AETC AIDS Education & Training Center Program Mountain West

HIV Pre-Exposure Prophylaxis (PrEP): New Meds, Guidelines, & Controversies

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Some slides & images courtesy of Dr. Joanne Stekler, Dr. Raphael Landovitz, & Dr. David Spach.

Disclosures

I have no financial disclosures or conflict of interest.

I am currently working remotely from Lusaka, Zambia.

The latest guidelines and meds are still very new!

I will mention investigational therapies.

Learning Objectives

- Review the latest guidelines for HIV PrEP, including selecting appropriate candidates, recommended baseline laboratory evaluation, and laboratory monitoring
- Discuss medication options for PrEP, including oral options and the new long-acting injectable agent
- Highlight areas of controversy in the new guidelines and describe the potential future of PrEP, including new medications in development

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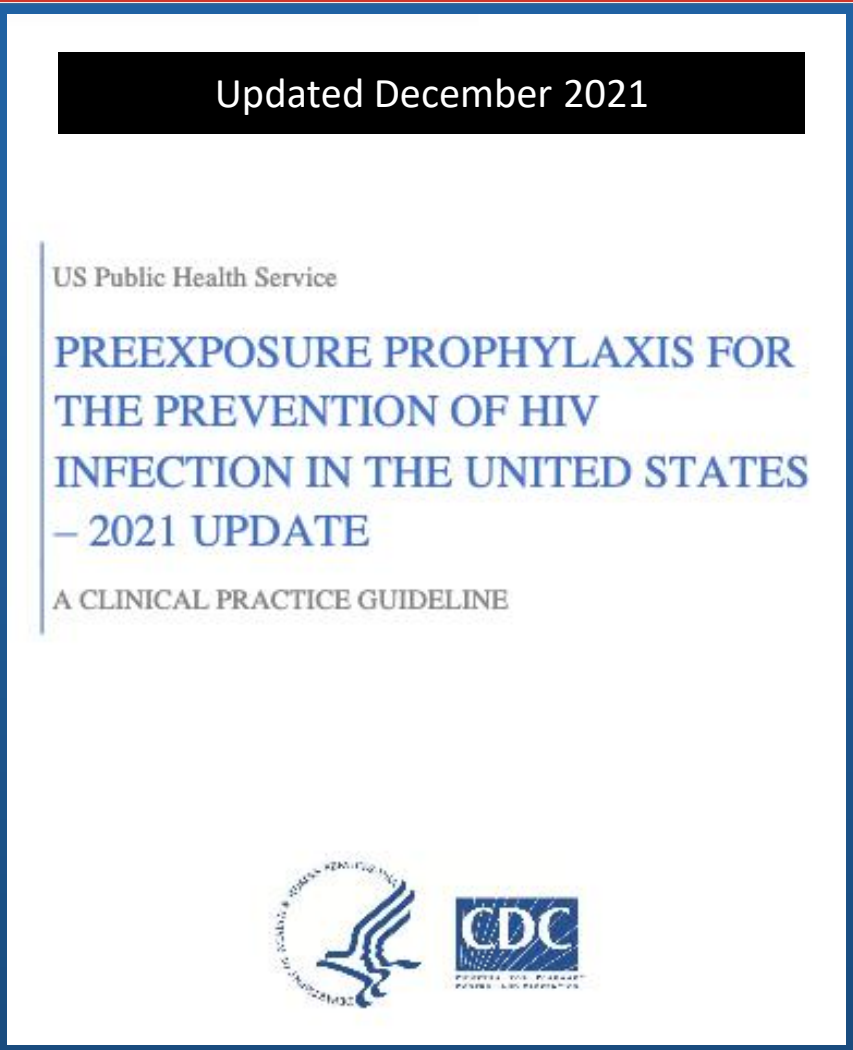
PrEP Guidelines & Resources



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

AIDSVu:
To see local data, help locate services
aidsvu.org

National HIV Curriculum:
www.hiv.uw.edu

Clinical Consultation:
PrEPLine (855-448-7737)
For urgent Q's/ambiguous test results

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

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What is HIV PrEP & Why Discuss It?

