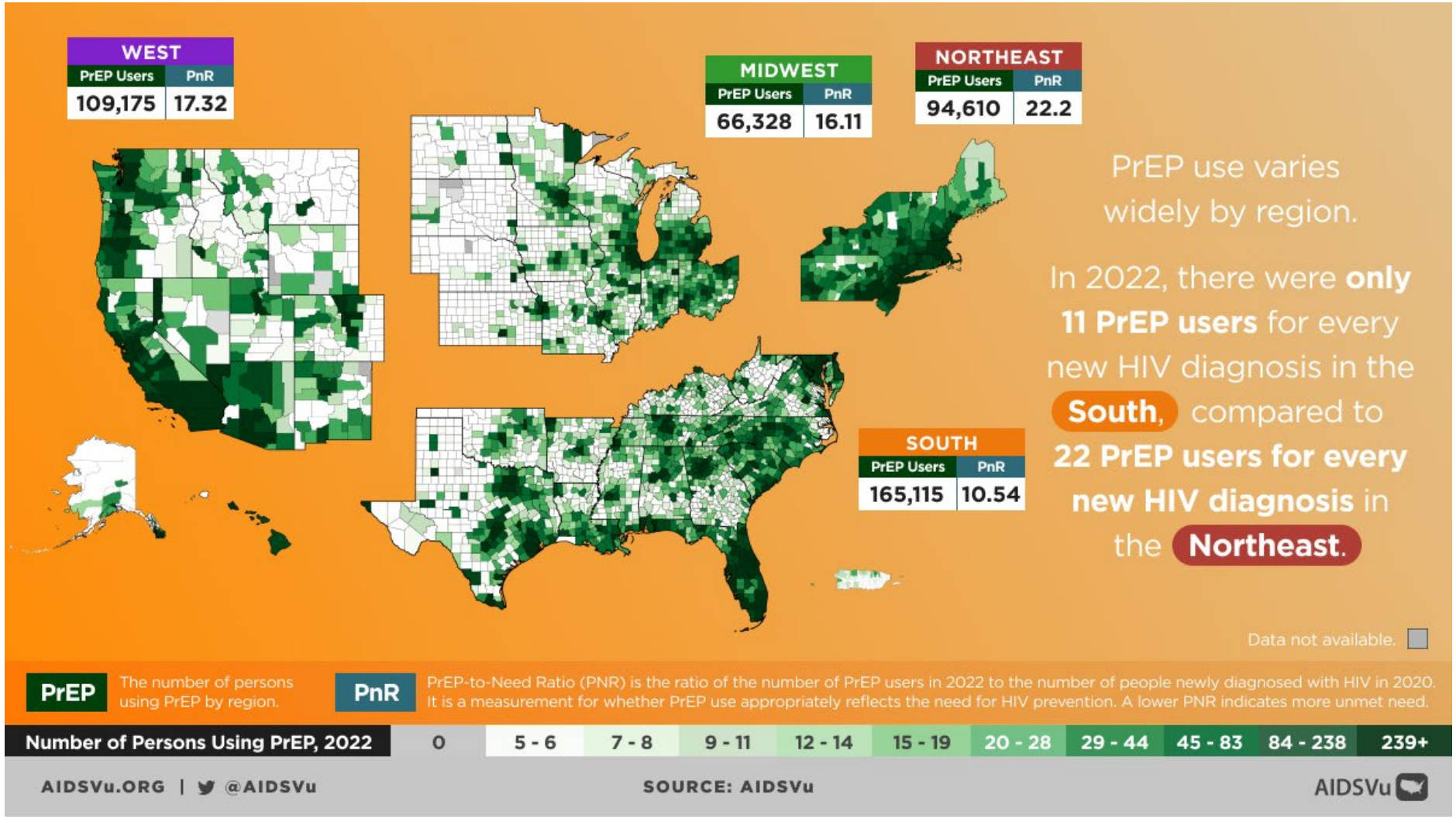


Image: aidsvu.org. Accessed June 2023.

Disparities in PrEP access and use are significant in the US

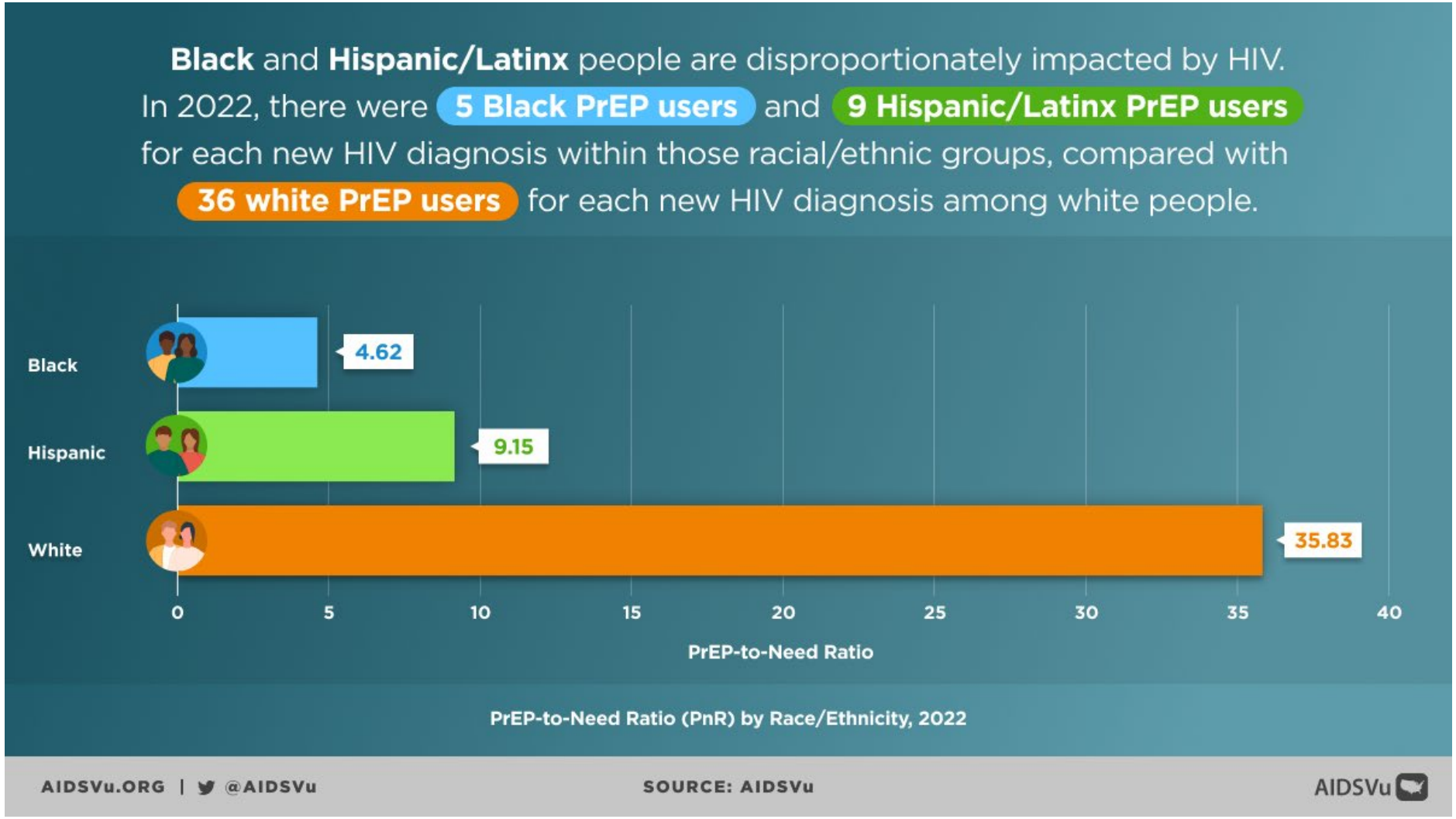


Image: aidsvu.org. Accessed June 2023.

Inequities in PrEP access and use are worsening

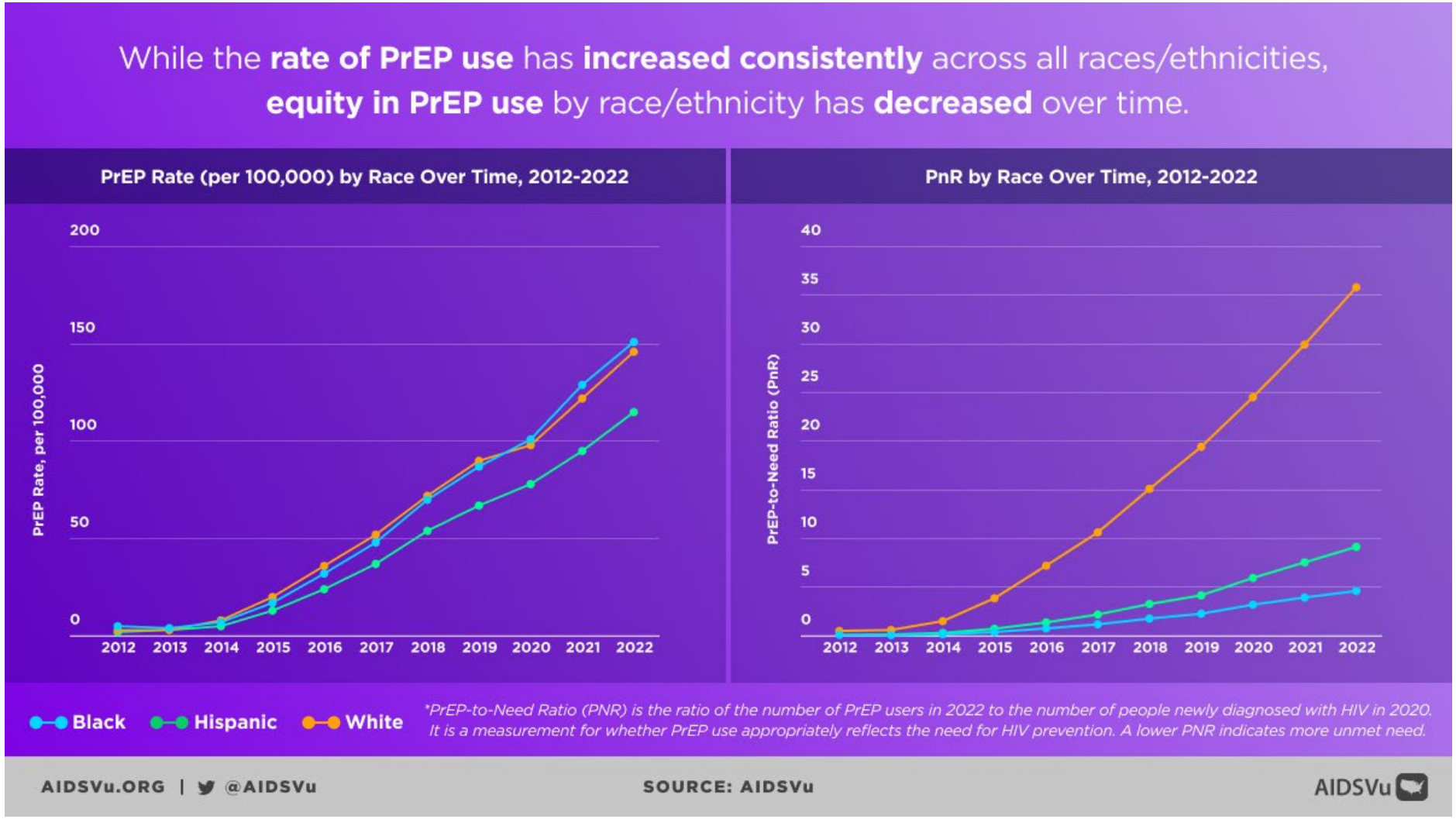


Image: aidsvu.org. Accessed June 2023.

