## Table 1: Suggested Step-by-Step Checklist for Providers Initiating PrEP

§ indicates detailed info available in Table 3

### 1 Assess need

**Having any <u>one or more</u> of the risk factors below places the individual at risk for HIV.**

**Risks for sexual transmission**
- ❑ Any condomless sex in prior 6 months
- ❑ Any STI diagnosed in prior 6 months
- ❑ Not in a monogamous relationship with a partner confirmed to be HIV-uninfected
- ❑ Having sex with HIV+ partner(s)
- ❑ Commercial sex work

**Risks for parenteral transmission**
- ❑ Shared injection equipment
  - needles & "works" for illicit/recreational drugs
  - *consider anabolic steroids, body fillers, etc.*
- ❑ Known HIV+ injecting partner(s)
- ❑ Having sex with injecting partner(s)

### 2 Determine clinical eligibility

**<u>Within 30 days BEFORE</u> starting PrEP, check hepatitis B status and renal function**

- ❑ Hepatitis B surface **antigen** (sAg) REQUIRED
- ❑ Hepatitis B surface **antibody** (sAb) RECOMMENDED

- ❑ Serum creatinine REQUIRED
- ❑ Estimated creatinine clearance REQUIRED
- ❑ Urinalysis (to establish baseline) RECOMMENDED

**CAUTION if active hepatitis B (sAg+)**
- Truvada treats HBV; use may cause "flare" §

**eCrCl must be ≥ 60 mL/min by Cockcroft-Gault**
- Truvada dose reduction is **<u>not</u>** permitted for PrEP
- Descovy is **<u>NOT YET</u>** approved for use as PrEP

**<u>Within 7 days</u> BEFORE starting PrEP, test for HIV infection**

**Order <u>ONE</u> of these** REQUIRED – UNC's suggested order of preference
- ❑ Automated, lab-based antigen/antibody combination assay (4th or "5th" generation)
- ❑ Automated, lab-based IgM/IgG-sensitive antibody assay (3rd generation)
- ❑ HIV RNA ("viral load"), **quantitative**
- ❑ Point-of-care (rapid) test with **fingerstick blood**

**Must be confirmed as HIV-uninfected before PrEP**
- Rapid 4th gen (Determine HIV-1/2 Ag/Ab Combo) has had poor performance for detection of p24 antigen, missing many early infections §
- If high-risk exposures, consider RNA **<u>and</u>** 4th gen
- Do **<u>NOT</u>** rely on oral fluid testing; sensitivity is lower with oral fluid than with blood

**Any of these symptoms in prior month?**
- ❑ Fever
- ❑ Fatigue
- ❑ Skin rash
- ❑ Pharyngitis
- ❑ Cervical adenopathy

**Cannot have recent symptoms of acute HIV**
- **Must** be free of these symptoms in the month prior to starting PrEP
- **If ANY symptoms are present, rule out acute HIV by ordering quantitative HIV RNA**

### 3 Consider other tests

**If not already done in the prior 3-6 months** RECOMMENDED
- ❑ **Serum RPR** for syphilis
- ❑ **Nucleic acid amplification tests (NAATs) for gonorrhea and chlamydia**
  - Cervix or vaginal swab for women, urine for men – along with pharynx and rectum, as appropriate
- ❑ **Nucleic acid amplification test for *Trichomonas vaginalis*** (or wet prep), as appropriate
- ❑ **Hepatitis C antibody** §

### 4 Counsel patient

**"Startup syndrome"**
- Around 1 in 6 patients develop mild headaches, nausea, or flatulence; resolves in 1-2 months (for most)
- Patient should notify provider with any unexpected reactions, especially rashes

**Adherence strategies**
- Pair pill-taking with daily task (something consistent every day – even on weekends)
- Set an alarm, use a pill box, and keep an extra dose handy (in car, at work, etc.)