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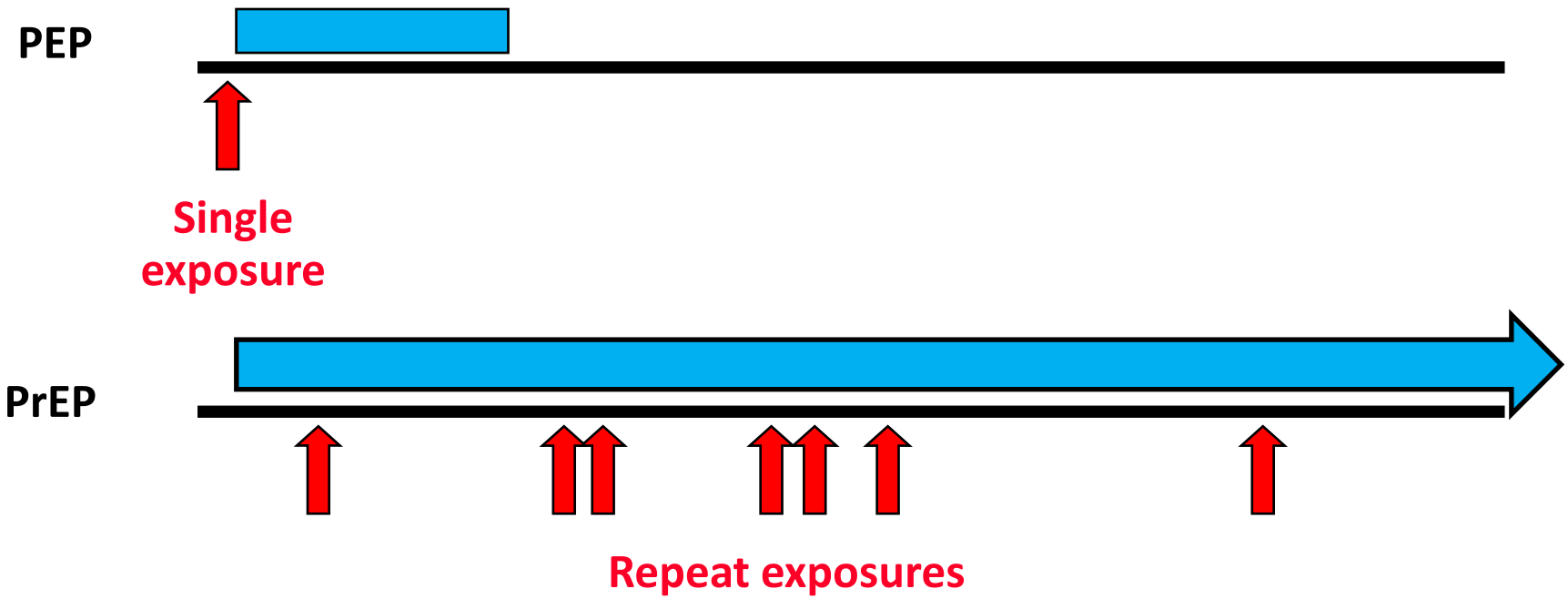
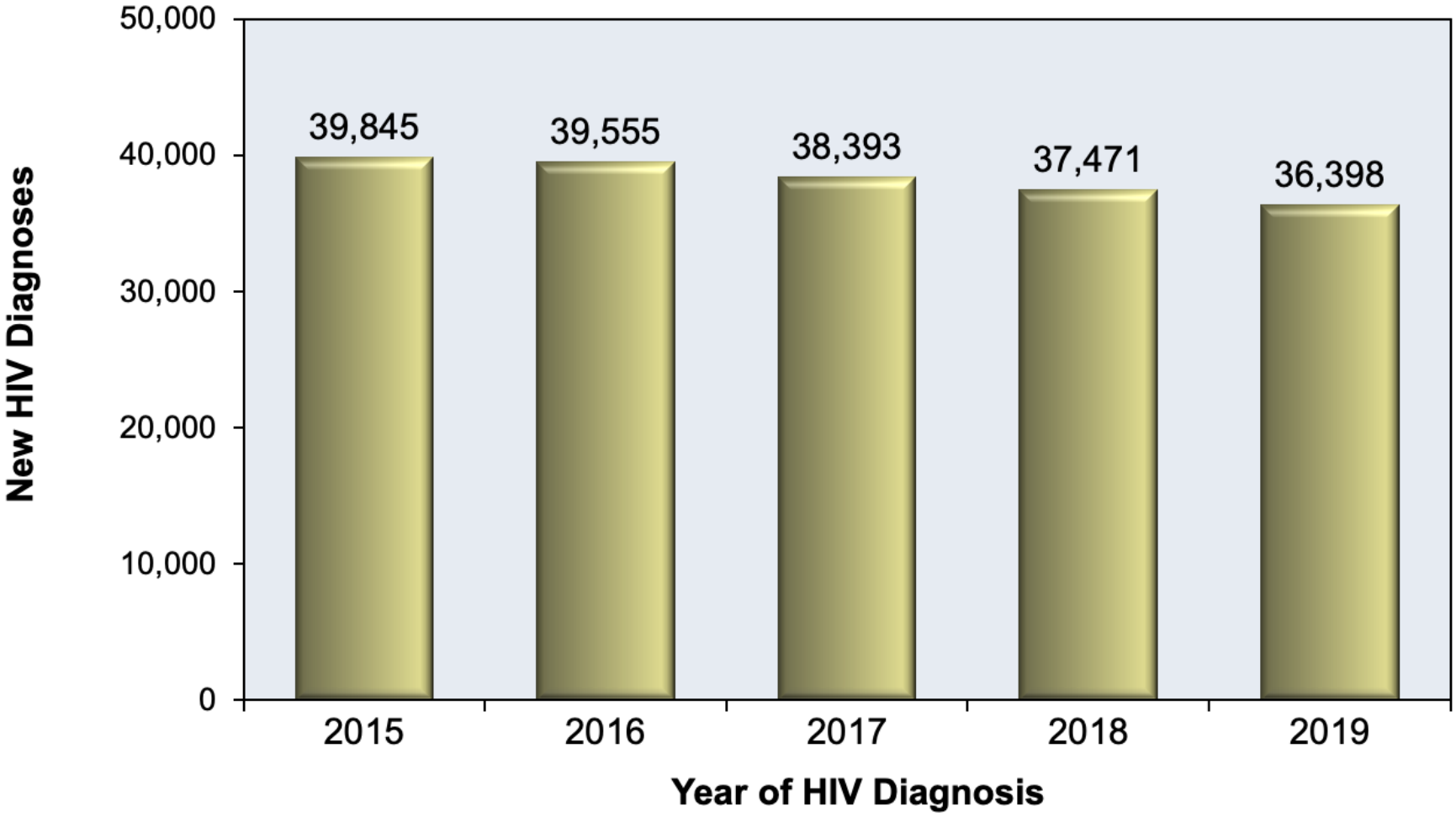
What is Pre-Exposure Prophylaxis (PrEP)?



*Blue bar represents taking an HIV medication to prevent infection

HIV PrEP: A prevention strategy in which an individual at **high risk** takes a medication **regularly** (along with continued behavioral **risk-reduction** strategies) to prevent HIV

