ACHA Guidelines

HIV Pre-Exposure Prophylaxis

Position Statement

The American College Health Association (ACHA) believes that the on-going HIV epidemic is an urgent health priority, one that our membership must actively embrace. ACHA endorses the wide availability of HIV pre-exposure prophylaxis (PrEP) in college and university health services. We believe that college health is uniquely positioned to make a significant impact in the health of young adults in the U.S. by offering PrEP as a standard health care service.

Given the prescriptive nature of the administration of PrEP as presented in this document and the ready availability of free consultation on this practice through the University of California, San Francisco (UCSF) Clinician Consultation Center, any college health center with a medical prescriber can offer PrEP. Establishing a relationship with a PrEP provider in the community with easy access to students/clients is an acceptable alternative to delivering PrEP for those health centers without a medical prescriber. This document was created to provide a roadmap and a resource for college health services in providing PrEP and to assist with front line implementation.

Introduction

While HIV rates have recently decreased among the general population, HIV remains a serious issue for young adults. According to the U.S. Centers for Disease Control and Prevention (CDC), young adults ages 13–24 accounted for 21% of new HIV infections in the United States in 2016.[1] In addition, 4 out of 5 young adults newly diagnosed with HIV were between 20 and 24 years old, and 81% were among young gay and bisexual men.[1] If current HIV rates persist among men who have sex with men (MSM), then it is estimated that 1 in 2 black MSM, 1 in 4 Latinx MSM, and 1 in 11 white MSM will be diagnosed with HIV during their lifetime.[2] These statistics serve as a call-to-action for college health professionals to be intentional about how their work addresses health disparities among marginalized students.

Approved by the Food and Drug Administration (FDA) in 2012, PrEP is a medical intervention that can reduce the risk of HIV infection by over 90% if taken daily as prescribed and is intended to be used in combination with other prevention strategies—such as using condoms.[3]

The National HIV/AIDS Strategy—the United States' guiding document for HIV prevention and care—calls for the expansion of PrEP services that target populations most affected by HIV:[4]

- Youth aged 13-24
- Gay, bisexual, and other MSM of all races and ethnicities, particularly MSM of color
- Transgender and non-binary individuals, particularly black transgender women
- Persons who inject drugs (PWID)

In November 2018, the United States Preventative Service Taskforce (USPSTF) published a draft recommendation statement that clinicians offer pre-exposure prophylaxis (PrEP) with effective antiretroviral therapy to persons who are at high risk of HIV acquisition, giving this recommendation its highest rating of A.[1]

College health centers are in a unique position to implement comprehensive, evidenced-based prevention strategies that will promote overall well-being and help to end the HIV epidemic among young adults.

Basic Science

Summary:

- **Daily Tenofovir/Emtricitabine (TDF/FTC) is over 90% effective in preventing HIV if taken regularly.**
- **TDC/FTC does not offer protection from other STIs and is meant to be used with barrier protection.**

The use of antiviral HIV treatment medications as prophylaxis, also known as HIV PrEP, has been studied extensively and demonstrated to be extremely effective in preventing HIV infection.[5,6] The currently approved

[1] See the USPSTF Draft Recommendation Statement "Prevention of Human Immunodeficiency Virus (HIV) Infection: Pre-Exposure Prophylaxis" at https://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementDraft/prevention-of-human-immunodeficiency-virus-hiv-infection-pre-exposure-prophylaxis#consider

oral regimen for PrEP, a combination of Tenofovir and Emtricitabine (TDF/FTC), is a non-nucleoside reverse transcriptase inhibitor (NNRTI). NNRTIs prevent the conversion of HIV RNA to DNA, thus preventing viral replication.

