

## Perspective

# HIV Preexposure Prophylaxis in the Real World

*According to evolving guidelines, candidates for HIV preexposure prophylaxis (PrEP) include HIV-uninfected men who have sex with men who engage in condomless anal intercourse, individuals in HIV-serodifferent sexual relationships, those with frequent anogenital sexually transmitted infections, and those who have received repeated nonoccupational postexposure prophylaxis treatment courses. In the real-world setting, indications for PrEP and management of PrEP candidates and patients may be less than clear-cut. Factors to be considered when assessing candidacy for PrEP and maximizing efficacy of treatment are discussed. This article summarizes a presentation by Demetre C. Daskalakis, MD, MPH, at the IAS–USA continuing education program held in Los Angeles, California, in April 2014.*

**Keywords:** HIV, risk behavior, serodiscordant, serodifferent, preexposure prophylaxis, PrEP, tenofovir, emtricitabine

Preexposure prophylaxis (PrEP) for HIV is not intended as a lifelong intervention, but rather a temporary method of increasing the chances of prevention of HIV acquisition during phases of increased high-risk behaviors. Although guidelines vary, potential candidates for PrEP include the following HIV-uninfected individuals: men who have sex with men (MSM) who engage in unprotected anal intercourse; individuals in a sexual relationship with an HIV-infected partner; transgender individuals engaging in high-risk sexual behaviors; individuals engaging in transactional sex; injection drug users engaging in injection-related or sexual risk behaviors; users of stimulant drugs, such as methamphetamine, that are associated with high-risk behaviors; individuals diagnosed with more than 1 anogenital sexually transmitted infection (STI) in the previous year; and individuals who have received nonoccupational postexposure prophylaxis (nPEP) but continue to engage in high-risk behaviors or have received repeated nPEP treatment courses (Table 1).<sup>1</sup>

Dr Daskalakis is Associate Professor of Medicine at Icahn School of Medicine at Mount Sinai in New York, New York.

### Case 1: Continued Exposures

Patient 1 is a 27-year-old man who visits his primary care practitioner to discuss his risk for HIV infection. He states that he engages in behaviors that place him at high risk for acquisition of HIV and other STIs. He confides that he sometimes engages in condomless anal sex with men, often anonymously and in the context of drug use. He has received 3 courses of nPEP in the past year and was diagnosed with rectal lymphogranuloma venereum

2 months ago and rectal gonorrhea a few weeks before that. The patient asks his physician about the possibility of starting PrEP. He has heard in the news that there is a daily pill that could lower his risk for HIV infection. The physician must consider whether this patient is a candidate for PrEP.

Patient 1 meets several PrEP candidacy criteria, including the recent diagnosis of more than 1 anogenital STI. Studies in San Francisco, California, have shown that risk of HIV infection increases 8-fold for MSM with 2 prior rectal chlamydial or gonococcal infections and that the annual incidence of HIV infection was 15 per 100 person-years among MSM with an average of 1 rectal infection per year.<sup>2</sup> Studies in New York City indicate an annual HIV infection incidence of 6.7% in MSM diagnosed with rectal STIs compared with 2.5% in MSM who did not have rectal STIs.<sup>3</sup>

The patient is also a candidate for PrEP on the basis of his having received repeated courses of nPEP, an indicator that his risk behaviors are ongoing. Data from studies in Amsterdam indicate a high frequency of HIV seroconversions following nPEP, owing not

**Table 1.** HIV-Uninfected Individuals Meeting Criteria for PrEP

- MSM who engage in unprotected anal sex
- Individuals in HIV-serodifferent sexual relationships
- Transgender individuals who engage in high-risk sexual behaviors
- Individuals who engage in transactional sex (eg, provide sex in exchange for money, drugs, housing, etc)
- IDUs who report:
  - Sharing injection equipment, including to inject hormones
  - Injecting 1 or more times per day
  - Injecting cocaine or methamphetamine
  - Engaging in high-risk sexual behaviors
- Individuals who use stimulant drugs (eg, methamphetamine) associated with high-risk behaviors
- Individuals diagnosed with more than 1 anogenital STI in the past year
- Individuals who have been prescribed nPEP who continue to engage in high-risk behaviors or have taken repeated courses of nPEP