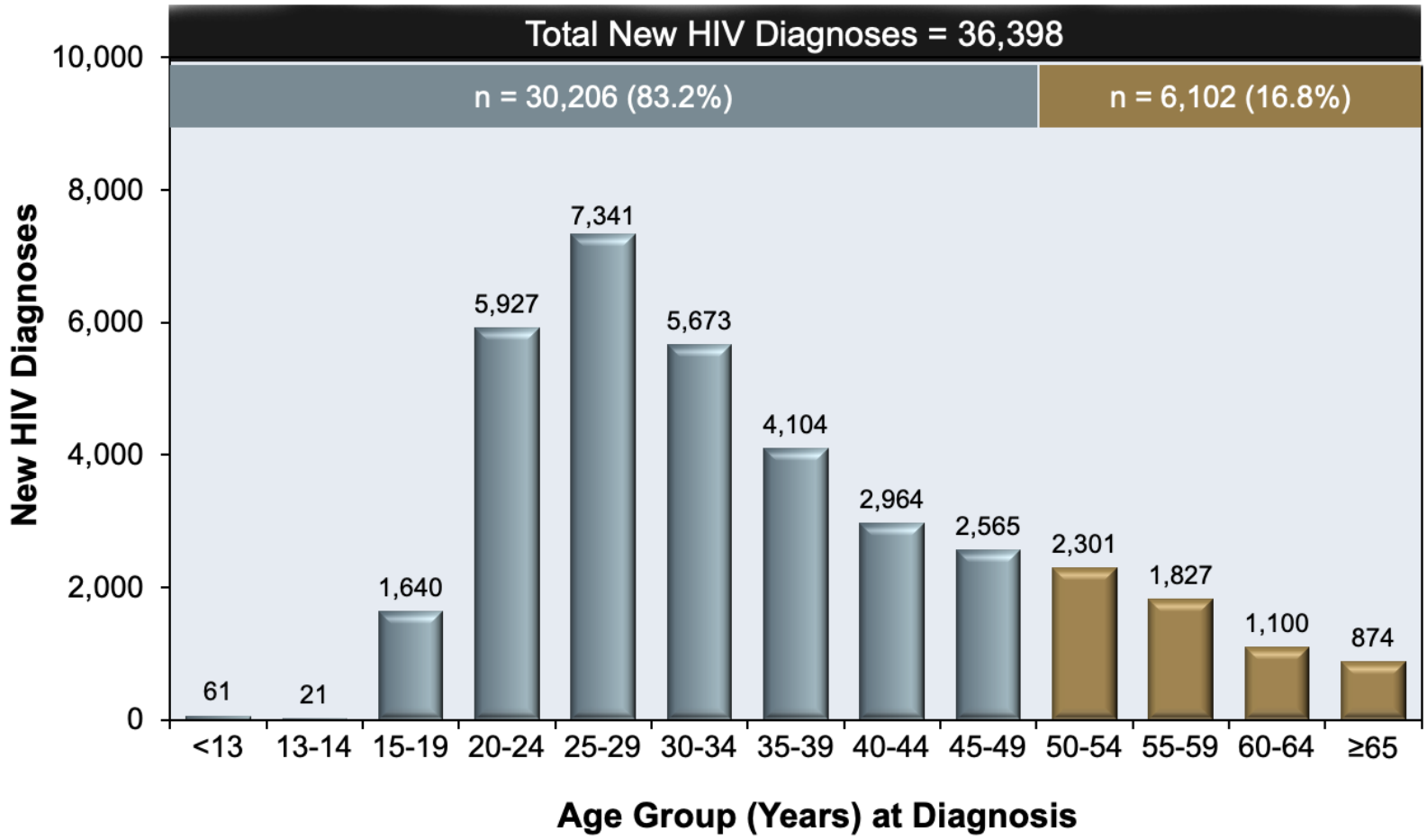
New HIV Diagnoses Each Year



Slide from: National HIV Curriculum (hiv.uw.edu)

Data source: CDC

New HIV Diagnoses Each Year by Age Group

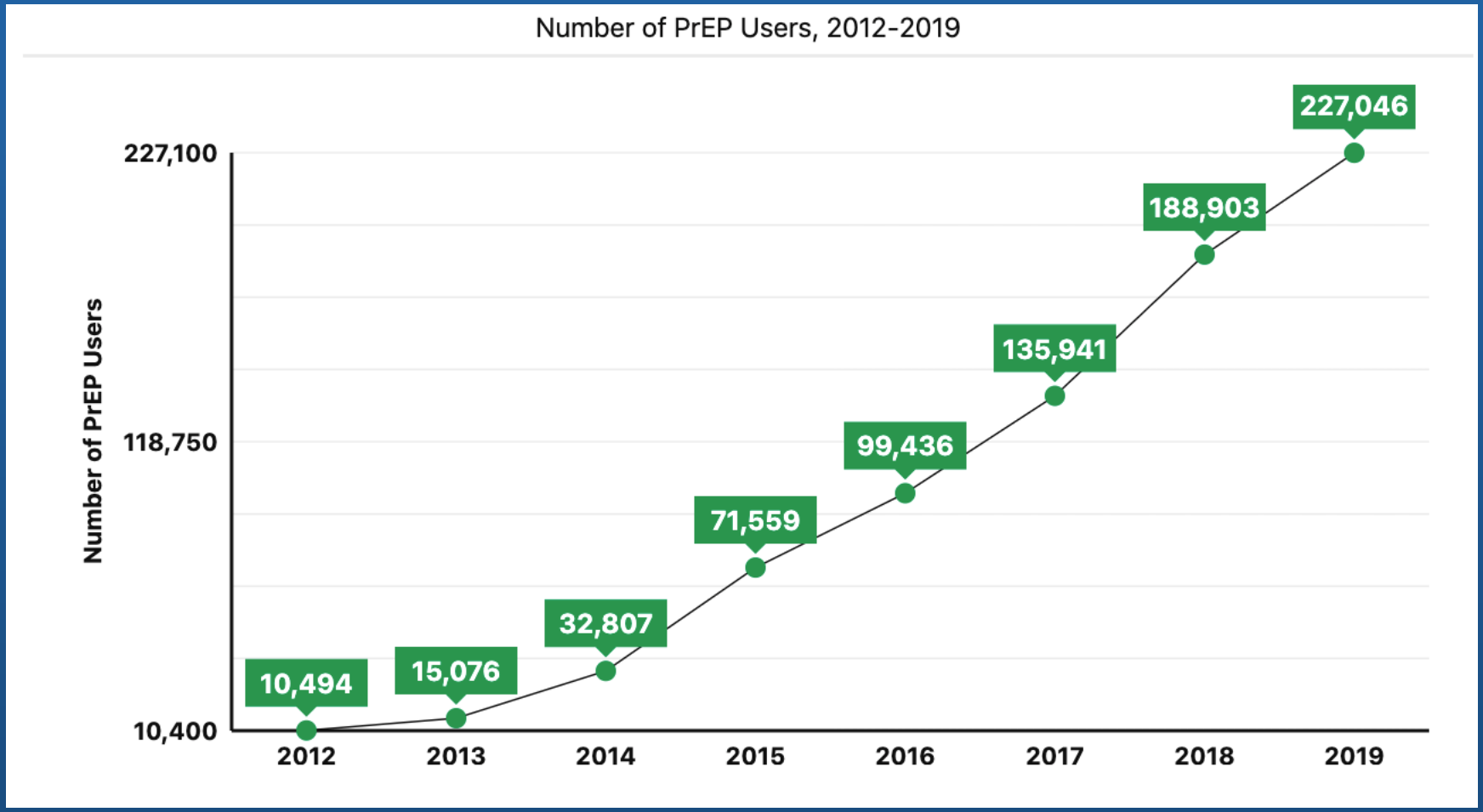


Slide from: National HIV Curriculum (hiv.uw.edu)