Nearly all PrEP users in the US are men

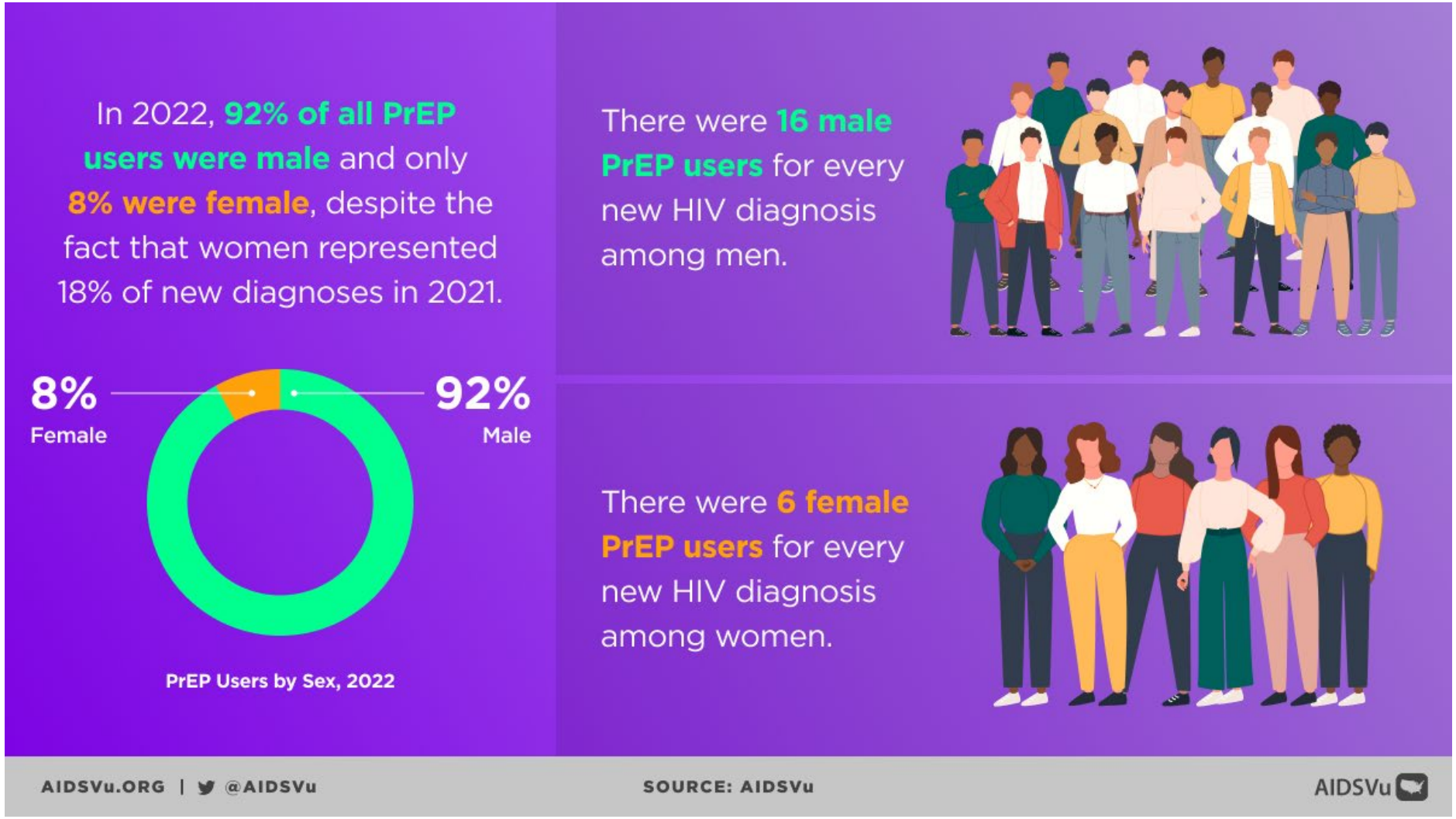
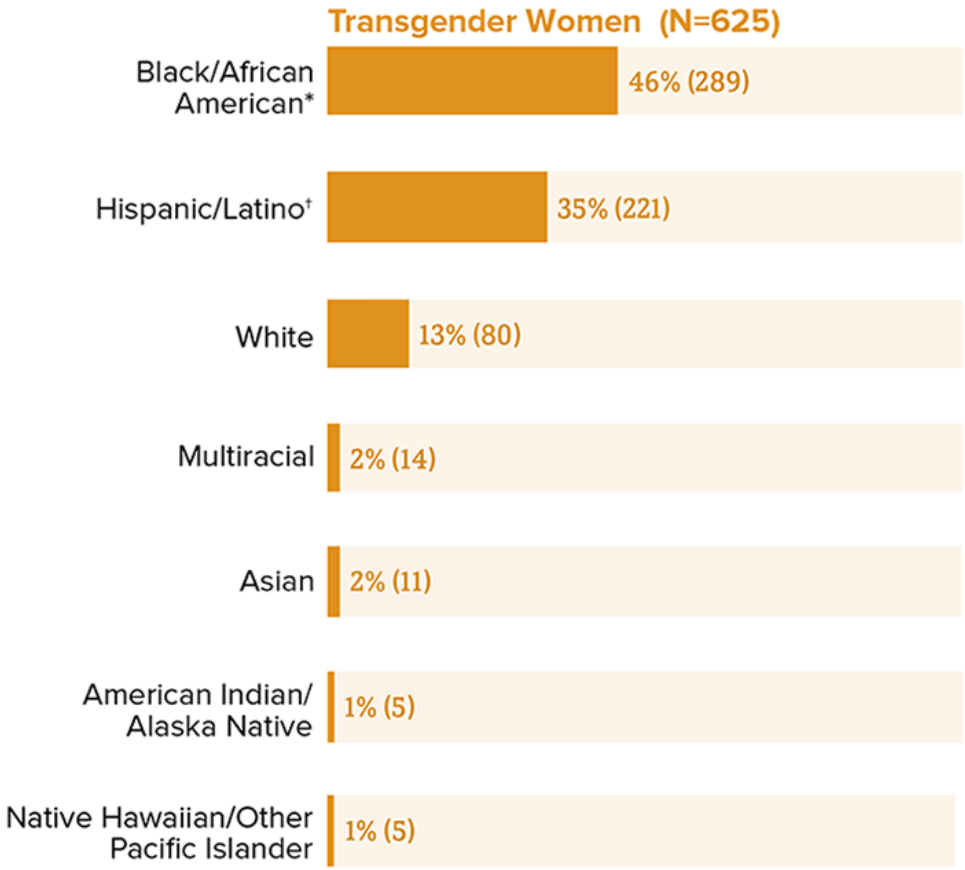
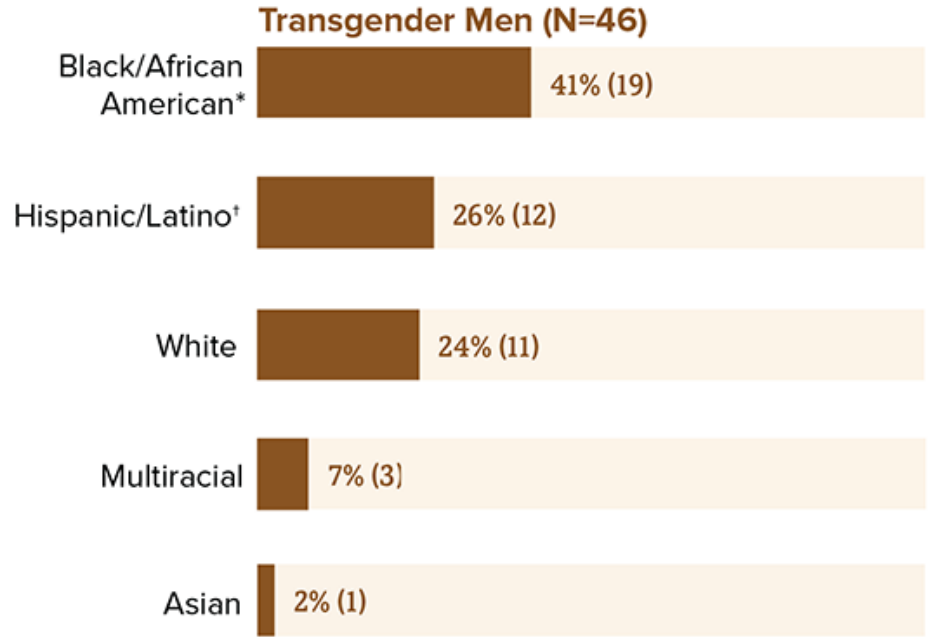


Image: aidsvu.org. Accessed June 2023.

Racial/ethnic disparities highest among transgender people

Of the **36,801 new HIV diagnoses** in the US and dependent areas in 2019, 2% (671) were among transgender people.





Source: CDC. HIV Surveillance Report. 2021;32

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A 32 y/o biracial non-binary person assigned male at birth (they/them) presents to clinic to start PrEP. They have engaged in receptive and insertive anal sex with 3 male partners this month.

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A 32 y/o biracial non-binary person assigned male at birth (they/them) presents to clinic to start PrEP. They have engaged in receptive and insertive anal sex with 3 male partners this month.

What PrEP medications are indicated for this person?

PrEP options by population

PrEP medication	Cisgender men	Cisgender women	Transgender & nonbinary people	Adolescents 12 or 13-17 y/o	PWID	Pregnancy	Comments
Oral F/TDF (RA/VI, IA/VI, receptive syringe sharing)	☑	☑	☑	☑	☑	☑	Must be ≥35 kg, CrCl ≥60
Oral F/TAF (RAI, IA/VI)	☑	CDC/HHS ⊘ IAS/USA ☑	CDC/HHS (TGW only) IAS/USA (RAI, IA/VI)	☑	Discuss	Discuss	Not for vaginal/front hole sex, CrCl ≥30
Injectable cabotegravir (RA/VI, IA/VI)	☑	☑	CDC/HHS (-) IAS/USA ☑	☑	Discuss	Insufficient data	Must be ≥35 kg
SQ/PO lenacapavir, oral islatravir, etc. *Studies ongoing*							

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PrEP options by population

PrEP medication	Cisgender men	Cisgender women	Transgender & nonbinary people	Adolescents 12 or 13-17 y/o	PWID	Pregnancy	Comments
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Oral F/TAF (RAI, IA/VI)	✓	CDC/HHS ⊘ IAS/USA ✓	CDC/HHS (TGW only) IAS/USA (RAI, IA/VI)	✓	Discuss	Discuss	Not for vaginal/front hole sex, CrCl ≥30
Injectable cabotegravir (RA/VI, IA/VI)	✓	✓	CDC/HHS (-) IAS/USA ✓	✓	Discuss	Insufficient data	Must be ≥35 kg
SQ/PO lenacapavir, oral islatravir, etc. Discuss							

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Comorbidities and PrEP

- Renal
  - TDF/FTC is contraindicated with CrCl ≤60
  - TAF/FTC is contraindicated with CrCl ≤30
  - Consider CAB for patients with significant renal disease in whom tenofovir-containing regimens are not recommended
- Bone
  - If high risk for osteoporosis, consider bone scan and consultation with bone health specialist prior to TDF or TAF use; TAF is more bone friendly than TDF
- If contraindications to CAB, do not prescribe PrEP

Krakower et al, *OFID* 2017

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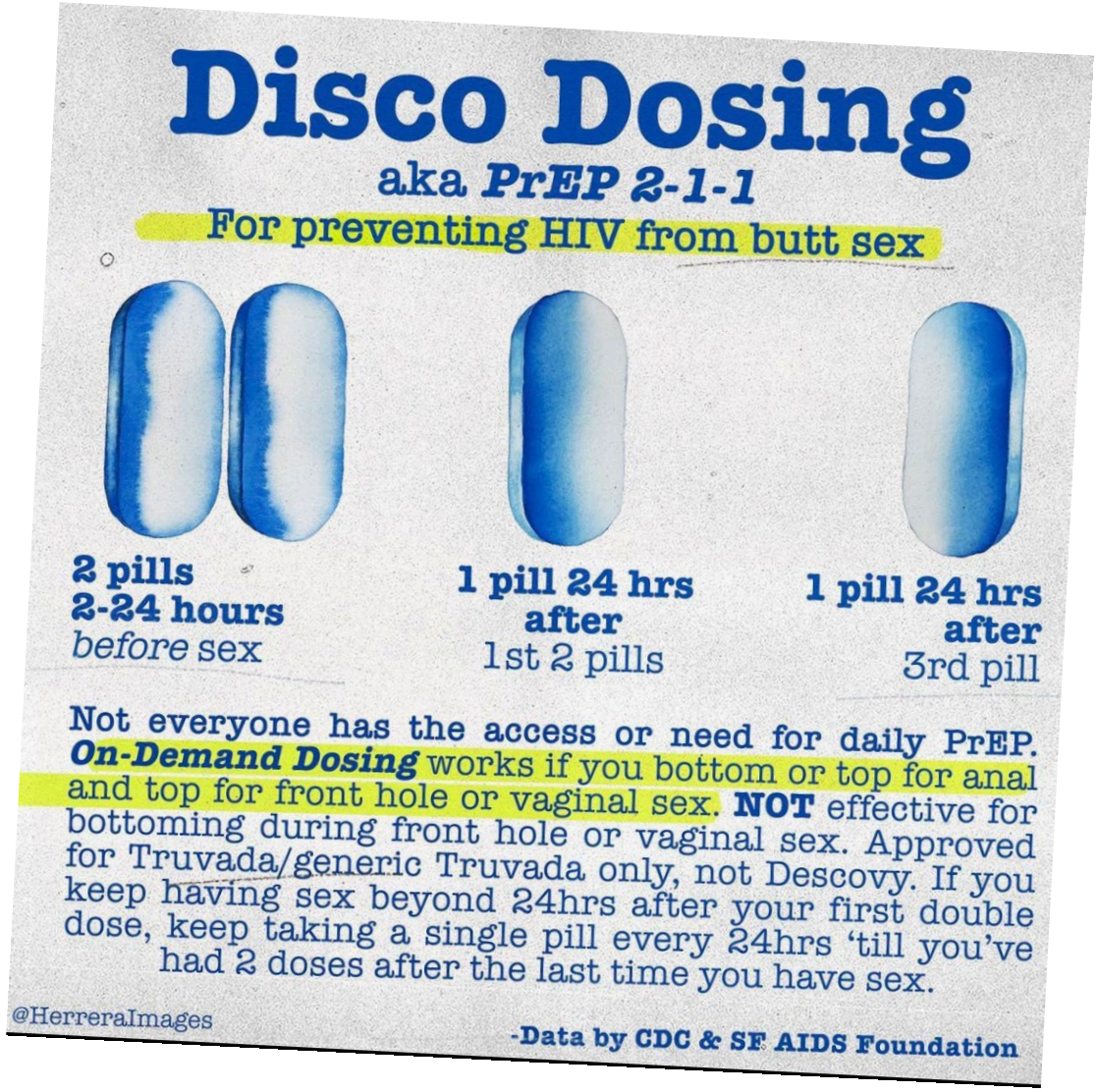
When should “2-1-1" or on-demand PrEP be considered?

