HIV prevention: A 3-pronged approach

HIV infection may not command the headlines it once did, but the public health threat it poses is still formidable. These steps can help us get ahead of it.

Despite advances in human immunodeficiency virus (HIV) screening and treatment over the last 30 years, HIV remains a public health concern. In the United States, after an initial decline, total HIV incidence has failed to significantly decrease in the last 25 years. More than 1.2 million people are living with HIV in the United States, and 12.8% of them (156,300) are unaware they are affected. Of those diagnosed with HIV, only 30% are receiving treatment and are virally suppressed. Due to structural inequalities and psychosocial factors, African American and Latino patients remain disproportionately affected. The incidence of HIV infection among men who have sex with men has increased, and the incidence of HIV infection among people who inject drugs has plateaued after years of progressive decline.

HIV prevention strategies are highly effective, but in general are underutilized. This article reviews 3 prevention strategies that can be administered by family physicians: HIV screening, pre-exposure prophylaxis (PrEP), and harm reduction.

Who and how to screen for HIV

Early identification of HIV infection generally leads to reduced transmission because diagnosis is associated with decreases in risky behavior. In addition, antiretroviral therapy (ART) is more effective when initiated early, before the development of advanced immunosuppression.

The “window period” of acute HIV infection (AHI) is the time from when the virus is transmitted to when markers of infection can be detected. Because this window period is associated with high viral transmission rates, family physicians must be familiar with symptoms of AHI and associated risk factors (eg, recent condomless sex or sharing of drug injection equipment with someone who is HIV-positive or of unknown HIV status).

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Screening for HIV solely based on the presence of risk factors or clinical symptoms is not enough, however. The United States Preventive Services Task Force (USPSTF) recommends screening all pregnant women and individuals ages 15 to 65 for HIV. Screening based solely on risk factors or clinical symptoms frequently leads to missed diagnoses and identification of HIV infection at more advanced stages. Both the USPSTF and the Centers for Disease Control and Prevention (CDC) recommend universal opt-out screening (patients are informed that HIV screening will be performed and that they may decline testing) because such screening identifies HIV earlier and is associated with higher testing rates than opt-in screening, which requires explicit written consent and extensive pre-test counseling.

Which test to use. HIV screening with a fourth-generation antigen/antibody combination immunoassay—which detects both HIV p24 antigen and HIV antibodies—provides greater diagnostic accuracy than older tests. These newer tests detect HIV approximately 15 days after initial infection, reducing the window period of AHI. If you suspect a patient has AHI, consider early repeat HIV testing with a fourth-generation assay, or initial co-testing with a fourth-generation assay and a nucleic acid amplification test for HIV RNA, which makes it possible to detect infection approximately 5 days earlier than fourth-generation assays.

Offer pre-exposure prophylaxis to high-risk patients
PrEP is the use of ART prior to HIV exposure to prevent transmission of the virus. It should be used with conventional risk reduction strategies, such as providing condoms, counseling patients about reducing risky behaviors, supporting medication adherence, and screening for and treating other sexually transmitted infections.

The US Food and Drug Administration (FDA) has approved only one medication, Truvada (tenofovir disoproxil fumarate/emtricitabine; TDF/FTC), for use as PrEP. Oral tenofovir-based regimens can effectively prevent HIV transmission, and strong adherence is associated with a risk reduction of 90% to 100%. The protective effect of oral PrEP is particularly strong in high-risk populations (eg, men who have sex with men, people who inject drugs), where the number needed to treat to prevent one HIV infection ranges from 12 to 100, depending on the patients’ risk profile. The CDC and Department of Health and Human Services have issued guidelines for using PrEP in high-risk patients.

Barriers to implementing PrEP. Despite being highly effective, PrEP is not routinely prescribed to high-risk patients; modeling suggests that current use of PrEP is insufficient to significantly impact the incidence of HIV. Demand for PrEP is high among target groups, but patients have expressed concerns about adverse effects and stigma related to ART, HIV, and being at risk for HIV. Young age, lack of social support, low perception of risk, and failure to show up for appointments are also barriers to PrEP use.

Some physicians have expressed concern that prescribing PrEP may promote high-risk sexual behavior. However, because PrEP is most beneficial in individuals who already engage in high-risk sexual behavior, strategic delivery of PrEP remains an effective risk-reducing strategy. Even in instances where PrEP has been associated with higher-risk sexual behavior and higher rates of sexually transmitted infections, it still prevents as much as 100% of new HIV infections.

