Monitoring PrEP

JANET CIFUENTES, PHARMD, BCPS, AAHIVP

LCDR US PUBLIC HEALTH SERVICE

HCV/HIV CLINICAL PHARMACIST

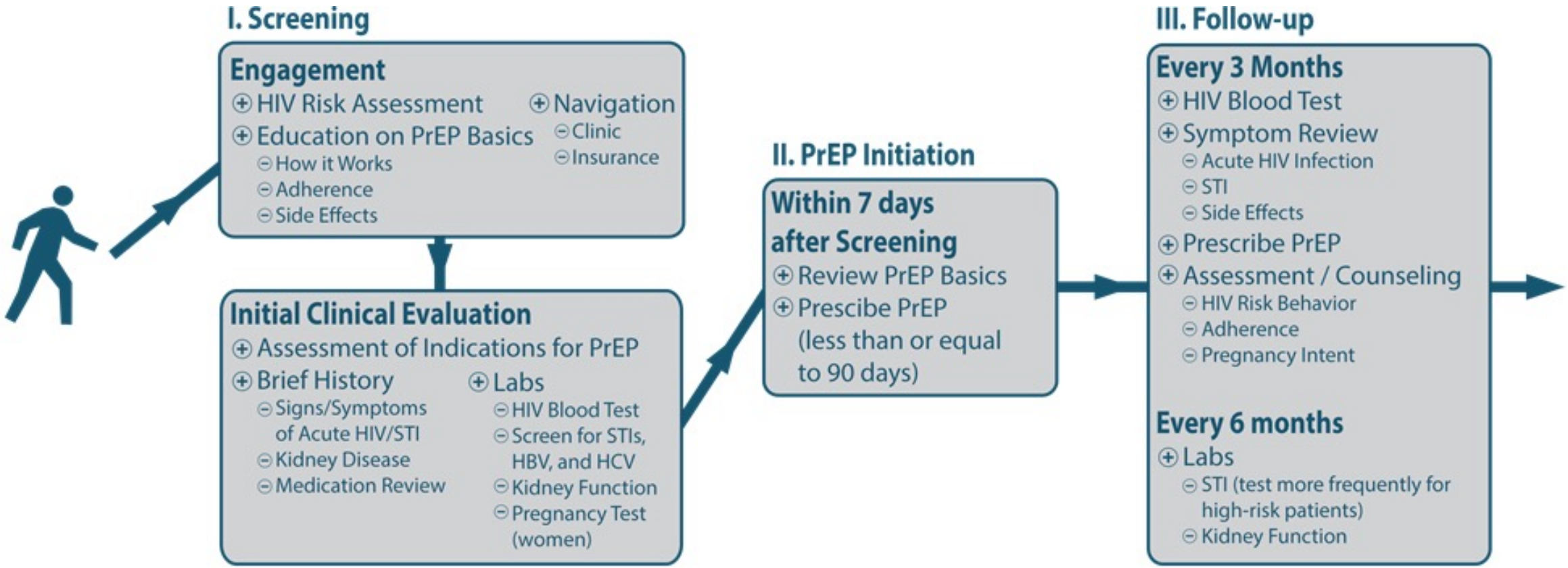
PHOENIX INDIAN MEDICAL CENTER

JANET.CIFUENTES@IHS.GOV

Objectives

- Know what biochemical parameters to monitor for people on PrEP
  - Lab monitoring
- Know what patient factors to monitor for people on PrEP
  - Side effects of medication
  - Adherence
- Know how and when to consider transitioning from non-occupational ***post***-exposure prophylaxis (nPEP) to ***pre***-exposure prophylaxis (PrEP)
- Know when to stop PrEP

Monitoring PrEP



https://www.cdc.gov/hiv/effective-interventions/prevent/prep/index.html#PrEP-Care-System

Monitoring on PrEP

At least every 3 months:

- Repeat HIV testing and assess for signs or symptoms of acute infection to document that patients are still HIV negative
- Repeat pregnancy testing for women who may become pregnant
- Provide a prescription or refill authorization of daily TDF/FTC (or FTC/TAF) for no more than 90 days
- Assess side effects, adherence, and HIV acquisition risk behaviors
- Provide support for medication adherence and risk-reduction behaviors
- Respond to new questions and provide any new information about PrEP use
- Conduct STI testing for sexually active persons with signs or symptoms of infection and screening for asymptomatic MSM at high risk for recurrent bacterial STIs (e.g., those with syphilis, gonorrhea, or chlamydia at prior visits or multiple sex partners)