On-demand PrEP dosing: How to “2-1-1”



Images: @HerreraImages (Instagram); prepdaily.org

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“2-1-1” or on-demand dosing (F/TDF only?)

	IAS-USA (2022)	HHS/CDC (2021)	WHO update (2022)
Cisgender men	Recommended regardless of sexual orientation	For adult MSM who have sex less than 1x/week and can anticipate sex	Recommended for sexual exposures
Transgender women	Use with caution in TGW receiving hormone therapy		Not recommended if using exogenous estradiol products
Cisgender women, transgender men, PWID with no sexual risk	Insufficient data		Not recommended
HBV co-infection	No specific guidance	Contraindicated	Ok to use

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They opt for daily PrEP.

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They opt for daily PrEP.

What should be explained about medication adherence?

Efficacy in open-label projects: iPrEx OLE (open label extension)

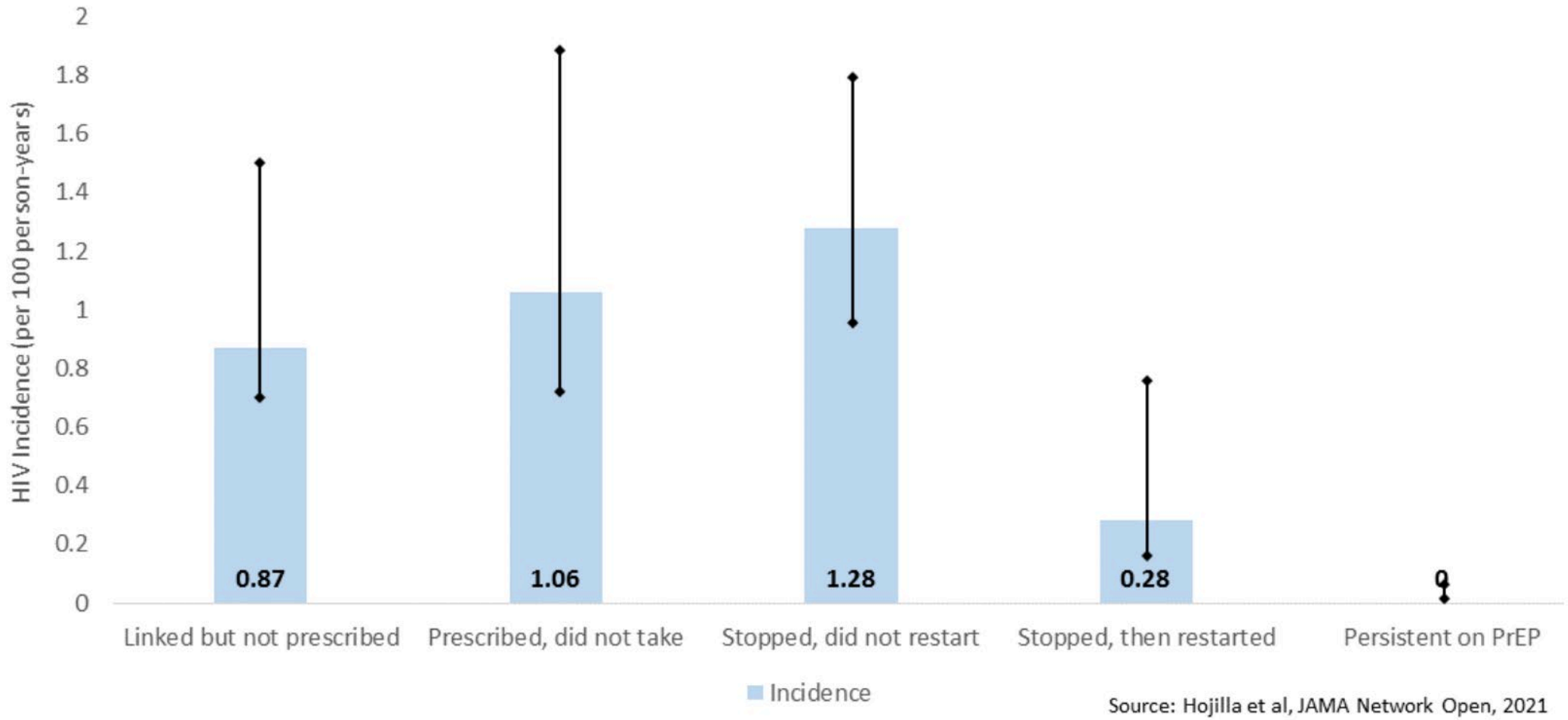
Estimated adherence (TDF in DBS)	Incidence	Protection
Not detected	4.7/100 person-years	
<2 tab/week	2.3/100 person-years	51%
2-3 tab/week	0.6/100 person-years	87%
4-7 tab/week	0/100 person-years	100%

Source: Grant et al (iPrEx OLE), Lancet. 2014: 14; 819-829.

We know of <10 well-documented cases of persons who acquired HIV despite excellent adherence to PrEP, but there may be others.

Examples: Knox et al NEJM 2017; 376: 501-502
Markowitz et al JAIDS 2017; 76(4): e104-106
Hoornenborg et al, Lancet HIV 2017; 4: e522-28

No HIV infections among people who persist on PrEP



Hojilla et al, *JAMA Network Open* 2021.

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Strategies to increase PrEP adherence

- Work into an existing routine
- Manage expectations around side effects
  - “Start up syndrome” with GI sx (oral PrEP) vs injection site reactions (IM CAB)
  - Preemptive discussion about rare bone and renal issues
- Reinforce benefit relative to few and uncommon harms
- Reminder that effectiveness is directly related to adherence
- Normalize missed doses
- Strategies that may be helpful
  - Check-ins/reminders using the patient’s preferred method of communication
  - Pillboxes, keychain pill cases
  - Peer-based PrEP navigation and adherence support

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Barriers to PrEP persistence are individual, social, and structural

- Young adults, Latinx and African American people, women, transgender people, those with lower SES, people in rural areas, and those with a substance use disorder are more likely to discontinue PrEP during follow-up
- Awareness and knowledge of PrEP among both patients and providers
  - Biased marketing of PrEP
  - Regional and cultural differences for prioritization of sexual health
- Mismatch in perceived and actual risk of HIV among both patients and providers
- Lack of access to appropriate, unbiased, anti-racist, trauma-informed care
- Stigma related to HIV infection and PrEP use

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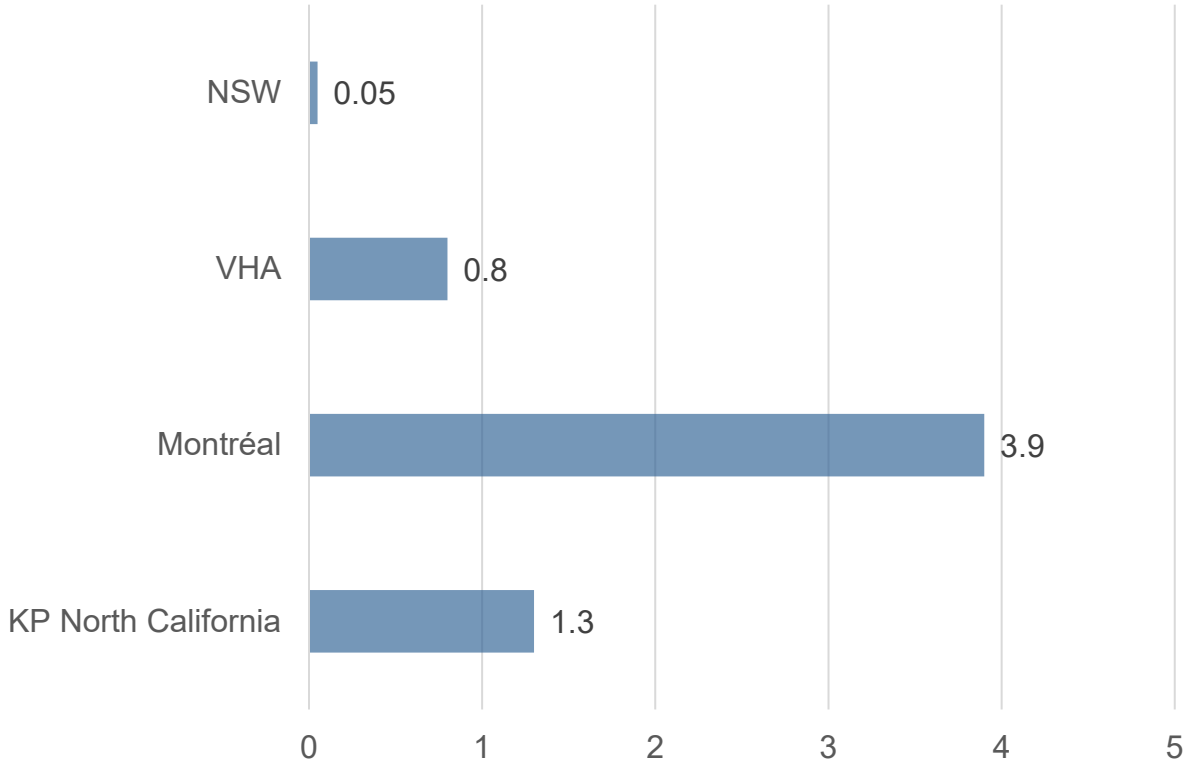
Risk for HIV acquisition is high after stopping PrEP

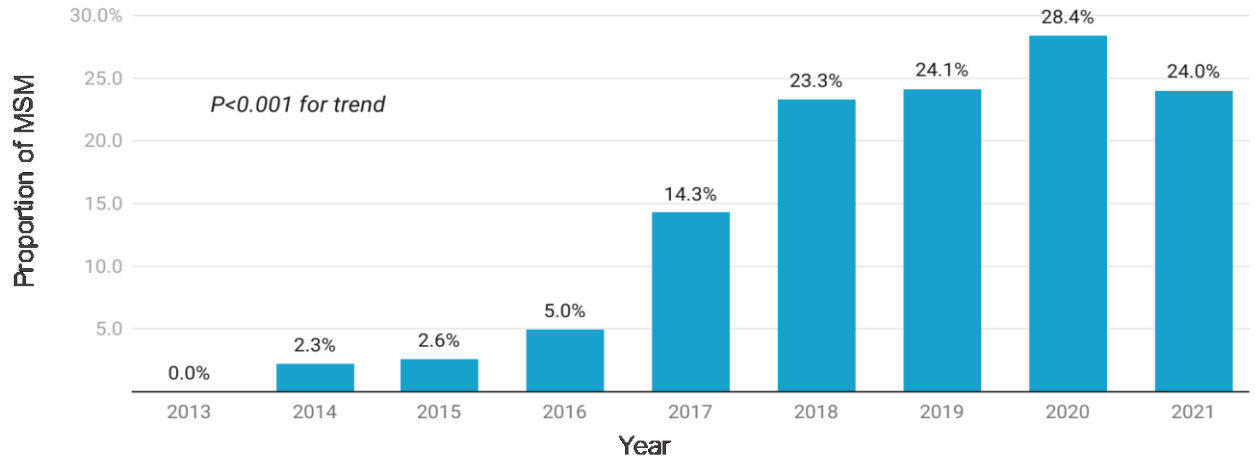
HIV incidence per 100 person-years after PrEP discontinuation



Grulich et al, *Lancet HIV* 2018; Van Epps et al, *JAIDS* 2019; Greenwald et al, *BMJ Open* 2019; Marcus et al, *CID* 2017

Over 20% of MSM with new HIV diagnoses in King County had used and discontinued PrEP

Figure 1: Number and Proportion of MSM Newly Diagnosed with HIV in King County, Washington Who Report Previous PrEP Use, 2013-2021



	2013	2014	2015	2016	2017	2018	2019	2020	2021
Used PrEP	0	3	3	5	12	17	21	21	12
Total # MSM	5	133	115	101	84	73	87	74	50

Cannon, et al. *JAIDS* 2022

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What do you tell them about time to protection?
How do you counsel about condom use?

