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Pre-Exposure Prophylaxis (PrEP) Implementation Guidelines 2024

These guidelines update local guidance issued in 2015 related to HIV PrEP implementation and are designed to complement the U.S Public Health Service PrEP guidelines[1]. Approximately 70% of all HIV infections in King County, WA occur in men who have sex with men (MSM), and MSM are the primary candidate population for PrEP use in the area. MSM who are young, Black, Indigenous, unhoused, and/or who use methamphetamine have the lowest levels of PrEP use and lowest rates of PrEP persistence (continued use) following initiation.

Identifying persons to consider for PrEP:

- Public Health recommends that medical providers routinely ask all adolescent and adult patients about the gender of their sex partners.
- Providers should ensure that all of their patients who are MSM, transgender or non-binary (TNB) and have any sex partners with a penis know about PrEP.

Analyses of local data suggest that the strongest risk factors for HIV acquisition among MSM are methamphetamine use, condomless receptive anal sex in the prior year, having > 10 sex partners in the prior year, and a history of gonorrhea or syphilis in the prior year [2], and these analyses have helped inform local guideline development. Local MSM with one of these risk factors have an annual HIV incidence of 0.5-1%, with higher incidence observed in men with more than one risk factor.

Guidelines for initiating PrEP in persons without HIV:

Medical providers should <u>recommend that patients initiate PrEP</u> if they meet the following criteria:

1) MSM or TNB persons who have sex with men (or any partners with a penis) and have one or more of the following risks in the prior 12 months:
    a. Diagnosis of gonorrhea or early syphilis
    b. Methamphetamine use
    c. Condomless receptive anal sex with someone other than a mutually monogamous partner
    d. >10 sex partners
    e. Trading sex for money, drugs, housing, or other things of value
2) Persons in ongoing sexual relationships with a partner living with HIV who is not on antiretroviral therapy (ART), **OR** is on ART but is not virologically suppressed **OR** who is within 2 months of initiating ART.

Medical providers should <u>discuss initiating PrEP</u> with any person seeking a prescription for PrEP or based on any of the following risks:

1) MSM and TNB persons who have sex with men (or any partners with a penis) outside of a long-term, mutually monogamous relationship with another HIV-negative person
2) Persons in HIV-serodifferent relationships who are planning to get pregnant
3) Women who trade sex for money, drugs, housing, or other things of value
4) Persons who inject drugs and/or who use methamphetamine or opioids that are not prescribed by a medical provider
5) Persons diagnosed with syphilis
6) Persons in ongoing sexual relationships with partners living with HIV who are on antiretroviral therapy and virologically suppressed. (<u>Note</u>: If a person with HIV is virologically suppressed, they cannot transmit HIV to others through sex. This concept is known as undetectable equals untransmittable or U=U[3]. All PrEP patients should be informed about U=U. U=U does not apply to nonsexual routes of transmission, such as shared injection drug use or breastfeeding.) Some HIV-negative people who have partners with well-controlled HIV may feel more comfortable taking PrEP and thus should be offered it.

CDC guidelines recommend discussing PrEP with all sexually active patients, but this is often not feasible given constraints on clinician time, and in many clinical settings most patients are at low risk for HIV. Beyond the patients with the characteristics listed above, PHSKC recommends that medical providers use their clinical judgement to determine with whom to discuss PrEP.

Patients should decide together with their medical providers what prevention strategies are best for them. Providers should evaluate patient's knowledge about the various PrEP use strategies and should counsel and educate patients to facilitate their success on PrEP. The most recent CDC practice guidelines (see below) and the National HIV PrEP Curriculum (hivprep.uw.edu) provide detailed information on how to prescribe PrEP and monitor persons on PrEP[1].

