THE UNIVERSITY OF ALABAMA AT BIRMINGHAM
SCHOOL OF MEDICINE

PrEP Prescribing and Monitoring
September 11, 2024

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Disclosures

Ad hoc Advisor ViiV

NIH/NIMH K23MH126794

There are no conflicts of interest.

Objectives

1. Understand the role of PrEP in ending HIV
2. Explain PrEP medication effectiveness and safety
3. Understand Guideline -Based PrEP provision

POLL #1

I know about PrEP

Not at all, a little bit, some what, a lot

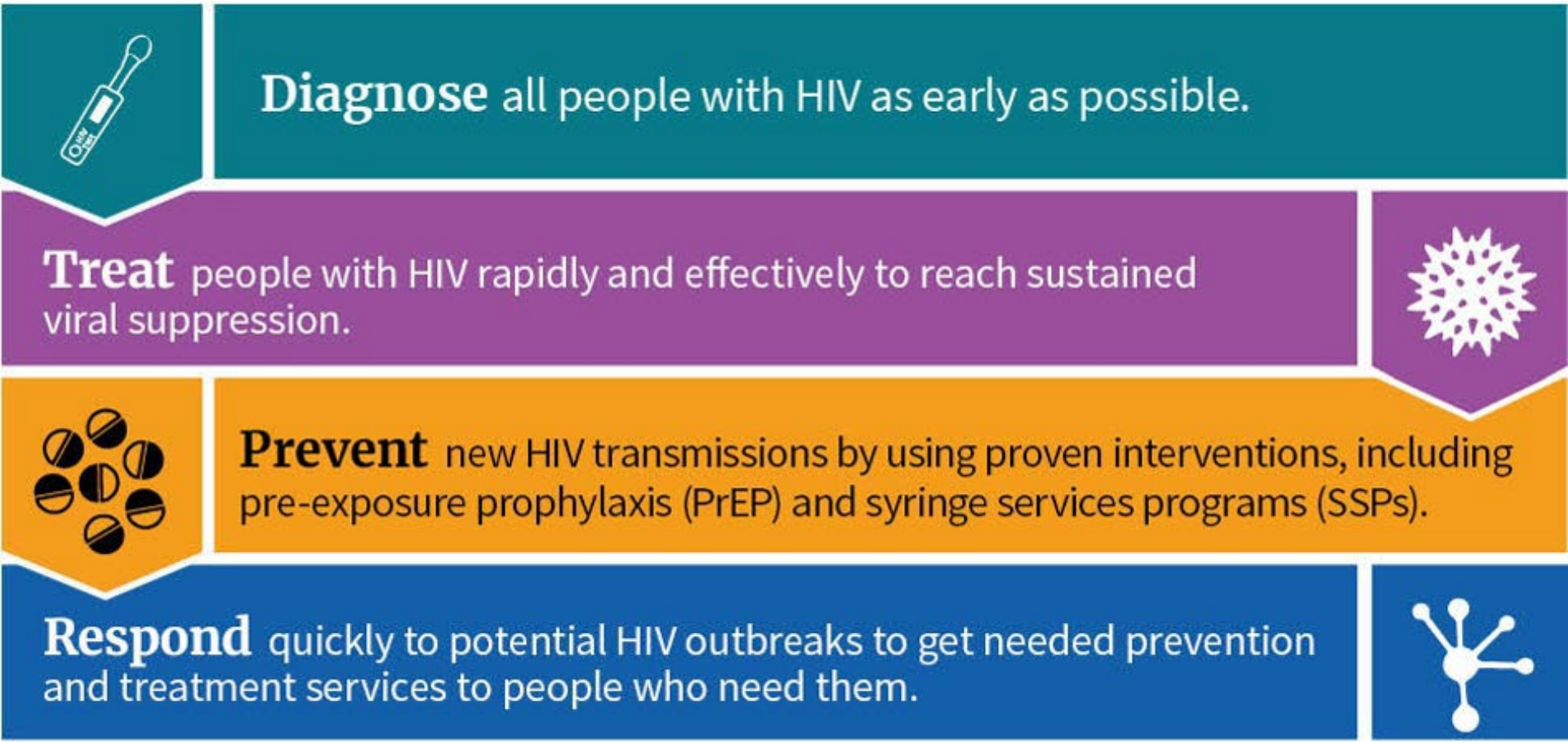
I have experience with PrEP provision.

Yes or No

“My biggest question or concern about PrEP is….

_____”

Ending the HIV Epidemic Strategies



DHHS, accessed 2021

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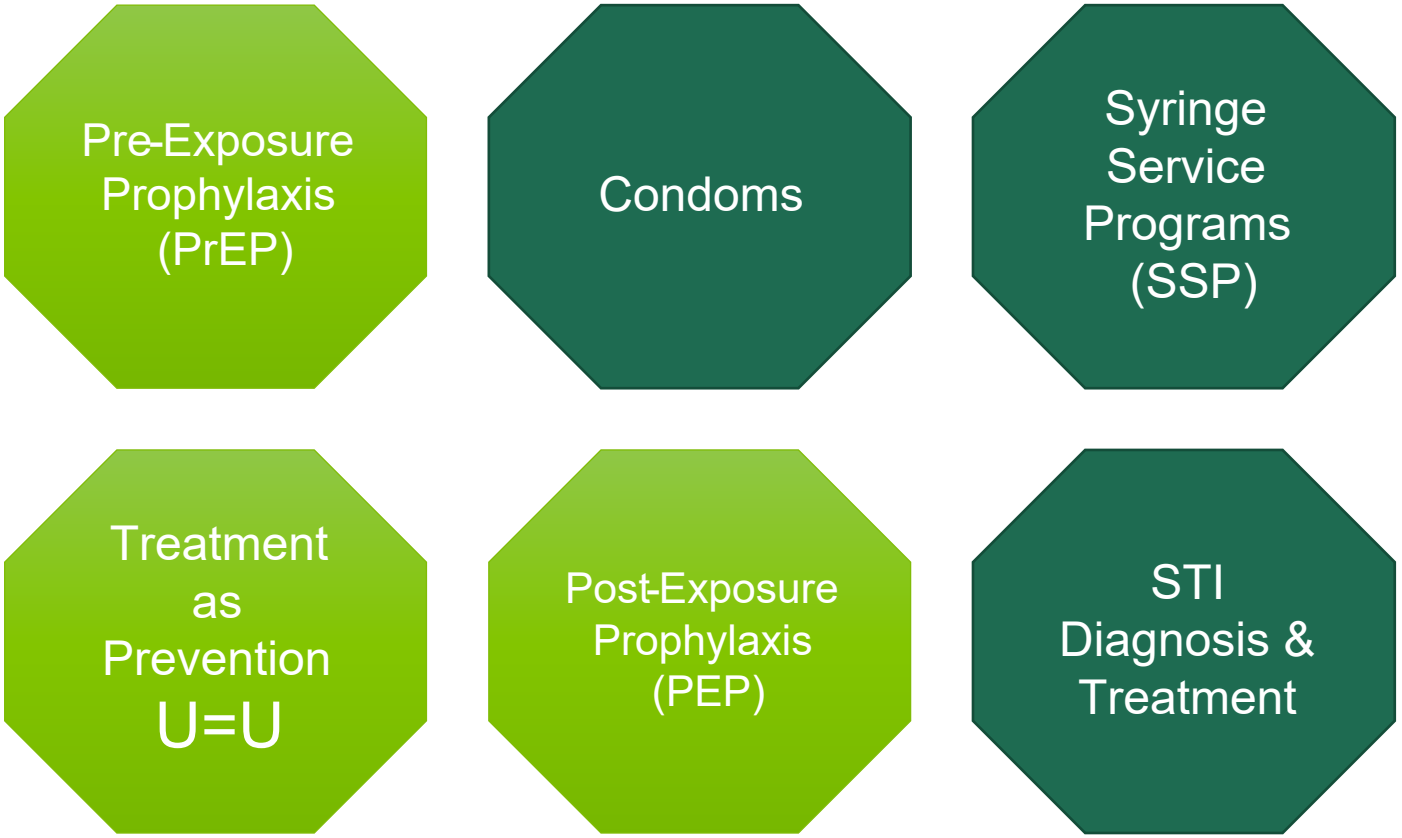
Status Neutral
Strategies to stop HIV transmission



Biomedical prevention strategies using antiretrovirals (ARVs)

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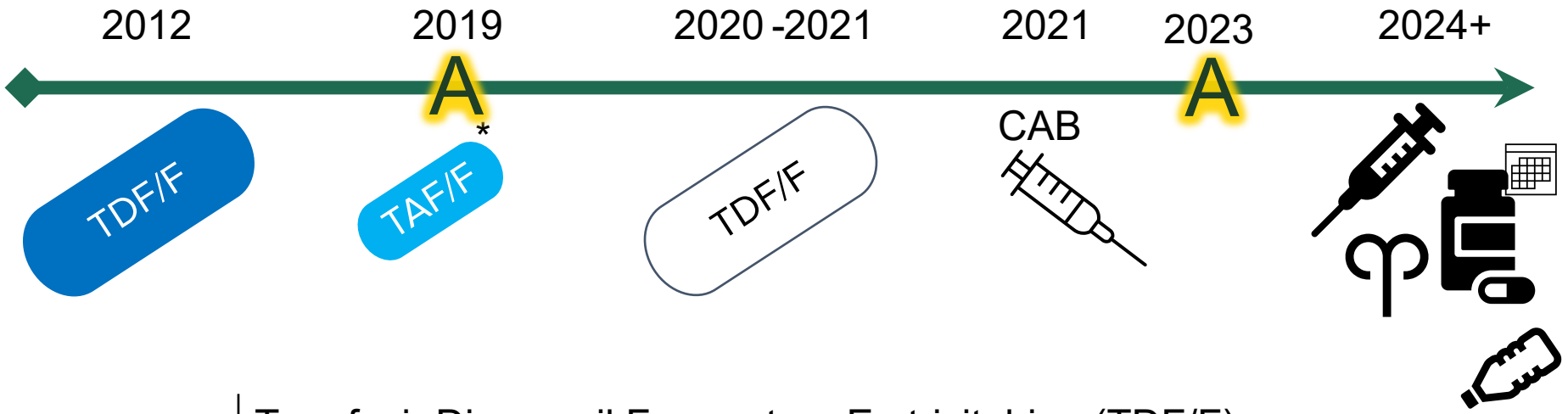
What is Pre-Exposure Prophylaxis?