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What do you tell them about time to protection?
How do you counsel about condom use?

What if this were a person whose primary risk of HIV infection is <u>not</u> through receptive anal intercourse?

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Time to protection and condoms with PrEP

- Oral daily PrEP initiation: Condoms recommended for 7-20 days after starting
- Differences in time to protection by anatomic compartment (for F/TDF)
  - Cervicovaginal: 20 days
  - Peripheral blood mononuclear cells: 7 days
  - Rectal: 7 days
  - Urethral: ?
- We know some people will never use condoms
  - 2-1-1 might be preferred for initiations in some people at highest risk
  - IAS-USA 2022 guidelines: May start with double dose of F/TDF to shorten time to protection to 24 hours
- Injectable PrEP initiation and F/TAF: 7 days?? Insufficient data

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Practical considerations for PrEP initiations and monitoring

- Ensure HIV test with short window period (e.g., ag/ab) is negative within 1 week
  - PrEP can lead to delayed seroconversion and false negative testing (esp. oral fluid)
  - False positive tests will occur in a PrEP program (low HIV incidence + freq. testing)
- POCT (e.g., INSTI) ok if blood drawn for ag/ab testing at the same time
- Screen for signs/sx of acute HIV infection – fever, fatigue, rash, headaches, etc.
- Taking double dose at initiation is reasonable to “jump start” time to protection for MSM/TGW choosing daily PrEP

Curlin et al, *CID* 2017; Donnell et al, *AIDS* 2017

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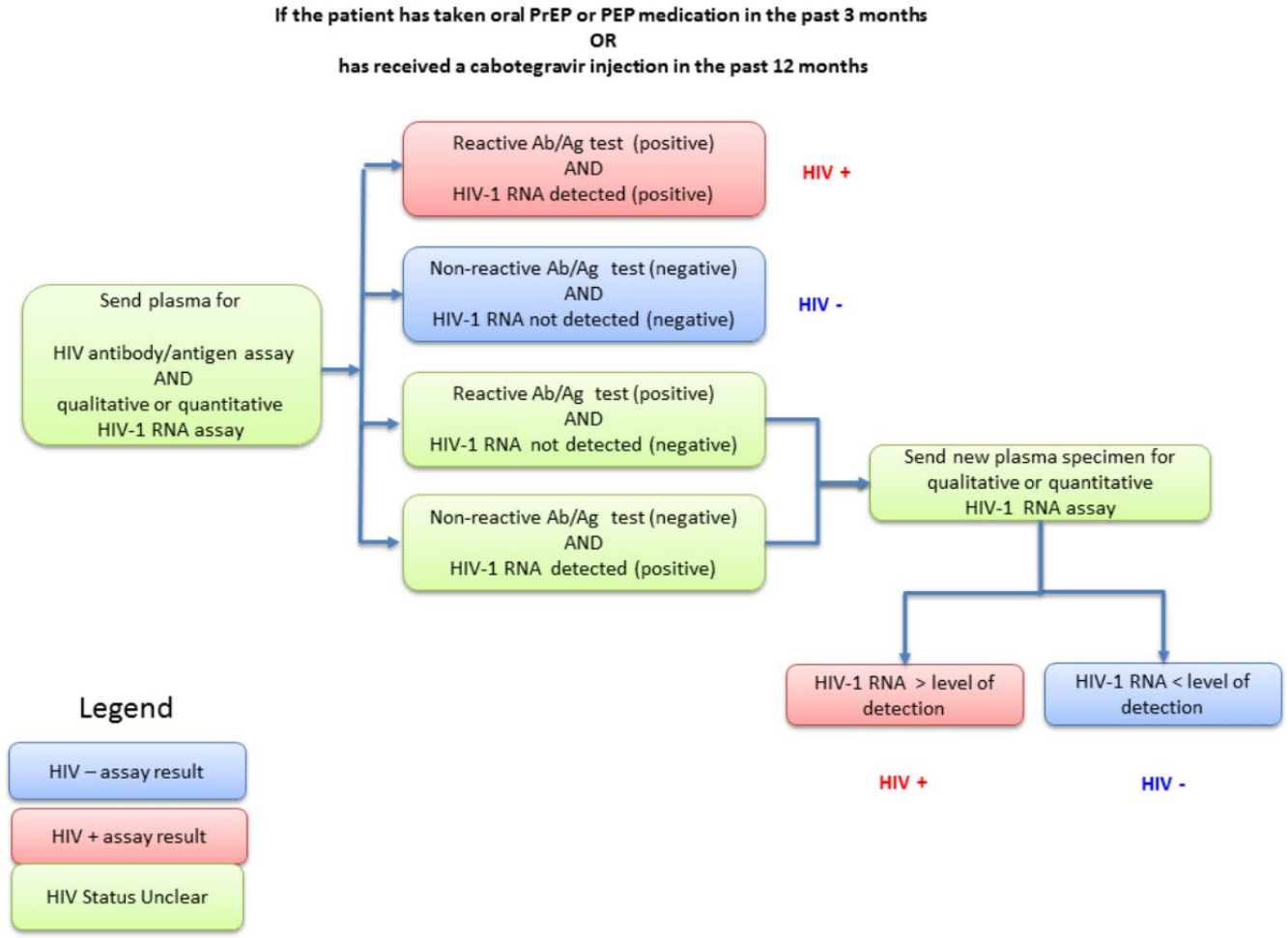
They return for their 3 month visit for refills and labs.

They return for their 3 month visit for refills and labs.

Is HIV RNA/NAAT for monitoring necessary?

CDC guidelines: HIV testing for those with recent or ongoing PrEP use

Figure 4b Clinician Determination of HIV Status for PrEP Provision to Persons with Recent or Ongoing Antiretroviral Prophylaxis Use



CDC, PrEP Clinical Practice Guidelines 2021

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Delayed detection of HIV on F/TDF in HPTN 083 (n=42)

	Baseline (n=3)	Incident infections (n=39)
Median delay 1st pos (range)	34 (14-36) days	31* (7-68 days*)
Median log VL at 1st pos visit	3.3 (2.1-4.7)	4.1 (NQ-4.3)**
# of cases VL would detect	3/3	6/39

*excluding case with visit interval 372 days
**for the 6 participants with detectable VL

4 participants continued to receive oral PrEP

5 M184V/I, 1 K65R

Marzinke et al, *JID* 2021

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PrEP USE DURING ACUTE HIV INFECTION IN A COMMUNITY SETTING COMPROMISES HIV DIAGNOSIS

Table: Clinical and diagnostic test results from 6 Thai MSM who started PrEP during acute HIV infection.
xG=x generation HIV antibody test, Gn= Geenius, □=nonreactive, ■=reactive, ND=not done

Partici-pant	# days on PrEP	HIV diagnosis	Pre-PrEP VL (cps/mL)	Pre-ART VL (cps/mL)	Pre-ART CD4 (cells/μL)	Week 0			Week 24			Week 48			
						2G	3G	4G	2G	3G	4G	2G	3G	4G	Gn
3145	7	NAAT	16,780	216	685	□	■	□	□	■	□	ND	ND	□	□
4634	2	NAAT	219	2,317	528	□	□	□	□	■	□	□	ND	□	□
5803	29	Ab	58	37,222	302	□	■	□	■	■	□	ND	ND	■	□
6313	91	Ab	223,361	389	690	■	■	□	■	■	□	ND	ND	□	□
6934	2	NAAT	32	276	739	□	□	□	□	□	□	□	□	□	□
7167	15	NAAT	317	8,802	521	□	□	□	■	■	■	ND	ND	ND.	□

WB = Indeterminate or NEG at all time points in all participants

Colby et al. CROI 2021. Abstract #179

Real issue: cost and back of envelope cost-effectiveness

- CAB: VL recommended at every visit (CDC & IAS-USA)
- Oral PrEP guidelines:
  - CDC (2021): Initiation? and RNA every 3 months
  - IAS-USA (2022): RNA at initiation if high-risk exposure in last 4 weeks or signs/sx of HIV
  - WHO: RNA is optional
- FTC/TDF: 2287 participants in HPTN 083

  Follow-up (Q3mo) = 2287 x $164 x 5 tests = $1,875,340

  With 5 M184V/I = additional **~$375,000/case identified**
- Some payers currently refusing to cover screening with HIV NAAT for PrEP
- In practice, ordering VL for monitoring on oral PrEP seems to be uncommon

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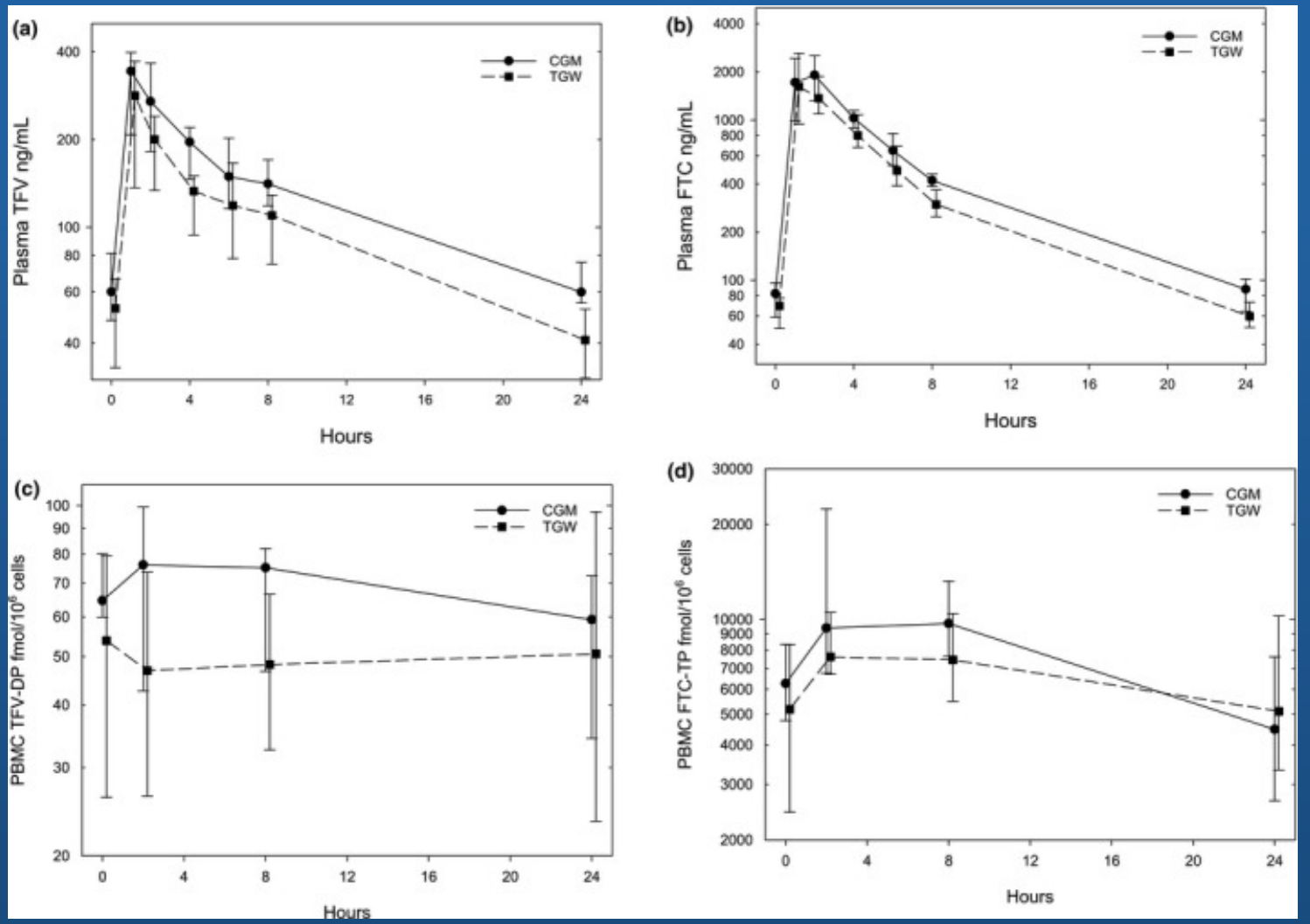
They return at 6 months for refills and labs. They report that they've been thinking about starting feminizing hormone therapy.