Data source: CDC

Estimated Number Who May Benefit from PrEP

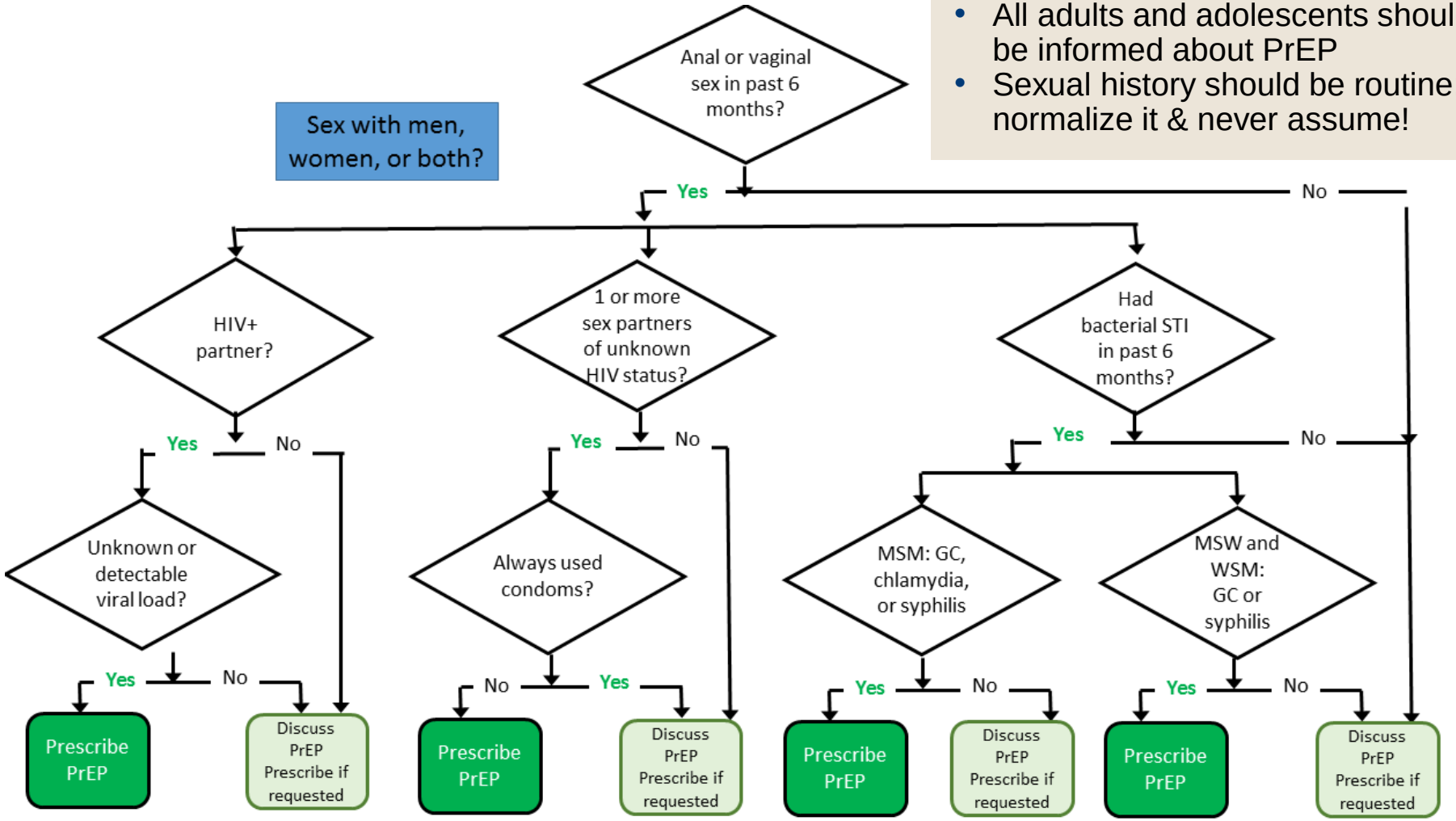
Current Estimate of PrEP Users



Who may benefit from HIV PrEP? And how effective is it?

Assessing Indications for PrEP in Sexually Active Persons

- All adults and adolescents should be informed about PrEP
- Sexual history should be routine; normalize it & never assume!



2021 CDC PrEP Guidelines

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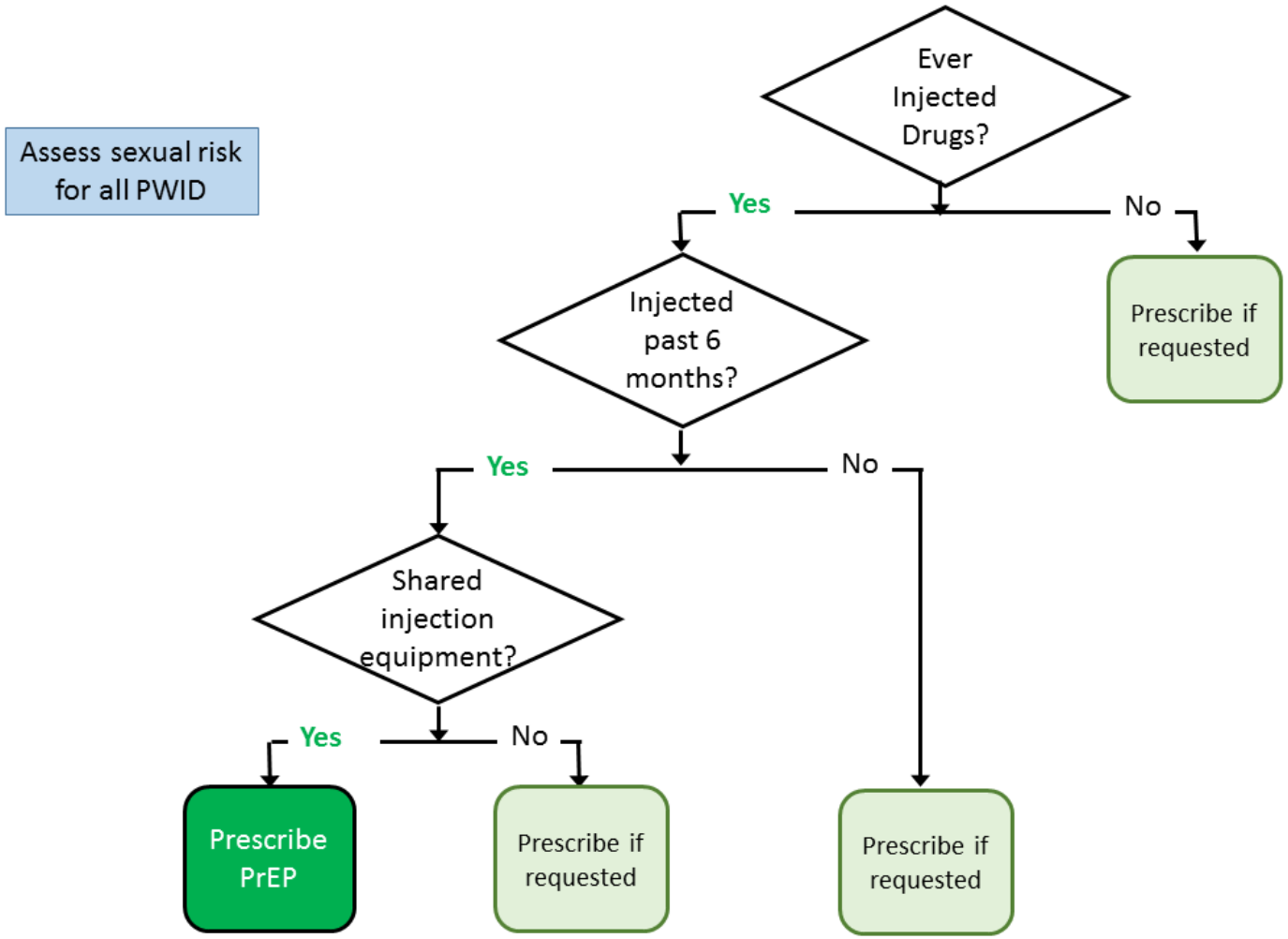
Assessing Indications for PrEP in Persons Who Inject Drugs



