PrEP Program Resource Binder

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PrEP Program Resource Binder

Table of Contents

Provider Resources

1. PrEP Overview
   - PrEP for HIV Prevention (CDC 2014)
2. PrEP in your practice
   - 5 steps for delivering PrEP care (CDC 2014)
   - What Primary Care Providers Need to Know about PrEP (Krakower & Mayer 2012)
3. Clinical guidance
   - Patient Eligibility & Clinical Guide Summary (HCHD, adapted from CDC 2014)
   - PrEP Consultation Line – Clinician Consultation Center & Johns Hopkins REACH Initiative
   - CDC Clinical Practice Guideline (2017)
   - CDC Clinical Providers' Supplement (2017)
   - MSM Risk Index – Additional copies (CDC 2017)
   - PWID (IDU) Risk Index – Additional copies (CDC 2017)
4. Billing for services
   - NASTAD Billing Coding Guide (2016)
   - Sample Clinical Services Billing Policy (HCHD 2018)
   - Sliding Scale Examples (HCHD 2018)

Patient Resources

5. What is PrEP?
   - PrEP 101 (CDC 2018)
   - PrEP FAQ (CDC 2017)
   - PrEP Myths & Facts (MDH 2018)
6. Is PrEP right for me?
   - "Talk to Your Doctor" brochure (CDC 2014)
   - Truvada Medication Information Sheet (CDC 2017)
   - Population-Specific PrEP FAQs (JHU REACH 2018)
7. Paying for PrEP
   - CDC "Paying for PrEP" brochure (CDC 2015)
   - PrEP Medication & Co-Pay Assistance Program Flowchart (MDH 2018)
   - "How can I pay for PrEP?" (HCHD 2017)

8. Additional Resources for Providers
   - Maryland Department of Health PrEP Newsletter
   - MSM Sexual Health Standards of Care (NCSD & NASTAD 2017)
   - Taking Routine Histories of Sexual Health (Fenway Institute 2015)
   - Emtricitabine-tenofovir concentrations and PrEP efficacy in MSM (Anderson et al. 2012)
   - Sexual risk behavior among HIV-uninfected MSM participating in PrEP trial (Liu et al. 2013)
   - Addressing Stigma Toolkit for Improving HIV-STD Outcomes for Black & Latino MSM (NASTAD & NCSD 2014)
   - PrEP from a Family Planning client's perspective (HCHC 2017)
   - Preconception counseling and care for women of childbearing age in living with HIV (or HIV-negative and in a serodiscordant relationship) (2017)
   - nPEP (Non-Occupational Post-Exposure Prophylaxis) Guidelines (CDC 2016)

PROVIDER RESOURCES

PrEP Overview

Pre-exposure Prophylaxis (PrEP) for HIV Prevention

May 2014

Fast Facts

- Pre-exposure prophylaxis, or PrEP, is a way to help prevent HIV by taking a pill every day.
- People who are at substantial risk for HIV should talk to their doctor about PrEP.
- PrEP must be taken every day to be most effective.

Pre-exposure prophylaxis, or PrEP, is a way for people who do not have HIV to help prevent HIV infection by taking a pill every day. The pill contains two medicines that are also used, in combination with other medicines, to treat HIV. When someone is exposed to HIV through sex or injection drug use, PrEP can help stop the virus from establishing a permanent infection.

When used consistently, PrEP has been shown to greatly reduce the risk of HIV infection in people who are at substantial risk. PrEP is much less effective when it is not taken consistently.

PrEP is a powerful HIV prevention tool, and can be combined with condoms and other prevention methods to provide even greater protection than when used alone. People who use PrEP must commit to taking the drug daily and seeing their health care provider every 3 months for HIV testing and other follow-up.

PrEP Medicines

Most PrEP clinical trials have tested a combination of two antiretroviral drugs, tenofovir disoproxil fumarate (also called TDF, or tenofovir) and emtricitabine (also called FTC), taken in a single pill daily for HIV prevention. This combination pill (brand name **Truvada**) was approved by the US Food and Drug Administration (FDA) for use as an HIV treatment in 2004, and was approved as PrEP in July 2012. Some clinical studies have also evaluated the use of tenofovir on its own as a preventive drug, but this drug alone is not FDA-approved for PrEP.