They return at 6 months for refills and labs. They report that they've been thinking about starting feminizing hormone therapy.

Are there interactions between PrEP and hormone therapy?

Feminizing hormones may affect rectal PrEP levels

- 8 TGW on oral or IM estrogens + spironolactone and/or medroxyprogesterone were compared with 8 cis men
- Trough TFV and FTC conc'n both 32% lower in TGW (*P*=0.010)
- AUC_{0-24} 27% lower and clearance 38% higher in TGW (*P*=0.065)
- No difference in PBMC/colon tissue
- Caution with 2-1-1 dosing in TGW on hormones



Shieh et al, *JIAS* 2019

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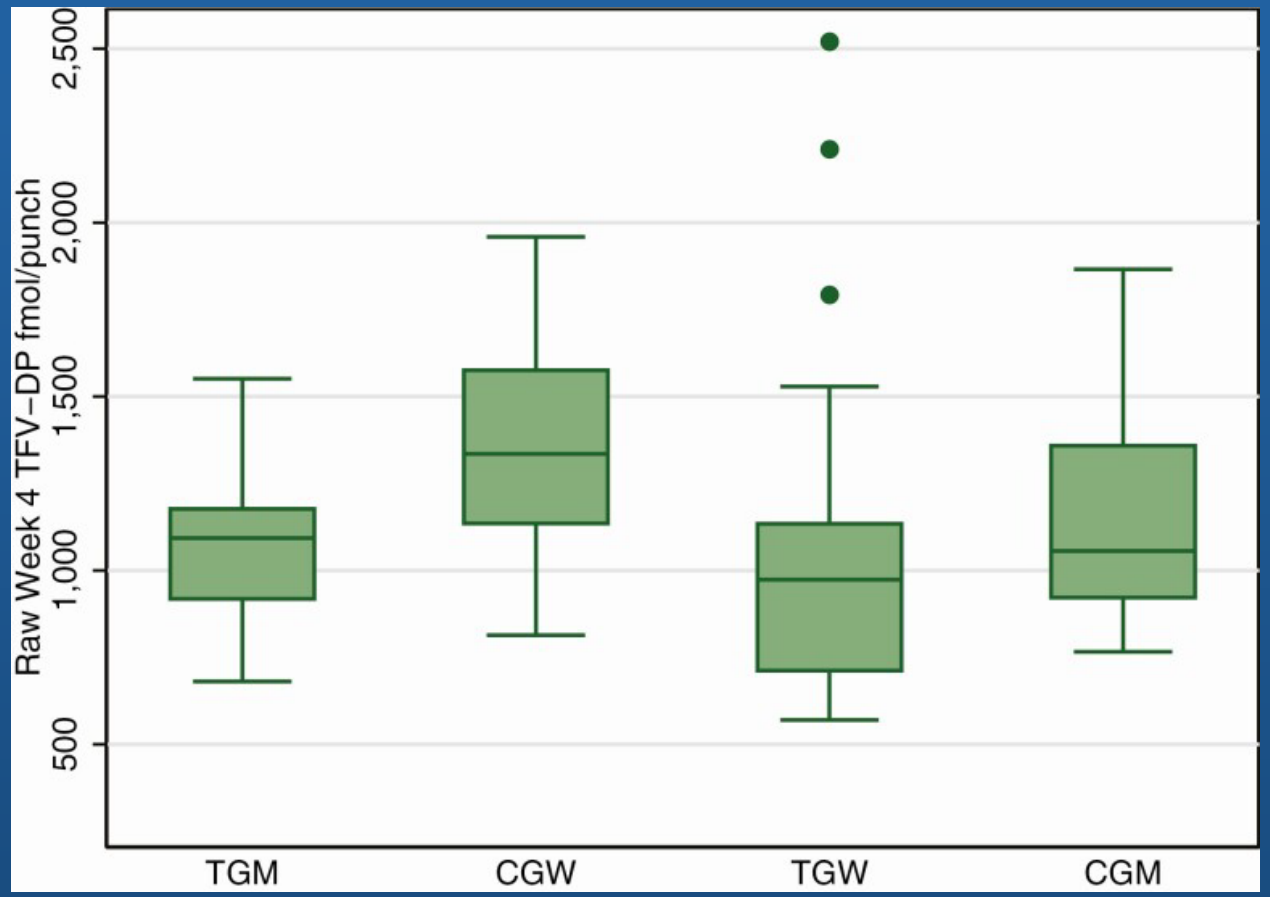
PrEP metabolites reach protective levels with GAHT

- 24 TGW and 24 TGM received 1 month of DOT; DBS collected for TFV
- TFV-DP levels were 23% lower among TGM compared to CGW (*P*=0.007)
- Otherwise, no difference in conc'n between other groups
- Serum hormone conc'n not affected by F/TDF use
- For all groups, levels projected at 8 weeks were equivalent to 4+ days/week of PrEP use



Grant et al, *CID* 2021.

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No change in TFV-DP by DBS at 12 weeks in TG persons taking and not taking HT

Table 1. PrEP Drug Concentrations and Satisfaction Scores by Gender Identity				
	Transgender Women (n=112)	p-value	Transgender Men (n=60)	p-value
Week 12 TFV-DP Concentration, fmol/punch (SD)*		0.26		0.49
No hormone therapy	1885.8 (1058.7) (n=28)		1682.0 (791.6) (n=10)	
Yes hormone therapy	1589.5 (819.1) (n=67)		1961.6 (966.4) (n=39)	
Body Image Satisfaction (SD)**		0.83		0.20
Week 0	2.7 (0.80) (n=23)		2.2 (0.60) (n=10)	
Week 24	2.6 (0.91) (n=19)		1.9 (0.62) (n=9)	
Satisfaction with HT on gender transition (SD)***		0.35		1.0
Week 0	1.9 (1.04) (n=23)		1.6 (0.70) (n=10)	
Week 24	1.9 (0.89) (n=19)		1.7 (0.87) (n=9)	

TFV-DP= tenofovir-diphosphate; SD= standard deviation; HT= hormone therapy
*Adjusting for confounding factors age, creatinine clearance and weight.
**Body Image Satisfaction summed 5 questions about desired physical effects from HT (low body image is 1, high body image is 5)
***Satisfaction with HT on gender transition is based on question "how satisfied are you with your HT on your gender transition?" (low satisfaction score is 1, high satisfaction score is 5)

Blumenthal J et al, OA84 - CROI 2022

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The patient recently started a new relationship and wants to “give PrEP a break.”

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The patient recently started a new relationship and wants to "give PrEP a break."

How long should they continue PrEP after their last condomless sexual exposure?

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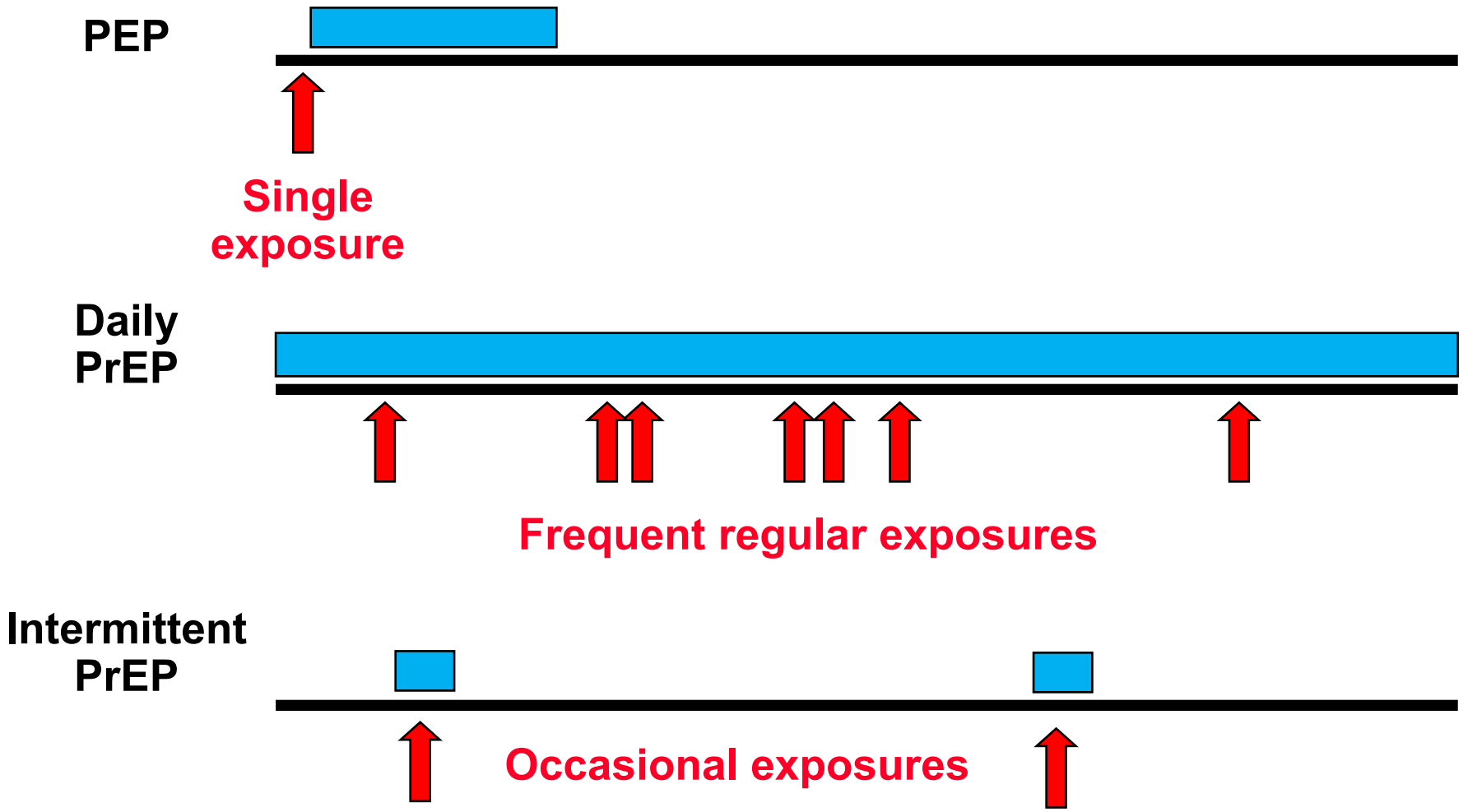
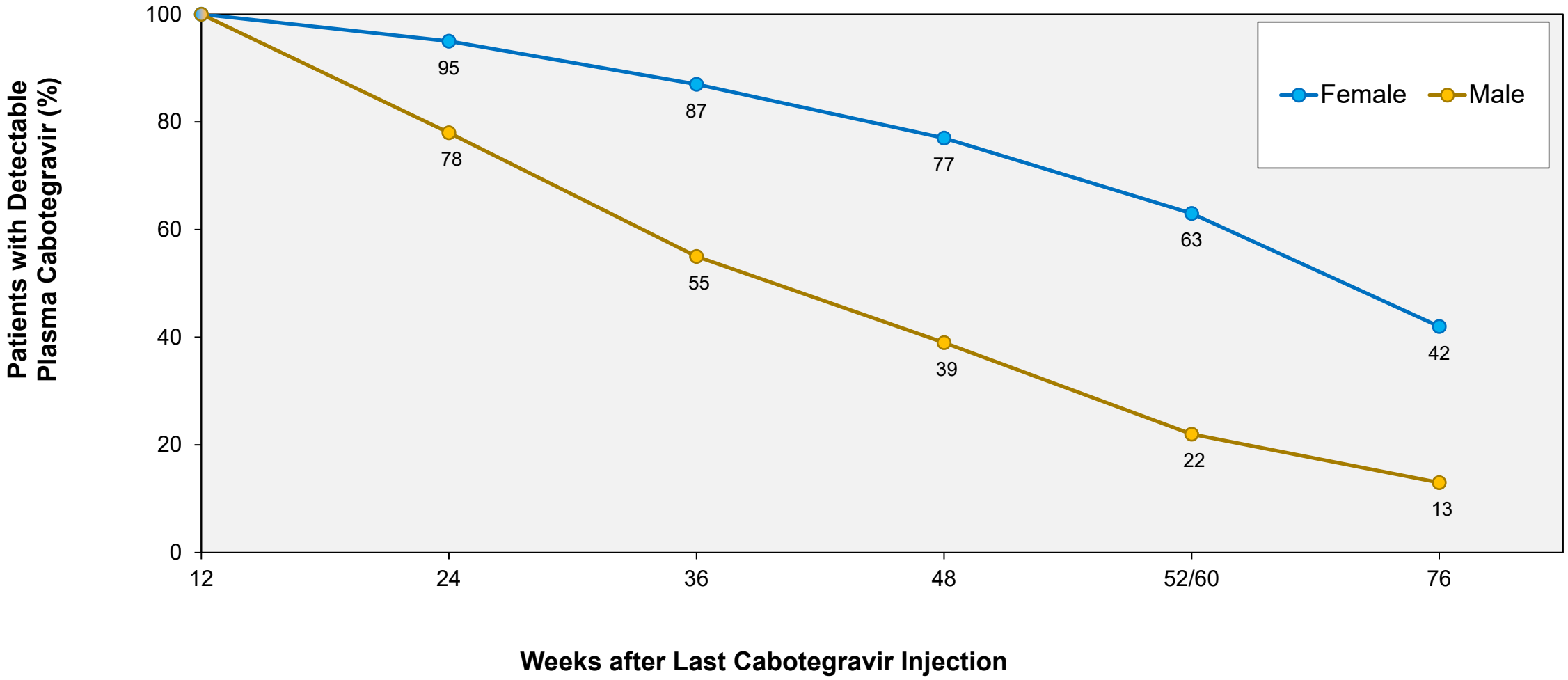
How long to continue PrEP?