2021 CDC PrEP Guidelines

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So how effective is oral HIV PrEP?
Quotes from the CDC

"PrEP reduces the risk of getting HIV from sex by about 99% when taken as prescribed"

"Although there is less information about how effective PrEP is among people who inject drugs, we do know that PrEP reduces the risk of getting HIV by at least 74% when taken as prescribed"

https://www.cdc.gov/hiv/basics/prep/prep-effectiveness.html

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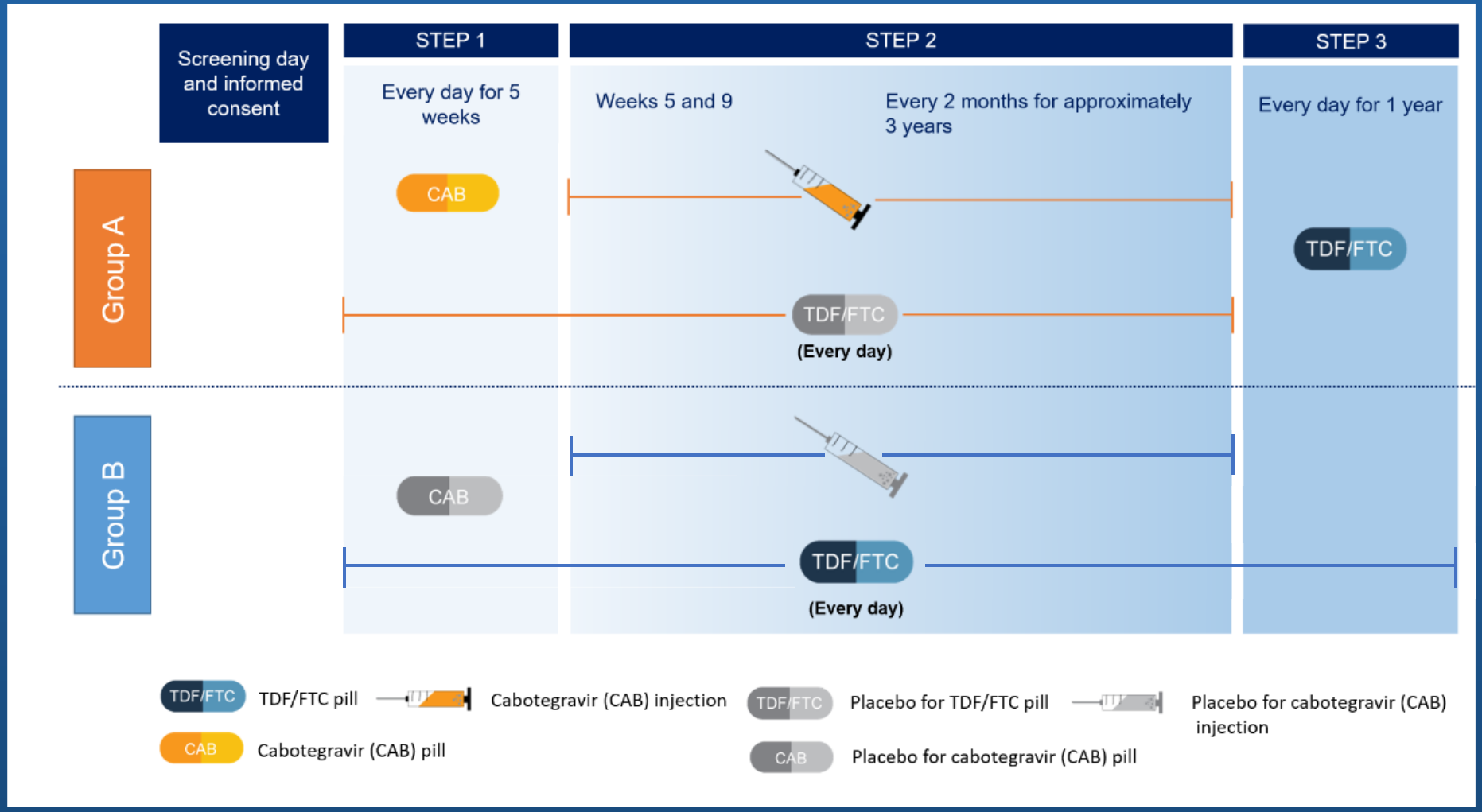
HPTN 083: Cisgender MSM & Transgender Women
HPTN 084: Cisgender Women



Slide courtesy of Dr. Raphael Landovitz, UCLA

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Injectable Cabotegravir (CAB)
Compared to Oral TDF/FTC in 2 Double-Blind RCT's

*CAB: efficacy **superior** to oral TDF/FTC & well-tolerated

- HPTN 083 (4,570 cisgender MSM 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: **0.34 (95% CI 0.18-0.62)**

- HPTN 084 (3,223 cisgender women).
  4 infections in the CAB arm (incidence rate 0.21%)
  34 infections in the FTC/TDF arm (incidence rate 1.79%)
  Hazard ratio for CAB versus FTC/TDF: **0.11 (95% CI 0.04-0.32)**

HPTN 083: Landovitz RJ et al. NEJM 2021.
HPTN 084: www.hptn.org, also data presented at IAS 2021 and HIVR4P 2021

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What are the FDA-approved medication options for PrEP?