Abbreviations: IDU, injection drug user; MSM, men who have sex with men; nPEP, nonoccupational postexposure prophylaxis; PrEP, preexposure prophylaxis; STI, sexually transmitted infection. Adapted from New York State Department of Health.<sup>1</sup>

to nonadherence or a lack of efficacy but to continuation of risk activity after the nPEP treatment course. One study showed that 8 of 11 seroconversions among nPEP users occurred more than 3 months after they received nPEP.<sup>4</sup> Another study showed 5 seroconversions out of 239 nPEP users, all occurring late in follow-up.<sup>5</sup>

The patient's physician is unsure about using tenofovir disoproxil fumarate and emtricitabine for PrEP. He has never prescribed this medication and is uncomfortable with the patient's revelation that he engages in ongoing condomless sex, and he believes that prescribing PrEP would be condoning the patient's risk behavior. Further, he does not believe that the protective efficacy of PrEP is as great as that of other protective treatments used for other disease states in his practice, such as statins to prevent cardiovascular events. He guides the patient away from considering PrEP but offers to refer him to an HIV specialist for further discussion of the intervention.

Using malaria as an example of an infection for which we have experience providing chemoprophylaxis, 2 models may exist for infection prevention. Unfortunately, the physician in this case was embracing an unhelpful model of infection prevention. In this model, the answer to the question "When traveling to parts of the world where malaria can be contracted, how can this be avoided?" might be something like "Always use bed nets, avoid mosquito exposure, and never leave your hotel." Extrapolating this to HIV prevention, the answer to "When in a behavioral or epidemiologic environment where HIV infection risk is high, how can this risk be reduced?" might be "Always use condoms, have only 1 sexual partner, and do not have sex with an HIV-infected partner." A more reasonable and realistic model might answer the first question for malaria with "Use bed nets, avoid mosquitoes as much as possible, and take antimalarial medications as malaria preexposure prophylaxis" and the second question with "Use condoms, but if condoms are not used consistently or at all, talk to a physician about HIV

medications that may help to prevent the acquisition of HIV infection."

The physician should confirm to the patient that PrEP is a reasonable choice and should heavily emphasize the need for strict adherence to a PrEP regimen, because the degree of adherence dictates the degree of efficacy. In the iPrEx (Chemoprophylaxis for HIV Prevention in Men) trial, there was a 44% reduction in HIV acquisition with the use of tenofovir and emtricitabine, in a modified intent-to-treat analysis. However, in a case-control study of the iPrEx population, analysis showed a 92% reduction in risk in patients with detectable intracellular tenofovir diphosphate levels. PrEP, like antiretroviral therapy for chronic HIV infection, works when it is taken. This finding is consistent across PrEP studies, with a higher percentage of patients with blood samples showing detectable levels of tenofovir correlating with higher protective efficacy rates in randomized comparisons—81% and 75%, respectively, in the Partners PrEP study; 79% and 62%, respectively, in the TDF2 study; 51% and 44%, respectively, in the iPrEx study; and only 26% and 6%, respectively, in the FEM-PrEP (Preexposure Prophylaxis Trial for HIV Prevention among African Women) study.<sup>6-9</sup>

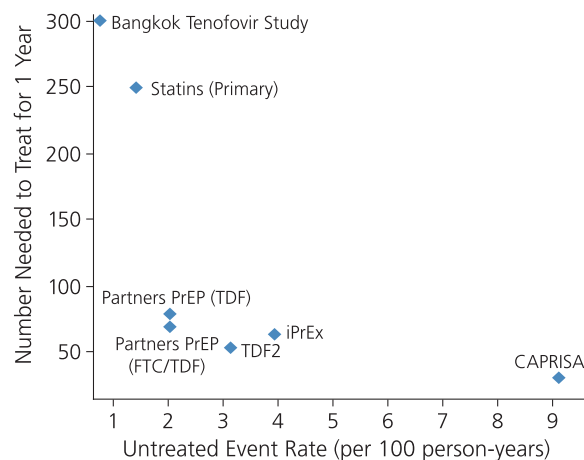
Nonadherence to a PrEP regimen lowers the barrier to acquisition of HIV infection. Physicians should be mindful of this and patients should be reminded of this, particularly in light of the finding that there appears to be no change in risk behaviors in many patients taking PrEP. In the iPrEx study, for example, there was no marked change in condom use between patients who perceived themselves to be taking a placebo and those who perceived themselves to be taking PrEP.<sup>10</sup> Physicians should not expect to see large reductions or increases in risk behaviors among patients taking

PrEP. Risk-reduction counseling and risk assessment should be part of every PrEP-related office visit.