HIV Pre-Exposure Prophylaxis (PrEP)

- Chemoprophylaxis using antiretrovirals (ARV) taken before exposure to HIV



Oral	Tenofovir Disoproxil Fumarate + Emtricitabine (TDF/F)
	Tenofovir Alafenamide + Emtricitabine (TAF/F)*
Injectable	Cabotegravir (CAB)

*not approved for vaginal exposures

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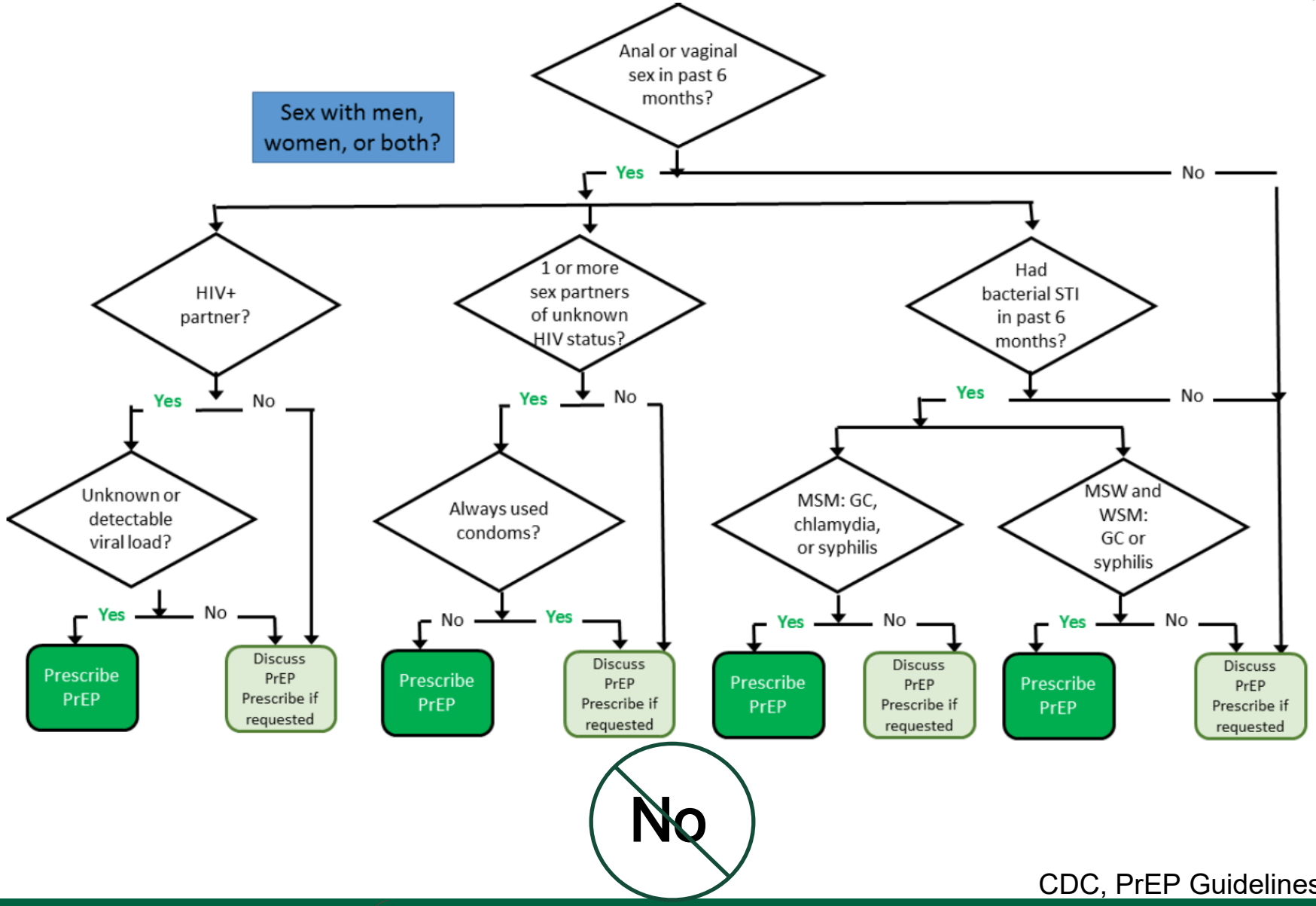
Identifying PrEP Candidates



CDC, PrEP Guidelines 2021

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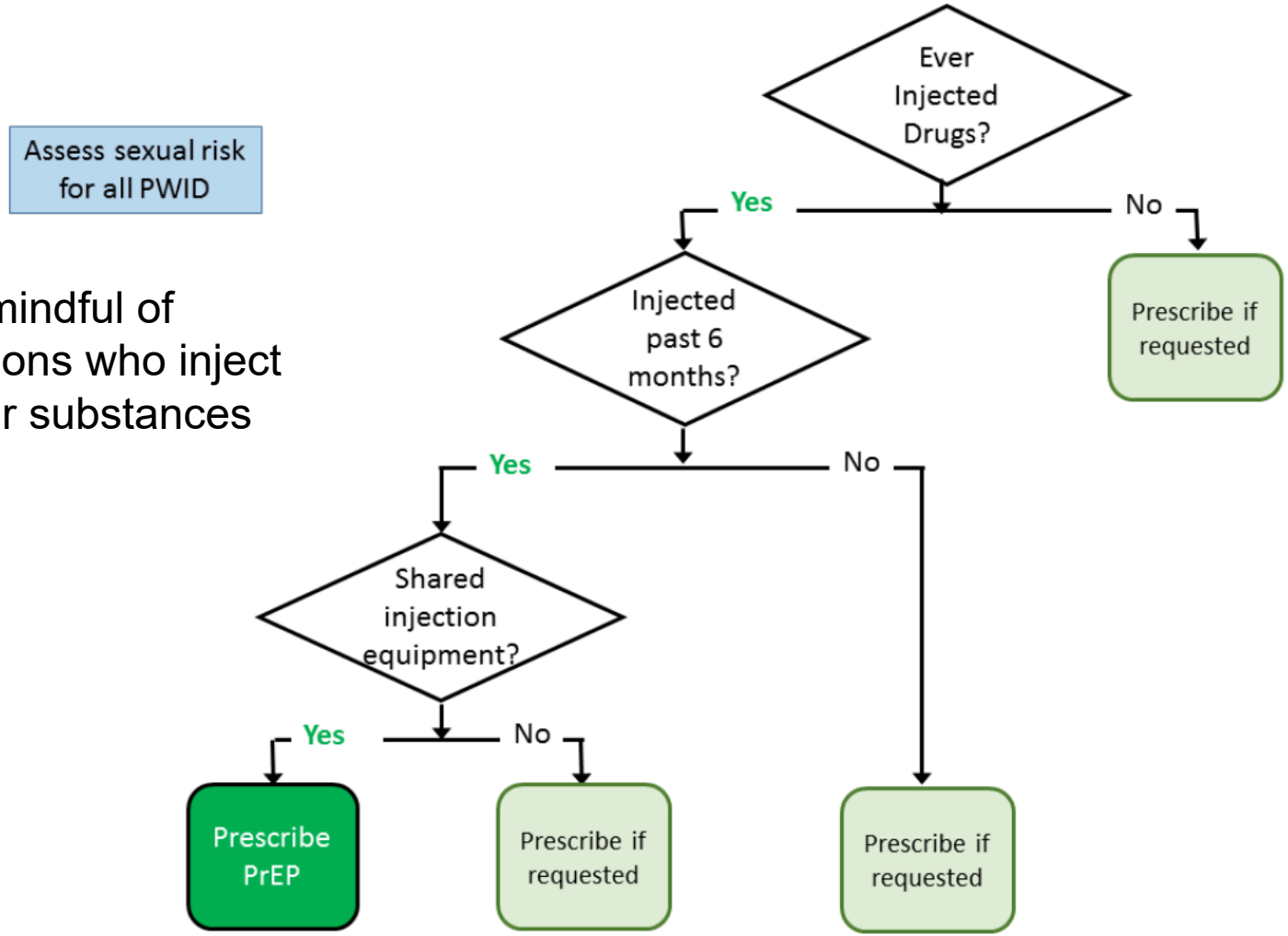
Identifying PrEP Candidates

Figure 3 Assessing Indications for PrEP in Persons Who Inject Drugs



Be mindful of persons who inject other substances

CDC, PrEP Guidelines 2021

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PrEP Efficacy – Tenofovir

Trial	Population	Intervention	Outcome	Interpretation
iPrex	MSM & TGW	TDF/FTC vsplac.	44% reduction, 92% if adherent	TDF/FTC effective
Partners PrEP	Serodifferent Heterosexual	TDF/FTC vs TDF vs plac.	75% reduction among all	TDF/FTC effective
VOICE	Cis-Women	5 arms (oral & vag TDF v plac)	Not effective, but poor adherence	Adherence matters most
Bangkok Study	PWID	TDF vs Placebo	49% reduction, 74% if adherent	TFV effective in PWID also
DISCOVER	MSM & TGW	TDF/F v TAF/F	0.34/100PY vs 0.16/100PY	TAF/F Noninferior
ANRS Ipergay	MSM & TGW	On-Demand TDF/F v Placebo	86% Risk Reduction	On-Demand effective also
*PURPOSE 1	Cis-Women	LEN v TDF TAF v TDF	Background: 2.41 LEN 0, TAF 2.02 (39), TDF 1.69	Adherence still matters

Grant et al, NEJM 2010; Baeten et al, NEJM 2012; Marrazzo et al, NEJM 2015; Choopanya et al. Lancet 2013; Mayer et al. Lancet 2020; Molina et al, NEJM 2015; Bekker et al., NEJM 2024