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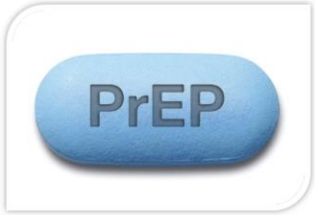
FDA-Approved for HIV PrEP (as of February 2022)

- Daily tenofovir DF/emtricitabine (TDF/FTC; *Truvada*)
  - For all adults or adolescents >35 kg, including persons who inject drugs
  - Requires CrCl >60 mL/min
- Daily tenofovir alafenamide/emtricitabine (TAF/FTC; *Descovy*)
  - For cisgender MSM and transgender women
  - Not for cisgender women/other persons at risk via receptive vaginal sex
  - Requires CrCl >30 mL/min
- Injectable, long-acting cabotegravir q2 months (CAB, *Apretude*)
  - For all adults and adolescents >35 kg
- *Dapivirine vaginal ring has been withdrawn*



PrEP Options Pros/Cons (Speaker's Opinion)

TDF/FTC (*Truvada*)	TAF/FTC (*Descovy*)	CAB (*Apretude*)
Pros:	**Pros:**	**Pros:**
Proven efficacy in many risk groups	Proven efficacy for cisgender MSM and transgender women (TGW)	Long-acting, injectable; superior efficacy to TDF/FTC for MSM, TGW, cisgender women
Generic options available	Likely less long-term renal and bone risk than TDF/FTC	Ok with renal insufficiency; no risks to kidneys/bones
Nondaily (2-1-1) dosing option for cisgender MSM	Smaller tablet	Neutral effect on weight/lipids
Cons:	**Cons:**	**Cons:**
Renal risks; do not start if CrCl <60 mL/min	Not approved for cisgender women/individuals at risk due to vaginal sex	Must be administered by a healthcare professional
Long-term risk to bone mineral density	Do not start if CrCl <30 mL/min	HIV RNA monitoring
Decreased weight (mechanism uncertain)	Only daily dosing studied	Cost/insurance barriers

Oral PrEP: TAF/FTC vs. TDF/FTC
Short-Term Side Effects

Short-term side effects in the DISCOVER TRIAL: similar “start-up syndrome” in both groups

	TAF/FTC (*Descovy*) N=2,694	**TDF/FTC (*Truvada*) N=2,693**
Diarrhea	5%	6%
Nausea	4%	5%
Headache	2%	2%
Fatigue	2%	3%
Abdominal pain	2%	3%

Neither needs to be taken with food

Descovy FDA Package Insert, 10/2019.

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What to Prescribe as PrEP?

- Choosing oral PrEP:
  - For most patients taking TDF/FTC, no need to switch to TAF/FTC
  - TAF/FTC is indicated for patients with eCrCl 30-60 ml/min
  - Clinicians may prefer TAF/FTC for patients with previously documented osteoporosis or related bone disease
- Injectable CAB:
  - May be preferred if significant renal disease, difficulty adhering to oral pills, or patient preference for injectable medication (plus no difficulty coming to clinic every 2 months)

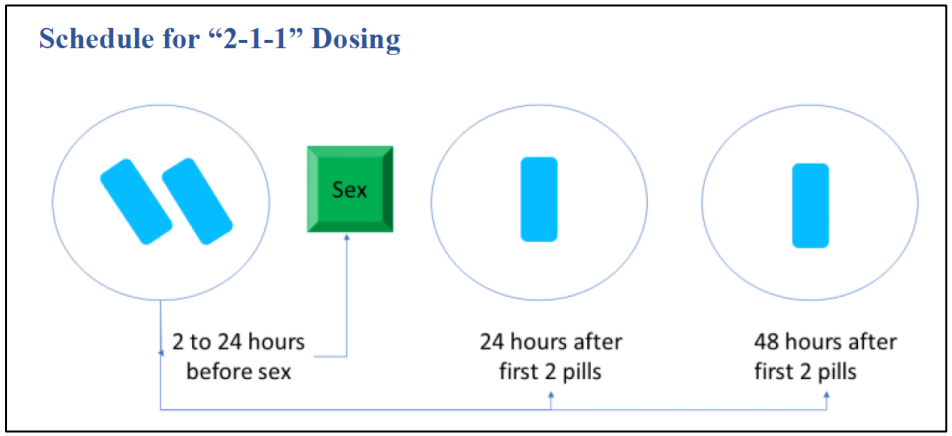
*Review drug-drug interactions before prescribing PrEP: only a few significant ones (rifamycins, some anticonvulsants, St. John's wort, etc.; CAB may decrease methadone levels)

Clinical Considerations:
Same-Day PrEP and Tele-PrEP

- Prescribe PrEP at patient's first visit prior to lab results?
  - Acceptable, assuming no significant risk within past 72 hours, good contact info, negative rapid HIV (not oral fluid)
  - Still need to send blood tests for confirmation; contact patient immediately if results come back concerning
  - Not appropriate if: patient ambivalent about starting, blood can't be drawn, signs/symptoms of acute HIV, history of renal disease or risk factors, no insurance, no contact info
- Prescribe PrEP by telemedicine?
  - Reasonable to initiate or refill PrEP based on tele-visits
  - Still need labs; home HIV/STI testing ok if feasible

What is 2-1-1? (a.k.a. event-driven, on-demand, pericoital)
Dosing option only with TDF/FTC, only for cisgender MSM

- Clinicians may choose to prescribe **TDF/FTC off-label** for **adult MSM** who have **sex less than once/week and anticipate sex**
  - Don't prescribe >30 pills without documenting repeat negative HIV
  - HBV is a contraindication
  - Discuss with patient:
    - Importance of taking all doses & using with all sexual encounters
    - Possibility of recurrent "start-up syndrome" symptoms
    - Option to change between 2-1-1 and daily dosing
    - Continued need for follow-up visits + labs
    - Off-label so may not be covered by insurance



