PrEP Medical Protocol, v1.0

In 2014, the CDC published guidelines that establish medical standards and protocols for the evaluation, initiation and management of pre-exposure prophylaxis (PrEP) against acquisition of HIV infection. These guidelines follow the 2012 FDA approval of Truvada for PrEP in those individuals determined to be at high risk for incident HIV infection. In accordance with CDC guidelines, numerous guidelines exist in order to tailor the medical management of PrEP to specific sites. The following proposed protocol is meant to apply to the "PrEP Home" of the HIV Program at the Wilmington Hospital Annex (WHA) of Christiana Care Health System (CCHS) in Wilmington, DE.

Evaluation of Potential PrEP Candidates

The first step in PrEP evaluation is the accurate identification of those candidates who are 18 years of age or older and are at high risk of HIV infection vis-à-vis a detailed social history, including sexual and drug use history AND gauging an individual's interest in PrEP. There are various assessment tools depending upon the individual's risk factor(s), including men who have sex with men (MSM), injection drug users (IDU), transgender individuals, heterosexuals, serodiscordant relationships, et al., to aid in HIV risk stratification. Ultimately, the final determination for PrEP suitability lies in the hands of the prescribing provider after a thoughtful individual risk/benefit analysis and consideration of the local epidemiology of HIV.

Potential Candidates for PrEP (Adapted from NY State Guidelines)

- MSM who engage in unprotected anal intercourse
- Individuals who are in a serodiscordant sexual relationship with a known HIV-infected partner
- Male-to-female and female-to male transgender individuals engaging in high-risk sexual behaviors
- Individuals engaging in transactional sex, such as sex for money, drugs, or housing
- IDU who report any of the following behaviors: sharing injection equipment (including to inject hormones among transgender individuals), injecting one or more times per day, injecting cocaine or methamphetamine, engaging in high-risk sexual behaviors
- Individuals who use stimulant drugs associated with high-risk behaviors, such as methamphetamine
- Individuals diagnosed with at least one anogenital sexually transmitted infection in the last year
- Individuals who have been prescribed non-occupational post-exposure prophylaxis (nPEP) who demonstrate continued high-risk behavior or have used multiple courses of nPEP

HIV Risk Assessment Tools

HIRI-MSM Risk Index*

1	How old are you today (yrs)?	<18 years	score 0
		18–28 years	score 8
		29–40 years	score 5
		41–48 years	score 2
		≥49 years	score 0
2	How many men have you had sex with in the last 6 months?	>10 male partners	score 7
		6–10 male partners	score 4
		0–5 male partners	score 0
3	In the last 6 months, how many times did you have receptive anal sex (you were the bottom) with a man?	1 or more times	score 10
		0 times	score 0
4	How many of your male sex partners were HIV positive?	>1 positive partner	score 8
		1 positive partner	score 4
		<1 positive partner	score 0
5	In the last 6 months, how many times did you have insertive anal sex (you were the top) with a man who was HIV positive?	5 or more times	score 6
		0 times	score 0
6	In the last 6 months, have you used methamphetamines such as crystal or speed?	Yes	score 5
		No	score 0
7	In the last 6 months, have you used poppers (amyl nitrate)?	Yes	score 3
		No	score 0
		Add down entries in right column to calculate total score	Total score†

*To identify sexually active MSM in their practice, we recommend clinicians ask all their male patients a routine question: "In the past (time) have you had sex? (if yes), with men, women, or both?"

†If score is 10 or greater, evaluate for PrEP or other intensive HIV prevention services; If score is 9 or less, provide indicated standard HIV prevention services.

Risk Assessment Tool for Heterosexual Men and Women

In the past 6 months:

- How many men/women have you had sex with?
- How many times did you have vaginal or anal sex when neither you nor your partner wore a condom?
- How many of your sex partners were HIV-positive?
- *(if any positive)* With these HIV-positive partners, how many times did you have vaginal or anal sex without a condom?