At least every 6 months:

- Monitor eCrCl
- If other threats to renal safety are present (e.g., HTN, diabetes), renal function may require more frequent monitoring or may need to include additional tests (e.g., urinalysis for proteinuria)
- A rise in serum creatinine is not a reason to withhold treatment if eCrCl remains ≥60 ml/min.
- If eCrCl is declining steadily (but still ≥60 ml/min), consultation with a nephrologist or other evaluation of possible threats to renal health may be indicated.
- Conduct STI screening for sexually active adolescents and adults (i.e., syphilis and gonorrhea for both men and women, chlamydia for MSM) even if asymptomatic

At least every 12 months:

- Evaluate the need to continue PrEP as a component of HIV prevention

https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf

Monitoring

TRUVADA	DESCOVY
Safety: general	**Safety: general**
Both medicines have very low rates of side effects overall. Some people experience "start-up" symptoms including diarrhea, nausea and vomiting, which usually resolve in the first three months of PrEP use.	Both medicines have very low rates of side effects overall. Some people experience "start-up" symptoms including diarrhea, nausea and vomiting, which usually resolve in the first three months of PrEP use.
Bone health	**Bone health**
People with osteoporosis should avoid	Safer to take for people with osteoporosis
Kidney health	**Kidney health**
People with kidney issues or a strong family history of kidney disease should avoid	Safer to take for people with kidney issues or a strong family history of kidney disease, though monitoring still recommended
Weight loss/gain	**Weight loss/gain**
May cause a small degree of weight loss[1]	May cause a small degree of weight gain[2]
Cholesterol	**Cholesterol**
May cause small decreases in HDL, LDL and total cholesterol[1]	May cause small increases in LDL cholesterol and triglycerides[2,3]

https://www.sfaf.org/resource-library/side-by-side-comparison-truvada-and-descovy-for-prep/

What to Monitor: Biochemistry

Biochemistry:

- HIV serology
- STI assays
- Kidney function
- Liver health

FTC/TDF (& FTC/TAF) Black Box Warning

BOXED WARNING: RISK OF DRUG RESISTANCE WITH USE OF FTC/TDF (or FTC/TAF) FOR PrEP IN UNDIAGNOSED EARLY HIV-1 INFECTION and POST TREATMENT ACUTE EXACERBATION OF HEPATITIS B

- FTC/TDF or FTC/TAF for PrEP must only be prescribed to individuals confirmed to be HIV-negative immediately prior to initiation and at least every 3 months during use. Drug-resistant HIV-1 variants have been identified with use of TRUVADA FOR PrEP following undetected acute HIV-1 infection. Do not initiate if signs or symptoms of acute HIV-1 infection are present unless HIV-negative status is confirmed

- Severe acute exacerbations of hepatitis B have been reported in HBV-infected patients who discontinued TRUVADA. Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in patients with HBV after discontinuing TRUVADA. If appropriate, initiation of anti-hepatitis B therapy may be warranted

Gilead Sciences. Truvada Package Insert. 2018. http://gilead.com/~/media/files/pdfs/medicines/hiv/truvada/truvada_pi.pdf. Accessed 30Sep2019.
Gilead Sciences. Descovy Package Insert. 2021. https://www.gilead.com/~/media/Files/pdfs/medicines/hiv/descovy/descovy_pi.pdf. Accessed 11Jun2021

HIV Serology

- Requires a negative HIV test in the previous 7 days before renewing medication
- A negative HIV test is required before resuming PrEP after a period of non-adherence
- A high index of suspicion for Acute HIV when assessing current HIV status
  - Does the person on PrEP have poor adherence?
  - Does the person on PrEP have elevated risk?
    - Presence of STIs, known exposure to HIV + partner
  - Does the person on PrEP have clinical indicia of acute HIV?

Perform an HIV viral load test if concern for acute HIV

- Positive HIV serology (4^{th} gen) is confirmed with:
  - HIV 1/2 antibody differentiation test
    - If lack of concurrence between 1/2 differentiation and 4^{th} gen. screen then:
      - HIV RNA test (either a viral load or a qualitative HIV RNA)

STI testing

- Refer to Dr. Iralu's comprehensive presentation from last session
- Ulcerative STIs such as herpes and syphilis can raise HIV acquisition risk by 2.5 times, and prompt treatment reduces that risk back to baseline
- Routine STI screening is part of PrEP monitoring
  - Opens a great opportunity for risk assessment/risk reduction discussion
  - Helps with recruitment-inquire about partners when an STI is documented, and offer partners PrEP
    - If partner is non-Native, refer to local PrEP navigators
      - https://npin.cdc.gov/preplocator
      - https://preplocator.org/