2021 CDC PrEP Guidelines

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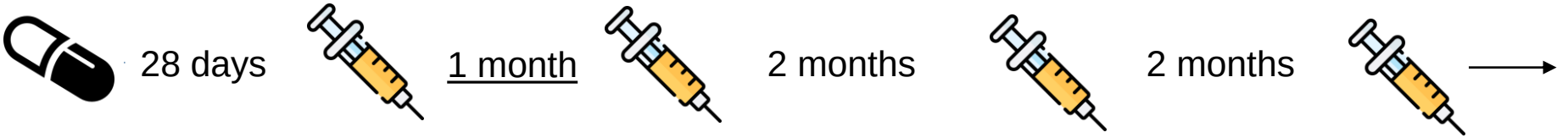
Cabotegravir Dosing & Administration
Oral Lead-In Phase is Optional

With oral lead-in (OLI):

Oral CAB 30 mg daily x at least 28 days → CAB 600 mg (3 mL) IM gluteal injection initial[a] + at 1 month → CAB 600 mg (3 mL) IM gluteal injection every 2 months thereafter[b]



Without oral lead-in, aka direct-to-inject (DTI):

CAB 600 mg (3 mL) IM gluteal injection initial + at 1 month → CAB 600 mg (3 mL) IM gluteal injection every 2 months thereafter[b]

a. Give initial CAB injection on last day or within 3 days of completing oral lead-in
b. Individual may receive CAB injection up to 7 days before or after scheduled injection date if needed
*If at any time an injection is missed by >2 months, restart with injection x 1 then repeat at 1 month

Cabotegravir FDA Prescribing Information (December 2021)

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Laboratory Evaluation & Monitoring

New in the Guidelines
HIV RNA Monitoring: Why?

- In HPTN 083, detection of HIV among participants in CAB group with Ag/Ab testing was delayed:
  - Mean 62 days compared to qualitative HIV-1 RNA assay for infections determined to have been present at baseline
  - Mean 98 days for incident infections
- Among participants in the TDF/FTC group, detection by Ag/Ab testing was delayed:
  - Mean 34 days compared to qualitative HIV-1 RNA detection for baseline infections
  - Mean 31 days for incident infections

Baseline HIV Testing

- **TDF/FTC or TAF/FTC**:
  - Document an HIV test within one week before PrEP
  - Ideally lab-based antigen/antibody (Ag/Ab) test
  - Point-of-care (POC) Ag/Ab testing is acceptable
    - When PrEP is prescribed based on POC results, a laboratory Ag/Ab test should always be drawn as well
    - Oral fluid tests should not be used
  - Add HIV RNA if patient has taken oral PrEP within last 3 months
- **CAB**:
  - Negative Ab/Ag test results should be confirmed with HIV RNA
  - Document within one week before PrEP
  - If starting based on rapid Ag/Ab, still draw HIV RNA

Additional Baseline Lab Tests

- Bacterial STI screening
  - Blood, urine, vaginal, rectal, oral (as indicated)
- Baseline renal function (prior to TAF/FTC or TDF/FTC)
- Hepatitis B serologies*
- Pregnancy test for individuals who may become pregnant**
- HCV test for MSM, TGW, and PWID
- Baseline lipids/weight if starting TAF/FTC

*Not absolutely required for CAB, but I think worthwhile
**Not in the updated guidelines, but I think worthwhile

Laboratory Monitoring

- HIV infection monitoring:
  - Oral PrEP: every 3-month Ag/Ab + HIV RNA (controversy!)
  - CAB: Ag/Ab + HIV RNA at 1 month then every 2 months
- Renal monitoring (oral PrEP only):
  - Check eCrCl every 6 months if ≥ age 50 or eCrCl <90 ml/min
  - Otherwise, every 12 months
- Triglycerides and cholesterol:
  - Check annually for all persons taking TAF/FTC
- Tests NOT routinely indicated, per guidelines:
  - Oral PrEP: DEXA, LFT's, CBC, UA
  - CAB: eCrCl, lipids, LFT's, HBV (personally, I check HBV)

Questions Without Answers

- How long does it take to achieve protective levels (with oral or injectable PrEP)?
- Will IM CAB demonstrate superior efficacy to oral PrEP outside of clinical trials?
- How will injectable PrEP be implemented? Will healthcare insurance cover injectable PrEP *and* lab monitoring?
- What is the most cost-effective option?

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Paying for PrEP
U.S. Preventative Services Task Force (2019)

Recommendation Summary

Population	Recommendation	Grade
Persons at high risk of HIV acquisition	The USPSTF recommends that clinicians offer preexposure prophylaxis (PrEP) with effective antiretroviral therapy to persons who are at high risk of HIV acquisition. See the Clinical Considerations section for information about identification of persons at high risk and selection of effective antiretroviral therapy.	A

- Private health plans must cover PrEP without cost-sharing (copay or coinsurance) beginning no later than the 2021 plan year
  - However, prior authorizations are allowed, as is placing generics on zero cost-sharing tiers with cost sharing for brand equivalents
- CMS/HHS: coverage must include baseline & monitoring services*

***See: ACA Implementation Part 47**
https://www.dol.gov/sites/dolgov/files/EBSA/about-ebsa/our-activities/resource-center/faqs/aca-part-47.pdf

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Additional Resources

- CDC Guidelines Provider Supplement:
  Checklists, FAQ's for patients, MSM risk index, PWID risk index, ICD10 and CPT codes for billing
  www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-provider-supplement-2021.pdf
- PrEPLine: 855-448-7737
- HHS "Ready, Set, PrEP:" 855-447-8410; www.getyourprep.com
- Find a PrEP provider: www.pleaseprepme.org
- Gilead Medication Assistance Program:
  https://www.gilead.com/purpose/medication-access/us-patient-access#truvadaid
- Project Inform (see flow sheet):
  http://www.projectinform.org/pdf/PrEP_Flow_Chart.pdf

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Summary of Oral PrEP Guidance (page 15)