Risk Assessment Tool for IDU

- When did you last inject unprescribed drugs?
- In the past 6 months, have you injected by using needles, syringes, or other drug preparation equipment that had already been used by another person?
- In the past 6 months, have you been in a methadone or other medication-based drug treatment program?

At the same time that an individual is preliminarily identified to be a suitable candidate for PrEP, each individual will require a social work visit (as well as a pharmacy consultation for those individuals who are uninsured) and a baseline medical evaluation. The full medical and laboratory evaluation is vital to confirm the patient is without pre-existing HIV infection or any other medical contra-indication to the receipt of PrEP AND without any pre-existing medical co-morbidities that will necessitate closer monitoring upon PrEP initiation. Providers need to obtain a complete medical history (including a targeted assessment of signs and symptoms to assess for risk of acute HIV infection, a full review of systems, past medical history, active medications, allergies, familial history and physical examination) and the following baseline studies: **4th generation HIV Ag/Ab testing, rapid plasma reagin (RPR), hepatitis B surface antigen (HepBsAg), hepatitis B surface antibody (HBVsAb), hepatitis B core antibody (HBVcAb), hepatitis C antibody (HCV Ab), Hepatitis A antibody (HAV IgG), urine gonorrhea and chlamydia nucleic acid amplification testing (Gc/Chl NAAT), basic metabolic panel and urinalysis**. ***MSM will additionally undergo extra-genital Gc/Chl NAAT of the oropharynx and the rectum. Females will all receive a urine pregnancy test.*** For those individuals in whom there is concern of acute HIV infection within the last 14 days, an HIV-1 RNA viral load will additionally be collected.

At the time of this initial visit, all patients will be scheduled for a return clinic visit within one calendar week of the time of laboratory evaluation. This initial provider visit is also an opportunity to link those patients not already receiving routine healthcare to primary care providers and to connect patients with specific specialty and ancillary services on an as-needed basis. All potential candidates will receive upfront risk reduction counseling (including but not limited to linkage to needle exchange programs and counseling on and provision of barrier protection).

Contraindications to PrEP

Patients who have pre-existing or newly diagnosed HIV infection, a baseline estimated creatinine clearance of less than 60ml/min, are unable to adhere to a daily medication, are determined to not be PrEP ready, or have a history of fragility fracture(s), will not be eligible to receive PrEP. Patients with osteopenia, osteoporosis or currently pregnant will be evaluated on a case-by-case basis. Patients with acute HIV infection will immediately be linked to HIV specialty care within WHA for management. Individuals diagnosed with other sexually transmitted infections will be treated according to 2015 CDC sexually transmitted diseases (STD) guidelines and remain viable PrEP candidates. All patients non-immune to hepatitis A and B should receive vaccinations according to the adult CDC vaccination schedule.

Initiation of PrEP

At this second clinic appointment [which needs to occur within one calendar week after completion of baseline laboratory collection], patient interest and ability to adhere to a daily medication regimen will be reconfirmed AND a targeted history of signs and symptoms of acute HIV infection will again be performed. If there is concern for interim incident HIV infection, 4th generation HIV Ab/Ag testing and serum HIV-1 RNA viral load testing will be collected and PrEP initiation deferred until there is confirmation of no primary HIV infection. The prescribing provider will review medication administration instructions, potential medication side effects, management/required medical follow-up and reasons for discontinuation as outlined in a patient-provider contract. PrEP candidates will be

required to sign a patient-provider contract prior to PrEP initiation. Upon contract review and signature, patients will receive a 30 day supply with zero refills of oral Truvada (co-formulated Tenofovir disoproxil 300mg/Emtricitabine 200mg). Patients in need of Hepatitis A and/or B vaccination series will initiate the series at this visit and those in need of acute STI treatment (excluding HIV) will be able to receive treatment at this appointment. Patients will again receive personalized risk reduction counseling and be advised to contact the clinic should they develop any signs or symptoms concerning for acute sexually transmitted infections and/or medication adverse effects. Patients will be scheduled for 1 month follow-up at this visit.