Finally, there is the concern of the physician in this case that PrEP does not have the preventive efficacy of other treatments, such as statins, that he routinely prescribes in practice. As shown in Figure 1, the number of patients needed to treat for 1 year to prevent 1 HIV infection is smaller in trials of HIV PrEP than the number needed to treat with statins in primary prevention to prevent 1 cardiovascular event, suggesting that PrEP is indeed an efficient but costly intervention, at \$8,000 to \$14,000 per year.<sup>11</sup>

The patient in this case visits an HIV specialist, who reviews the patient's risk and decides that a PrEP regimen of tenofovir and emtricitabine is a potentially good intervention to supplement barriers to HIV infection and STIs, as long as the patient is medically cleared to start PrEP. The patient then reports that he engaged in condomless receptive anal sex 3 weeks ago with a partner whose HIV serostatus is unknown.

Baseline HIV testing is part of the prescription evaluation of all patients being considered for PrEP. Considerations for prescription



**Figure 1.** Number of patients needed to treat for 1 year to prevent 1 case of HIV acquisition in preexposure prophylaxis (PrEP) trials or 1 cardiovascular event with statin use for primary prevention. CAPRISA indicates Center for the AIDS Program of Research in South Africa; FTC, emtricitabine; iPrEx, Chemoprophylaxis for HIV Prevention in Men; TDF, tenofovir disoproxil fumarate. Adapted with permission from Glidden.<sup>11</sup>

**Table 2.** Preprescription Considerations for PrEP

Education	Assessment	Laboratory
<ul style="list-style-type: none"> <li>■ Teach how PrEP works</li> <li>■ Define the limits of PrEP               <ul style="list-style-type: none"> <li>□ Adherence</li> <li>□ Lack of protection against STIs</li> <li>□ Does not offer 100% protection against HIV</li> </ul> </li> <li>■ Reinforce daily dosing of PrEP</li> <li>■ Review adverse effects</li> <li>■ Discuss the long-term safety of PrEP in HIV-seronegative individuals</li> <li>■ Confirm a schedule for follow-up and testing, especially HIV testing every 90 days</li> <li>■ Review stopping criteria for PrEP               <ul style="list-style-type: none"> <li>□ Positive HIV test result</li> <li>□ Renal disease</li> <li>□ Nonadherence</li> <li>□ Change in risk-taking behavior</li> </ul> </li> <li>■ Teach about symptoms of acute HIV infection</li> <li>■ Discuss with women:               <ul style="list-style-type: none"> <li>□ How PrEP can help prevent HIV infection acquisition during pregnancy</li> <li>□ Potential but undemonstrated risk of birth defects</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>■ Screen for symptoms of acute HIV infection within the past 6 weeks</li> <li>■ Review medication list               <ul style="list-style-type: none"> <li>□ Are there any potential interactions or synergistic toxicities?</li> </ul> </li> <li>■ Assess mental health and substance use</li> <li>■ Explore patient knowledge of PrEP and motivation for initiating medication</li> <li>■ Evaluate willingness to take PrEP daily</li> <li>■ Is the patient connected to primary care?</li> <li>■ Is patient involved with HIV-seropositive sexual partners?               <ul style="list-style-type: none"> <li>□ Are any HIV-seropositive sexual partners taking antiretroviral therapy?</li> <li>□ Are resistance data available?</li> </ul> </li> <li>■ Screen for domestic violence</li> <li>■ Assess housing status</li> <li>■ Does patient have the means to pay for PrEP?</li> <li>■ Evaluate fertility goals and contraception use in women who are PrEP candidates</li> </ul>	<ul style="list-style-type: none"> <li>■ Baseline HIV testing               <ul style="list-style-type: none"> <li>□ Third- or fourth-generation HIV test</li> <li>□ NAAT for HIV in:                   <ul style="list-style-type: none"> <li>– Patients with symptoms of acute HIV infection</li> <li>– Patients whose HIV antibody test results are negative but who have reported engaging in unprotected sex with an HIV-infected partner within the past month</li> </ul> </li> </ul> </li> <li>■ Drug-resistant HIV has been observed in patients with undiagnosed HIV infection taking a PrEP regimen of tenofovir and emtricitabine</li> <li>■ Basic metabolic panel               <ul style="list-style-type: none"> <li>□ PrEP should not be initiated for patients with a creatinine clearance &lt;60 mL/min</li> </ul> </li> <li>■ Urinalysis               <ul style="list-style-type: none"> <li>□ Proteinuria can be an early warning sign of tenofovir toxicity</li> <li>□ Baseline urinalysis should be used to identify any preexisting proteinuria</li> </ul> </li> <li>■ Serologies for hepatitis A, B, and C viruses               <ul style="list-style-type: none"> <li>□ Immunize patients against hepatitis A and B viruses as needed</li> </ul> </li> <li>■ STI screening               <ul style="list-style-type: none"> <li>□ NAAT for gonococcal and chlamydial infection; 3-site screening (genital, rectal, pharyngeal)</li> <li>□ Rapid plasma reagin test for syphilis</li> </ul> </li> <li>■ Pregnancy testing               <ul style="list-style-type: none"> <li>□ If a woman is pregnant when starting PrEP or becomes pregnant while taking PrEP, known risks and benefits should be discussed</li> </ul> </li> </ul>