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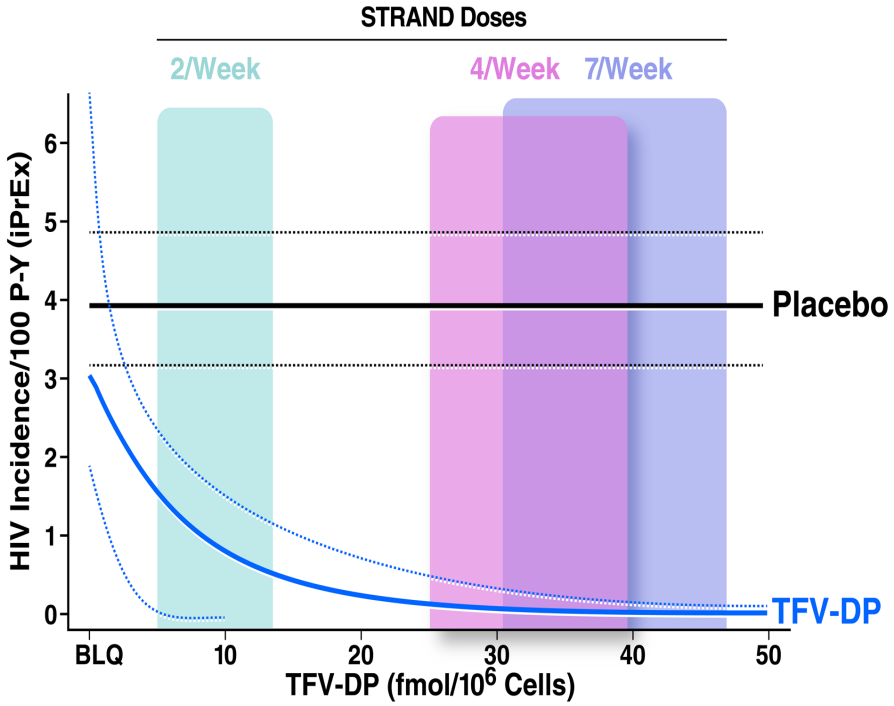
Drug Levels and Adherence

Effectiveness relies on appropriate dosing.

Men = 4x/week Women = 6-7x/week



- 7 days until protective in rectal tissues
  - Rectal TFV-dp levels at least 10x higher than cervicovaginal tissues
- 21 days until protective in cervicovaginal tissues or blood

Anderson et al, Sci Transl Med 2012
Grant et al, Lancet ID 2014
CDC PrEP Guidelines, 2021

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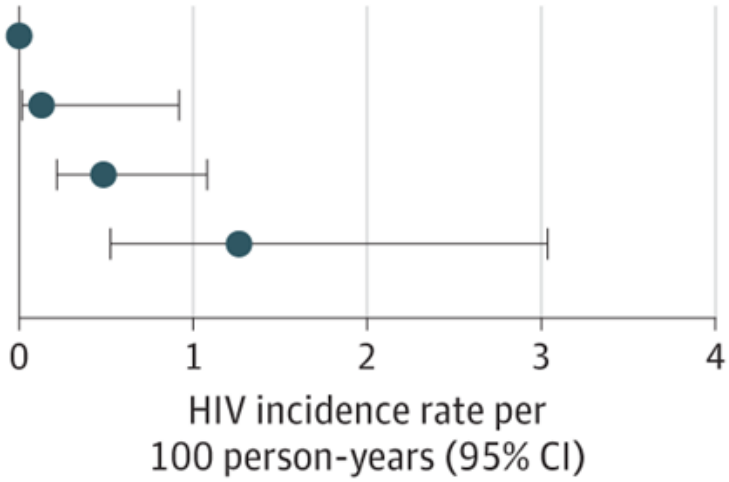
HIV Preexposure Prophylaxis With Emtricitabine and Tenofovir Disoproxil Fumarate Among Cisgender Women

Jeanne Marrazzo, MD; Li Tao, PhD; Marissa Becker, MD; Ashley A. Leech, PhD, MS; Allan W. Taylor, MD, MPH; Faith Ussery, MPH; Michael Kiragu, MBBS; Sushena Reza-Paul, MBBS, MPH, PhD; Janet Myers, PhD, MPH; Linda-Gail Bekker, PhD; Juan Yang, PhD; Christoph Carter, MD, PhD; Melanie de Boer, PhD; Moupali Das, MD; Jared M. Baeten, MD; Connie Celum, MD, MPH

7 Post-approval studies (2012-2020)
-Botswana
-India
-Kenya
-South Africa
-Uganda
-US

Adherence	HIV incidence rate per 100 person-years (95% CI)
Consistently daily	0 [Reference]
Consistently high	0.13 (0.02-0.92)
High but declining	0.49 (0.22-1.08)
Consistently low	1.27 (0.53-3.04)



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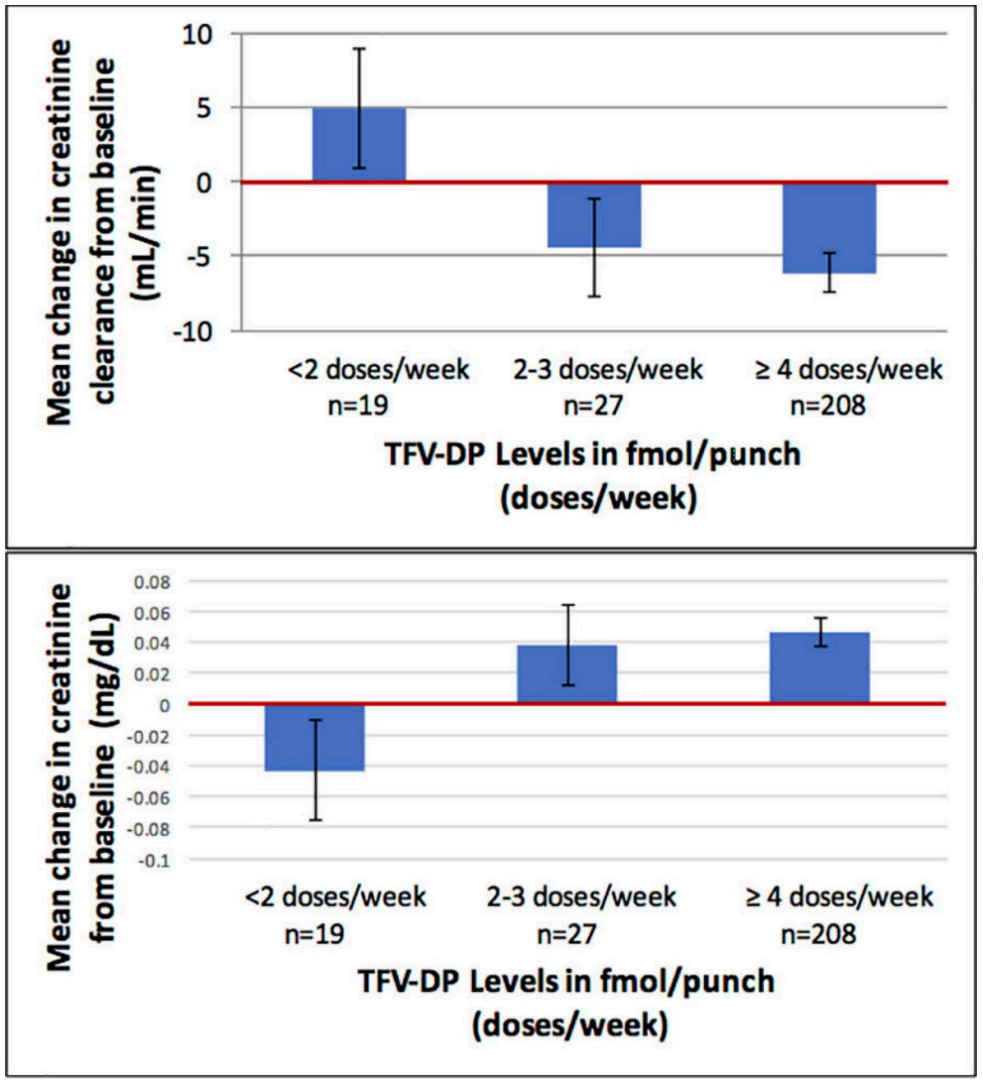
PrEP and Renal Safety

- TDF/FTC
  - statistically significant GFR decline, but clinically significant?
- TDF/FTC as PrEP only indicated for GFR >60ml/min



Ascher et al. AIDS 2020
Tang et al. JAIDS 2018

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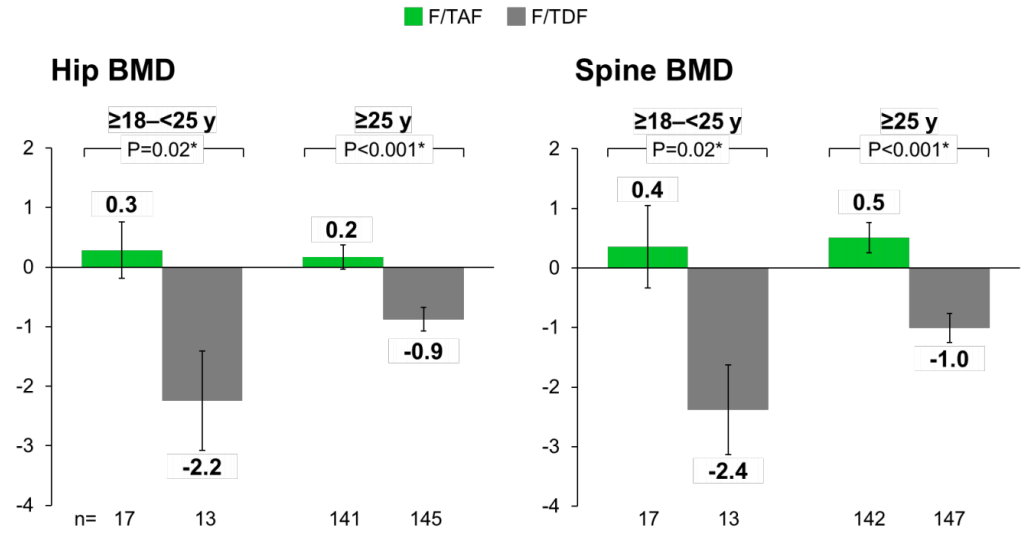
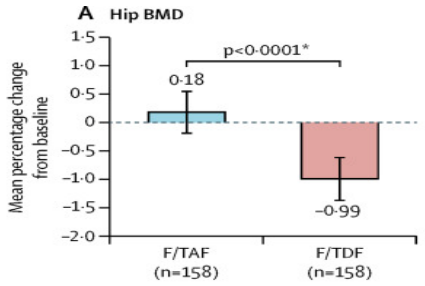
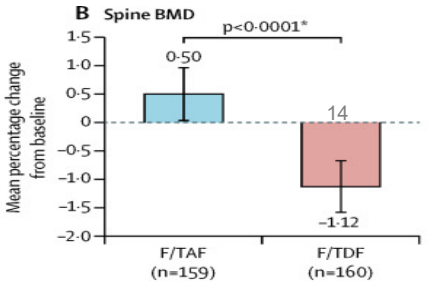
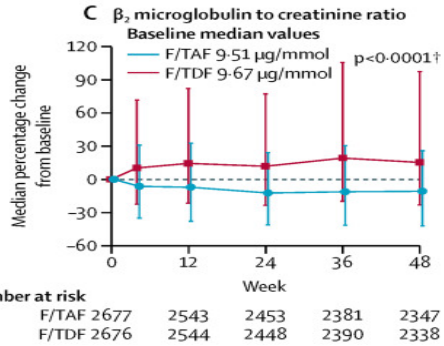
DISCOVER– TAF/F