There have since been multiple studies on HIV PrEP, investigating different modes of delivery. One of the more well-known studies is iPrEx, the first randomized controlled study of oral PrEP. The initial results showed efficacy rates of over 77% when pills were taken 90% of the time, and then later over 90% when taken daily.[5]

The success of the iPrEx study, and the preceding timeline of studies, led to the FDA approval in July 2012 of using daily oral TDF/FTC for HIV prevention. PrEP research is ongoing, looking at other modes of HIV PrEP delivery, as well as intermittent use vs. daily use. Currently, the FDA has approved only oral daily HIV PrEP use.[6, 7] TDF/FTC is currently the only approved formulation for use as pre-exposure prophylaxis, but other products are expected to become available in the future.

Side Effects and Contraindications

Summary:

- **The contraindications for PrEP are unknown or positive HIV status and chronic renal insufficiency defined as eCrCL <60 ml.**
- **Hepatitis B infection is not a contraindication to PrEP use, but students with chronic active hepatitis B should receive expert consultation**
- **Side effects are minimal.**
- **The development of drug resistance to TDF/FTC during PrEP has occurred very rarely.**

Long term daily use of TDF/FTC as PrEP is generally well-tolerated by patients with no severe or life-threatening side effects[6,8] although long-term data on safety is lacking. The most common adverse reactions are related to the gastrointestinal tract (nausea, vomiting, flatulence) and occur in <10 % of patients. Other adverse reactions occurring in <1% of patients include rash, headache, fatigue and dizziness.[6,8] Most of these side effects resolve within the first month and can be treated using over-the-counter medications.

Contraindications to TDF/FTC as PrEP include acute HIV infection and chronic renal insufficiency (defined as creatinine clearance (CrCl) <60 ml/min). The regimen of TDF/FTC in PrEP is not adequate for treating acute HIV infection,[6] so it is important to screen patients for symptoms of acute HIV infection and perform appropriate testing for HIV to determine that the patient is not living with HIV prior to initiating PrEP.[6] Among people who are living with HIV and are prescribed TDF-containing regimens, decreases in renal function have been documented and occasional cases of acute renal insufficiency have occurred. CDC guidelines for the eligibility for PrEP includes a CrCl of >60 ml/min. The renal effects are seen least frequently in people under age 40 and those with normal baseline renal function.[9, 10]

Although there may be a possible decrease in bone mineral density by 1-4%, no increased risk of facture has been found, and bone density has been shown to return to normal once TDF/FTC is discontinued. There is limited data on the safety of PrEP on the developing fetus, but a small study on HIV-discordant couples (n=46) demonstrated no ill effects on the pregnancy and no HIV infection in the baby or the person giving birth.

Prior to initiating PrEP, screening for chronic active hepatitis B is indicated. TDF is a treatment for chronic active hepatitis B. Sudden discontinuation of TDF can cause a rebound increase in hepatitis B replication and intermittent use of TDF may lead to hepatitis B viral resistance. As such, initial and periodic hepatitis B viral levels are indicated for the patient with chronic infection on PrEP. Management of individuals on PrEP with chronic active hepatitis B is best coordinated with a clinician with expertise in this area. While hepatitis B vaccination is not needed to initiate PrEP, it is recommended for all people having anal sex, MSM, and PWID.[6]

The development of drug resistance to TDF/FTC during the course of treatment has been a major concern for medical providers but has happened only rarely. As of this printing, less than ten cases of seroconversion have been reported among nearly 100,000 PrEP users.[11-15]

Indications for PrEP

PrEP is indicated for clients who are HIV-negative and at substantial risk for HIV infection. Although there is no single definitive definition of what "substantial risk" means, factors to consider include sexual behaviors and social or sexual networks.[6]

In May 2018, the FDA revised the lower age limit for the use of TDF/FTC as PrEP in adolescents younger than 18 years old who weight more than 35 kg (77lbs).

Potential candidates for PrEP include (but are not limited to):

- MSM who have had condomless anal sex within past 6 months.
- Transgender individuals engaging in high risk sexual behavior: e.g. multiple partners, condomless anal sex.
- Individuals who have been diagnosed with anogenital gonorrhea or syphilis in past 6 months.
- Individuals who have a partner who is living with HIV.
- Heterosexual women who have sex with MSM or PWID.
- Individuals engaging in transactional sex.
- People who inject drugs.
- Individuals using stimulant drugs (cocaine, methamphetamine) in association with high risk sexual behavior
- Individuals who have been prescribed post-exposure prophylaxis (PEP).
- Someone requesting PrEP.