Research Supporting PrEP Use

On May 14, 2014, the US Public Health Service released the first comprehensive clinical practice guidelines for PrEP (www.cdc.gov/hiv/pdf/guidelines/PrEPguidelines2014.pdf). This follows the earlier publication of brief interim guidelines that were based on findings from several large national and international clinical trials. These trials evaluated PrEP among gay and bisexual men, heterosexual men and women, and injection drug users. All participants in these trials received pills containing either PrEP or placebo, along with intensive counseling on safe-sex behavior, regular testing for sexually transmitted diseases (STDs), and a regular supply of condoms.

In all of these studies, the risk of getting HIV infection was lower—up to 92% lower—for **participants who took the medicines consistently** than for those who did not take the medicines. (See our PrEP web page at www.cdc.gov/hiv/prevention/research/prep/ for a brief description of the clinical trials, with links to the published studies.)

Guidelines for PrEP Use

The new federal guidelines for health care providers recommend that PrEP be considered for people who are HIV-negative and **at substantial risk for HIV infection**.

For sexual transmission, this includes anyone who is in an ongoing relationship with an HIV-positive partner. It also includes anyone who 1) is not in a mutually monogamous relationship with a partner who recently tested HIV-negative, and 2) is a

- gay or bisexual man who has had anal sex without a condom or been diagnosed with an STD in the past 6 months; or
- heterosexual man or woman who does not regularly use condoms during sex with partners of unknown HIV status who are at substantial risk of HIV infection (e.g., people who inject drugs or have bisexual male partners).

For people who inject drugs, this includes those who have injected illicit drugs in past 6 months and who have shared injection equipment or been in drug treatment for injection drug use in the past 6 months.

Health care providers should also discuss PrEP with heterosexual couples in which one partner is HIV-positive and the other is HIV-negative as one of several options to protect the partner who is HIV-negative during conception and pregnancy.

For a summary of clinical indications and treatment recommendations for PrEP, see the Table on the next page.

Summary of Guidance for PrEP Use

	Men Who Have Sex With Men	Heterosexual Women and Men	Injection Drug Users
Detecting substantial risk of acquiring HIV infection:	• Sexual partner with HIV • Recent bacterial STD • High number of sex partners • History of inconsistent or no condom use • Commercial sex work	• Sexual partner with HIV • Recent bacterial STD • High number of sex partners • History of inconsistent or no condom use • Commercial sex work • Lives in high-prevalence area or network	• HIV-positive injecting partner • Sharing injection equipment • Recent drug treatment (but currently injecting)
Clinically eligible:	• Documented negative HIV test before prescribing PrEP • No signs/symptoms of acute HIV infection • Normal renal function, no contraindicated medications • Documented hepatitis B virus infection and vaccination status		
Prescription	Daily, continuing, oral doeses of TDF/FTC (Truvada), ≤90 day supply		
Other services:	• Follow-up visits at least every 3 months to provide: • HIV test, medication adherence counseling, behavioral risk reduction support, side effect assessment, STD symptom assessment • At 3 months and every 6 months after, assess renal function • Every 6 months test for bacterial STDs		
	• Do oral/rectal STD testing	• Assess pregnancy intent • Pregnancy test every 3 months	• Access to clean needles/ syringes and drug treatment services

Source: US Public Health Service. Preexposure prophylaxis for the prevention of HIV infection in the United States —2014: a clinical practice guideline.

Because no prevention strategy for sexually active people is 100% effective, patients taking PrEP are encouraged to use other effective prevention strategies to maximally reduce their risk, including:

- Using condoms consistently and correctly.
- Getting HIV testing with partners.
- Choosing less risky sexual behaviors, such as oral sex.
- For people who inject drugs, getting into drug treatment programs and using sterile equipment.

The more prevention options patients choose, the greater their protection. Some HIV prevention strategies, such as using condoms, can also provide protection against other STDs, which PrEP does not prevent.

PrEP is only for people who are at ongoing substantial risk of HIV infection. For people who need to prevent HIV after a single high-risk event of potential HIV exposure—such as unprotected sex, needle-sharing injection drug use, or sexual assault —there is another option called postexposure prophylaxis, or PEP. PEP must begin within 72 hours of exposure. See our PEP Q&A (www.cdc.gov/hiv/basics/pep.html) for more information.