Liver Health

- AST/ALT/T.bili: while medications for PrEP RARELY cause liver problems, it must be kept in mind for people on PrEP with HBV history due to black box warning
- Most common cause of liver enzyme abnormality in PrEP clinic is unrelated liver problems (not PrEP)
- Alcohol can be responsible for increased risk for HIV acquisition with poor adherence and black-out-sex being 2 common issues
  - EtOH use/ SUDs are NOT a contraindication for PrEP

Kidney Health

- FTC/TDF has contraindication for GFR below 50 ml/min
- FTC/TAF is ok down to GFR of 30ml/min
- Urinalysis may also demonstrate proteinuria and glucosuria together are suggestive of Fanconi's syndrome
- Serum creatinine is recommended prior to initiation, at end of first 3 months then Q 6 months there after (may change soon)

*No PrEP option currently exists for patients on dialysis or GFR less than 30 ml/minute**

Proposed Changes to Monitoring

- Continue to test for HIV, sexually transmitted infections and pregnancy should be repeated at least every three months.
- Kidney function should be checked periodically, as the TDF in Truvada can cause kidney impairment. This is recommended:
  - Every six months for people over age 50 and those with low kidney function at baseline or other risk factors and
  - Once yearly for everyone else
- The tenofovir alafenamide (TAF) in Descovy is less likely to cause kidney problems but more likely to be linked to elevated cholesterol and triglyceride levels and weight gain; these should be monitored at least every six months.

https://www.poz.com/article/cdc-releases-draft-updated-prep-guidelines

Bone Health

- iPrEx trial (TDF/FTC) and the CDC PrEP safety trial in MSM (TDF) conducted serial dual-emission x-ray absorptiometry (DEXA) scans on a subset of MSM in the trials and determined that a small (~1%) decline in BMD that occurred during the first few months of PrEP either stabilized or returned to normal
- ***NO*** increase in fragility (atraumatic) fractures over the 1-2 years of observation in these studies comparing those persons randomized to receive PrEP medication and those randomized to receive placebo
- DEXA scans or other assessments of bone health are not recommended before the initiation of PrEP or for the monitoring of persons while taking PrEP.
- BUT… any person being considered for PrEP who has a history of pathologic or fragility bone fractures or who has significant risk factors for osteoporosis should be referred for appropriate consultation and management.

https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf

Monitoring in Patients with HBV

- In persons with substantial risk of both HIV acquisition and active HBV infection, daily doses of TDF/FTC may be especially indicated
- All persons screened for PrEP who test positive for hepatitis B surface antigen (HBsAg) should be evaluated by a clinician experienced in HBV treatment
  - For clinicians without this experience, co-management with an infectious disease or a hepatic disease specialist should be considered
- Test for HBV DNA with a quantitative assay to determine the level of HBV replication ***before*** PrEP is prescribed ***and*** every 6-12 months while taking PrEP
- Reinforce the need for adherence to prevent reactivation of HBV infection and to minimize the risk of developing TDF-resistant HBV

https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf

Adverse Events

Few discontinuations due to adverse events

1%	VS	2%
of patients discontinued DESCOVY FOR PrEP® (n=2694)		of patients discontinued FTC/TDF (n=2693)

Adverse reactions (all grades) reported in ≥2% of patients were similar in both study arms

	DESCOVY® (n=2694)	FTC/TDF (n=2693)
Diarrhea	5%	6%
Nausea	4%	5%
Headache	2%	2%
Fatigue	2%	3%
Abdominal pain	2%	3%

Mean change in lipid values[2–4,a]

		DESCOVY		FTC/TDF	
Lipid value	Target level	Baseline (mg/dL)	Week 96 change	Baseline (mg/dL)	Week 96 change
Total cholesterol (fasted)	<200 mg/dL	175	-2	176	-13
HDL cholesterol (fasted)	≥60 mg/dL	51	-2	51	-4
LDL cholesterol (fasted)	<100 mg/dL	103	-1	103	-8
Triglycerides (fasted)	<150 mg/dL	108	+6	111	-7
Total-cholesterol-to-HDL ratio	<4.5	3.7	+0.1	3.7	0.0

https://www.descovyhcp.com/adverse-reactions-and-discontinuations#

PrEP Adherence

iPrEx Study

- 44% reduction in HIV overall (includes all levels of adherence)
- 92%-99% reduction in those with good adherence (PWID = 74% +)
  - 7 PrEP pills per week -> 99% estimated level of protection
  - 4 PrEP pills per week -> 96% estimated level of protection
  - 2 PrEP pills per week -> 76% estimated level of protection

iPrEX: Grant RM, Lama JR, Anderson PL, et al; iPrEx Study Team. *N Engl J Med* 2010;363(27):2587-99