For people who need to prevent HIV after a single high-risk potential HIV exposure, such as condomless anal sex or a sexual assault, there is another option, post-exposure prophylaxis, or PEP. PEP must be given within 72 hours of exposure to be effective (preferably 24 hours). PEP includes a course of three anti-retroviral medications given for 28 days. Patients completing a course of PEP are often candidates to initiate PrEP immediately after their course of PEP is completed

Introducing PrEP

Summary: Be proactive in talking about PrEP—don't wait for the student to ask. Dispel myths.

Some students will request PrEP, but many will not know they are candidates unless their provider brings it up. A visit with a client who presents for sexually transmitted infection (STI) testing is an excellent opportunity to share information about PrEP. The diagnosis of an STI is clearly an indication to discuss PrEP and further explore risk factors. Screening for risk factors for HIV during visits related to sexual health will help to identify patients for whom PrEP may be indicated.

Many people have misconceptions about PrEP. Discussing safety, tolerability, and affordability is crucial (see section below on financial concerns). Some students will be ready to start PrEP on their first visit. Others will want to think about it and explore the confidentiality and coverage of their health insurance.

Initial Evaluation

Summary: Initial testing includes an HIV test, serum creatinine (Cr) and estimated GFR (eGFR), hepatitis B surface antigen (HBsAg), and STI testing. See Appendix for sample protocols.

Prior to starting PrEP, the clinician needs to ensure that the student is HIV-negative and without signs of acute retroviral infection. An HIV test is best performed within one week of initiation, preferably a fourth generation combined Ab/Ag test. A third generation HIV test is an acceptable alternative. Direct review of official HIV test results performed by an accredited laboratory by the PrEP clinician is a best practice.

Always ask about symptoms of acute HIV infection within the past four weeks: a flu like illness with fever, body aches, sore throat, and often rash. Inquire when the last high-risk exposure occurred; if it was within 72 hours, PEP (post-exposure prophylaxis) may be indicated. If there are concerns about acute HIV or a recent exposure in the last 7-28 days (the window period for fourth generation HIV test), a quantitative RNA viral load should be obtained.

Renal function assessment in someone without known renal disease can be measured with a serum Cr and estimated GFR (eGFR), a calculation that is included in the report from the lab. A full CrCl requires a 24-hour urine and does not need to be done unless there is an abnormality in the serum Cr or eGFR.

STI testing is important and includes testing based on sex practices of all sites of potential chlamydia and gonorrhea infection, as well as syphilis and hepatitis C testing. Screening for hepatitis B infection can be done with a HBsAg. Perform a pregnancy test in people of childbearing potential. All MSM, whether on PrEP or not, should receive appropriate vaccinations: hepatitis A, hepatitis B, and HPV.

Once TDF/FTC is initiated, it takes seven days to detect measurable levels in anal tissue and up to 20 days to detect levels in blood and cervical/vaginal secretions. There are no data yet available about intracellular drug concentration in penile tissues to help inform considerations of protection for insertive sex partners.[6]

Examples of two step-by-step protocols are included as appendices. These protocols may be downloaded and edited to fit your needs.

Providing the Prescription

TDF/FTC is available in one fixed-dose combination for adults—no dosage adjustments are needed. Prescriptions are generally written for a 30-day supply with two refills, or a 90-day supply, depending on insurance parameters and patient preference. It is acceptable to start medication before the HIV test result is available, as long as the provider can confirm that a test has been done. A pharmacy benefits prior authorization may be necessary. Some insurance plans require the use of specialty pharmacies or mail order service. This usually becomes apparent when the prescription is first submitted.