Supporting PrEP Uptake

To support the new guidelines and provider's supplement, CDC is leading efforts on multiple fronts to improve PrEP awareness and delivery in community settings. For example, the agency is implementing a pilot study examining practical requirements, costs, and impact of PrEP delivered at four federally qualified health centers, and will support state and local health departments by providing webinars and program guidance on using CDC funds to support PrEP implementation.

Many other groups will also play a vital role in achieving the full promise of PrEP. Health care providers can prescribe PrEP to those patients with indications for its use and increase awareness and uptake of PrEP for their patients who are at substantial risk. Advocates can raise PrEP awareness in at-risk populations, and groups implementing HIV prevention efforts can integrate PrEP education into existing programs.

Resources

- Basic PrEP Q&As (www.cdc.gov/hiv/basics/prep.html)
- Clinical Practice Guidelines (www.cdc.gov/hiv/pdf/guidelines/PrEPguidelines2014.pdf)
- Clinical Practice Guidelines—Providers' Supplement (www.cdc.gov/hiv/pdf/guidelines/PrEPProviderSupplement2014.pdf)
- Basic PEP Q&As (www.cdc.gov/hiv/basics/pep.html)

Additional Resources

CDC-INFO
1-800-CDC-INFO (232-4636)
www.cdc.gov/info

CDC HIV Website
www.cdc.gov/hiv

CDC Act Against AIDS Campaign
www.cdc.gov/actagainstaids

PrEP in your practice

Any prescribing health care provider can deliver PrEP care.

1 Test
for HIV including acute infection.

If HIV negative, ask about sex and drug use behaviors.

If HIV positive, provide or refer patient for HIV treatment and other services to maintain health and prevent further spread of HIV.

If HIV risk is low, discuss prevention methods.

If HIV risk is high, discuss risk behaviors, PrEP, and use of other prevention methods.

2 Order
recommended tests if patient is interested in PrEP and could benefit from it.

If tests show reason not to prescribe PrEP *(e.g. abnormal kidney function)*, discuss other prevention methods.

If tests show patient still benefits from taking PrEP, go to Step 3.

3 Help
patient apply for insurance or other programs to pay for PrEP.

Most public and private insurance programs cover PrEP, and patients can get help with their co-payments.

Drug assistance programs can help patients without insurance pay for PrEP.

4 Prescribe
PrEP and instruct patient to take one pill every day.

Currently Truvada®* is the only medicine approved by the FDA for PrEP.

**Tenofovir disoproxil fumarate/emtricitabine*

5 Follow-up
Schedule appointments every 3 months for follow-up, including HIV testing and prescription refills.

SOURCE: 2014 PrEP Clinical Practice Guidelines.

Have questions?

Read the full 2014 PrEP Clinical Practice Guidelines:
www.cdc.gov/hiv/pdf/PrEPguidelines2014.pdf

Call the PrEP Clinician Helpline:
(855) 448-7737
or (855) HIV-PrEP

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What Primary Care Providers Need to Know about Pre-Exposure Prophylaxis (PrEP) for HIV Prevention: Narrative Review

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Abstract

As HIV prevalence climbs globally, including more than 50,000 new infections per year in the United States, we need effective HIV prevention strategies. The use of antiretrovirals for pre-exposure prophylaxis (known as "PrEP") among high-risk HIV-uninfected persons is emerging as one such strategy. Randomized controlled trials have demonstrated that once daily oral PrEP decreased HIV incidence among at-risk MSM and African heterosexuals, including HIV serodiscordant couples. An additional randomized control trial of a pericoital topical application of antiretroviral microbicide gel reduced HIV incidence among at-risk heterosexual South African women. Two other studies in African women did not demonstrate the efficacy of oral or topical PrEP, raising concerns about adherence patterns and efficacy in this population. The FDA Antiretroviral Advisory Panel reviewed these studies and additional data in May 2012 and recommended the approval of oral tenofovir-emtricitabine for PrEP in high-risk populations. Patients may seek PrEP from their primary care providers and those on PrEP require monitoring. Thus, primary care providers should become familiar with PrEP. This review outlines the current state of knowledge about PrEP as it pertains to primary care including identification of individuals likely to benefit from PrEP, counseling to maximize adherence and minimize potential increases in risky behavior, and monitoring for potential drug toxicities, HIV acquisition, and antiretroviral drug resistance. Issues related to cost and insurance coverage are also discussed. Recent data suggest that PrEP, in conjunction with other prevention strategies, holds promise in helping to curtail the HIV epidemic.