**Anticipatory guidance**
- Dose can be safely taken 3-4 hours before or 3-4 hours after a regularly scheduled dosing time
- No interactions with alcohol or recreational drugs – but encourage patient to avoid sex under the influence
- No drug interactions with hormones for transgender individuals on replacement therapy

**MUST RETEST FOR HIV BEFORE RESTARTING PrEP, IF SIGNIFICANT GAP** (e.g., self d/c, insurance lapse, lost bottle)

### 5 Prescribe, monitor, and support

**First prescription:** Truvada, one tablet PO daily, dispense #30, zero refills ← UNC'S PRACTICE – CDC says #90, no rf is OK

**Return to clinic in 3-4 weeks** to assess adherence, side effects, and risk-reduction behaviors ← UNC'S PRACTICE

**Subsequent prescriptions:** Truvada, one tablet PO daily, dispense #30, two refills

**At least every 3 months:**
- ❑ **Repeat HIV testing for ALL PATIENTS ON PrEP**
- ❑ Assess adherence, side effects, & risk behaviors

**At least every 6 months:**
- ❑ Check creatinine and eCrCl
- ❑ Screen for STIs, if not done in interim
- ❑ Assess ongoing need for PrEP

**Table 2: Recommended *Minimum* Follow-up Assessments for Patients on PrEP, by Time on Therapy ***

| Assessment | At 3 Months | At 6 Months | At 9 Months | At 12 Months |
|---|---|---|---|---|
| HIV antibody testing† | ❑ | ❑ | ❑ | ❑ |
| Pregnancy testing (if appropriate) | ❑ | ❑ | ❑ | ❑ |
| Ask about side effects | ❑ | ❑ | ❑ | ❑ |
| Ask about adherence | ❑ | ❑ | ❑ | ❑ |
| Ask about risk-reduction behaviors | ❑ | ❑ | ❑ | ❑ |
| Determine need for continuing PrEP | ❑ | ❑ | ❑ | ❑ |
| | | | | |
| **30-day prescription with 2 refills** | ❑ | ❑ | ❑ | ❑ |
| | | | | |
| Creatinine and eCrCl calculation | | ❑ | | ❑ |
| Serum RPR for syphilis | ❑ | ❑ | | ❑ |
| NAAT for gonorrhea & chlamydia‡ | ❑ | ❑ | | ❑ |
| Urinalysis with dipstick | | | | ❑ |

* If patient continues on PrEP after 12 months, restart schedule (i.e., assessments at month 15 are same as those at month 3)

† **Strong consideration should be given to using ONLY automated 4th or "5th" gen antigen/antibody combo assays**, instead of "standard" antibody testing. *See notes in Table 3 for details*.

‡ Nucleic acid amplification test (NAAT) kits used for cervical, vaginal, or urethral swabs can also be used for specimens from the pharynx and rectum. Studies show that a substantial number of infections go unrecognized because "extragenital" anatomical sites are not tested often enough – especially among men who have sex with men.