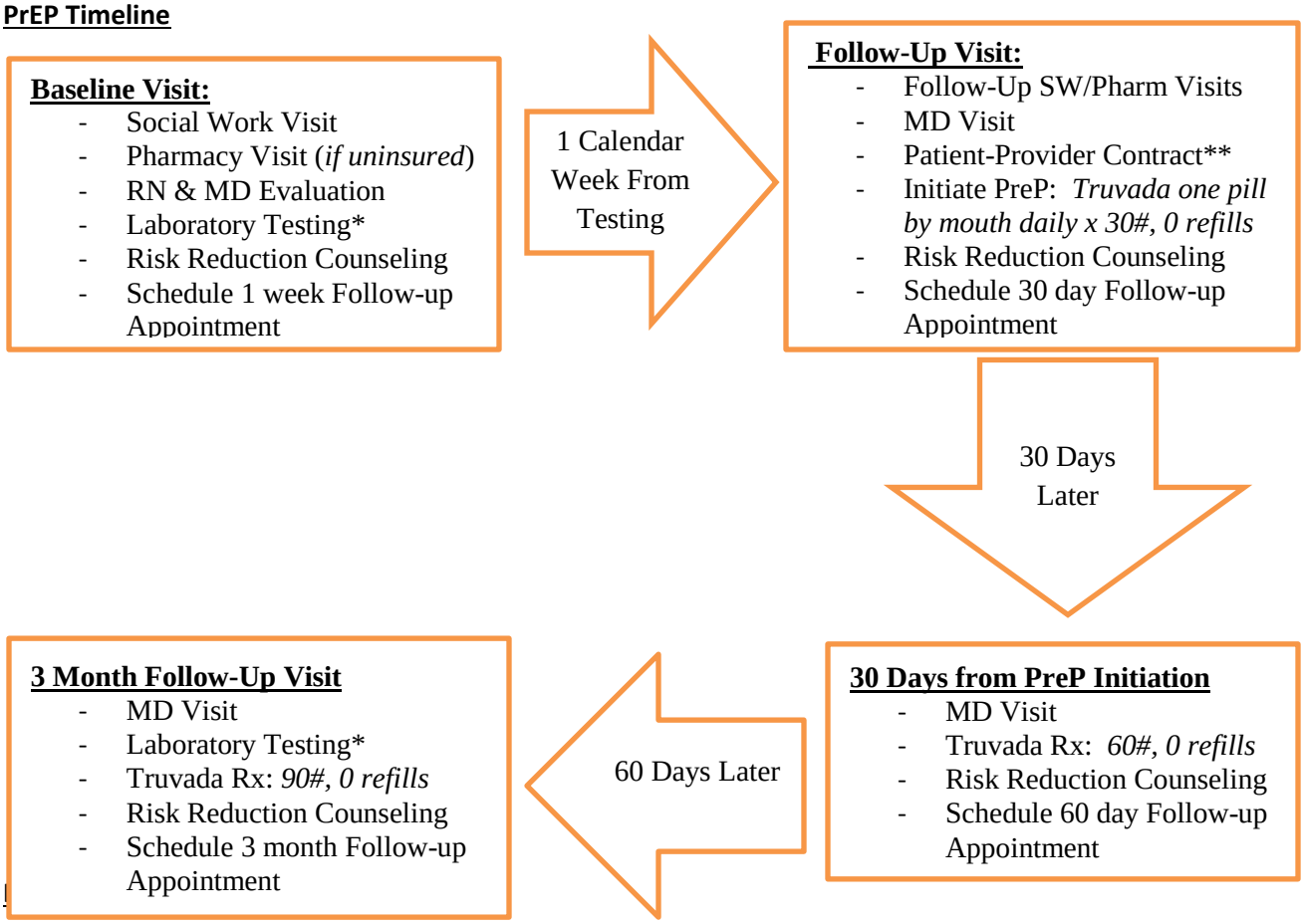
Management of PrEP

Patients will need to present for on-site appointments 30 days and 90 days after PrEP initiation and then every 3 months thereafter. During the 30 day follow-up appointment, patient adherence and medication side effects should be evaluated and targeted eCrCl testing should be collected on those patients with pre-existing kidney disease or those at increased risk for the development of kidney disease. At this appointment, patients should be provided a 60 day prescription with zero refills for Truvada and scheduled for a 3 month [from the time of PrEP initiation] follow-up appointment. At each appointment, prescribing providers will assess PrEP adherence and potential side effects, confirm patient's ongoing indication for PrEP and perform targeted interval histories and physicals as well as risk reduction counseling**. Serial STI screening, including HIV Ag/Ab testing [to confirm no acute seroconversions], urine Gc/Chl NAAT, RPR and eCrCl will be collected every 3 months**. **Urinalysis should be collected bi-annually in those patients with risk factors for the development of renal disease or known renal disease and annually in all other PrEP patients.** ***MSM will additionally undergo targeted extra-genital Gc/Chl NAAT every 3 months***. ***MSM and IDU will receive HCV Ab testing every 6 months; all other PrEP patients will receive annual HCV Ab testing***. Patients with chronic hepatitis B will require baseline HBV DNA testing followed by bi-annual monitoring and liver function tests every 3 months. **Females will undergo urine pregnancy testing every 3 months**. Concern for acute HIV infection or acute HCV infection will further prompt respective viral load testing. HAV and HBV vaccination series will be advanced as appropriate.

Discontinuation PrEP

There are a multitude of potential reasons for PrEP discontinuation which may be patient and/or provider-driven including but not limited to medication toxicities/intolerance, breach of the patient-provider contract, or a change in life circumstances such that there is no longer an indication for PrEP. Patients with documented