TDF/FTC is a very high cost medication, but robust patient assistance programs exist that can provide resources to cover the costs for most students (see Financial Concerns below).

On-Going Monitoring

People on PrEP should have follow up testing and monitoring every three months. See the appendix for step by step protocols. Regular follow up visits provide an opportunity to assess any barriers to medication adherence, review behavioral risk reduction, and perform ongoing testing. Regular laboratory monitoring includes: HIV testing, with pregnancy testing if appropriate, every three months. STI testing is performed every 3-6 months depending on history, and renal function evaluated every 6 months. The on-going need for PrEP over time can also be discussed.

Retention in Care

Once PrEP has been started, it is important to help patients succeed. Barriers to PrEP persistence include: issues with obtaining or using the patient assistance copay relief card, picking up the prescription, and making regular follow up appointments. One study showed that drop off was most common in the first month and was more pronounced for younger users.[14]

Consider contacting the student early in their treatment course to help with any problem solving. Proactively remind students when they are due for a follow up and, when resources exist on campus to do so, allow walk-in appointments for PrEP follow up.

Common Concerns

Financial Barriers

Summary: Substantive financial resources exist for college students that will allow most to obtain TDF/FTC without any out of pocket expense.

A major barrier to considering taking PrEP for many students may be concern about costs associated with the medication and associated testing and office visits. Fortunately, excellent resources exist to help remove or reduce financial barriers. Proactively addressing financial concerns is key to improving PrEP uptake among those at risk.

For patients who do not have health insurance, whose insurance does not cover PrEP medication, or whose personal resources are inadequate to pay the monthly co-pays, Gilead Sciences, a manufacturer of PrEP, has established a PrEP medication assistance program. The Gilead Advancing Access patient assistance program provides resources for medication costs for those in financial need based on self-reported income. As of August 2018, each patient registered can receive up to $7,200 per year to cover co-pays or insurance deductibles.

Students can easily register for Gilead's assistance program online at www.gileadadvancingaccess.com or by calling 1-877-505-6986. For uninsured students or those with very high deductible plans, the advancing access program can often help them find additional resources. Many states have programs to further support vulnerable populations, therefore it is useful to connect with local public health departments.

The costs of initial laboratory testing and ongoing STI screening can create a barrier to accessing PrEP. STI testing is covered as preventive health under the Affordable Care Act (ACA), so deductibles would not apply, but not all students have insurance or insurance that meets ACA guidelines. Local public health departments may have resources to provide free testing to eligible students.

Confidentiality

Summary: Confidentiality is a real concern for students who are on another person's insurance plan, and they may need help navigating Explanations of Benefits (EOBs). Some insurances are open to redirecting EOBs.

Even if lab testing is covered by a student's insurance, it may not be confidential coverage. Every time an insurance company receives a bill from a provider for services rendered to a covered individual, the insurance company generates a statement, also known as an EOB. The EOB is then sent to the patient or policy holder explaining what medical treatments and/or services were paid for on their behalf and what portion is the patient's responsibility.

All insurance companies are different. Some insurance companies provide a statement to the policy holder (usually a parent) detailing the services received. If confidentiality about PrEP is important to the student, they will need to explore how their insurance company handles EOB by calling the customer service number on the back of the insurance card to inquire. Some insurers will allow the EOB to be sent directly to the student or to a patient portal that can be accessed only by the student.

Legislation is starting to address this threat to confidentiality around sensitive health care, and as of the time of this publication, 13 states have provisions that serve to protect the confidentiality of individuals insured as dependents. For now, however, this is a very real concern and students need to be educated on this issue.

Providing PrEP During the Summer

Summary: Suggestions for providing PrEP over summer break include providing a four-month supply, having a telehealth visit, and having student obtain an HIV test locally that is emailed to their college health service provider.

CDC recommends individuals on PrEP have HIV testing every three months. Since the typical summer for most colleges is four months long, the college health provider and the student must make plans to enable access to PrEP despite the break.
One option is to ask the student to get an HIV test where they are spending their summer, scan their result, and email it to their provider. A brief interaction over phone or by video conferencing (Skype, WebEx, etc.) can then take the place of a traditional office visit, and a new prescription can be generated.