**Table 3: Notes on Laboratory Tests for Initiating and Managing Patients on PrEP**

| Test | Notes |
|---|---|
| HIV antibody testing | • For an overview of HIV testing, see: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5718364/<br>• **Strong consideration should be given to ordering automated, lab-based 4th (or 5th) generation antigen/antibody combination assays for all PrEP-related HIV testing**. These newer tests are capable of detecting recent infections more reliably than the older, IgM/IgG sensitive, third generation EIA/ELISA tests. Antigen/antibody combination tests on serum or plasma can identify the presence of viral antigens *before* anti-HIV antibodies develop, narrowing the "window" period of early infection.<br>**Point-of-care (rapid) antigen/antibody combination tests are NOT as sensitive as lab-based, automated 4th gen tests.** Unfortunately, the initial version of the only FDA-approved rapid 4th gen (Alere Determine HIV-1/2 Ag/Ab Combo) had exceptionally poor sensitivity in detecting p24 antigen in post-marketing field studies, so it **cannot** be relied upon to exclude acute infection. (For a review, see: http://www.ncbi.nlm.nih.gov/pubmed/26558545 ). The manufacturer has revised this assay, but as of May 2019, its performance from prospectively collected samples has yet to be reported; see https://www.ncbi.nlm.nih.gov/pubmed/27272704 .<br>**If any concern exists that a patient may have acute (seronegative) HIV infection, order HIV RNA (viral load) in addition to OR instead of a 4th generation assay.**<br>• To order a lab-based, automated 4th generation Ag/Ab combo assay:<br>  ○ Quest Diagnostics<br>  ▪ Test code 91431, CPT code 87389<br>  ▪ "HIV 1/2 Antigen and Antibodies, Fourth Generation, with Reflexes"<br>  ○ LabCorp<br>  ▪ Test number 083935, CPT code 87389<br>  ▪ "Human Immunodeficiency Virus 1/O/2 (HIV-1/O/2) Antigen/Antibody (Fourth Generation) Preliminary Test with Cascade Reflex to Supplementary Testing"<br>• An IgG-sensitive (2nd generation) point-of-care (rapid) test (e.g., OraQuick ADVANCE HIV-1/2) may be considered **ONLY IF** fingerstick blood is used as the specimen – NOT oral fluid. Antibody concentrations are much lower in oral transudate than in blood, so the "window" period for antibody detection in oral fluid is longer than in fingerstick blood. For an overview of HIV testing, see: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5718364/ . |
| Serum creatinine | • Estimated creatinine clearance (eCrCl) must be ≥ 60 mL/min to receive Truvada-based PrEP<br>• **Patients with impaired renal function should not be prescribed Truvada.**<br>Dose adjustment of Truvada has not been studied in the context of PrEP and is ABSOLUTELY NOT recommended in HIV-uninfected patients. Descovy is **NOT YET** approved for use as PrEP, and there are no data on Descovy's preventive benefit for cisgender heterosexual men or women. |
| Hepatitis serologies | • Baseline serologies should include AT LEAST the following:<br>  ○ Hepatitis B surface antigen (HBsAg) to rule out active, chronic HBV infection<br>  ○ Hepatitis B surface antibody (anti-HBs) to assess for the need for immunization<br>• Since Truvada has anti-HBV activity, concern exists for the possibility of HBV "flares" among individuals with chronic, replicative HBV who are prescribed PrEP. Data from the iPrEx study showed no evidence of flares, however only 12 of 2499 participants had chronic HBV and only 6 were randomized to receive Truvada. (See: http://www.ncbi.nlm.nih.gov/pubmed/26413853 ). Patients with chronic, replicative HBV should be referred to an infectious disease or liver specialist for anti-HBV therapy – which might be PrEP.<br>• Hepatitis C antibody (anti-HCV) testing is encouraged for all patients, however the best evidence supporting this recommendation applies to individuals:<br>  ○ born between 1945-1965 (the "HCV birth cohort")<br>  ○ who have ever injected drugs (with or without shared equipment)<br>  ○ who have ever snorted drugs (implements are often shared)<br>  ○ having sex of any kind that results in visible mucosal or tissue bleeding<br>  ○ engaging in anal sex practices that could produce bleeding or tears in tissue (e.g., sex toys, fisting, rough sex, group sex, or sex under the influence of alcohol or drugs) |
| Urinalysis with dipstick | • Establishes a baseline so that if any tenofovir-associated renal issues develop, you have a reference point |
| Serum RPR for syphilis | • If not already done in the prior year |
| NAA tests for gonorrhea & chlamydia | • If not already done in the prior year<br>• Include pharyngeal testing for gonorrhea (± chlamydia) if the patient reports performing oral sex<br>• Include rectal testing for gonorrhea and chlamydia if the patient reports receptive anal sex |

**Table 4: ICD-10 Diagnostic Codes for PrEP-Related Visits ***

| Description | Code | Baseline | Follow-Up |
|---|---|---|---|
| Encounter for screening for HIV | Z11.4 | ❑ | ❑ |
| Encounter for screening for infections with a predominantly sexual mode of transmission (i.e., screening for STIs) | Z11.3 | ❑ | ❑ |
| Counseling related to patient's sexual behavior and orientation | Z70.1 | ❑ | ❑ |
| High-risk sexual behavior | Z72.5 | ❑ | ❑ |
| Contact with and (suspected) exposure to HIV | Z20.6 | ❑ | ❑ |
| Other long-term (current) drug therapy | Z79.899 | | ❑ |

* Excerpted from CDC/USPHS PrEP Guidelines, 2014