Adherence Check-Ins

Box D: Key Components of Medication Adherence Counseling

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

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

https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf

Post-Exposure Prophylaxis (nPEP) to Pre-Exposure Prophylaxis (PrEP)

Two types of patients may be candidates for PrEP use after a course of non-occupational post-exposure prophylaxis (nPEP):

- Patients who request PrEP and also have had a possible sexual or injection drug-related HIV exposure in the prior 72 hours (i.e., are within the recommended window to start nPEP)
- Patients who request repeated courses of nPEP, particularly over a relatively recent period (e.g., more than twice during the past 6 months)

Discuss transition from nPEP x 28 days to PrEP (without a break in meds) and repeat HIV screen in 4 weeks if patient meets PrEP criteria and is willing to fulfill monitoring requirements

- Discuss PrEP with patient at initial nPEP visit, if appropriate
- Follow up with patient a few days after start of nPEP to assess adherence and tolerability
- Have patient RTC for repeat HIV screen and PrEP discussion just prior to completion of nPEP
- If no suspicion of acute HIV, complete any outstanding baseline PrEP labs
  - If suspicion of acute HIV, continue nPEP regimen pending confirmation of patient's HIV status
- Dispense (or have plan to acquire) PrEP med by the time nPEP runs out to avoid break in meds
- Schedule 3-month follow up with PrEP clinic/provider before patient leaves visit

When To Stop

- When a person on PrEP no longer has risk factors for HIV acquisition
- When a person on PrEP acquires HIV
- When a person on PrEP declines to participate in monitoring
- When a person on PrEP develops a serious ADR to PrEP

Be sure to document status at end of PrEP & reason for discontinuation!

Patient Risk Factors (patient risk and partner risk)

- **U=U**: PrEP may no longer be necessary when a partner with known HIV is undetectable on meds
- Person on PrEP in committed relationship with partner(s) who all do testing together
- Person on PrEP no longer engages in unprotected sex or needle sharing
- Person on PrEP choosing low risk behaviors such as oral only
- Person on PrEP committing to consistent and correct condom use

HBV Considerations after PrEP

- If PrEP no longer needed to prevent HIV infection,
  - Separate determination should be made about whether to continue TDF/FTC to treat HBV
- When HBsAg + patients discontinue PrEP,
  - Acute flares from the reactivation of HBV infection have been seen in HIV-infected persons
  - Continue to see a clinician experienced in HBV management so flares can be detected promptly and treated appropriately

https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf

References

- Centers for Disease Control and Prevention. US Public Health Service. Preexposure prophylaxis for the prevention of HIV infection in the United States – 2014: a clinical practice guideline. Retrieved from https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf. Accessed 30Sep2019.
- Centers for Disease Control and Prevention: US Public Health Service: Preexposure prophylaxis for the prevention of HIV infection in the United States—2017 Update: a clinical practice guideline. https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf. Published March 2018.
- https://www.cdc.gov/hiv/effective-interventions/prevent/prep/index.html#PrEP-Care-System
- https://www.sfaf.org/resource-library/side-by-side-comparison-truvada-and-descovy-for-prep/
- iPrEX: Grant RM, Lama JR, Anderson PL, et al; iPrEx Study Team. N Engl J Med 2010;363(27):2587-99
- https://www.poz.com/article/cdc-releases-draft-updated-prep-guidelines
- Gilead Sciences. Truvada Package Insert. 2018. http://gilead.com/~/media/files/pdfs/medicines/hiv/truvada/truvada_pi.pdf. Accessed 30Sep2019.
- Gilead Sciences. Descovy Package Insert. 2021. https://www.gilead.com/~/media/Files/pdfs/medicines/hiv/descovy/descovy_pi.pdf. Accessed 11Jun2021

Monitoring PrEP

JANET CIFUENTES, PHARMD, BCPS, AAHIVP

LCDR US PUBLIC HEALTH SERVICE

HCV/HIV CLINICAL PHARMACIST

PHOENIX INDIAN MEDICAL CENTER

JANET.CIFUENTES@IHS.GOV