Another option is to consider extending the testing interval. Although every-three-month testing is clearly recommended, it is not required. Most insurances will provide more refills or vacation over-rides for longer than three months. It is important for the provider to balance the risk for development of a TDF/FTC resistant HIV strain (very rare), with the risks of acquiring HIV because PrEP has been discontinued. Providing a four-month or even five-month prescription may actually provide the best medical care.

International study abroad is most problematic, as U.S. clinicians cannot prescribe internationally. Sending the student with a six-month supply of medication and having them get an HIV test at three months that can be sent to the provider might feel reasonable. Consulting with local infectious disease specialist for HIV PrEP resources abroad may help identify clinics abroad in the location of study.

Increased Risk-Taking

Summary: Data is mixed on whether PrEP causes riskier sex, thereby increasing rates of STIs, but overall the effect seems minimal or even to decrease rates of STIs.

Some health care providers are concerned that prescribing PrEP may change students' perception of risk and encourage risky sexual choices ("risk compensation"). Although there are data to support both sides of this issue, some studies indicate that sexual risk taking actually declines with PrEP use.[9-11] Most recently, the findings of a recent joint study by the CDC and the Rollins School of Public Health at Emory University suggest there is a significant reduction in the transmission of HIV and other STIs for those who are using PrEP and receiving regular STI screenings and treatment.[15]

Providing PrEP for patients at risk of HIV affords the opportunity to not only reduce the risk of an incurable, potentially life-threatening illness, but also to screen for curable STIs and counsel individuals on ways to mitigate the risk of acquiring any of these infections.

Implementation

Summary: Utilize sample protocols and the expertise of colleagues with experience in implementing PrEP.

When introducing a new clinical skill in a health service, an important first step is to identify a leader or champion. The champion can prepare the way by providing a protocol and serving as the point person for questions or barriers. The champion can also provide coaching in how to take a nonjudgmental sexual history.

Sample protocols are included in the appendix to assist health centers in implementation. If the health service uses an electronic health record, developing a template can be helpful in simplifying visits and increasing clinician confidence.

As with all clinical skills, comfort will increase over time. The champion may find it helpful to connect with a knowledgeable colleague outside of their school for questions or support. National and regional professional organizations, such as the American College Health Association, can help connect providers to experienced colleagues. Local infectious disease specialists are also a good resource for patient management questions.

Finally, the University of California, San Francisco provides a telephone consultation service that provides direct access to experts in HIV and STI care:

Telephone consultation line: 1-855-448-7737
9 am to 8 pm ET Monday–Friday

Online: https://nccc.ucsf.edu.

Resources in the Community

In some situations, students may need information about PrEP services outside of the student health service—for example, if the health service has limited prescriber presence or when the student graduates or leaves the institution. The following links are resources that aide in the location of PrEP providers:

www.cdc.gov/hiv/risk/prep

www.pleaseprepme.org

www.preplocator.org

Considerations for Higher Education Settings

Having conversations about HIV prevention requires bringing up topics that can be stigmatizing—such as sex and drugs—and college health center providers must keep this in mind when dealing with their patient population.[4] It is important for college health practitioners to recognize PrEP as an HIV prevention tool that can be used in combination with broader strategies to promote sexual health.[4]

The ACHA Clinical Medicine Section has included prescribing PrEP in its list of core competencies for medical providers in college health. In order to decide whether or not a patient might benefit from PrEP, for example, clinicians must be comfortable taking inclusive, nonjudgmental sexual histories.[4] For the patient to be willing to discuss these issues, it is crucial that they feel they are in a welcoming, safe, and comfortable space with a trusted provider. This is especially true for members of those historically marginalized communities who are most affected by HIV (e.g., queer and trans persons; persons of color; people who inject drugs), who have not felt supported, respected, or seen by the health care system. Some strategies for making a health center a safe space for these students include:

- Making sex-positive, lesbian, gay, bisexual, transgender, queer, intersex, asexual (LGBTQIA+)-inclusive resources available.
- Integrating PrEP appointments into online scheduling systems.
- Emphasizing privacy and confidentiality in student-facing resources.
- Allowing patients to identify their sexual orientation, gender identity, and sex assigned at birth in electronic medical record systems.
- Integrating LGBTQIA+ identities into non-discrimination statements and Patient Rights and Responsibilities.
- Integrating best practices in sexual health care into routine visits, including (but not limited to):
  - Adding LGBTQIA+-inclusive sexual history sections to health questionnaires.
  - Performing extra-genital STI testing as indicated.
  - Implementing routine/opt-out HIV testing into clinical practice.
  - Testing patients for HIV when testing for STIs, and vice versa.
- Training all clinic staff in proactively discussing PrEP and adhering to best practices for inclusive health care.

Summary

Rates of HIV continue unchanged among college age adults, particularly MSM of color. HIV prevention with a daily pill, called pre-exposure prophylaxis (PrEP) is safe, well tolerated, effective and financially accessible. The management of PrEP is straightforward—it is always just one pill a day, no levels to measure, no medication adjustments needed. With PrEP, college health providers can make a dramatic contribution to the current and long-term health and well-being of their students.

Additional Resources

For additional information, please read "Viewpoint: Why you should provide HIV pre-exposure prophylaxis (PrEP) at your college health center" in the *Journal of American College Health:*

Michael J. Huey, Margaret Higham & Ariel L. Watriss (2018) Viewpoint: Why you should provide HIV pre-exposure prophylaxis (PrEP) at your college health center, Journal of American College Health, DOI: 10.1080/07448481.2018.1529673

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Prepared by the ACHA PrEP in College Health Task Force

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Appendix A: HIV Pre-Exposure Prophylaxis Protocol

Overview

Since the summer of 2012 when the FDA approved the use of combination of Tenofovir and Emtricitabine (TDF/FTC) for HIV pre-exposure prophylaxis (PrEP) in high risk patients, college health services have seen increasing numbers of students who qualify for and are interested in taking PrEP. In 2018, the FDA approved TDF/FTC for use in 13–17-year-olds weighing more than 77 lbs.

Initial Evaluation

- Identify high risk students and discuss the option of PrEP with them. This might come up at a visit scheduled to discuss PrEP, or it might come up during treatment of an STI, or at an STI screening visit.
- Potential candidates for PrEP include (but are not limited to):
  - Individuals who have an HIV positive partner
  - MSM who has had condomless anal sex within past 6 months
  - Transgender individuals engaging in high risk sexual behavior such as condomless sex or multiple partners
  - Individuals (male or female) who have been diagnosed with anogenital STI in past year.
  - Individuals engaging in transactional sex
  - Heterosexual women who have sex with male partners at substantial risk of HIV infection
  - Injection drug users
  - Individuals using stimulant drugs in association with high risk behavior: condomless anal sex, multiple partners
  - Individuals who have been prescribed post-exposure prophylaxis (PEP)
- Discuss PrEP with student—data on efficacy, crucial importance of compliance, short term side effects, lack of information about very long-term use, importance of condom use, co-pays, importance of frequent follow up to make sure no HIV infection has developed.
- When was their last high-risk exposure? Do they need PEP?
- Screen for symptoms of acute HIV infection in past 3 weeks—a flu-like illness with fever, body aches, often sore throat, sometimes rash.
- Indicated initial labs:
  - HIV test 4th generation preferred and performed within 1 week before starting PrEP
  - If last exposure was within 7-21 days (i.e., window period), consider a viral load test
  - Consider Hep C Ab for those who have ever injected drugs
  - HBsAg—even in immunized students
  - Creatinine
  - E-GFR (Estimated GFR)
  - Pregnancy test if applicable
- STI testing if not recently done:
  - Gonorrhea of appropriate sites: urine, throat, and anal (can use self-swab)
  - Chlamydia of appropriate sites: urine and anal (can use self-swab)
  - Syphilis
  - HPV vaccine if needed
- Provide educational materials:
  - CDC website: www.cdc.gov/hiv/basics/prep.html
  - San Francisco AIDS Foundation: www.prepfacts.org