PrEP prescribing, follow up and continuation:

In the absence of clinical signs or symptoms of HIV infection (including acute HIV), medical providers should not wait to receive negative HIV tests results before prescribing PrEP. It is safe to provide patients with PrEP on the same day as their clinical evaluation if the following criteria are met: **1)** blood is collected and sent for lab-based HIV antigen/antibody testing or such a test was negative within the last 2-4 weeks with no recent concerning HIV exposures, and **2)** creatinine and hepatitis B serostatus are already known or blood is collected and sent for these tests, and **3)** results will be available within 7 days and the provider can contact the patient if HIV test is positive. If possible, patients should also undergo HIV testing with a blood-based (not oral fluid testing) point of care rapid HIV test on the day of their clinical evaluation prior to receiving a PrEP prescription. Of note, the lack of availability of HIV RNA testing should not be a limiting factor in prescribing oral PrEP. Patients who test positive for HIV and are confirmed to have HIV infection should be given a full HIV treatment regimen as recommended in national guidelines[4]. PHSKC recommends that medical providers prescribe patients 90 days of PrEP at their initial visit.

Medical providers should consider following up with patients 1-2 months following PrEP initiation to inquire about side effects and adherence; this can be done by telephone or telemedicine visit or secure messaging. However, this should not be a requirement for continuing PrEP.

Providers and their staff should implement procedures that make PrEP follow up simple and flexible. PHSKC endorses the use of standing orders for PrEP monitoring tests to allow patients to present to a laboratory for a blood draw and self-sampling for gonorrhea and chlamydia screening without being seen by a medical provider.

While patients on PrEP should ideally be tested for HIV every 3 months, PHSKC advises against stopping PrEP in patients who miss HIV testing appointments as PrEP discontinuation increases the risk of HIV acquisition[5]. It is reasonable to allow up to 6 months without testing before considering discontinuation of PrEP refills.

PHSKC encourages providers and their staff to reach out to patients who discontinue PrEP to encourage follow up. Several community-based organizations have staff that can assist patients to stay on PrEP (https://doh.wa.gov/sites/default/files/2024-04/150083-PreventionServiceNavigationProviders.pdf).

In some cases, home-based self-collection of swabs and/or blood samples for laboratory-based testing may be an option for PrEP monitoring. However, there are some limitations to using commercial, direct-to-consumer companies for PrEP monitoring and STI screening. These may include the inability to perform quantitative RPR testing for persons with a history of syphilis, promotion of inappropriate or unnecessary testing for non-pathogenic organisms (e.g., Ureaplasma), and additional out-of-pocket cost to the patient.

PrEP Regimens

Tenofovir disoproxil fumarate/emtricitabine (TDF/FTC):

Given the high efficacy of TDF/FTC as PrEP[6], local data demonstrating the drugs' high effectiveness[7], evidence for use in multiple populations of all genders,[1] and the dramatic difference in cost between TDF/FTC and other PrEP regimens, PHSKC recommends that medical providers use daily generic TDF/FTC as the primary PrEP regimen and that other regimens should be used only if clinically indicated (Table 1). This recommendation is aligned with those of the New York City Department of Health and Mental Hygiene as well as published expert opinion[8,9].

MSM and TNB persons who primarily engage in insertive vaginal or any anal sex may also use TDF/FTC for event-driven PrEP (sometimes called on-demand, event-driven or 2-1-1 dosing)[10,1112]; this regimen may be particularly useful in persons who infrequently have condomless sex and can accurately predict when they will have sex.

Tenofovir alafenamide (TAF/FTC):

Although TAF/FTC is efficacious in MSM and transgender women, it is not superior to TDF/FTC[13].