Abbreviations: NAAT, nucleic acid amplification test; PrEP, preexposure prophylaxis; STI, sexually transmitted infection. Adapted from New York State Department of Health.<sup>1</sup>

education and evaluation are shown in Table 2. Important components of education include informing patients about the nature and limitations of PrEP, stressing the need for adherence, and ensuring that the patient understands that treatment is part of a larger package that includes HIV testing, with the invitation to visit every 3 months for repeat testing, and STI prevention, testing, and treatment. Potential adverse effects of treatment with tenofovir and emtricitabine, including bone and kidney effects, should be considered. Fertility goals and potential embryo-fetal toxicity should be discussed with patients when appropriate. Clinical evaluation includes screening for symptoms of acute HIV infection, review of current medications for potential drug interactions and augmented toxicity, and assessment of a patient's motivation for taking PrEP, mental health, substance use status, and status with regard to

such psychosocial factors as stable housing and domestic violence. Laboratory evaluation includes assessment of kidney function, urinalysis to identify preexisting proteinuria (proteinuria may be an early sign of tenofovir renal toxicity), STI screening, viral hepatitis serology (including ensuring that patients are up to date with their vaccinations), and pregnancy testing. With regard to HIV testing, current PrEP preprescription guidelines state that nucleic acid amplification testing for HIV viral load should be performed in patients with symptoms of acute HIV infection and in those with a negative HIV antibody test who report engaging in unprotected sex with an HIV-infected partner in the past month.<sup>1</sup> It is important for physicians and patients to know that drug-resistant HIV has been found in patients with undiagnosed HIV infection who were taking a PrEP regimen of tenofovir and emtricitabine.

For the patient in this case, the HIV specialist performs HIV viral load testing, which shows no evidence of infection, and attempts to get approval from the patient's insurance company to initiate PrEP. However, the insurance company denies coverage on the basis of the treatment's being "not medically necessary." The insurance company's statement notes that "as per health plan criteria for tenofovir and emtricitabine, coverage cannot be approved at this time. This drug cannot be approved if recent exposure (less than a month) to the HIV virus is not suspected." The HIV specialist responds by engaging the insurance company in a discussion and ultimately gaining approval for the treatment. Responses such as this from insurance companies have become somewhat less common in practice. However, it is important for physicians to note that some barriers do exist to obtaining coverage for PrEP and that an aggressive approach may



be necessary in order to incorporate PrEP into a practice.