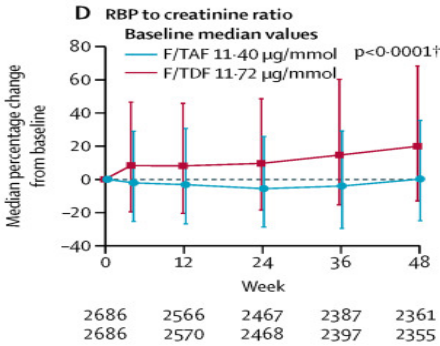
- TAF/F superior to TDF/F in bone/renal endpoints

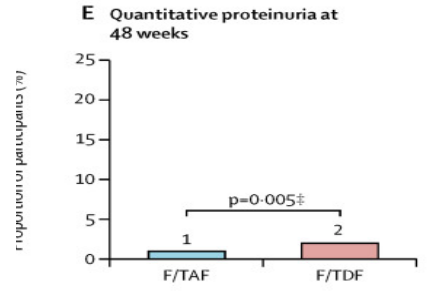


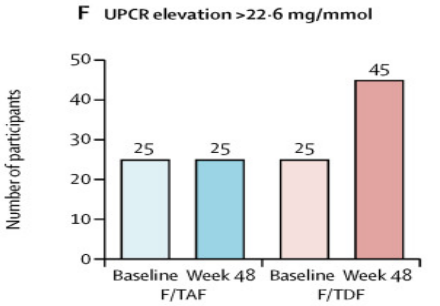


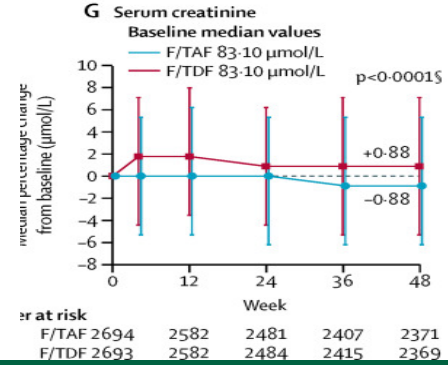


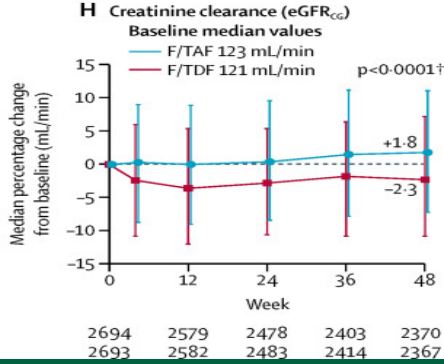












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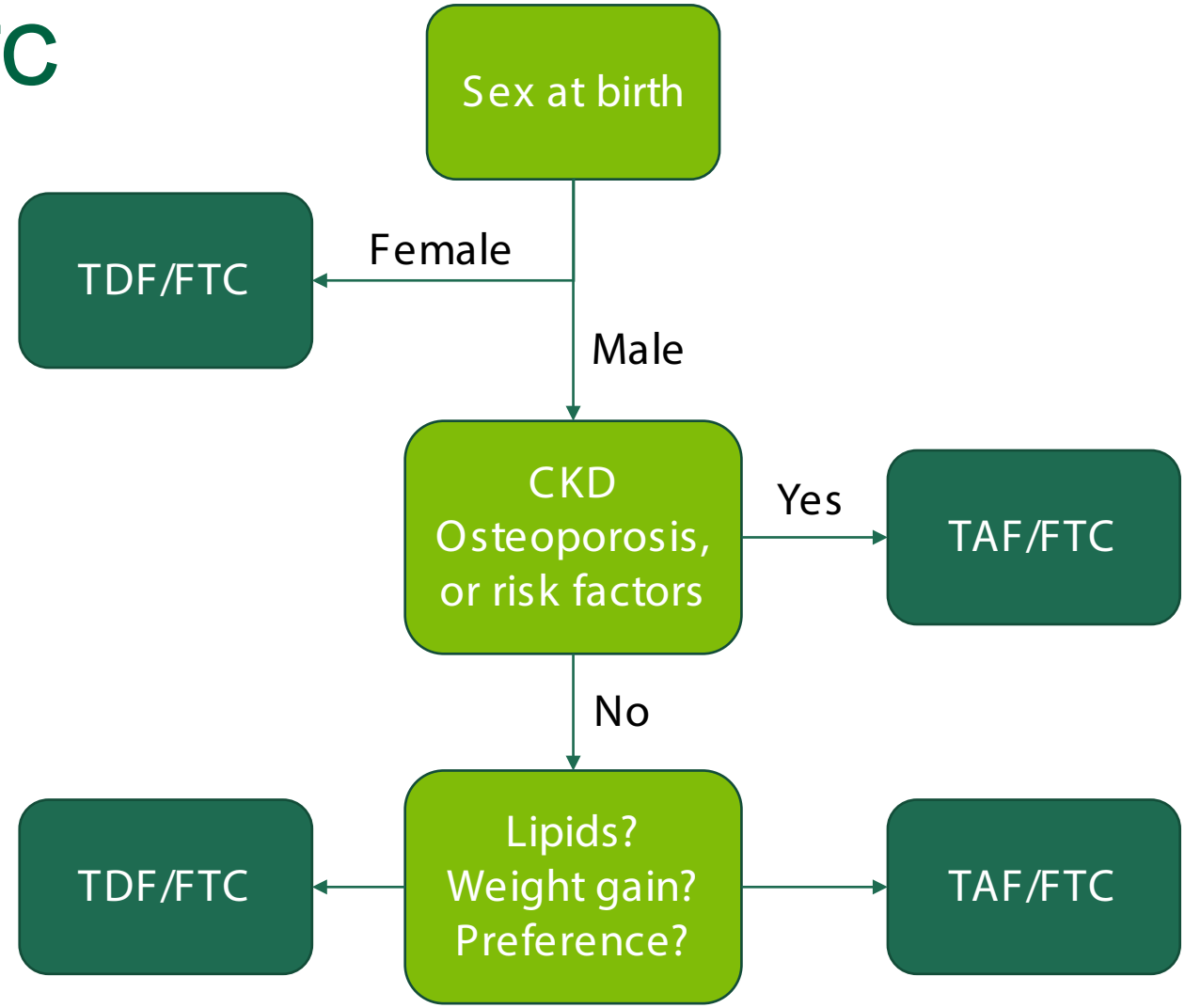
Choosing PrEP TDF/FTC or TAF/FTC



This is a general guide and is subject to change

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Tenofovir Adverse Effects

	TAF/FTC (n=2694)	TDF/FTC (n=2693)
Any SE	545 (20%)	630 (23%)
Diarrhea	135 (5%)	160 (6%)
Nausea	114 (4%)	123 (5%)
Headache	59 (2%)	57 (2%)
Fatigue	43 (2%)	72 (3%)
Abdominal Pain	26 (1%)	35 (1%)
Flatulence	22 (<1%)	32 (1%)
Abdominal discomfort	18 (<1%)	30 (1%)
Weight Change	+1.1kg	-0.1kg
Fractures	53 (2%)	53 (2%)
Non-traumatic*	1 (<0.1%)	2 (<0.1%)

GI Effects rapidly declined over ~~2~~4 weeks after starting PrEP

Mayer et al. Lancet 2020

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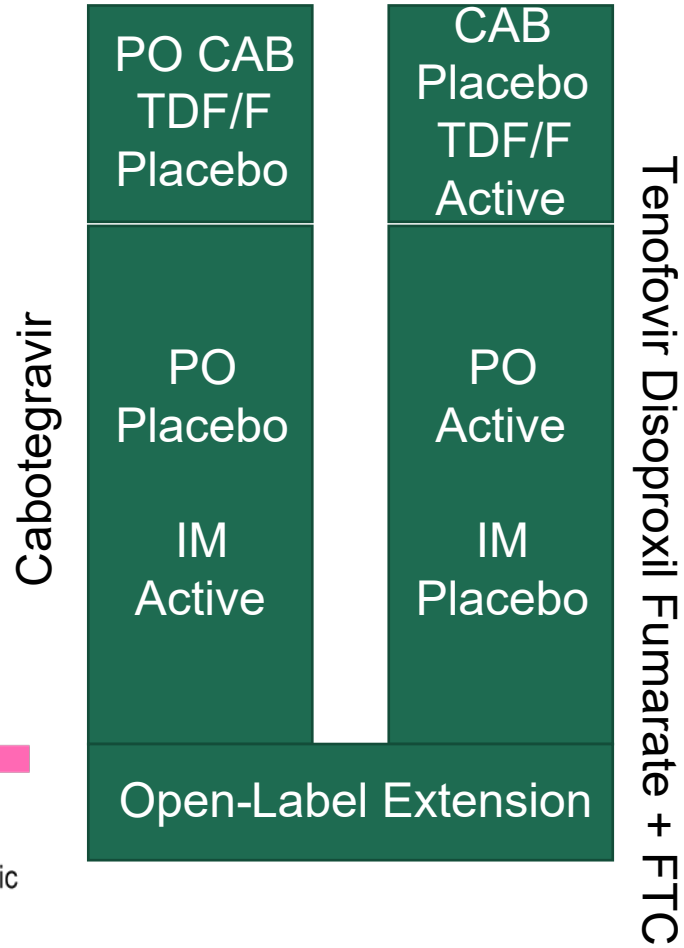
Long-Acting Cabotegravir

