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 90 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 & Descovy treat HBV; use may cause "flare" §

Calculate eCrCl using Cockroft-Gault
- For Truvada, eCrCl must be ≥ 60 mL/min
  → You can NOT dose-reduce Truvada for PrEP if eCrCl <60 mL/min
- For Descovy, eCrCl must be ≥ 30 mL/min
  <u>DO NOT</u> PRESCRIBE DESCOVY TO PREVENT HIV ACQUISITION THROUGH VAGINAL SEX OR INJECTION DRUG USE – <u>NO DATA!</u>

<u>Within 7 days BEFORE</u> 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>** HIV Ag/Ab test
- 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 <u>month</u> 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 from <u>any</u> exposed anatomical sites**
  - Screen the vagina with a swab. Screen the penile urethra with <u>urine</u>. Swab 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 or Descovy, 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 or Descovy, 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	❑	❑	❑	❑
Prescription for 90d worth of PrEP	❑	❑	❑	❑
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/
	• **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.
	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 revised this assay, but as of May 2020, its performance from prospectively collected samples has yet to be reported; see https://www.ncbi.nlm.nih.gov/pubmed/27272704 & https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7125248 .
	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.
	• To order a lab-based, automated 4th generation Ag/Ab combo assay:
	  ○ Quest Diagnostics
	  ▪ Test code 91431, CPT code 87389
	  ▪ "HIV 1/2 Antigen and Antibodies, Fourth Generation, with Reflexes"
	  ○ LabCorp
	  ▪ Test number 083935, CPT code 87389
	  ▪ "Human Immunodeficiency Virus 1/O/2 (HIV-1/O/2) Antigen/Antibody (Fourth Generation) Preliminary Test with Cascade Reflex to Supplementary Testing"
	• 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, and ≥ 30 mL/min to receive Descovy-based PrEP. • **Patients with impaired renal function should not be prescribed Truvada.** Dose adjustment of Truvada has not been studied in the context of PrEP and is ABSOLUTELY NOT recommended in HIV-uninfected patients.

Hepatitis serologies	• Baseline serologies should include AT LEAST the following:
	  ○ Hepatitis B surface antigen (HBsAg) to rule out active, chronic HBV infection
	  ○ Hepatitis B surface antibody (anti-HBs) to assess for the need for immunization
	• Since Truvada and Descovy have 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 HBV should be referred to an infectious disease or liver specialist for anti-HBV therapy – which might be PrEP.
	• Hepatitis C antibody (anti-HCV) testing is encouraged for all patients, however the best evidence supporting this recommendation applies to individuals:
	  ○ aged 18-79 years old (see USPSTF updated recommendation issued 2 March 2020)
	  ○ who have ever injected drugs (with or without shared equipment)
	  ○ who have ever snorted drugs (implements are often shared)
	  ○ having sex of any kind that results in visible mucosal or tissue bleeding
	  ○ 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 • Include pharyngeal testing for gonorrhea (± chlamydia) if the patient reports performing oral sex • 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

† If you use this ICD-10 code, it may appear on after visit summaries or patient-facing documents. **Strongly consider** letting your patient know in advance that this is not a judgment you're making, it's just one of the diagnostic codes that is necessary to use in order to make sure that PrEP is covered by their insurer.