Fear of drug resistance also contributes to slow implementation of PrEP. Drug resistance has been observed in clinical trials of PrEP, but...
it has been exceedingly rare and predominantly limited to patients who had unrecognized AHI when they started PrEP.39 Furthermore, the few cases of drug resistance attributable to PrEP pale in comparison to the large number of estimated HIV infections averted—infections that would require lifelong ART with its own associated risks of drug resistance. By decreasing HIV transmission, PrEP is expected to decrease total drug resistance.40

Cost is another obstacle. Truvada costs approximately $1,540 per month.41 However, analysis has demonstrated that PrEP is cost-effective when targeted to high-risk patients.42 Most insurance plans cover PrEP, but often require high deductibles and copays; fortunately, this financial burden for patients can be mitigated or eliminated by co-pay assistance programs. The manufacturer of Truvada offers assistance programs for both insured and uninsured patients who are candidates for PrEP; details are available at http://www.truvada.com/truvada-patient-assistance.

Stigma has historically burdened individuals who seek to protect their sexual health, including HIV-negative individuals who are candidates for PrEP. Stigma surrounding HIV may decrease ART-based HIV prevention in men who have sex with men,43 while increasing high-risk behaviors44 and all-cause mortality.45

The resources listed in TABLE 2 can help physicians overcome some of the barriers to implementing PrEP.

### How to deliver PrEP

Whether HIV specialists or primary care clinicians are best suited to provide PrEP is a subject of debate. HIV specialists are most familiar with ART and routine monitoring of adherence; however, they have less access to HIV-negative patients, who are the target group for PrEP.35 Family physicians tend to work in closer proximity and maintain longitudinal relationships with PrEP target groups, but in general have less experience with ART and evaluating AHI. Some may argue that competing demands may make it impractical to take a detailed sexual history during a primary care visit.46 In truth, both HIV specialists and family physicians can be appropriately equipped to provide PrEP.

**TABLE 3** outlines the steps necessary to provide a patient with PrEP.47 Assessing risk is the initial step; PrEP is beneficial for patients who have one or more risk factors for HIV infection. To be eligible for TDF/FTC, a patient must be HIV-negative, and should be tested for hepatitis B virus (HBV) infection and kidney disease. Because TDF/FTC treats HBV infection, candidates for PrEP who test positive for HBV should be evaluated for treatment of HBV before initiating PrEP. Candidates for PrEP who test negative for HBV infection and immunity should be vaccinated.

Candidates for PrEP should also be screened and monitored for kidney disease. TDF can cause increased serum creatinine due to tubular toxicity. A patient who has an estimated creatinine clearance <60 mL/min should not receive TDF/FTC for PrEP. If a patient’s estimated creatinine clearance falls below 60 mL/min or serum creatinine increases by 0.3 mg/dL above baseline after PrEP is started, TDF/FTC should be discontinued, and the patient should be evaluated for the underlying cause of the kidney disease.27

### TABLE 2

**Resources for implementing pre-exposure prophylaxis for HIV**

<table>
<thead>
<tr>
<th>Resource</th>
<th>Contact information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinician Consultation Center PrEPline</td>
<td>855-448-7737 (11 am-6 pm EST) <a href="http://nccc.ucsf.edu/2014/09/29/introducing-the-ccc-prepline/">http://nccc.ucsf.edu/2014/09/29/introducing-the-ccc-prepline/</a></td>
</tr>
<tr>
<td>North Carolina AIDS Training and Education Center</td>
<td><a href="http://www.med.unc.edu/ncaidtraining/prep/for-providers/for-prep-prescribers">http://www.med.unc.edu/ncaidtraining/prep/for-providers/for-prep-prescribers</a></td>
</tr>
<tr>
<td>Centers for Disease Control and Prevention</td>
<td><a href="http://www.cdc.gov/hiv/risk/prep/index.html">www.cdc.gov/hiv/risk/prep/index.html</a></td>
</tr>
</tbody>
</table>

HIV, human immunodeficiency virus.
Before starting PrEP, candidates should be screened for HIV infection and symptoms of AHI. Strongly consider testing for sexually transmitted infections that may increase the risk of HIV transmission, such as syphilis, gonorrhea, or chlamydia.