    - Gilead Advancing Access: www.gileadadvancingaccess.com Gilead (manufacturer of PrEP) co-pay program that covers co-pays and deductibles for most patients. Currently program can cover up to $7,200 annually. Provider can give an access card to student or student can register online.
    - State and local resources providing financial aid (for example, the Massachusetts Pre-Exposure Prophylaxis Drug Assistance Program [PrEPDAP] helps Massachusetts residents pay for approved medications that can prevent the transmission of HIV by covering out-of-pocket costs, including copays and co-insurance, and up-to-full-cost payments toward a deductible. PrEPDAP can also cover the full cost, if necessary, for individuals who lack health insurance.)
- Prescribe TDF/FTC—Can be done at first visit or at a second visit if student wants to think about it.
    - Medication can be started while awaiting HIV results.
    - Provide prescription for 90 days if allowed by insurance or 30 days with 2 refills.
    - Discuss strategies for taking the medication daily.
    - It can take up to 3 weeks for medication to reach adequate levels in all body compartments:
        - Rectal: 7-10 days
        - Vaginal: 21 days
        - Plasma: 21 days

Second Visit if Needed

- Review test results.
- Prescribe TDF/FTC—see above.
- Review strategies for taking medication daily.
- Review length of time until it is effective.
- Review importance of consistent condom use.

Follow Up Visits

- First follow up in 30 days.
    - Assess compliance.
    - Assess side effects.
    - Problem solve barriers to compliance.
- Subsequent follow ups every 3 months approximately—be flexible and accommodating.
    - Students should be seen approx. every 3 months. Consider sending students reminders 2-3 weeks before refill needed.
    - Assess sexual behavior and brainstorm strategies for safer sex as appropriate.
    - Assess general health, medication compliance, and side effects.
    - Follow up labs:
        - 4th generation HIV test at every visit.
        - Pregnancy test if applicable.
        - Cr and E-GFR every 6-12 months.
    - STI testing (chlamydia, gonorrhea, and syphilis) every 3-6 months depending on level of high risk activity. Remember to test all affected sites—urine, throat and anal.
    - Periodically assess level of ongoing risk and whether student wishes to continue PrEP.

For Additional Assistance

CDC PrEP Hotline: 855-448-7737

UCSF PrEP Consultation Service for Clinicians: http://nccc.ucsf.edu

Appendix B: Checklist for Initiating PrEP

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 bacterial 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+)
- TDF/FTC treats HBV; stopping may cause "flare"[§]

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

eCrCl must be ≥ 60 mL/min by Cockcroft-Gault
- TDF/FTC 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**
  - Vaginal self-collect or cervix in women and urine/urethra in men – also 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"
- 1 in 5 patients develop mild headaches, nausea, or flatulence which resolve within 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: TDF/FTC, 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: TDF/FTC, 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
- ❑ Screen for STIs**

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" third generation 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.

** STI testing every 3 months for sexually active persons who are symptomatic or asymptomatic MSM at high risk for recurrent bacterial STIs (e.g., those with syphilis, gonorrhea, or chlamydia at prior visits or multiple sex partners).

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 TDF/FTC-based PrEP • **Patients with impaired renal function should not be prescribed TDF/FTC.** Dose adjustment of TDF/FTC 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 TDF/FTC 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 TDF/FTC. (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 TDF/FTC, 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") - baseline testing
	  ○ who have ever injected drugs (with or without shared equipment) - annual testing for PWID
	  ○ who have ever snorted drugs (implements are often shared) having sex of any kind that results in visible mucosal or tissue bleeding – annual
	  ○ 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) - annua

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