### Cases 2 and 3: “Risk Vacation” or Pregnancy

Patient 2 is a 35-year-old, HIV-seronegative man who uses condoms 100% of the time when home in Los Angeles, California, but once a year he goes on vacation to Palm Springs, California, where he engages in condomless insertive and receptive anal sex. He foresees numerous possible exposures to HIV infection while on vacation. Patient 3 is a 35-year-old, HIV-seronegative woman who wants to have a baby with her HIV-seropositive husband. She does not intend to use any fertility technology to become pregnant. Her husband has undetectable HIV RNA levels, and they use condoms but are planning to stop using them in order to achieve their fertility goal. Both patient 2 and patient 3 want advice on PrEP from their physicians.

From an appropriately nonjudgmental medical point of view, these individuals are likely to have biologically similar exposures to HIV, notwithstanding the difference (pleasure vs fertility) in psychosocial context. Are they candidates for PrEP? If so, how should PrEP be managed in such settings?

Extant data indicate that PrEP works very well for heterosexual serodifferent couples. The Partners PrEP study showed a preventive efficacy rate of 66% among women and 84% among men taking tenofovir and emtricitabine.<sup>7</sup> Outside the context of serodifferent couples, PrEP also works well in the setting of heterosexual high-risk individuals and partners of unknown HIV serostatus. Results of the TDF2 trial examining HIV-seronegative individuals in Botswana revealed a 62% protective efficacy rate among men and women (combined) taking regimens of tenofovir and emtricitabine.<sup>8</sup>

It is important to note that there have also been disappointing results in PrEP studies—notably, in the FEM-PrEP and VOICE (Microbicide Trials Network-003 Vaginal and Oral Interventions to Control the Epidemic)

studies of high-risk HIV-seronegative African women. The FEM-PrEP study was stopped early owing to the lack of efficacy of tenofovir and emtricitabine; assessment of tenofovir levels in blood suggested an adherence rate of less than 40%, too low to allow assessment of efficacy.<sup>9</sup> The oral tenofovir and vaginal tenofovir gel arms in the VOICE study were also discontinued early owing to a lack of efficacy, and the oral tenofovir and emtricitabine arm showed no protective efficacy. As in the FEM-PrEP study, poor adherence also explained the lack of efficacy observed in the VOICE trial, and no relationship was found between reported adherence and tenofovir levels in blood.

These findings drive home the need for strong support of adherence for patients taking PrEP. In the setting of HIV infection, many clinics have resources and staff specifically devoted to supporting patients' adherence goals. The same level of resources does not exist in the preventive setting, and it is thus incumbent on physicians and partnerships with community-based organizations to generate and maintain support.

In considering how long before HIV exposure tenofovir and emtricitabine should be started, it is useful to know that protective drug levels do not necessarily depend on achievement of steady state blood levels. It takes between 4 and 7 half-lives for a drug to reach steady state. The intracellular half-life of tenofovir is 150 hours, indicating that achieving steady state takes approximately 25 days.<sup>12</sup> The intracellular half-life of emtricitabine is 39 hours, indicating that achieving steady state takes approximately 6 days.<sup>13</sup> However, efficacy may be achieved in the absence of steady state conditions if a drug reaches sufficiently high concentrations within a short time and those concentrations are maintained throughout the period of exposure to HIV. After oral administration of a single 300 mg dose of tenofovir, maximum tenofovir concentration is reached in approximately 2 hours.<sup>12</sup> Similarly, emtricitabine is rapidly absorbed and reaches maximum concentration in 1 hour to 2 hours.<sup>13</sup>

Dosing after exposure to HIV is also important, although when to stop tenofovir and emtricitabine dosing after exposure is less clear; guidelines for nPEP indicate that 28 days of treatment are needed for efficacy.<sup>14,15</sup>

In the absence of definitive data and guidance, a reasonable approach for the individuals in these 2 cases and others in similar settings is to start PrEP at least 1 week before a planned HIV exposure. If it is possible, starting PrEP 1 month before a planned HIV exposure makes sense given the steady state kinetics of PrEP drugs, particularly tenofovir. In extrapolation from the nPEP guidelines, PrEP should be continued for at least 28 days after the last HIV exposure. Further, continuation of PrEP should be discussed with both of these patients, given the potential for unplanned exposures; depending on their actual risk, they may be candidates for longer-term PrEP.