- FDA approved cabotegravir for PrEP in December 2021
  - Approved for all persons regardless of sex assigned at birth
  - Adults and Adolescents >35kg
  - HPTN 083 – MSM/TGW
  - HPTN 084 – CGW

HPTN 083
an HIV prevention clinical trial

HPTN 084
Long-acting Injectable For the Epidemic



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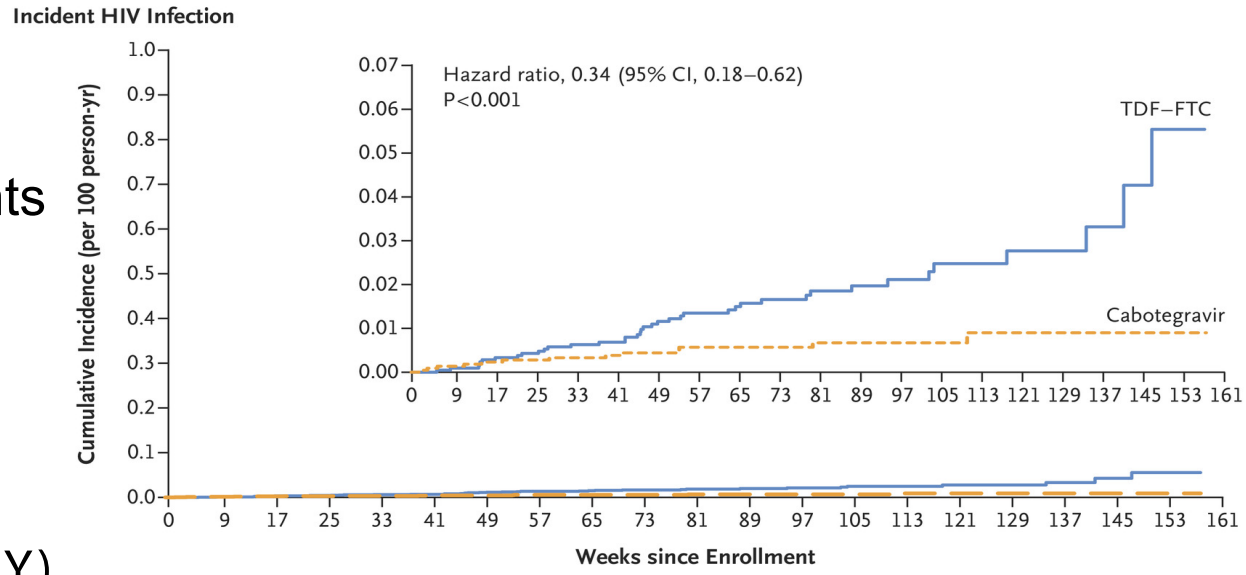
HPTN 083 - Cabotegravir LA

- 4566 Total Participants
  - 68% < 30years
  - 12% TGW
  - 1698 US participants
    - Median age 27
    - 50% Black/AA
    - 7% TGW
- 52 Infections
  - 13 in CAB (0.41/100PY)
  - 39 in TDF (1.22/100PY)
- 46 additional HIV infections in extension
  - 42 after unblinding (11 CAB/31TDF/F)



HR 0.33– 0.34:
66% Risk Reduction

Landovitz et al. NEJM 2021
Landovitz et al. CROI 2022

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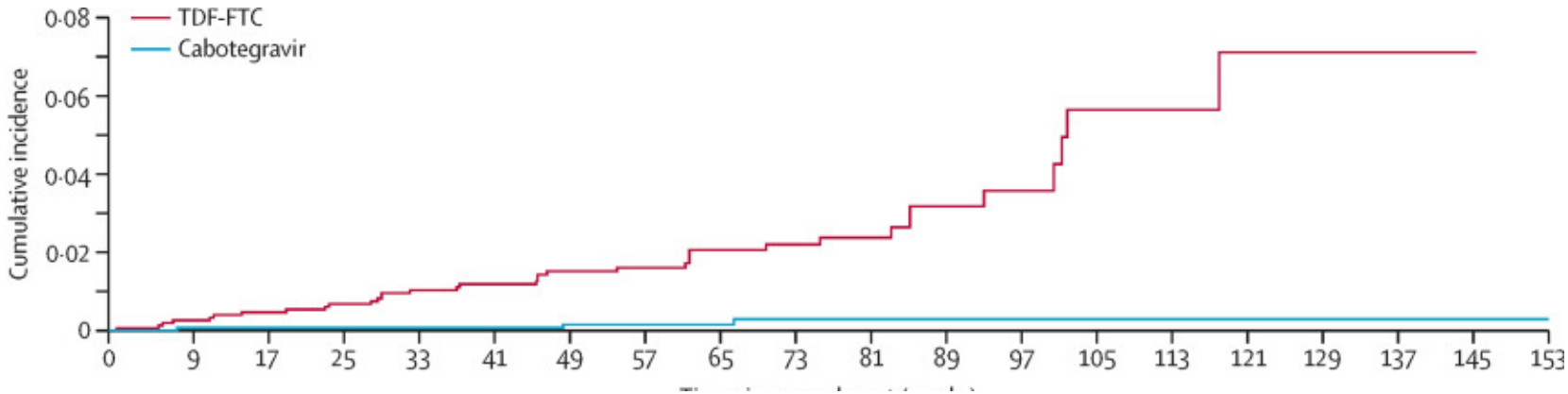
HPTN 084 – Cabotegravir LA



- >3,000 cisgender women, Median Age: 25y
- 38 total infections:
  - 4 CAB (0.2 incidence rate)
    - 1 baseline, 3 incident HIV
  - 34 TDF/FTC (1.79 incidence rate)
- HR 0.11 (95% CI 0.04-0.32)
- 62% detectable drug in TDF/FTC

HR 0.11
89% Risk Reduction

Delany-Moretlwe S, et al. Lancet 2022

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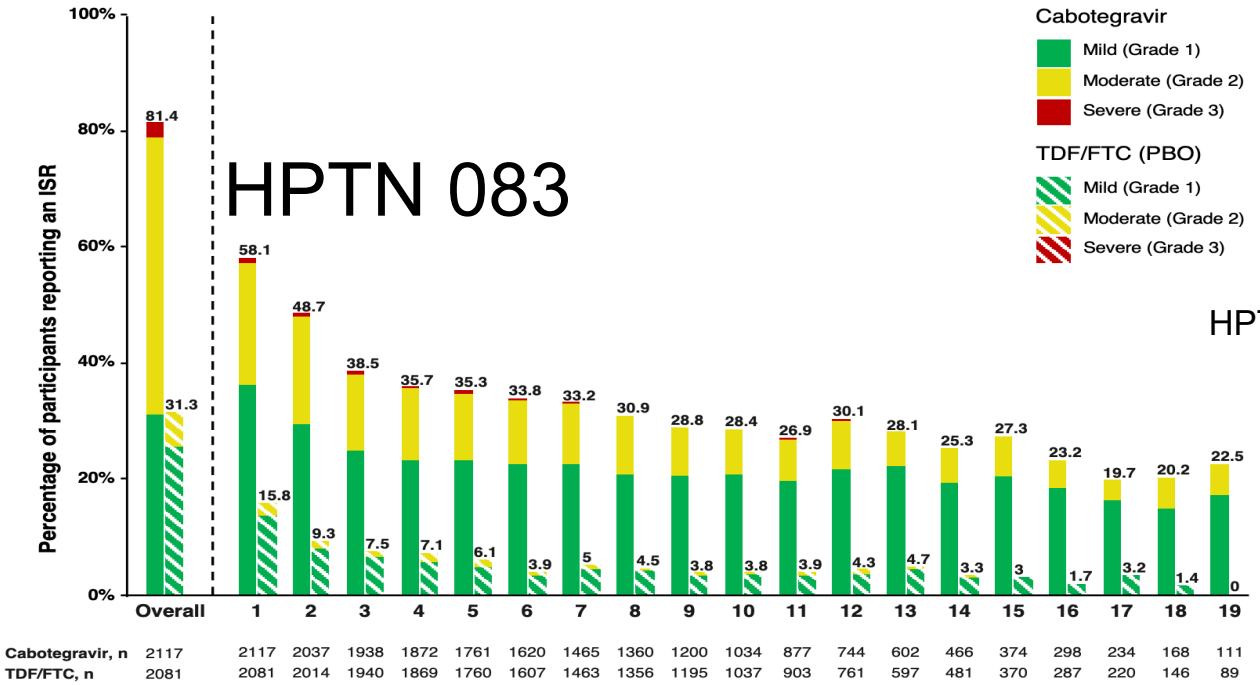
Cabotegravir – Injection Site Reactions



HPTN 083 Injection Site Reactions

- Most common in first 3 injections
- Pain (61%), tenderness (24%)
- Begin 1 d and resolve by 3d
- Improve over time
- Only 2.4% d/c due to ISR

HPTN 084

Injection site reactions§	Cabotegravir	TDF/F
Any	577/1519 (38·0%)	163/1516 (10·8%)
Grade ≥2	192/1519 (12·6%)	25/1516 (1·6%)