How to safely stop PrEP

- Oral PrEP
  - WHO update (2022)
    - One dose/day x 2d after last exposure for people AMAB
    - One dose/day x 7d after last exposure for people AFAB
  - CDC (2021)
    - Document HIV status at time of discontinuation
    - Protection will wane in 7-10 days after ceasing continuous daily PrEP use
    - Counsel re: risk for HBV flare if known to have HBV coinfection
- Injectable PrEP
  - IAS-USA (2021): Transition to oral PrEP regimen for period of ongoing risk

CAB levels persist >1 year after last dose administration



Landovitz RJ et al, *Lancet HIV* 2020

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They elected to try 2-1-1 dosing. Outreach attempts are unsuccessful for the next 6 months, but then a PrEP refill request comes in…

They elected to try 2-1-1 dosing. Outreach attempts are unsuccessful for the next 6 months, but then a PrEP refill request comes in…

How can the system better engage PrEP patients?

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Structural interventions for increased PrEP engagement and persistence

- Importance of bi-directional communication (direct text messages, email, MyChart, etc.)
- Telehealth
- Low-barrier care models (mobile clinics, DIS-driven, pharmacist-driven PrEP)
- Mail-order medications
- Peer-based adherence support
- For transgender and nonbinary people
  - Integrate PrEP into gender-affirming care (whatever that means for the patient)
  - Incorporate with primary care
- For people who use alcohol or other substances:
  - Integrate PrEP delivery into programs for syringe exchange, harm reduction, medication-assisted recovery (alcohol, opioids), contingency management (stimulants), and other recovery models, behavioral health

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They return to care several months later after having run out of PrEP two months ago. They report condomless RAI with a partner with HIV (not on ART) last night.

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They return to care several months later after having run out of PrEP two months ago. They report condomless RAI with a partner with HIV (not on ART) last night.

You want to prescribe PEP, but the patient is worried about needing to take >1 pill/day…

2016 Nonoccupational PEP Guidelines
Regimens for Nonoccupational PEP

2016 HHS Nonoccupational PEP Regimens for Adults and Adolescents
Preferred Regimen
Dolutegravir + Tenofovir DF-Emtricitabine
Raltegravir + Tenofovir DF-Emtricitabine
Alternative Regimen
Darunavir + Ritonavir + Tenofovir DF-Emtricitabine
Regimens for Patients with CrCl <60 ml/min
Replace Tenofovir DF-Emtricitabine with Zidovudine plus Lamivudine*
*Adjust doses for degree of renal impairment

Must be taken within 24-72 hours of exposure

Source: 2016 HHS Nonoccupational PEP Guidelines

Multiple barriers contribute to PEP underutilization

- Some providers are uncomfortable prescribing PEP
- Stigma associated with seeking PEP services
- Geographic disparities in knowledge and use of PEP
- Limited access to providers and ART within 72-hour window
- Adherence to 28-day regimen may be challenging: side effects, etc.
- Multiple examples of successful PEP to PrEP transition programs
- PEP use may be declining due to increased availability of PrEP

Kelley C, OA 34 – CROI 2023; Ayieko et al, *JAIDS* 2022; Bogoch et al, *CID* 2014; Ford et al, *AIDS* 2014; John et al, *AIDS Behav* 2020; Woodward et al, *Int J STD AIDS* 2022

Safety and Tolerability of Once Daily Coformulated Bictegravir, Emtricitabine, and Tenofovir Alafenamide for Postexposure Prophylaxis After Sexual Exposure

Mayer, Kenneth H. MD[a,b,c]; Gelman, Marcy NP[a]; Holmes, Johnathon NP[a]; Kraft, Jessica NP[a]; Melbourne, Kathleen PharmD[d]; Mimiaga, Matthew J. ScD, MPH[a,e]

Author Information

JAIDS Journal of Acquired Immune Deficiency Syndromes 9
10.1097/QAI.0000000000002912

An open-label evaluation of safety and tolerability of coformulated bictegravir/emtricitabine/tenofovir alafenamide for post-exposure prophylaxis following potential exposure to human immunodeficiency virus-1

Liu, An[1]; Xin, Ruolei[2]; Zhang, Hongwei[1]; Dai, Lili[1]; Wu, Ruojun (Esther)[3]; Wang, Xi[1]; Li, Aixin[1]; Hua, Wei[1]; Li, Jianwei[1]; Shao, Ying[1]; Gao, Yue[1]; Wang, Zhangli[1]; Ye, Jiangzhu[1]; bu dou re xi ti, Gulimila A[4]; Li, Zaicun[1]; Sun, Lijun[1]

Editor(s): Yin, Yanjie

Author Information

Chinese Medical Journal 135(22):p 2725-2729, November 20, 2022. | ***DOI:*** 10.1097/CM9.0000000000002494

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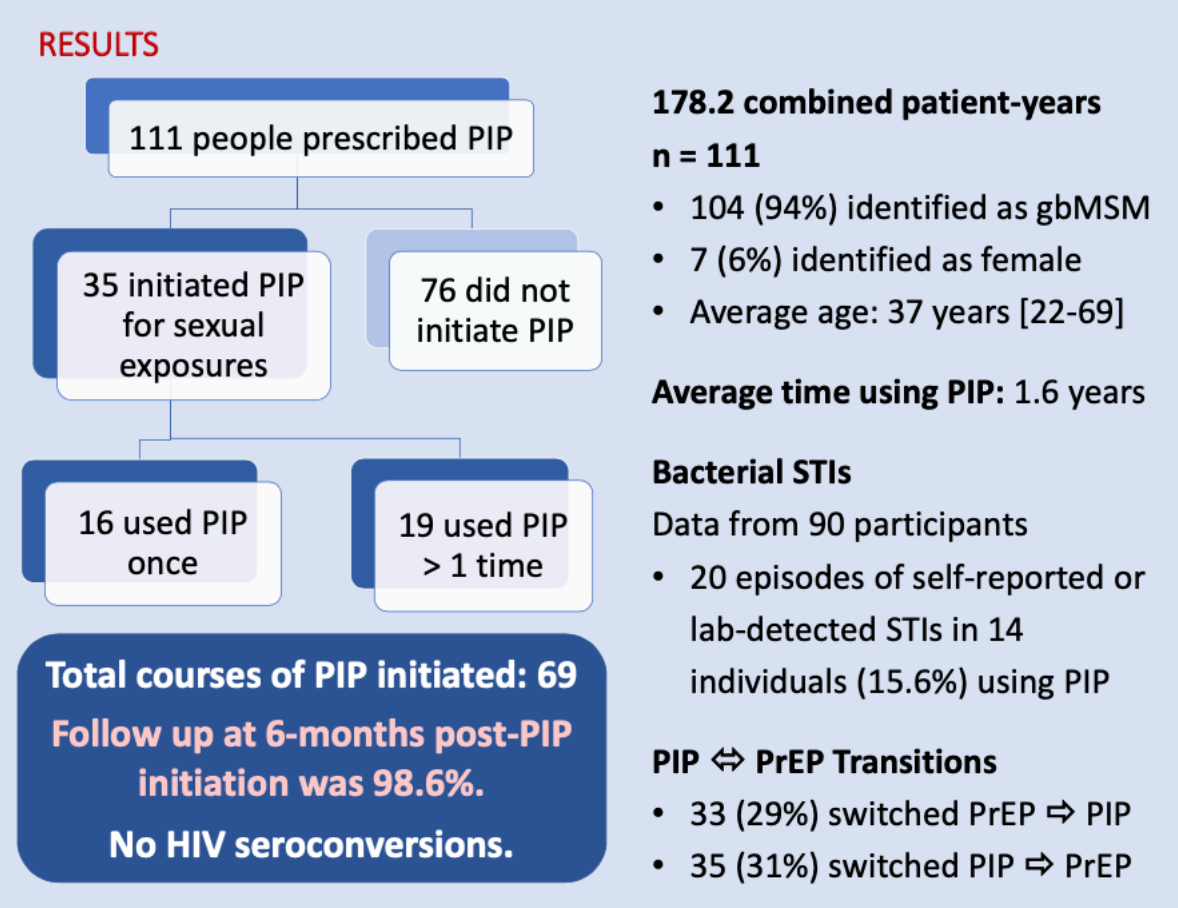
PEP in pocket (PIP) as a novel HIV prevention strategy



- Persons with low frequency (0-4/yr) high-risk HIV exposures offered PrEP or PIP using shared decision-making process
- Regimens: B/F/TAF (Biktarvy®) or F/TDF + DTG
- Full 28-day PEP prescription is given **prior** to an exposure with counseling on how to use and to f/u with provider within 1 week for HIV/STI testing
- Routine f/u every 5-6 months with re-evaluation to continue PIP vs switch to PrEP

Fisher KN et al, Poster 972 – CROI 2023

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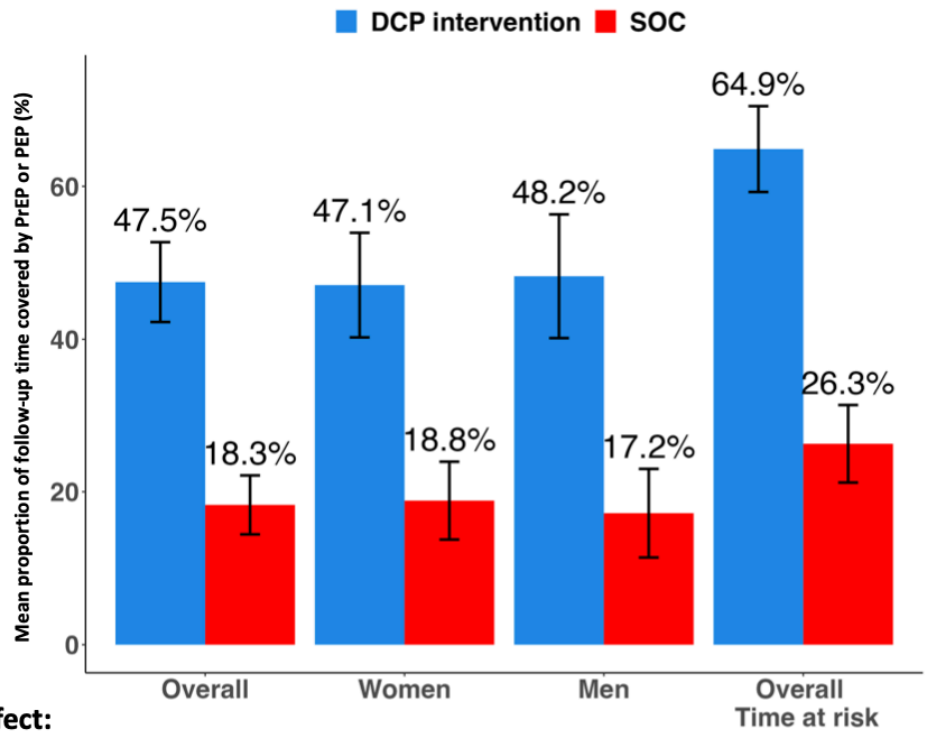
Dynamic choice for HIV prevention improves coverage

Figure 3. Primary outcome: Proportion of follow-up time covered by PrEP or PEP



	Overall	Women	Men	Overall Time at risk
Effect: DCP vs. SOC (95% CI)	**29.2%** (22.7-35.7)	**28.2%** (19.7-36.8)	**31%** (21.1-41)	**38.6%** (31-46.2)
P-value	p<0.001	p<0.001	p<0.001	p<0.001