Table 1a: Summary of Clinician Guidance for Daily Oral PrEP Use

	Sexually-Active Adults and Adolescents[1]	Persons Who Inject Drug[2]
Identifying substantial risk of acquiring HIV infection	Anal or vaginal sex in past 6 months AND any of the following: • HIV-positive sexual partner (especially if partner has an unknown or detectable viral load) • Bacterial STI in past 6 months[3] • History of inconsistent or no condom use with sexual partner(s)	HIV-positive injecting partner OR Sharing injection equipment
Clinically eligible	**ALL OF THE FOLLOWING CONDITIONS ARE MET:** • Documented negative HIV Ag/Ab test result within 1 week before initially prescribing PrEP • No signs/symptoms of acute HIV infection • Estimated creatinine clearance ≥30 ml/min[4] • No contraindicated medications	
Dosage	• Daily, continuing, oral doses of F/TDF (Truvada®), ≤90-day supply OR • For men and transgender women at risk for sexual acquisition of HIV; daily, continuing, oral doses of F/TAF (Descovy®), ≤90-day supply	

Summary of Oral PrEP Guidance (page 15)

Follow-up care	**Follow-up visits at least every 3 months to provide the following:** • HIV Ag/Ab test and HIV-1 RNA assay, medication adherence and behavioral risk reduction support • Bacterial STI screening for MSM and transgender women who have sex with men[3] – oral, rectal, urine, blood • Access to clean needles/syringes and drug treatment services for PWID **Follow-up visits every 6 months to provide the following:** • Assess renal function for patients aged ≥50 years or who have an eCrCl <90 ml/min at PrEP initiation • Bacterial STI screening for all sexually-active patients[3] – [vaginal, oral, rectal, urine- as indicated], blood **Follow-up visits every 12 months to provide the following:** • Assess renal function for all patients • Chlamydia screening for heterosexually active women and men – vaginal, urine • For patients on F/TAF, assess weight, triglyceride and cholesterol levels

?

[1] adolescents weighing at least 35 kg (77 lb)

[2] Because most PWID are also sexually active, they should be assessed for sexual risk and provided the option of CAB for PrEP when indicated

[3] Sexually transmitted infection (STI): Gonorrhea, chlamydia, and syphilis for MSM and transgender women who have sex with men including those who inject drugs; Gonorrhea and syphilis for heterosexual women and men including persons who inject drugs

[4] estimated creatine clearance (eCrCl) by Cockcroft Gault formula ≥60 ml/min for F/TDF use, ≥30 ml/min for F/TAF use

Summary of Oral PrEP Guidance (page 44)

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)

Summary of Injectable PrEP Guidance (page 16)

Table 1b: Summary of Clinician Guidance for Cabotegravir Injection PrEP Use

	Sexually-Active Adults	Persons Who Inject Drugs[1]
Identifying substantial risk of acquiring HIV infection	Anal or vaginal sex in past 6 months AND any of the following: • HIV-positive sexual partner (especially if partner has an unknown or detectable viral load) • Bacterial STI in past 6 months[2] • History of inconsistent or no condom use with sexual partner(s)	HIV-positive injecting partner OR Sharing injection equipment
Clinically eligible	**ALL OF THE FOLLOWING CONDITIONS ARE MET:** • Documented negative HIV Ag/Ab test result within 1 week before initial cabotegravir injection + negative HIV RNA • No signs/symptoms of acute HIV infection • No contraindicated medications or conditions	
Dosage	• 600 mg cabotegravir administered as one 3 ml intramuscular injection in the gluteal muscle o Initial dose o Second dose 4 weeks after first dose (month 1 follow-up visit) o Every 8 weeks thereafter (month 3,5,7, follow-up visits etc)	

Summary of Injectable PrEP Guidance (page 16)

Follow-up care	**At follow-up visit 1 month after first injection** • HIV Ag/Ab test and HIV-1 RNA assay **At follow-up visits every 2 months (beginning with the third injection – month 3) provide the following:** • HIV Ag/Ab test and HIV-1 RNA assay • Access to clean needles/syringes and drug treatment services for PWID **At follow-up visits every 4 months (beginning with the third injection- month 3) provide the following:** • Bacterial STI screening[2] for MSM and transgender women who have sex with men[2] – oral, rectal, urine, blood **At follow-up visits every 6 months (beginning with the fifth injection – month 7) provide the following:** • Bacterial STI screening[1] for all heterosexually-active women and men – [vaginal, rectal, urine - as indicated], blood **At follow-up visits at least every 12 months (after the first injection) provide the following:** • Assess desire to continue injections for PrEP • Chlamydia screening for heterosexually active women and men – vaginal, urine **At follow-up visits when discontinuing cabotegravir injections provide the following:**

[1] Because most PWID are also sexually active, they should be assessed for sexual risk and provided the option of CAB for PrEP when indicated

[2] Sexually transmitted infection (STI): Gonorrhea, chlamydia, and syphilis for MSM and transgender women who have sex with men including those who inject drugs; Gonorrhea and syphilis for heterosexual women and men including persons who inject drugs

Summary of Injectable PrEP Guidance (page 50)

Table 7 Timing of CAB PrEP-associated Laboratory Tests

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

X all PrEP patients

^ men who have sex with men

~ persons assigned male sex at birth whose gender identification is female

Managing PrEP with Ambiguous HIV Test Results

- All patients:
  - Assess medication adherence since last negative HIV test
  - Redraw labs after a few days (Ag/Ab + quantitative RNA)
  - If results still ambiguous, contact PrEPline (855-448-7737)
- While awaiting results, 3 options for oral PrEP patients:
  - Continue PrEP
  - Add a third drug to provide full HIV treatment
  - Discontinue PrEP for 1-2 weeks then draw new lab tests
- While awaiting results, for CAB patients:
  - Do not administer a new CAB injection
  - If labs confirm HIV infection, refer for care and start full ART
  - If labs rule out HIV infection, resume IM CAB

Adherence Support

A brief medication adherence question

"Many people find it difficult to take a medicine every day.

Thinking about the last week; on how many days have you **not** taken your medicine?"

Establish trust and bidirectional communication

Provide simple explanations and education

- Medication dosage and schedule
- Management of common side effects
- Relationship of adherence to the efficacy of PrEP
- Signs and symptoms of acute HIV infection and recommended actions

Support adherence

- Tailor daily dose to patient's daily routine
- Identify reminders and devices to minimize forgetting doses
- Identify and address barriers to adherence
- Reinforce benefit relative to uncommon harms

Monitor medication adherence in a non-judgmental manner

- Normalize occasional missed doses, while ensuring patient understands importance of daily dosing for optimal protection
- Reinforce success
- Identify factors interfering with adherence and plan with patient to address them
- Assess side effects and plan how to manage them

PrEP is One Piece of the HIV Prevention Puzzle