Q&As for the PrEP Curious Provider

What is PrEP?
PrEP is an abbreviation for “pre-exposure prophylaxis.” The concept behind PrEP is simple: having anti-HIV (antiretroviral) medications in an uninfected person’s body makes it very difficult for HIV to infect them if they are exposed. You can think of PrEP as a pharmacological “shield” that helps protect your patient from becoming infected if s/he is exposed through sex or the sharing of needles or “works” during drug use.

In 2012, the FDA approved an existing tablet called Truvada (truh-VAH-duh) for use as PrEP among individuals at risk for HIV infection. This decision was made on the basis of several large clinical trials showing this strategy works well at preventing HIV infection among uninfected heterosexual men and women, men who have sex with men, transgender women (male-to-female transsexuals), and injection drug users.

What exactly is Truvada?
Truvada is a fixed-dose, combination tablet containing two anti-HIV medications: emtricitabine (em-TRY-site-uh-bean) and tenofovir (ten-OFF-uh-veer). It’s about the size of a large multivitamin tablet. When used for treating patients already living with HIV, these drugs help prevent the virus from making copies of itself within infected cells. When an uninfected person takes Truvada before an exposure, the drugs accumulate in cells that are susceptible to infection – so any virus that does enter the body never has a chance to make any copies; replication is blocked from the very start.
Truvada is also used for treating hepatitis B virus (HBV) – so knowing the infection status of patients prior to initiating PrEP is important. If a patient who has HBV is started on Truvada and then discontinues it for some reason, s/he may experience a “flare” of hepatitis and can become ill. Though some evidence suggests Truvada may reduce the likelihood of acquiring HBV, it is not recommended for HBV prevention; vaccination is recommended for those who are susceptible based on serologic testing.

Why do we need a pill for HIV prevention? Aren’t condoms good enough?
Condoms prevent pregnancy and sexually transmitted diseases, but only if they’re used properly and consistently. Whether we like it or not, not everyone uses condoms. Some are in relationships and feel that condoms limit intimacy with their partner. Some aren’t in a position to negotiate for condom use with sex partner(s). Others have difficulty with sexual performance while wearing a condom. Still others simply prefer the way condomless sex feels. With PrEP, we now have a viable and effective option for HIV prevention to offer these individuals.

“Discordant” couples (one with HIV, one without) trying to conceive can also benefit from PrEP. If the HIV-infected partner is on treatment and her/his viral load is “undetectable,” and the negative partner is initiated on PrEP, the risk of the uninfected partner acquiring HIV is
extremely small – perhaps even zero. We can help connect such couples with high-risk obstetricians for additional counseling and support, as well.

How good is PrEP at preventing HIV infection?
At first glance, the results of the clinical trials are a little confusing and made some people question whether or not PrEP was ready for “prime time.” When considering all the participants in the clinical trials, the protective effect varied significantly, with reductions in the risk of acquiring HIV ranging from 44% to 75%. (“Perfect” protection would be a 100% reduction.) However, these main estimates included all participants – including those who took their medications as directed and those who did not. When sub-analyses were conducted looking at those individuals who were highly adherent (compliant), the protection afforded by PrEP was much higher – in the range of 90% to 99%.

Why does adherence (compliance) matter so much for PrEP?
As with any prescription, the medication doesn’t provide any benefit if it’s still in the bottle. This is especially true for PrEP. Studies showed that the protective effect of Truvada was directly related to how consistently the tablets were taken, with the best “adherers” having the lowest risk of becoming infected with HIV. Individuals who didn’t take their Truvada as directed (at about the same time every single day, without fail) were much more likely to acquire HIV.

Adherence can be made easier by scheduling pill-taking with something your patient already does routinely – like eating a meal, brushing her/his teeth, or plugging in a cell phone before going to sleep. Setting an alarm on a cell phone or clock also helps some people remember.