- 403 patients in SW Uganda & W Kenya randomized to dynamic choice vs SOC and followed for 48 weeks
- In choice arm: 86% ever chose PrEP, 15% ever chose PEP
- Choice to HIV self-test and follow up at community site both increased
- Dynamic choice resulted in >2x more time covered by PrEP or PEP compared to SOC

Kamya M et al, OA 128 – CROI 2023

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Products in the pipeline for PrEP and PEP

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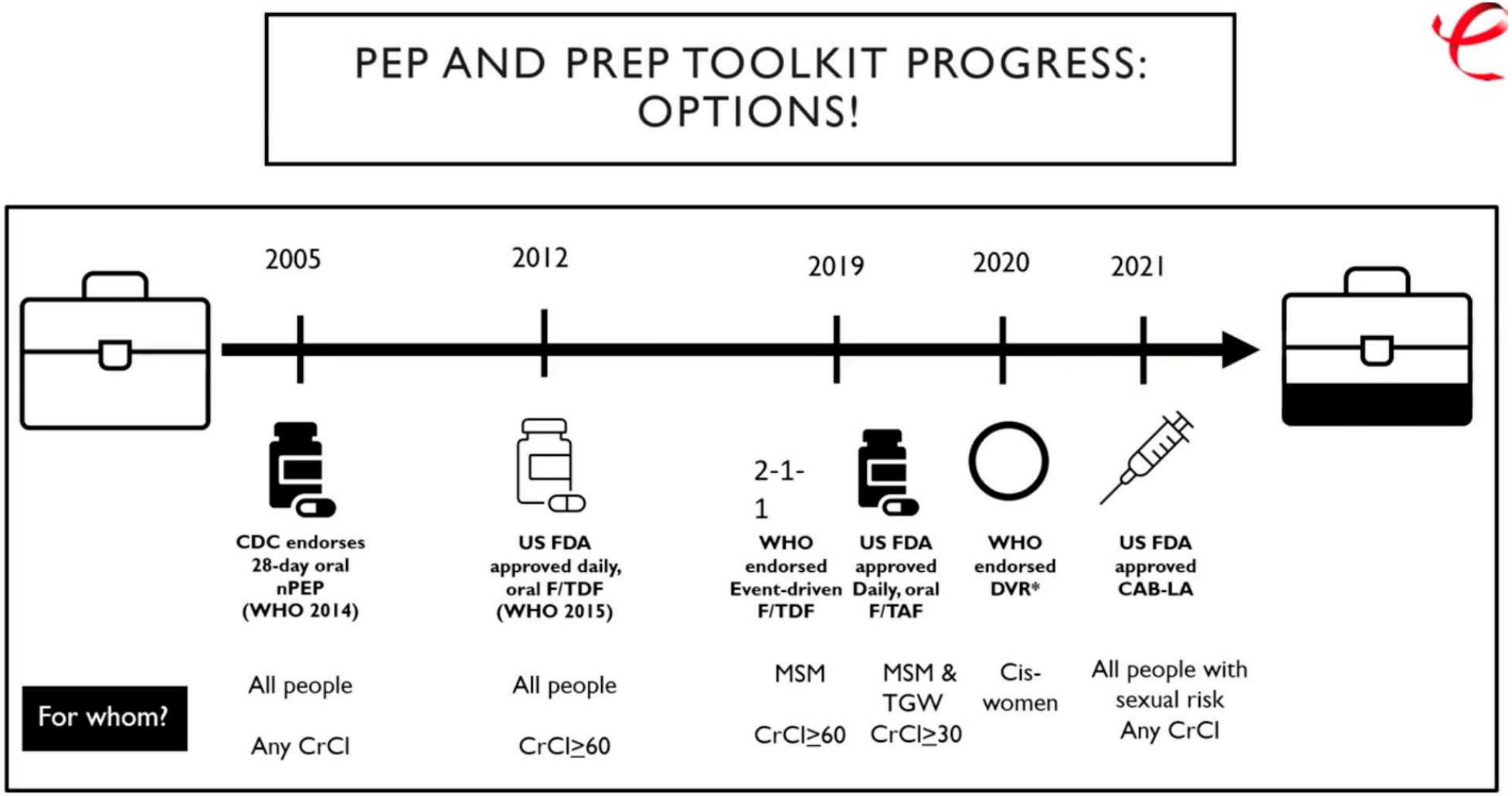
Current PrEP & PEP landscape

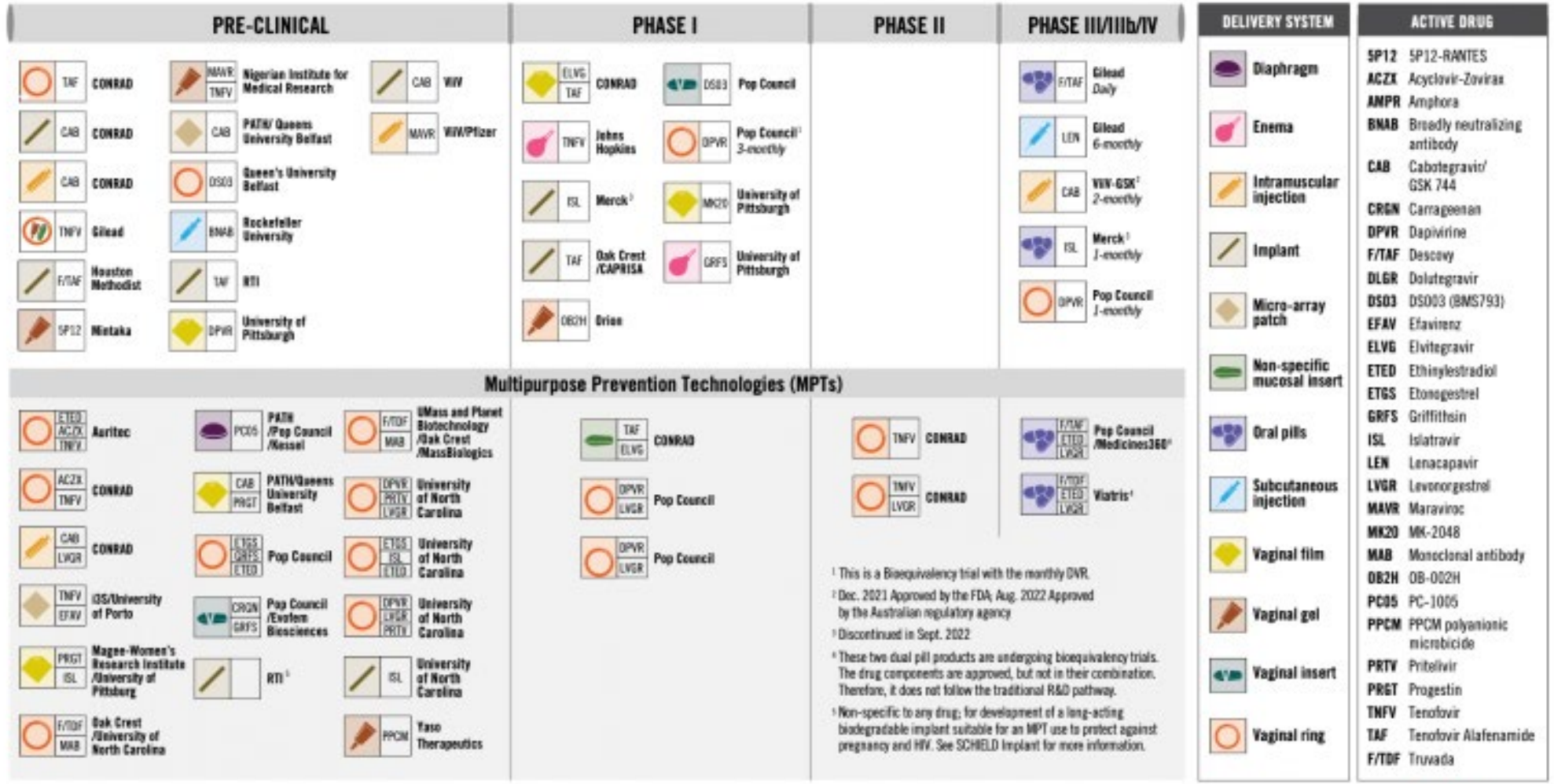


Kelley C, OA 34 – CROI 2023

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.)



AVAC www.avac.org October 2022

Image: avac.org

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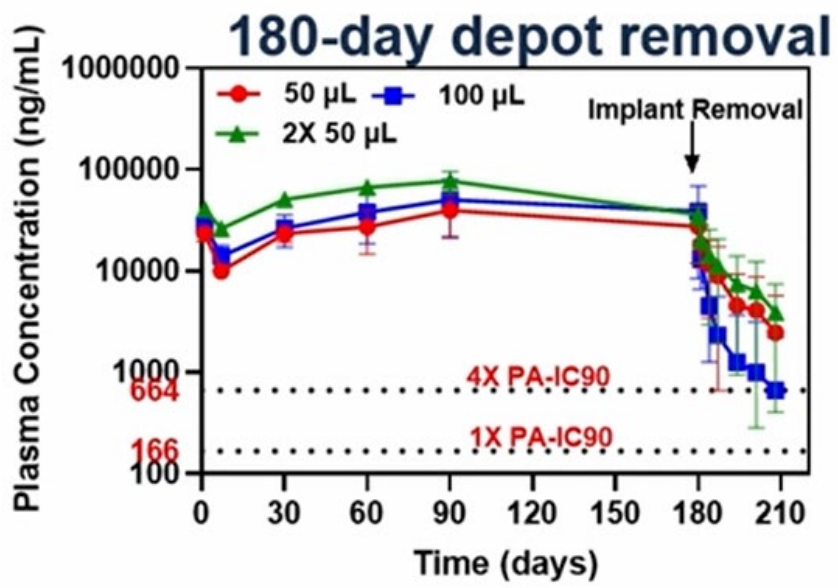
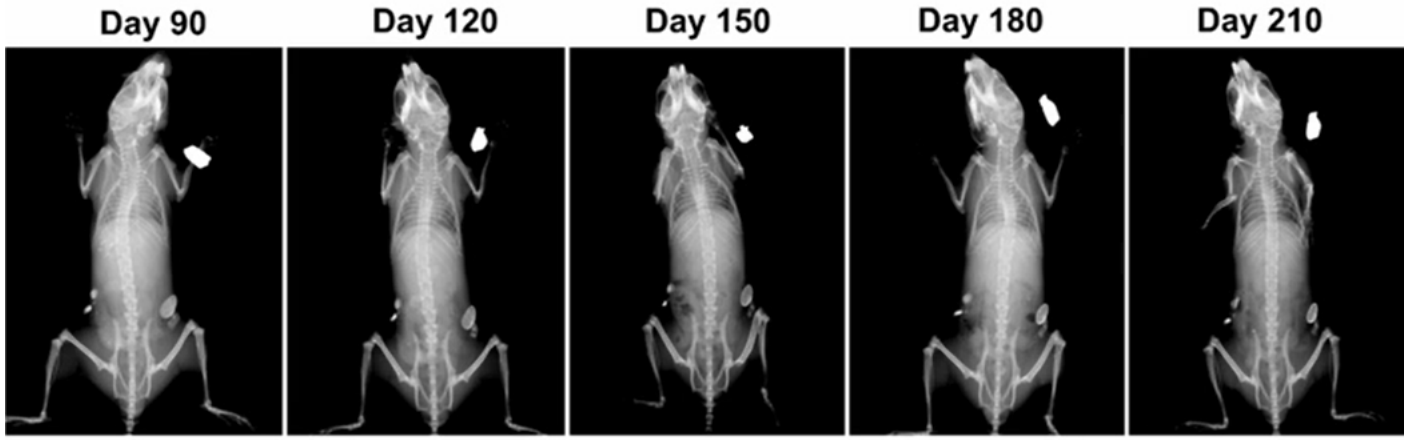
Ultra-long acting in-situ forming implant with CAB

- SQ injection of biodegradable polymer mixed with solvent and drug(s) of choice
- Expected duration of action: 1 year above target levels in macaques and mice
- After implant removal at 180 days, CAB plasma levels drop but persist (25% drug and 15% polymer left)





Young IC et al, *Nature Comm* 2023. Young I et al, Poster 991 - CROI 2023

On-demand inserts for HIV PEP or PrEP

- Fast-dissolving TAF 20mg + EVG 16mg insert demonstrated efficacy in NHP SHIV challenges using 1 vaginal or 2 rectal inserts

- Phase 1, single-arm, OL study assessing PK/PD after use of 1 or 2 rectal inserts in humans
  - 1 drug-related AE – mild anal erythema
  - EVG levels present 2-24 hrs, tenofovir sustained 48-72 hrs
  - Levels for TFV-DP exceeded those compared to steady state concentrations at 4 or 7 tabs/wk of oral TDF in HPTN 066