Human immunodeficiency virus (HIV) continues to spread with an estimated 2.6 million new infections globally (1) and 50,000 new infections in the United States per year (2). Thus, there is an urgent need for more effective HIV prevention strategies. Administration of antiretroviral medications to uninfected persons at high risk to protect against HIV

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acquisition, known as pre-exposure prophylaxis or "PrEP," has recently emerged as a promising prevention strategy. Over the past 2 years, randomized controlled trials have demonstrated that PrEP can decrease HIV incidence in high-risk populations. While FDA approval of oral tenofovir-emtricitabine for PrEP in high-risk populations is pending as we write this (3), clinicians can implement PrEP with off label use of available oral antiretroviral medications. Thus, it is important that practicing physicians understand this new evidence and its implications.

What is the Evidence Base for PrEP?

In 2010, the Center for the AIDS Programme of Research in South Africa 004 (CAPRISA-004) trial demonstrated that pericoital use of tenofovir 1% vaginal gel was associated with a 39% reduction in the risk of HIV acquisition among at-risk South African women after 2.5 years, as compared to placebo (4). This study was the first demonstration that PrEP can protect against HIV acquisition in humans. Several months later, the multi-national Pre-Exposure Prophylaxis Initiative (iPrEx) trial showed that a once-daily oral tablet containing a fixed-dose combination of tenofovir disoproxil fumarate and emtricitabine (TDF-FTC) led to a 44% reduction in HIV incidence among MSM after a median follow-up of 1.2 years (5). More recently, the Partners PrEP Study showed that daily oral PrEP reduced the risk of HIV acquisition by the HIV-uninfected partner in HIV discordant, heterosexual African couples by 67% with tenofovir and 75% with TDF-FTC after a median follow-up of nearly 2 years (6). In the TDF-2 Study, daily oral TDF-FTC for at-risk heterosexual men and women in Botswana decreased HIV incidence by 63% after 2 years (7). Although it is not known if the efficacy of PrEP protection will persist after long-term use, these studies demonstrated no waning of protection over the duration of follow-up.

Notably, two other trials failed to demonstrate the efficacy of oral or topical PrEP for African women. The FEM-PrEP study randomized at-risk women in several African countries to oral TDF-FTC or placebo. An independent data safety monitoring board terminated the study early due to ineffectiveness of the intervention (8, 9). The Vaginal and Oral Interventions to Control the Epidemic (VOICE) study randomized 5000 at-risk African women to receive either a gel (tenofovir versus placebo) or a pill (tenofovir or TDF-FTC versus placebo) to be used once daily. The oral tenofovir and topical gel arms were terminated due to a lack of efficacy (10). Suboptimal adherence to study medications is one possible explanation of the conflicting results among PrEP trials. The proportion of participants with detectable levels of study drug was far lower in FEM-PrEP than in Partners PrEP, suggesting substantially poorer adherence in the study that failed to show efficacy (8, 11). It is also possible that the women in studies that failed to show efficacy had riskier behaviors than women in other studies. The oral TDF-FTC arm of VOICE is ongoing and another trial of pericoitally-administered tenofovir gel among South African women is underway (12). While awaiting results of ongoing studies (Table 1), the urgency of the HIV epidemic and positive findings from several PrEP studies justify consideration of implementing PrEP before these results are available.

What Must Clinicians Consider when Implementing Pre-Exposure Prophylaxis?

Translating the efficacy of PrEP observed in trials to public health effectiveness will require successful implementation in real-world clinical settings. Realization of the benefits of PrEP will require identifying individuals who are most likely to benefit from it, monitoring for adverse effects, addressing costs, and training providers to responsibly prescribe PrEP. HIV specialists who routinely prescribe antiretroviral medications and may identify at-risk persons who are sexual partners of their HIV-infected patients are likely to be among the

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first clinicians involved in PrEP delivery. However, other types of settings such as sexually transmitted disease (STD) clinics and primary care practices are likely to be other venues for PrEP prescription. Since primary care physicians are likely to care for many at-risk individuals, the successful implementation of PrEP will also require their engagement.