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

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PURPOSE 1

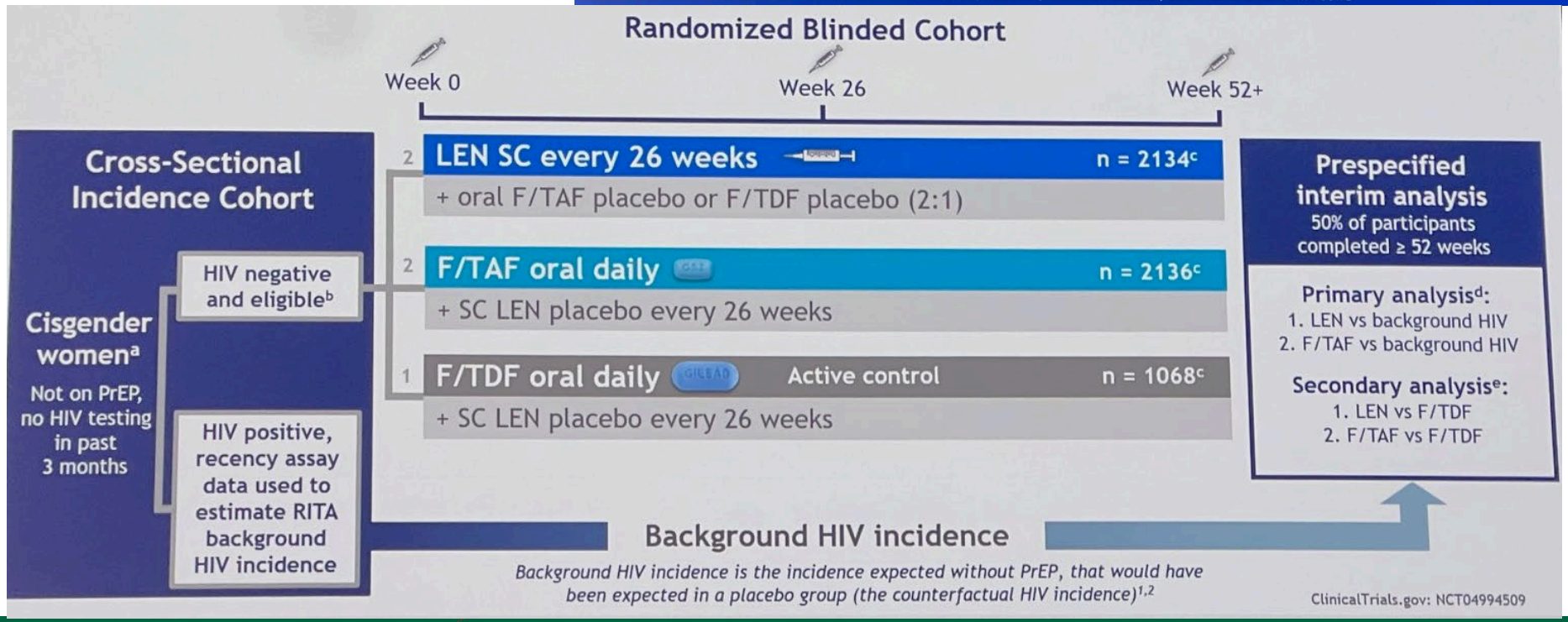
PURPOSE
Prevention with PURPOSE

AIDS 2024

Twice-Yearly Lenacapavir or Daily Oral Emtricitabine/Tenofovir Alafenamide for HIV Prevention in Cisgender Women: Interim Analysis Results from the PURPOSE 1 Study

Linda-Gail Bekker, MBChB, PhD, on behalf of the PURPOSE 1 Study Team
The Desmond Tutu HIV Centre, University of Cape Town, Cape Town, South Africa

Co-authors: Moupali Das, Quarraisha Abdool Karim, Khatija Ahmed, Joanne Batting, William Brumskine, Katherine Gill, Ishana Harkoo, Manjeetha Jaggernath, Godfrey Kigozi, Noah Kiwanuka, Philip Kotze, Limakatso Lebina, Cheryl E. Louw, Moelo Malahleha, Mmatsie Manentsa, Leila E. Mansoor, Dhayendre Moodley, Vimla Naicker, Logashvari Naidoo, Megeshinee Naidoo, Gonasagrie Nair, Nkosiphile Ndlovu, Thesla Palanee-Phillips, Ravindre Panchia, Saresha Pillay, Disebo Potloane, Pearl Selepe, Nishanta Singh, Yashna Singh, Elizabeth Spooner, Amy M. Ward, Zwelethu Zwane, Ramin Ebrahimi, Yang Zhao, Alexander Kintu, Chris Deaton, Christoph Carter, Jared M. Baeten, and Flavia Matovu Kiweewa



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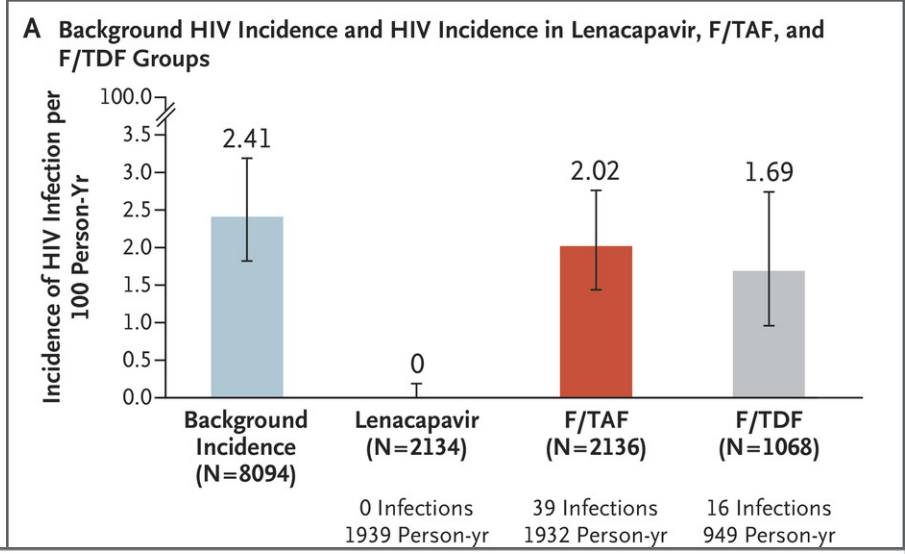
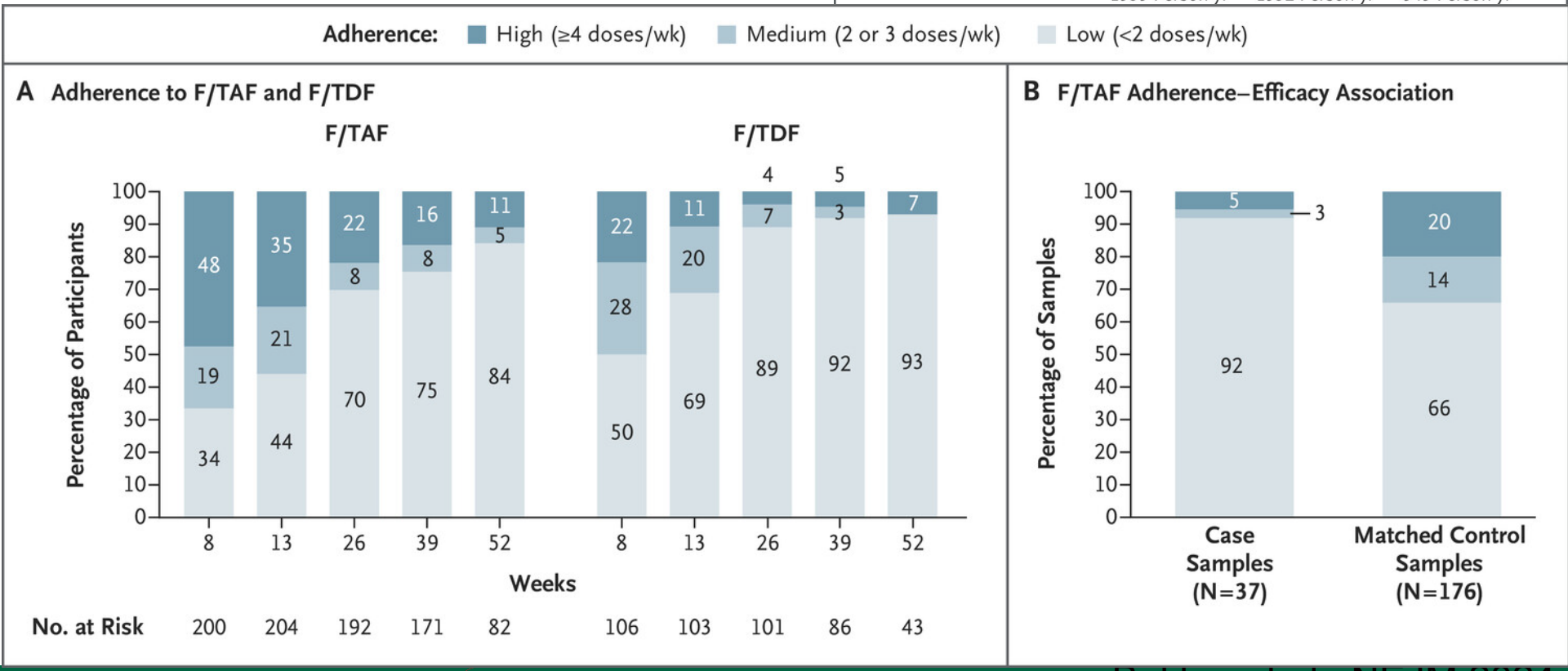
PURPOSE 1