Dobard et al, *eBioMedicine* 2022; Makarova et al, *eBioMedicine* 2022; Riddler S et al, OA 164 - CROI 2023

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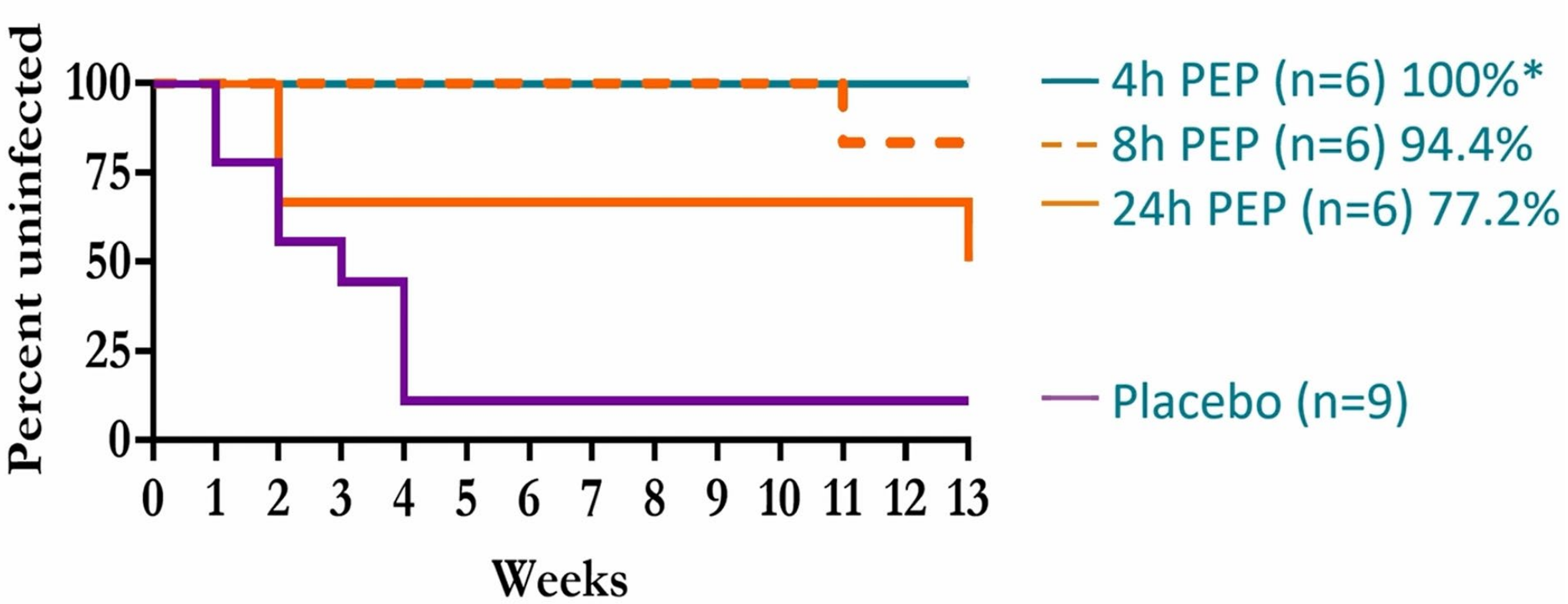
TAF/EVG insert efficacy as PEP after vaginal SHIV exposure

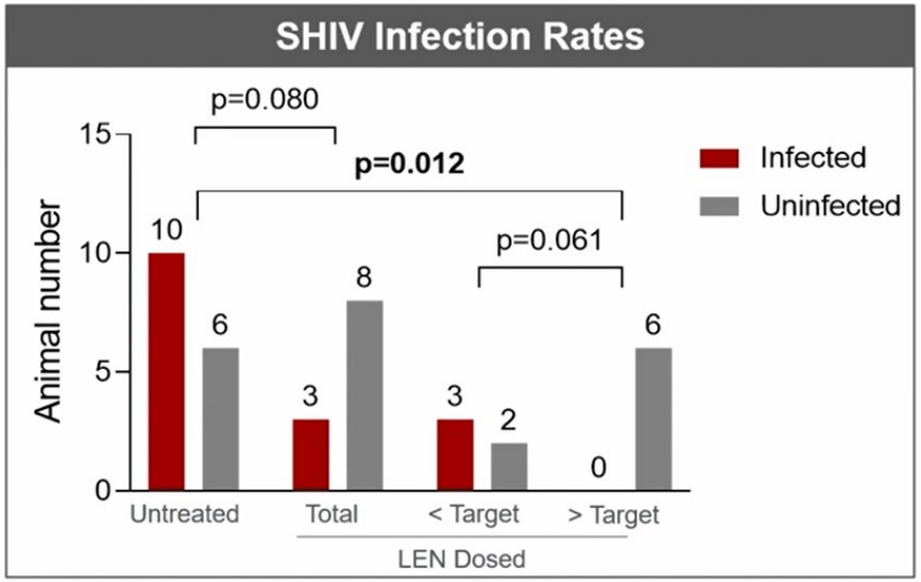


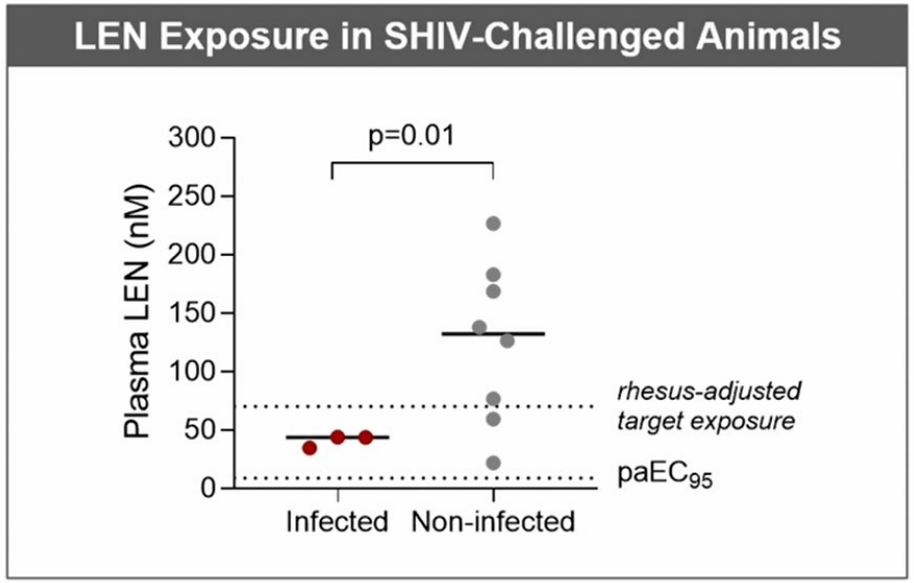
High protection for inserts applied 4-8h after exposure with good effect even if given as 24-hour PEP

Dobard et al, *eBioMedicine* 2022; Makarova et al, Poster 990 - CROI 2023

Lenacapavir and GS-CA1 for PrEP

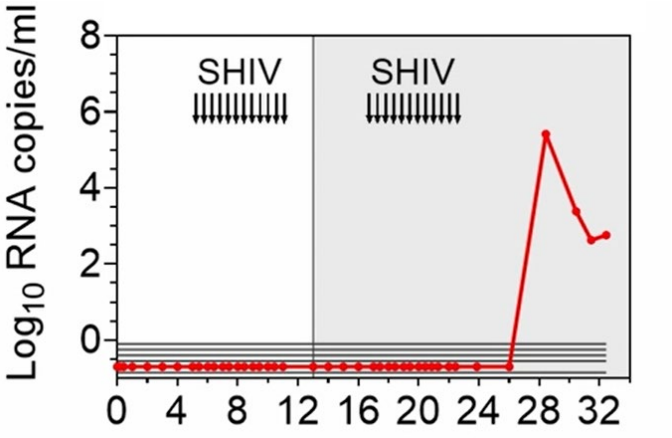
- Lenacapavir fully protected macaques after SHIV challenge 7 wks after SQ dosing (infection rate: 63% untreated vs 27% treated) if target levels reached
- PURPOSE-1 & PURPOSE-2 (soon: 3, 4) are phase 3 clinical studies of long-acting lenacapavir for PrEP

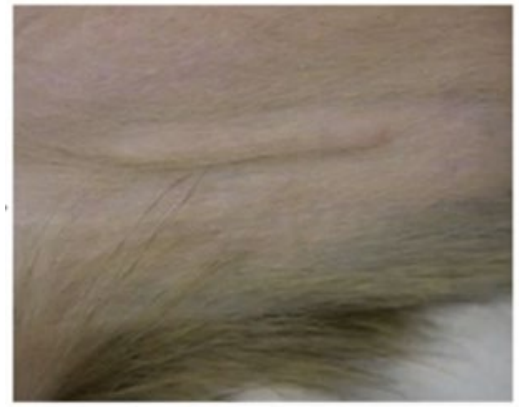




Bekerman E et al, Poster 992 - CROI 2023

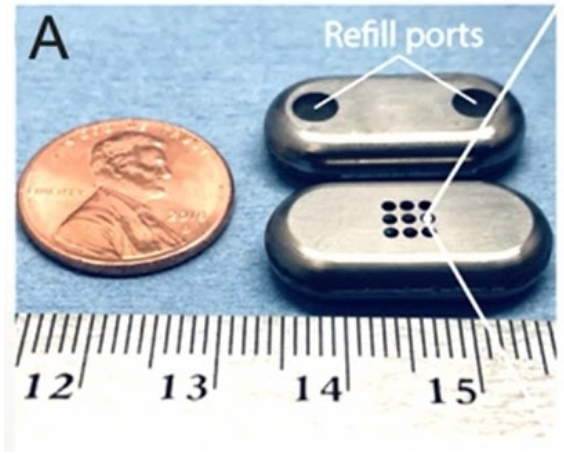
Biodegradable and refillable islatravir implants show promise

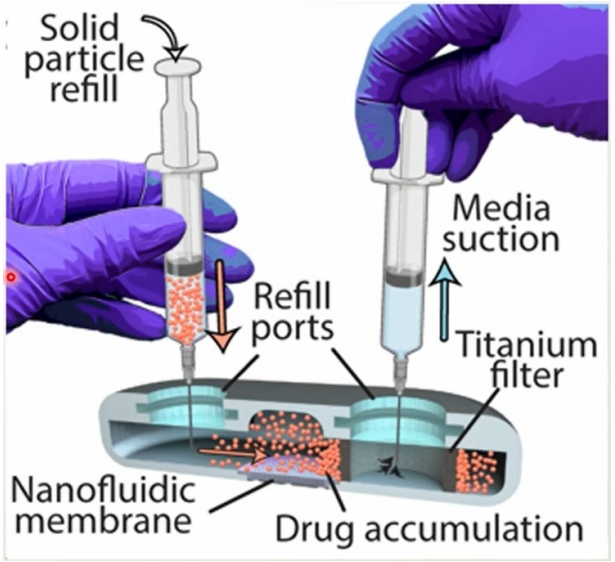




Week 13

SHIV protection in 5 of 6 macaques when plasma ISL levels were therapeutic





100% of infections prevented in rectal + vaginal SHIV challenges with therapeutic levels to 20 months

Daly M et al, Poster 989 - CROI 2023; Matthews et al, *JAIDS* 2021; Di Trani et al, *Advanced Therapeutics* 2022; Grattoni A et al. OA 165 - CROI 2023

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Conclusions

- PrEP uptake remains suboptimal in the US, especially among populations with highest HIV incidence
- Prevention options for nearly all: daily or 2-1-1 oral (F/TXF) vs injectable (CAB)
- Adherence can improve with proactive, anticipatory counseling
- PrEP persistence remains a challenge; discontinuations are common and associated with risk for future HIV acquisition
- PEP in pocket may be an emerging strategy in the HIV prevention toolkit
- Many exciting, new options for HIV prevention in the pipeline

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Coming soon: National HIV PrEP Curriculum

National HIV PrEP Curriculum

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HIV Prevention Resources

CDC/HHS
www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf
www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-provider-supplement-2021.pdf

IAS-USA
www.iasusa.org/resources/guidelines/

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

Consultation and assistance
MWAETC Prevention Detailing Program
mwaetc.org/washington-state-hiv-prevention-detailing-program

Consultation PrEPLine (855-448-7737)
For urgent questions or ambiguous test results

UCSF University of California, San Francisco | About UCSF

NATIONAL CLINICIAN CONSULTATION CENTER

CCC PEP line 888-448-4911
9a-8p ET (Mon-Fri)
11a-8p (weekends & holidays)

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QUESTIONS?

THANK YOU

Chase Cannon
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