What are Truvada’s side effects?
Most people experience very few side effects. The most common issues in clinical trials of PrEP have been fatigue, nausea (with or without vomiting) and flatulence. For the majority of participants, these side effects went away after the first month of use.
Extended use of tenofovir (one of the two agents in Truvada) has two adverse effects that are important to consider for patients who might be on PrEP long-term:

Nephrotoxicity. About 10% of HIV-infected patients taking tenofovir have slight elevations in serum creatinine. You don’t have to stop the drug, provided that the estimated creatinine clearance (eCrCl) remains at or above 60 mL/min. Although no patients in clinical trials of PrEP developed more severe renal impairment, we do sometimes see this in HIV-infected patients on Truvada long-term. Rarely, patients have developed proximal (type 2) renal tubular acidosis with or without the Fanconi syndrome (loss of glucose, phosphate, and bicarbonate into the urine). If you suspect renal injury, stopping tenofovir is recommended. Cessation of the drug allows for recovery of renal function for the majority of people.
Loss of bone mineral density. Within the first 6 months of taking tenofovir, at least 25% of patients on long-term tenofovir therapy have a small but measurable loss of bone density. This then stabilizes over time. Baseline bone densitometry is not routinely recommended unless otherwise clinically indicated.
How long does it take before PrEP is fully active? How long does it take to "wash out"? For blood and cervicovaginal tissues to be fully protected, it takes about 20 days of daily Truvada use. For rectal tissue to be maximally protected, it takes only about 7 days. About the same amount of time would be needed for these drugs to wash out from these different tissue types—with waning anti-HIV protection as those levels drop, over time.

Are there any other medications I should have my patient avoid, while taking PrEP? Because tenofovir can be nephrotoxic in some patients, it’s reasonable to try to avoid other known nephrotoxic agents, like high-dose NSAIDs.

How will my patient pay for PrEP? The manufacturer of Truvada, Gilead Sciences, has a medication assistance program that was specifically set up to handle requests related to PrEP. This program is available to insured patients as a copayment assistance program, and to uninsured patients as a medication access program. There are two ways you or your patient can begin this process:
• Call to determine eligibility, toll-free at 1-855-330-5479, M-F, 9A-8P EST
• Click here to download and fax the application directly from the Gilead website
To date, there have been no reports to the “watchdog” website MyPrEPExperience about insurance refusals from private companies or state Medicaid programs, though pre-authorizations may be required before the prescription will be approved.

How do I manage my patient who is interested in PrEP? NCATEC has detailed information on managing PrEP patients available on our Prescribing Providers page.

How often will tests need to be done to monitor my patient on PrEP? All patients should be seen and assessed every 1-3 months while on PrEP. Our recommended schedule of assessments and tests is available on our Prescribing Providers page. More frequent testing is reasonable, depending on how things are going with your patient – this is just a guide for the minimum number of assessments and tests needed during follow-up.

I’m concerned I may get a test result that I’m not sure what to do with. Is there someone who can help me? Absolutely. You can get in touch with someone from UNC Infectious Diseases in a couple of ways (listed below). We only ask that when you do call, please have the following information readily available:
• patient age
• risk factor for HIV acquisition
• date(s) and results of all available HIV tests
• date(s) and results of most recent serum creatinine level
• date(s) and results of most recent syphilis, gonorrhea, and chlamydia testing
For urgent or time-sensitive questions, call the North Carolina AIDS Training and Education Center (NCATEC) Clinician Line at 1-855-862-2832. As a backup, you can also call the Carolina Consultation Center and ask to speak with someone from UNC Infectious Diseases. The phone number is 1-800-862-6264. Between 8
AM and 5 PM on weekdays, you’ll be speaking with an attending physician; after hours and on weekends, you’ll be speaking with one of our fellows (who can reach an attending physician quickly, if needed). For non-urgent or general questions, please feel free to email one of our providers who has agreed to provide clinical guidance for PrEP. Please allow up to 48 hours for a response.

- Christopher Hurt, MD  christopher_hurt@med.unc.edu
- Lisa Hightow-Weidman, MD, MPH  lisa_hightow@med.unc.edu
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I’m still skeptical. Convince me that PrEP is a good idea for my at-risk patients.

Two of UNC’s providers, David Wohl and Christopher Hurt, have written opinion pieces for NCATEC related to PrEP. They are more resources and videos at:

http://www.med.unc.edu/ncaidstraining/prep/for-providers/for-interested-providers