Both drugs have a low risk of adverse events, including nephrotoxicity. TDF/FTC is associated with small, reversible decreases in creatinine clearance (median difference in serum creatine 0.02 mg/dL at 48 weeks follow up) and measures of bone mineral density (median 1.62% change at 48 weeks follow up) relative to TAF/FTC, while TAF/FTC is associated with more weight gain (mean difference in weight change 2.64 lbs at 48 weeks) and slightly less favorable lipid parameters than TDF/FTC[13]. The average wholesale acquisition price for TAF/FTC is approximately 70 times higher than the cost of generic TDF/FTC[4], though the prices different insurers pay varies. Given the minimal difference in clinical outcomes between the two medications, TAF/FTC is not cost effective (estimated $7 million cost for a single year of life in perfect health) compared to TDF/FTC[14]. There are no published efficacy data for TAF/FTC as PrEP for persons assigned female at birth or persons who inject drugs; trials are currently ongoing. Prior to making a switch from TDF/FTC to TAF/FTC due to concerns about decreased renal function, serum creatinine and estimated glomerular filtration rate should be assessed at least twice to document a sustained decrease in renal function. Several factors may contribute to elevated creatinine levels, including increased muscle mass, use of creatine or some exercise supplements, nonsteroidal anti-inflammatory drug (NSAID) use, and hypovolemia. These factors should be assessed and corrected before obtaining and interpreting a repeat creatinine. Clinicians should consider obtaining a cystatin C with the repeat creatinine test to calculate a more accurate estimate of the glomerular filtration rate (GFR) (https://www.kidney.org/professionals/kdoqi/gfr_calculator). If the GFR is ≥60 mL/min, TDF/FTC should remain the recommended option for PrEP.

Long acting cabotegravir (CAB-LA):

CAB-LA administered intramuscularly every 8 weeks was found to be more efficacious than daily TDF/FTC in a randomized trial conducted in a population at high risk for HIV composed of cis-gender MSM and transgender persons[15]. Adverse events in the two study arms were similar. As is common in randomized trials, the study included extensive efforts to promote participant retention, including outreach and monetary incentives for study visits during which participants received medication; these procedures are not typically part of PrEP programs and the extent to which they influenced the study outcome is unknown. In the trial, retention on PrEP was 86% at 12 months. By comparison, retention in PrEP at 12 months in the PHSKC Sexual Health Clinic is approximately 60%. Like TAF/FTC, CAB-LA costs approximately 70 times as much as generic TDF/FTC. Administering injectable CAB-LA can also present logistical challenges for busy clinics.

	Recommendation	Contraindications	Approximate Annual Cost*
Generic TDF/FTC	Preferred regimen to be used for most patients who desire PrEP	Creatine clearance <60 mL/min Osteoporosis	$350
TAF/FTC	Use in persons with the following clinical indications: • Creatine clearance 30-60 mL/min • Osteoporosis • Intolerance of TDF/FTC	Creatine clearance <30 mL/min	$25,908
CAB-LA	Use in persons at high risk for HIV who are unable to consistently take or tolerate oral PrEP or who have a creatinine clearance <30mL/min.	Allergic reaction to cabotegravir	$27,720

**Based on wholesale acquisition costs*

Additional considerations

In the absence of a clinical indication for an alternative regimen, PHSKC recommends generic TDF/FTC as the primary PrEP regimen for most people. In general, patient preference alone is not an indication for using TAF/FTC or CAB-LA. However, some patients at elevated risk for HIV infection face significant barriers to taking daily PrEP (e.g., houselessness, substance use, stigma, fear of partners or family knowing about their PrEP use) and, in some instances, CAB-LA is the best choice for such patients. Given disparities in rates of HIV and low levels of PrEP use and persistence among young, Black, and/or Indigenous MSM and TNB people, medical providers may opt to have a lower threshold for offering CAB-LA to patients from these populations. Medical providers should discuss doxycycline post-exposure prophylaxis with MSM and TNB persons for whom they prescribe PrEP.

PHSKC guidelines on the use doxy-PEP are available at https://cdn.kingcounty.gov/-/media/depts/health/communicable-diseases/documents/hivstd/DoxyPEP-Guidelines.ashx.

Additional resources:
The Washington State Department of Health provides financial assistance to help pay for PrEP. Information about this program is available at: https://doh.wa.gov/you-and-your-family/illness-and-disease-z/hiv/prevention/pre-exposure-prophylaxis-drug-assistance-program-prep-dap

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