### Case 4: Monogamous HIV-Serodifferent Sexual Partners

Patient 4 is an HIV-seronegative man in a monogamous relationship with his HIV-seropositive husband. His husband has a CD4+ cell count of 688/ $\mu$ L and his plasma HIV RNA level has been below 20 copies/mL for several years on antiretroviral therapy. The patient is tired of using condoms for insertive anal sex but uses condoms for all receptive anal sex. He wants to know if he should be taking PrEP.

The issue raised by this case is how PrEP fits into prevention efforts, given the success of treatment as prevention; that is, is PrEP indicated in the setting of a monogamous HIV-serodifferent relationship (same sex or heterosexual) if there is a decreased risk of transmission associated with viral suppression in the HIV-infected partner?

Data showing the efficacy of treatment as prevention come from the HIV Prevention Trials Network 052 trial, in which 1763 HIV-serodifferent couples were randomized to have the HIV-infected partner initiate antiretroviral therapy immediately or, according to then-current guidelines, when their

CD4+ cell count dropped below 250/ $\mu$ L or they developed other indications. Of the 28 linked transmissions of HIV infection observed in the study, only 1 occurred in the immediate treatment arm, a case in which the HIV-infected patient had not been taking antiretroviral therapy for long and still had detectable virus. The reduction in HIV acquisition was 96% with immediate treatment. However, HIV-serodifferent couples of MSM accounted for only 3% of couples in the trial, raising questions about the applicability of the findings to the MSM population.<sup>16</sup>

The PARTNER study, however, included 16,400 occasions of unprotected sex among 767 couples of MSM.<sup>17</sup> The HIV-infected partner had to be taking antiretroviral therapy and have an HIV RNA level of less than 200 copies/mL. Estimated rates of HIV transmission based on sexual behavior reported by the HIV-uninfected partners were 0 per 100 couple-years of follow-up among women who engaged in heterosexual vaginal sex with ejaculation (total, 192 couple-years); among men who engaged in heterosexual vaginal sex (total, 272 couple-years); and among MSM who engaged in receptive anal sex with ejaculation (total, 93 couple-years), receptive anal sex without ejaculation (total, 157 couple-years), and insertive anal sex (total, 262 couple-years). These data, however, should not be interpreted as indicating an absence of risk. The upper bound of the 95% confidence interval for the point estimates of risk imply that although the incidence of HIV infection was 0, the probability of infection may not be. These bounds were highest for MSM who engaged in receptive anal sex with ejaculation, followed by MSM who engaged in receptive anal sex without ejaculation, women who engaged in heterosexual vaginal sex with ejaculation, and men who engaged in heterosexual vaginal sex or MSM who engaged in insertive anal sex. Although sex with a virologically suppressed partner is likely low risk, it is not statistically correct to call it zero risk.

It is unclear whether patient 4 requires or should receive PrEP, given the protective effect of antiretroviral

therapy in his partner and the patient's 100% use of condoms for receptive anal sex. Given the current available data, it is possible that PrEP is not necessary in this setting.


### Case 5: PrEP Stigma

Patient 5 is a 23-year-old African American male who presents to a physician to be treated for syphilis. The patient states that he is heterosexual but sometimes has sex with other heterosexual men. He also states that he does not use condoms when engaging in anal sex because his older partners prefer it that way. The physician attempts to discuss PrEP with the patient, but the patient indicates that he does not think he needs it. He thinks PrEP is only for homosexual men and not for him.

It is clear that there are patient-level barriers to PrEP, including a stigma attached to its use. In addition, there appears to be substantial denial or lack of knowledge in some at-risk individuals' assessment of their own risk level. Daskalakis and colleagues recently surveyed individuals attending commercial sex venues in New York City (eg, bath houses and sex clubs) regarding whether they believed their risk for HIV infection was high enough to make them candidates for PrEP.<sup>18</sup> Because the study began before there were established guidelines for PrEP, iPrEx trial entry criteria were used to assess candidacy. Of the 511 men surveyed, 377 (73%) met these criteria and were thus PrEP candidates. Of these 377, only 84 (22%) believed HIV infection risk was sufficient to warrant PrEP.