HIV seroconversion will immediately be instructed to discontinue PrEP and will be linked to HIV care within WHA. Patients with new renal dysfunction and/or concern for PrEP-associated nephrotoxicity will require consideration for PrEP discontinuation. Those patients not using PrEP as intended in the patient-provider contract and/or participating in PrEP diversion will be evaluated on a case-by-case basis. At the time of PrEP discontinuation, the prescribing provider will clearly document the reason for discontinuation, recent medication adherence and risk behavior(s), and reassess the patient for acute HIV infection with a 4th generation HIV Ab/Ag test. If patients in conjunction with their prescribing provider elect to discontinue PrEP due to a change in personal circumstance, these individuals will be welcomed to return to the "PrEP Home."

PrEP Timeline



BASELINE VISIT:

HIV Ab/Ag
RPR
Urine Gc/Chl NAAT
Hepatitis A IgG (HAV IgG)
Hepatitis BsAg, BsAb, BcAb
Hepatitis C Ab (HCV Ab)
Basic Metabolic Panel (BMP)
Urinalysis (UA)
Pregnancy Test (Females of Reproductive Potential)
Extragenital OP/Rectal Gc/Chl NAAT (MSM)

3 MONTH VISIT (and every 3 months therafter):

HIV Ab/Ag
RPR
Urine Gc/Chl NAAT
BMP
Extragenital Gc/Chl NAAT (MSM)
Pregnancy Test (Females of Reproductive Potential)

6 MONTH VISIT (and every 6 months thereafter)

Same as 3 Month Visit AND

Urinalysis (every 6 months for patients with known renal disease or risk factors for development of renal disease; annually for all else)

HCV Ab (MSM, IDU every 6 months; annually for all else)

References:

1. Preexposure Prophylaxis for HIV Prevention in the United States – 2014. A Clinical Practice Guide. Centers for Disease Control and Prevention.
2. Preexposure Prophylaxis for the Prevention of HIV in the United States – 2014. Clinical Providers' Supplement. Centers for Disease Control and Prevention.
3. Guidance for the Use of Pre-Exposure Prophylaxis (PrEP) to Prevent HIV Transmission. HIV Clinical Resource: Office of the Medical Director, New York State Department of Health AIDS Institute in Collaboration with Johns Hopkins University Division of Infectious Diseases. January 2014.