Bekker et al., NEJM 2024

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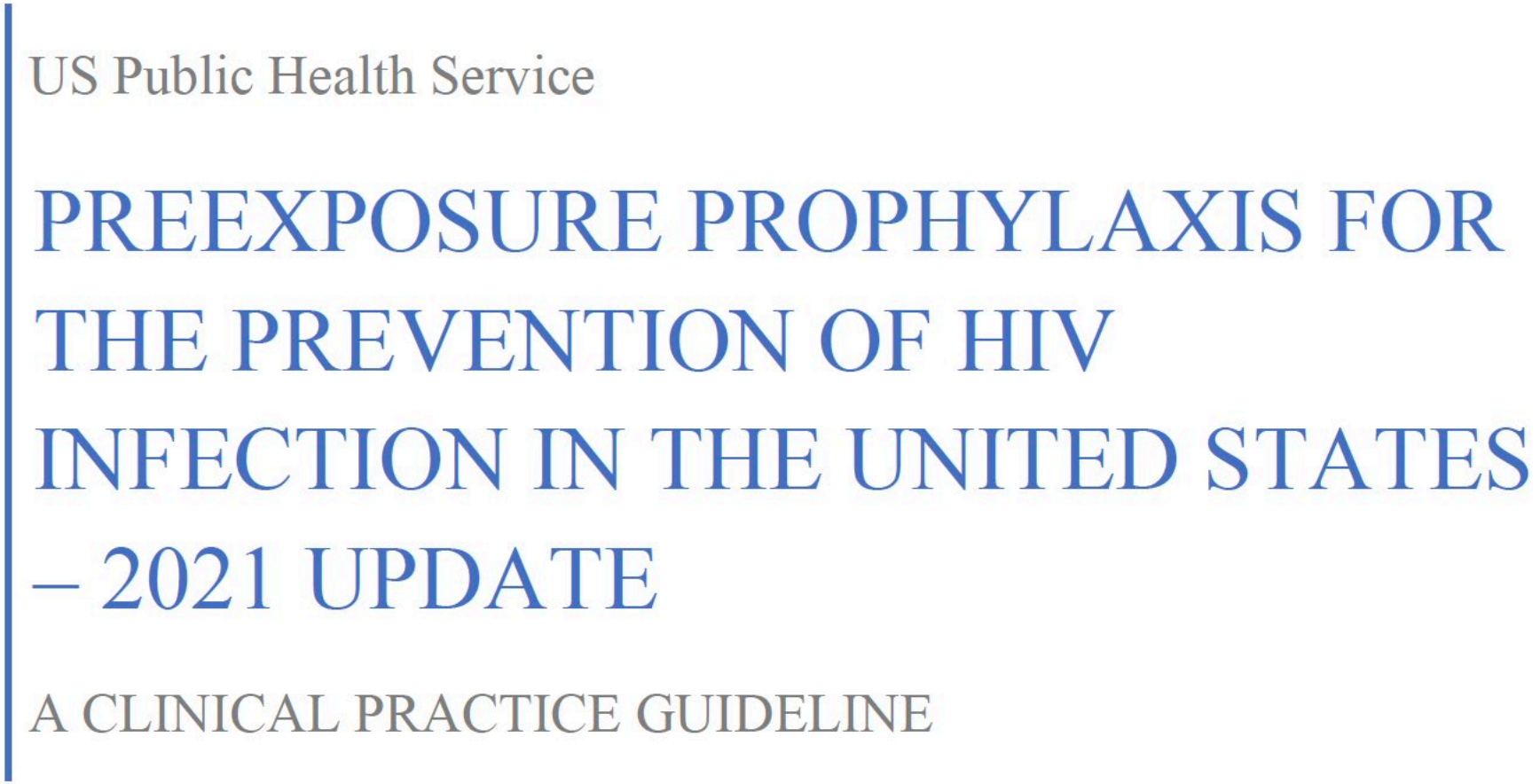
Reflection and Poll

Oral and injectable PrEP are all highly effective, and all are considered safe.

“My biggest question or concern about PrEP (so far) is…._____”

Updated CDC Guidelines



https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf

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Notable Changes in 2021 Guidelines

- Choice
  - Addition of cabotegravir
  - Clarification of TDF/F v TAF/F
  - Inform all sexual active adults and adolescents of PrEP
- Timing
  - Same-day starts
  - Event-driven dosing

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Providing PrEP

- Important factors regardless of PrEP agent:
  - HIV testing – must be confirmed HIV negative
  - STI testing
  - Adherence counseling
  - Sexual risk and behavioral counseling

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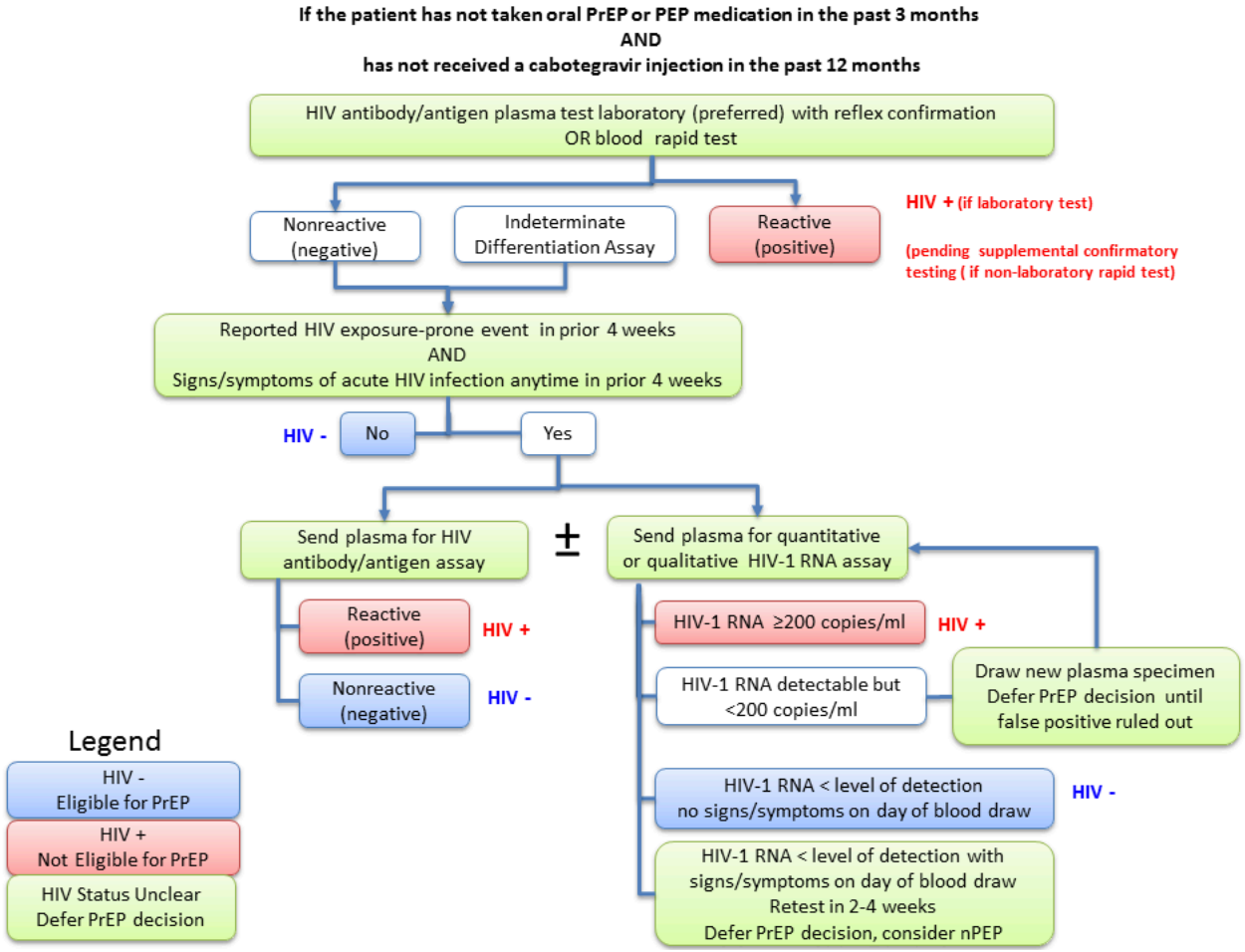
HIV Testing for PrEP – Initial

- If no recent PrEP use



CDC PrEP Guidelines, 2021

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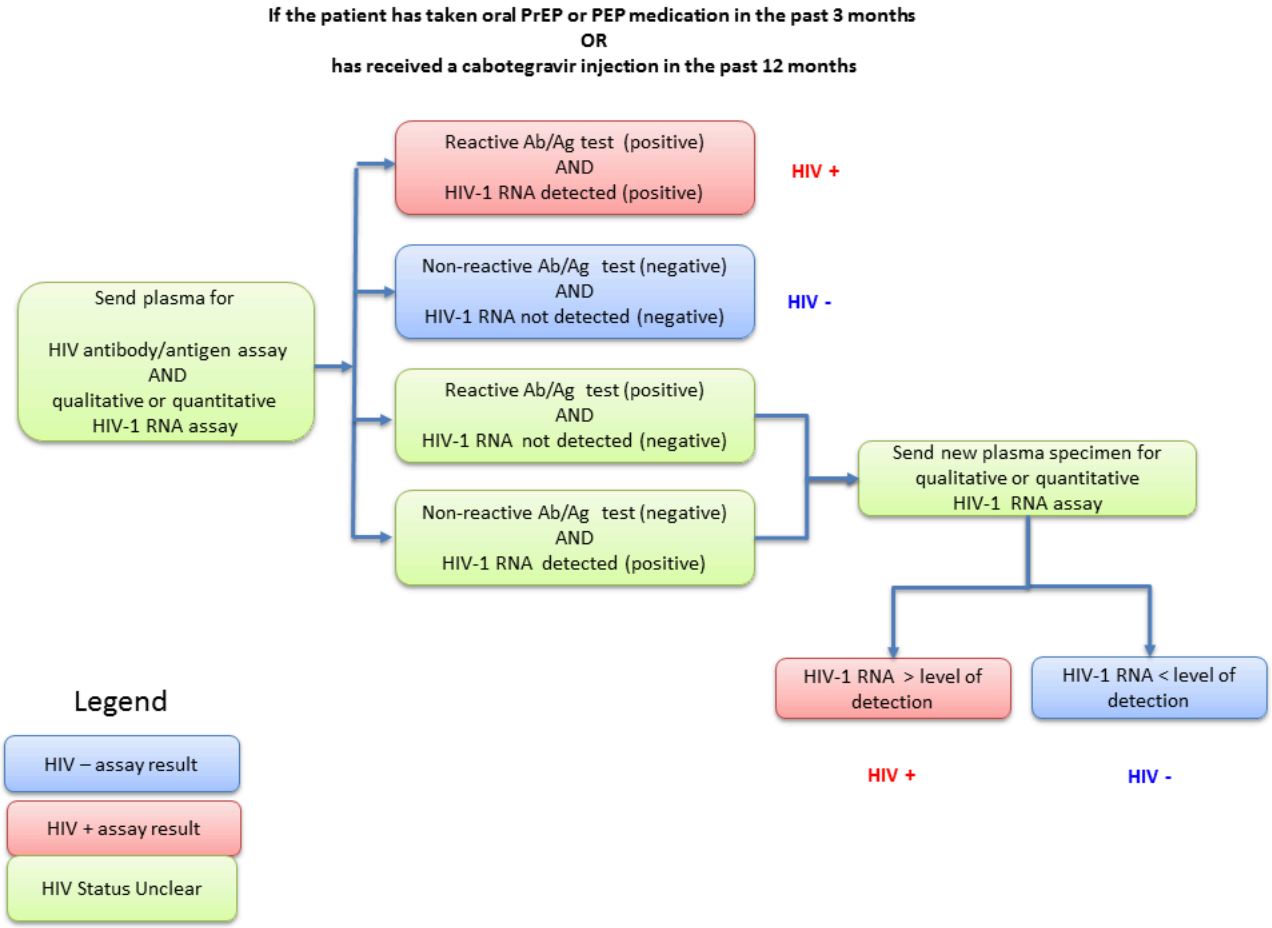
HIV Testing for PrEP – Follow-up