### Conclusion

Like many innovations in the realm of HIV medicine, technology has outpaced both implementation and social norms. With condoms being the only biomedical intervention available to HIV-uninfected individuals, PrEP has challenged the dogma of HIV prevention. Efficacious if adhered to, PrEP has demonstrated that it deserves a place in the biomedical compartment of the HIV prevention toolbox alongside

treatment as prevention, condoms, STI treatment or control, and postexposure prophylaxis. Real-world implementation and a shift in the dialogue of prevention toward risk acknowledgment and mitigation rather than zero tolerance will be the path to fully realizing the power of PrEP. 

*Presented by Dr Daskalakis in April 2014. First draft prepared from transcripts by Matthew Stenger. Reviewed and edited by Dr Daskalakis in September 2014.*

*Financial affiliations in the past 12 months: Dr Daskalakis has no relevant financial affiliations to disclose.*

### References

1. HIV Clinical Resource. Guidance for the use of pre-exposure prophylaxis (PrEP) to prevent HIV transmission. <http://www.hivguidelines.org/clinical-guidelines/pre-exposure-prophylaxis/guidance-for-the-use-of-pre-exposure-prophylaxis-prep-to-prevent-hiv-transmission/>. Accessed on October 2, 2014.
2. Bernstein KT, Marcus JL, Nieri G, Philip SS, Klausner JD. Rectal gonorrhoea and chlamydia reinfection is associated with increased risk of HIV seroconversion. *JAIDS*. 2010;53(4):537-543.
3. Pathela P, Braunstein SL, Blank S, Schilling JA. HIV incidence among men with and those without sexually transmitted rectal infections: estimates from matching against an HIV case registry. *Clin Infect Dis*. 2013;57(8):1203-1209.
4. Heuker J, Sonder GJ, Stolte I, Geskus R, van den Hoek A. High HIV incidence among MSM prescribed postexposure prophylaxis, 2000-2009: indications for ongoing sexual risk behaviour. *AIDS*. 2012;26(4):505-512.
5. Sonder GJ, Prins JM, Regez RM, et al. Comparison of two HIV postexposure prophylaxis regimens among men who have sex with men in Amsterdam: adverse effects do not influence compliance. *Sex Transm Dis*. 2010;37(11):681-686.
6. Grant RM, Lama JR, Anderson PL, et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *N Engl J Med*. 2010;363(27):2587-2599.
7. Baeten JM, Donnell D, Ndase P, et al. Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. *N Engl J Med*. 2012;367(5):399-410.
8. Thigpen MC, Kebaabetswe PM, Paxton LA, et al. Antiretroviral preexposure prophylaxis for heterosexual HIV transmission in Botswana. *N Engl J Med*. 2012;367(5):423-434.
9. Van Damme L, Corneli A, Ahmed K, et al. Preexposure prophylaxis for HIV infection among African women. *N Engl J Med*. 2012;367(5):411-422.
10. Marcus JL, Glidden DV, Mayer KH, et al. No evidence of sexual risk compensation