Candidates who are eligible for PrEP must be counseled on medication adverse effects, adherence strategies, and symptoms of sexually transmitted infections. To initiate PrEP, candidates may be given a one-month supply of TDF/FTC; adherence, adverse effects, and other risk-reduction strategies are assessed at an office visit 3 to 4 weeks later. Subsequent prescriptions are then dispensed as a 3-month supply, with office visits to monitor PrEP scheduled for at least once every 3 months. During these monitoring visits, evaluate the patient’s HIV status, pregnancy status, adherence, adverse effects, risk-reduction behav-

### TABLE 3
Step-by-step checklist for initiating pre-exposure prophylaxis for HIV

#### Step 1: Assess risk

**Risks for sexual transmission**
- Condomless sex in prior 6 mo
- Any STI diagnosed in prior 6 mo
- Not in a monogamous relationship with partner confirmed to be HIV-negative
- Relationship with HIV-positive partner(s)
- Commercial sex work

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

#### Step 2: Determine clinical eligibility

**Within 30 days before starting PrEP, check viral hepatitis status and renal function:**

- Hepatitis B surface antigen (sAg)
- Hepatitis B surface antibody (sAb)
- Serum creatinine
- eCrCl
- Urinalysis (to establish baseline)

**Must be hepatitis B sAg negative**
- Truvada (tenofovir disoproxil fumarate/emtricitabine) treats hepatitis B virus; stopping can cause "flare"
- eCrCl must be ≥60 mL/min (by Cockcroft-Gault equation)

**Within 7 days before starting PrEP, test for HIV infection**

**Test for HIV with ONE of the following:**
- HIV RNA (viral load)
- Antigen/antibody combination assay (4th generation)
- Rapid test with fingerstick blood
- Traditional blood test with ELISA (EIA) and reflexive confirmatory testing

**Must be HIV negative**
- Preference for HIV RNA (viral load) or 4th generation Ag/Ab assay; both can detect early HIV infection
- Do NOT rely on oral rapid testing; sensitivity lower than with blood

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

**No symptoms of 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)

See footnotes on facing page.
ors, and indications for continued PrEP. Every 6 months, renal function and sexually transmitted infection status should be reassessed.

Reducing risk of harm among patients who inject drugs
Nonsexual transmission of HIV is a route of high infectivity. It includes transfusion of infected blood, sharing of equipment during injection drug use, and percutaneous needle sticks. Sharing of equipment during injection drug use is estimated to account for 8% of new infections in the United States.4

Harm reduction is a collection of strategies meant to reduce complications of illicit drug use, including HIV transmission. These strategies include needle and syringe programs that provide injection drug users with sterile equipment, and opioid substitution therapy.

Needle and syringe programs decrease HIV transmission and risky behaviors related...
TABLE 4
Harm reduction training and support resources

<table>
<thead>
<tr>
<th>Resource</th>
<th>URL</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Harm Reduction International</td>
<td><a href="http://www.ihra.net/north-america-harm-reduction-programmes">http://www.ihra.net/north-america-harm-reduction-programmes</a></td>
<td>Education and advocacy related to harm reduction</td>
</tr>
<tr>
<td>Substance Abuse and Mental Health Services Administration</td>
<td><a href="http://www.samhsa.gov/medication-assisted-treatment">http://www.samhsa.gov/medication-assisted-treatment</a></td>
<td>Guidance for training and obtaining the waiver necessary to be able to prescribe buprenorphine products in any settings in which you are qualified to practice</td>
</tr>
<tr>
<td>Providers’ Clinical Support System for Medication Assisted Treatment</td>
<td><a href="http://pcssmat.org/">http://pcssmat.org/</a></td>
<td>Training and mentoring program for medication assisted treatment of opioid misuse</td>
</tr>
</tbody>
</table>

In clinical trials of pre-exposure prophylaxis, drug resistance has been rare and mostly limited to those who had unrecognized acute HIV infection.

References

34. Thigpen MC, Kebaabetswe PM, Paxton LA, et al. Antiretroviral
38. Henderson FL, Taylor AW, Chirwa LI, et al. Characteristics and
42. Gomez GB, Borquez A, Case KK, et al. The cost and impact of
43. Murnane PM, Celem C, Mugo N, et al. Efficacy of preexposure prophylaxis for HIV-1 prevention among high-risk heterosexuals:
45. Buchbinder SP, Gildden DV, Liu AY, et al. HIV pre-exposure prophylaxis in men who have sex with men and transgender women:
47. Grant RM. Scale-up of preexposure prophylaxis in San Francisco to impact HIV incidence. Abstract 25. Paper presented at Conference on Retroviruses and Opportunistic Infections; February 23-26, 2015; Seattle, WA.