INTRODUCING THE “PrEP PACKAGE” FOR ENHANCED HIV PREVENTION:
A Practical Guide for Clinicians
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Although advances in treatment have improved the quality and length of life for individuals infected with HIV, more than 50,000 new infections occur each year in the United States. Fortunately, clinicians now have an unprecedented and expanding number of effective HIV prevention tools at their fingertips, including behavioral and biomedical interventions that can play a critical role in reducing the incidence of new infections. This guide summarizes how clinicians can be most effective at preventing new HIV infections and provides information on one of the most promising new prevention tools: the use of daily antiretroviral medications by high-risk HIV-uninfected individuals as pre-exposure prophylaxis, or “PrEP.” PrEP has been shown to protect against HIV acquisition and has been approved by the FDA.

HIV TESTING: STILL THE CRITICAL FIRST STEP IN HIV PREVENTION

In the United States, 21% of HIV-infected persons do not know they are infected. Therefore, the CDC recommends that all persons aged 13 to 64 be tested for HIV at least once, independent of risk, and on a regular basis if they are at high-risk for HIV acquisition. HIV test results will determine whether HIV treatment or preventive services are indicated. Those patients who are HIV-infected should be immediately evaluated for HIV treatment, as early treatment can reduce their risk of HIV-related complications and greatly decreases their likelihood of transmitting HIV to their sexual partners.
CREATING A PATIENT-CENTERED PREVENTION PLAN

HIV-uninfected individuals should be offered a selection of prevention services, based on an individualized risk assessment. Those at increased risk for HIV acquisition include:

- People with sexual partner(s) known to be HIV-infected.
- Men who have sex with men; in particular, those who report inconsistent condom use, use recreational drugs or alcohol in conjunction with sex, or have been diagnosed with sexually transmitted infections.
- Sex workers or anyone who exchanges sex for money, goods, or services.
- Injection drug users.

Selection of the optimal prevention package will depend on each individual’s risk factors for HIV acquisition, their personal preferences, and the presence of medical co-morbidities. Key components of an individual’s prevention package may include:

- Safer-sex counseling, focusing on reduction in the number of sexual partners, avoidance of high-risk behaviors (e.g., unprotected receptive anal or vaginal sex), and correct and consistent condom and lubricant use.
- Provision of condoms and lubrication.
- Screening and treatment for other sexually transmitted infections, as these can facilitate HIV acquisition.
- Post-exposure prophylaxis, or “PEP,” consisting of antiretroviral medications taken for 28 days following a high-risk exposure to HIV.
- The PrEP Package: Antiretroviral medications coupled with the behavioral interventions listed above, for individuals at ongoing, high risk for HIV acquisition.
- Provision of clean syringes for injection drug users.

WHAT IS THE PrEP PACKAGE? A PILL AND A PROCESS!

The term “PrEP Package” is preferred over the shorter term “PrEP” to emphasize that taking a pill alone has not been proven to be effective for HIV prevention without an integrated package of evidence-based behavioral interventions. The PrEP Package consists of the prescription of antiretroviral medications to high-risk persons in addition to ongoing safer-sex counseling, condom provision, treatment of other sexually transmitted infections, and monitoring for adherence and adverse effects. In essence, it involves taking a pill as part of a process aimed at optimizing the prevention effect. In the United States, once-daily tenofovir-emtricitabine (TDF-FTC) is the only medication that is FDA-approved for use as part of the PrEP Package.
**HOW EFFECTIVE IS TDF-FTC AS PART OF THE PrEP PACKAGE?**

Daily oral TDF-FTC has been evaluated in several large clinical trials in a range of high-risk populations, including men who have sex with men and serodiscordant heterosexual couples (i.e., couples in which one partner is infected with HIV and the other is not). In these studies, TDF-FTC reduced the risk of HIV acquisition by 44% to 75%, although one study of high-risk African women did not show a benefit using the combination of TDF-FTC, while another did not show a benefit from oral TDF alone in a comparable population. Overall, these studies demonstrated that the effectiveness of TDF-FTC is highly contingent upon medication adherence. Those who were more adherent attained the greatest prevention benefit. A study to test the efficacy of PrEP among injection drug users is ongoing.