- in the iPrEx trial of daily oral HIV pre-exposure prophylaxis. *PLoS One*. 2013; 8(12):e81997.
11. Glidden DV. Choosing populations for Maximal Impact [CROI abstract 64]. In Special Issue: Abstracts From the 2014 Conference on Retroviruses and Opportunistic Infections. *Top Antivir Med*. 2014;22(e-1):32.
  12. Duwal S, Schutte C, von KM. Pharmacokinetics and pharmacodynamics of the reverse transcriptase inhibitor tenofovir and prophylactic efficacy against HIV-1 infection. *PLoS One*. 2012;7(7):e40382.
  13. Jackson A, Moyle G, Watson V, et al. Tenofovir, emtricitabine intracellular and plasma, and efavirenz plasma concentration decay following drug intake cessation: implications for HIV treatment and prevention. *J Acquir Immune Defic Syndr*. 2013;62(3):275-281.
  14. Centers for Disease Control and Prevention (CDC). Preexposure prophylaxis for the prevention of HIV infection in the United States - 2014: A Clinical Practice Guideline. <http://www.cdc.gov/hiv/pdf/guidelines/PrEPguidelines2014.pdf>. Accessed on October 2, 2014.
  15. Marrazzo JM, del Rio C, Holtgrave DR, et al. HIV prevention in clinical care settings: 2014 recommendations of the International Antiviral Society–USA Panel. *JAMA*. 2014;312(4):390-409.
  16. HIV Prevention Trials Network. Initiation of antiretroviral treatment protects uninfected sexual partners from HIV infection (HPTN Study 052) [press release]. [http://www.hptn.org/web%20documents/Press-Releases/HPTN052PressReleaseFINAL5\\_12\\_118am.pdf](http://www.hptn.org/web%20documents/Press-Releases/HPTN052PressReleaseFINAL5_12_118am.pdf). Accessed on October 2, 2011.
  17. Rodger A, Bruun T, Cambiano V, et al. HIV transmission risk through condomless sex if HIV+ partner on suppressive ART: PARTNER study [CROI abstract 153LB]. In Special Issue: Abstracts From the Conference on Retroviruses and Opportunistic Infections. *Top Antivir Med*. 2014;22(e-1):24-25.
  18. Gallagher T, Link L, Ramos M, Bottger E, Aberg J, Daskalakis D. Self-perception of HIV risk and candidacy for pre-exposure prophylaxis among men who have sex with men testing for HIV at commercial sex venues in New York City. *LGBT Health*. 2014;1(3):218-224.

### Additional Suggested Reading

Choopanya K, Martin M, Suntharasamai P, et al. Antiretroviral prophylaxis for HIV infection in injecting drug users in Bangkok, Thailand (the Bangkok Tenofovir Study): a randomised, double-blind, placebo-controlled phase 3 trial. *Lancet*. 2013;381(9883):2083-2090.

*Top Antivir Med*. 2014;22(4):670-675

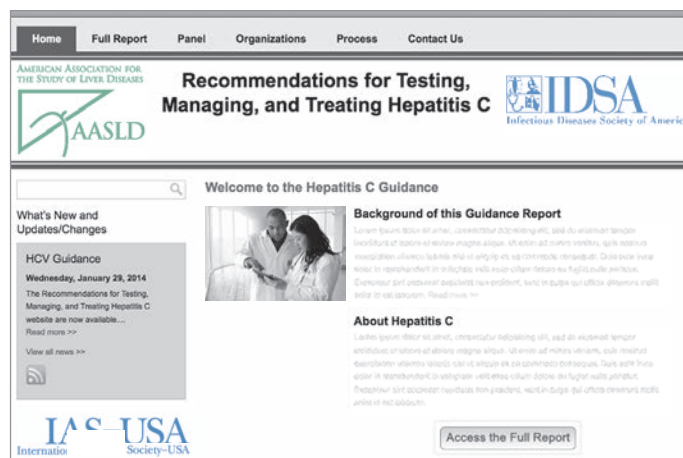
©2014, IAS–USA. All rights reserved

[www.HCVguidelines.org](http://www.HCVguidelines.org)

- Developed by a panel of experts in the field.
- Provides practitioners with regularly updated, evidence-based, consensus recommendations for screening, treating, and managing patients with HCV.
- Assists practitioners in treating the estimated 3 to 4 million Americans infected with HCV by highlighting the latest information in improved diagnostics and new drug options as they meet FDA approval.
- Offers guidance to practitioners about how to best use the next generation of direct-acting antivirals and other treatment options in the care of their patients.

## Recommendations for Testing, Managing, and Treating Hepatitis C

*Recommendations for Testing, Managing, and Treating Hepatitis C* is a website sponsored by the American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA) in collaboration with the International Antiviral Society–USA (IAS–USA) to provide the most current guidance for the treatment of hepatitis C virus (HCV).



### Available sections:

- HCV Testing and Linkage To Care
- When and in Whom to Initiate HCV Therapy
- Initial Treatment of HCV Infection in Patients Starting Treatment
- Retreatment of Persons in Whom Prior Therapy Has Failed
- Monitoring Patients Who Are Starting Hepatitis C Treatment, Are on Treatment, or Have Completed Therapy
- Unique Patient Populations
- Management of Acute HCV Infection