Table 1: 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
- ❑ 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
- ❑ Relationship with HIV+ partner(s)
- ❑ Commercial sex work

Risks for parenteral transmission
- ❑ Shared injection equipment (needles or "works")
- ❑ Known HIV+ injecting partner(s)
- ❑ Recent drug treatment (but currently still injecting)
- ❑ Sexually active with injecting partner(s)

2 Determine clinical eligibility

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

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

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

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

eCrCl must be ≥ 60 mL/min by Cockcroft-Gault
- Truvada dose reduction is not permitted for PrEP

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

Order ONE of these (in order of preference)
- ❑ Automated, lab-based 4th generation antigen/antibody combination assay
- ❑ HIV RNA (viral load)
- ❑ Rapid test with **fingerstick blood**
- ❑ "Traditional" blood test with ELISA (EIA) and reflexive confirmatory testing

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

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

No symptoms of acute HIV infection
- **Must** be free of these symptoms in the month prior to starting PrEP
- **If ANY symptoms are present, rule out acute HIV by ordering HIV RNA (viral load)**

3 Consider other tests

If not already done in the prior 6-12 months:
- ❑ **Serum RPR** for syphilis
- ❑ **Nucleic acid amplification tests (NAATs) for gonorrhea and chlamydia**
  - Cervix in women and urine/urethra in men – along with pharynx and rectum, as appropriate
- ❑ **Nucleic acid amplification test for *Trichomonas vaginalis*** (or wet prep), as appropriate
- ❑ **Hepatitis C antibody** is strongly encouraged §

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 after a regularly scheduled dosing time
- Truvada has no interactions with alcohol or recreational drugs – but avoid sex under the influence
- No drug interactions with hormones for transgender individuals on replacement therapy

5 Prescribe, monitor, and support

First prescription: Truvada, one tablet PO daily, dispense #30, zero refills
Return to clinic in 3-4 weeks to assess adherence, side effects, and risk-reduction behaviors
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, and risk-reduction 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 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 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 extra-genital anatomical sites are tested infrequently – 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	• **Strong consideration should be given to ordering automated, lab-based 4th generation antigen/antibody combination assay for all PrEP-related HIV testing**. These newer tests are capable of detecting recent infections more reliably than the older, third generation EIA/ELISA tests. Fourth generation tests can identify the presence of viral antigens *before* anti-HIV antibodies develop, narrowing the "window" period of early infection.
	
	Rapid 4th gen tests are not as sensitive as lab-based, automated 4th gen tests. Unfortunately, the only FDA-approved rapid 4th gen (Alere Determine HIV-1/2 Ag/Ab Combo) has 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).
	
	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"
	
	• May use a 2nd generation rapid test (e.g., OraQuick ADVANCE HIV-1/2) **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.

Serum creatinine	• Estimated creatinine clearance (eCrCl) must be ≥ 60 mL/min to receive Truvada-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)
	  ○ Hepatitis B surface antibody (anti-HBs)
	
	• 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 for antiviral therapy of their infection; if prescribed Truvada, then their HBV will be treated and they are also therefore on PrEP.
	
	• Hepatitis C antibody (anti-HCV) is encouraged for all patients, however the best evidence supporting this recommendation applies to individuals:
	  ○ born between 1945-1965 (the "HCV birth cohort")
	  ○ 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 measurement 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