**HOW SAFE IS TDF-FTC AS PART OF THE PrEP PACKAGE?**

There have been no differences in serious adverse effects between the use of TDF-FTC and placebo medications in clinical trials of PrEP to date. Use of TDF-FTC may be associated with nausea or other gastrointestinal symptoms (in less than 5% of study participants) that generally resolve within days, and certainly within 4 weeks of use. Counseling patients about this possibility could decrease self-discontinuation of TDF-FTC. When used for the long-term treatment of HIV infection, TDF-FTC has been associated with renal toxicity and decreased bone mineral density, but clinically significant changes in these parameters have not been seen in PrEP trials. However, the duration of follow-up for study participants has generally been about 1-2 years, so clinicians must be alert for potential adverse effects as long-term safety data are not yet available. Use of TDF-FTC in those with pre-existing renal failure or osteoporosis is not recommended.

It is possible that PrEP use could be associated with an increase in high-risk sexual behaviors or with selection of antiretroviral resistance in those who acquire HIV while using TDF-FTC as PrEP. However, in the context of clinical studies, all of which have featured intensive behavioral counseling, PrEP use has not been associated with increased sexual risk, and antiretroviral resistance among those who acquire HIV while using PrEP has been rare.

**HOW DO I PRESCRIBE TDF-FTC FOR THE PrEP PACKAGE?**

Before prescribing TDF-FTC, clinicians should consider whether the patient is capable of taking a daily pill and of coming in for regular follow-up visits. In addition, all patients should have:

- Documentation of a negative HIV antibody test.
- Assessment for acute HIV with an HIV RNA test if the patient has signs or symptoms consistent with acute infection (e.g., fever, rash, lymphadenopathy, a “viral syndrome”) or a recent, high-risk exposure.
- Baseline creatinine assessment to document an estimated creatinine clearance ≥ 60 mL/minute.
- Screening for hepatitis B infection, as both TDF and FTC can be used to treat this condition, and their abrupt discontinuation can cause flares of chronic hepatitis B.
- Safer-sex counseling.
- Determination if women are pregnant, planning to become pregnant, or are breastfeeding, and counseling around the use of barrier and hormonal contraception while using PrEP. TDF-FTC is not recommended for women who are breastfeeding.
During prescription of TDF-FTC, all patients should have:

- HIV antibody tests every 2-3 months. If patients experience signs or symptoms of acute HIV infection, HIV RNA testing should be performed.
- Follow-up visits at least every 2-3 months to assess medication adherence and adverse effects, to evaluate for sexually transmitted infections, and to provide safer-sex counseling and condoms.
- Screening for sexually transmitted infections at least every six months, even if asymptomatic, with treatment as needed.
- Serum creatinine checked after 3 months on the medication and yearly thereafter if baseline and 3 month values are within normal limits.
- For women, pregnancy testing every 3 months. In case of pregnancy, continued use of the medication should be discussed with the patient and their prenatal-care provider given limited safety data for the fetus in this setting.

REIMBURSEMENT

Public and private payors are currently undergoing a review process to determine if they will provide reimbursement for PrEP, as they typically do for newly approved treatments. Clinicians and patients will need to determine whether each patient’s insurer will cover the cost of PrEP. Some payors have already agreed to cover payment, while others are considering it.

WHAT ARE OTHER RESOURCES ON THE USE OF TDF-FTC?

- Interim guidelines for health care providers who may prescribe PrEP have been published by the CDC: http://www.cdc.gov/hiv/prep/pdf/PrEPfactsheet.pdf.
- Gilead Sciences, the manufacturer of TDF-FTC, has developed a website which contains an online training module and checklist for clinicians providing PrEP as well as information on identifying individuals at high risk of HIV acquisition: https://truvadapreprems.com.
- The CDC’s Compendium of Evidence-Based Behavioral HIV Interventions: www.cdc.gov/topics/research/prs/prs_rep_debi.htm provides extensive information on risk-reduction counseling and other non-pharmacologic strategies to help prevent HIV infection.
- The CDC has published recommendations for HIV testing in health care settings: www.cdc.gov/MMWR/preview/mmwrhtml/rr5514a1.htm.

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