- Delayed seroconversion or detection of HIV infection due to presence of PrEP agent.
- ~98d from time of infection to detection in CAB
- ~32d among TDF/F



CDC PrEP Guidelines, 2021
Marzinke et al. *JID* 2021

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Daily Oral PrEP – Labs/Visits

Table 5 Timing of Oral PrEP-associated Laboratory Tests

Test	Screening/Baseline Visit	Q 3 months	Q 6 months	Q 12 months	When stopping PrEP
HIV Test	X*	X			X*
eCrCl	X		If age ≥50 or eCrCL <90 ml/min at PrEP initiation	If age <50 and eCrCl ≥90 ml/min at PrEP initiation	X
Syphilis	X	MSM /TGW	X		MSM/TGW
Gonorrhea	X	MSM /TGW	X		MSM /TGW
Chlamydia	X	MSM /TGW	X		MSM /TGW
Lipid panel (F/TAF)	X			X	
Hep B serology	X				
Hep C serology	MSM, TGW, and PWID only			MSM,TGW, and PWID only	

* Assess for acute HIV infection (see Figure 4)

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Daily Oral PrEP – Tenofovir Prescribing

- Adherence and sexual health assessment and counseling
- Prescription for 90 days TDF/FTC or TAF/FTC
- Follow-up appointment in 3 months

CDC PrEP Guidelines, 2021

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CAB PrEP

Test	Initiation Visit	1 month visit	Q2 months	Q4 months	Q6 months	Q12 months	When Stopping CAB
HIV*	X	X	X	X	X	X	X
Syphilis	X			MSM^/TGW~ only	Heterosexually active women and men only	X	MSM/TGW only
Gonorrhea	X			MSM/TGW only	Heterosexually active women and men only	X	MSM/TGW only
Chlamydia	X			MSM/TGW only	MSM/TGW only	Heterosexually active women and men only	MSM/TGW only

* HIV-1 RNA assay

CDC PrEP Guidelines, 2021

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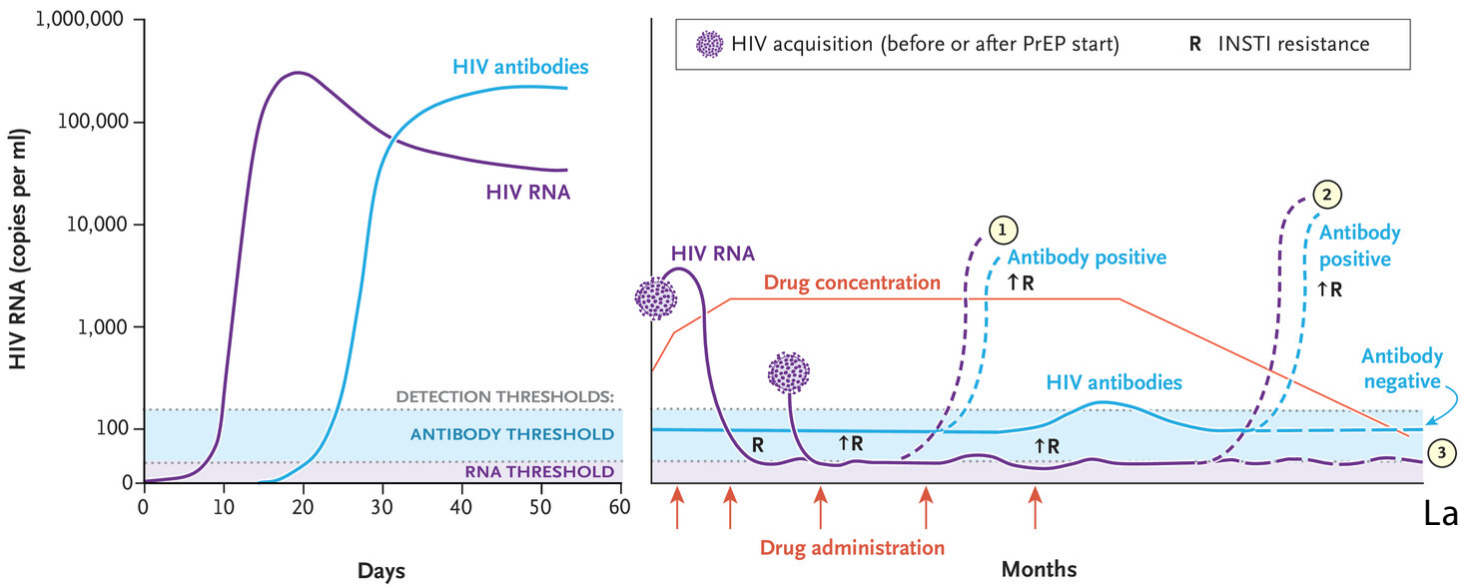
A

	Classic Acute HIV Infection	Acute HIV Infection Involving LEVI
Context	No antiretroviral therapy	Long-acting antiviral PrEP agent (prototype: CAB-LA)
Onset	New infection	Infection during PrEP Initiation of PrEP agent during acute or early infection
Symptoms	Fever, chills, rash, night sweats, muscle aches, sore throat, fatigue, swollen glands	Minimal, varied, often no symptoms reported
Viral replication	Explosive	Smoldering
Viral load	Very high	Low or undetectable
Detection	Antigen and antibody assay, RNA assays (including less sensitive point-of-care assays)	Ultrasensitive RNA assay (often low or undetectable RNA, low or undetectable DNA, diminished or delayed antibody production)
Assay reversion	Rare	Common for many test types
Duration	1–2 weeks (until antibody detection)	Months (until breakthrough infection, drug clearance, or start of PrEP agent); can persist for months after the antiviral agent is discontinued
Drug resistance	No (unless transmitted)	Yes (can emerge early when the viral load is low)

B



Landovitz et al., NEJM 2024

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CAB-LA – Other Considerations

- Cost
  - Copay and medication assistance throughViiV (www.viivconnect.com)
  - Cost effectiveness (compared to TDF/F or TAF/F)
  - Clinic acquisition
- Implementation
  - More frequent visits (every two months)
  - Viral load testing
- Equity
  - Disparities in uptake and persistence

Neilan et al. Ann Int Med 2022
Sharfstein et al. JAMA 2022

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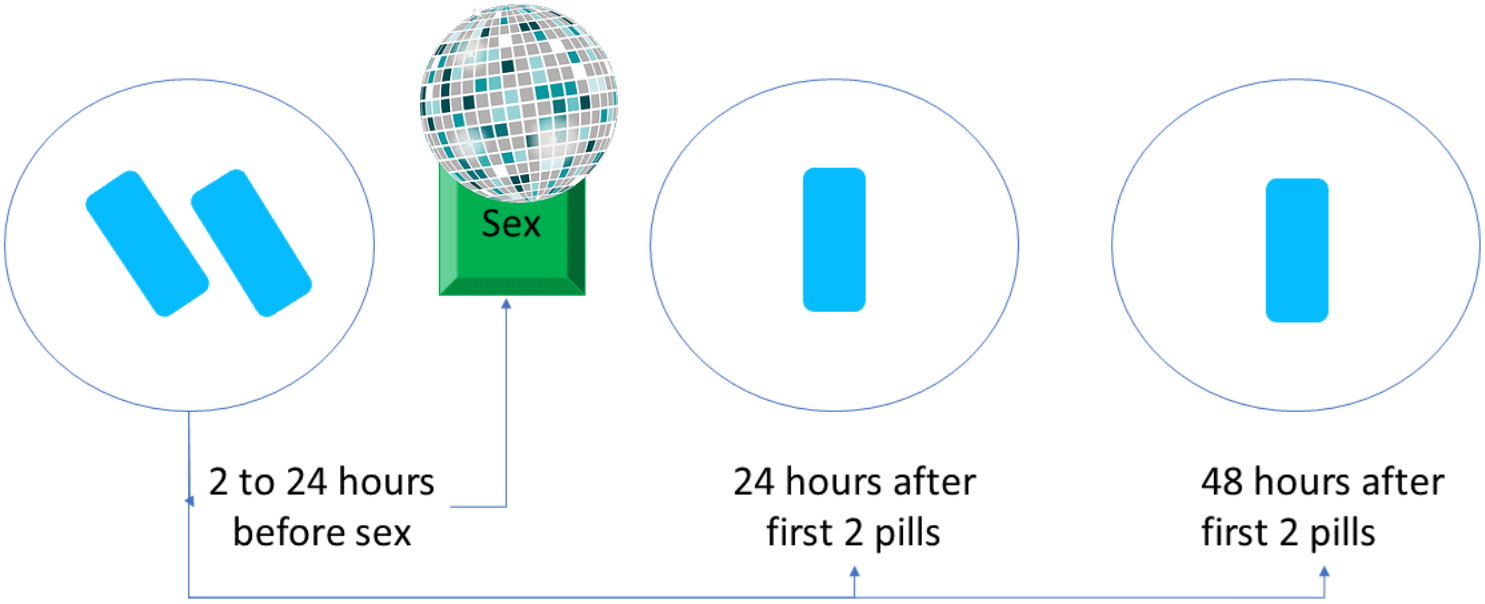
Event-Driven (On-Demand) PrEP

- "2-1-1 Dosing" is very effective but it is not currently approved by FDA but is included in CDC recommendations
- IAS-USA gives alternative recommendation for this modality compared to daily but *only* in MSM/TGW



CDC PrEP Guidelines 2021
Saag et al. JAMA 2018

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When to avoid Event-Driven PrEP

- Persons who are AFAB (due to insufficient evidence and concern of drug levels in cervicovaginal tissues)
- MSM who cannot adhere to this regimen
- When using TAF/F due to lack of data
- Chronic HBV Infection

- Other considerations to discuss with patient
  - **What do they think about spontaneity?**
  - **Can they plan their encounters at least 2 hours in advance?**

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Conclusion

- HIV can be effectively prevented
- USPSTF gives PrEP a GRADE A Recommendation
- PrEP is safe and highly effective
- Adherence is key for oral PrEP and ART.
- New agents will help make this easier but new agents require renewed attention to implementation and equity!

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Final Reflection and Poll

CDC Guidelines help us provide PrEP effectively and safely.

I feel more confident in my understanding of PrEP.

No way, kinda, definitely.

“I am still concerned about _____”

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Thank you!

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