Are Other Drugs Likely to be Useful for PrEP?

The only PrEP regimen that has demonstrated efficacy and is currently recommended and available for prescribing is TDF-FTC (5–7). Tenofovir, a nucleotide reverse transcriptase inhibitor, is rapidly absorbed and provides sustained drug concentrations in blood and genital tissues and secretions for many days (14). Its long intracellular half-life could allow for intermittent dosing strategies to minimize cost and side effects. The nucleoside analogs emtricitabine and lamivudine are also well-tolerated and concentrate well in genital tissues (14, 15), but have a propensity to quickly select for resistant mutants. Other agents under study for PrEP include oral agents from drug classes not commonly used for HIV treatment, (e.g., the chemokine receptor 5 antagonist maraviroc) and topical agents that can be delivered via gel or intravaginal rings (e.g., the non-nucleoside reverse transcriptase inhibitor dapivirine) (16). Agents that should be avoided as PrEP include nevirapine and abacavir given risks of severe hypersensitivity reactions (17, 18).

Oral and topical PrEP each have theoretical merits and drawbacks, but only oral TDF-FTC is currently available. Tenofovir gel is still being evaluated in the FACTS-001 trial, and these data will be an important part of submission for FDA approval of tenofovir gel for PrEP.

Daily ingestion of oral PrEP results in sustained systemic and genital antiretroviral concentrations, which provides a continuous antiretroviral barrier to establishment of HIV infection, by inhibiting HIV integration into host cell genomes. Continuous protection is desirable when potential exposure is frequent, as with HIV serodiscordant couples, MSM with multiple partners, or sex workers, particularly when exposure is largely through unplanned sexual encounters. In addition, HIV-uninfected individuals who are unable to negotiate the use of condoms during sexual contact due to power inequality between partners (19) or cultural and legal barriers (20) could use oral PrEP without notifying their partners. Potential challenges for implementing daily oral PrEP include cost (over $10,000 per person annually in the U.S. for the drugs alone), the need for ongoing clinical monitoring for drug toxicities, and suboptimal adherence with a daily regimen, especially if risky behavior is intermittent.

The benefits of pericoital topical PrEP include high local drug exposure with lower systemic drug levels (21), presumably leading to decreased likelihood of drug toxicity, and potentially improved adherence. Less frequent dosing may make PrEP more affordable, especially in resource-constrained environments. Yet, topical PrEP will be more difficult to employ without partner knowledge. It is also possible that unless the gel is used on a daily basis, even in the absence of sex, it may not provide sufficient protective drug exposure if intercourse is unplanned.

Is PrEP Safe?

Available data suggests that PrEP with TDF-FTC has no serious, short term safety or tolerability concerns. Yet, tenofovir use has been associated with renal toxicity and decreased bone mineral density when used as part of treatment regimens in HIV-infected persons (22, 23), so clinicians will need to be alert for similar toxicities in patients who use tenofovir-based PrEP.

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The iPrEx study reported infrequent and comparable rates of serious adverse between daily oral TDF-FTC and placebo, although participants randomized to TDF-FTC experienced more nausea and minimal, but statistically significant, weight loss in the first few weeks of the study compared to the placebo arm (5). Counseling patients who initiate TFC-TDF about these potential symptoms might minimize self-discontinuation of drugs. In iPrEx, those assigned to TDF-FTC more often developed elevated serum creatinine (2%) compared to those in the placebo group (1%), but this difference was not statistically significant, and creatinine elevations normalized after discontinuation of study drug (5). Among 5 iPrEx participants who developed creatinine elevations, 4 did not experience a new elevation when TDF-FTC was restarted. Other PrEP trials have also been reassuring with no differences in adverse renal events being seen between men receiving daily oral tenofovir or placebo in a U.S. safety study (24) or among heterosexuals in 3 African PrEP studies (6–8). Long-term effects of tenofovir on bone demineralization will also need to be assessed given minor changes in bone density seen in the U.S. PrEP safety study and iPrEx (25, 26). However, in both of these studies, the level of demineralization was not clinically significant, and there was no evidence of increased fractures or other adverse clinical sequelae (25, 26). Although the safety findings in these first PrEP studies are reassuring, long term safety data are lacking and patients who initiate PrEP will need ongoing monitoring for adverse effects.

With regard to the safety of topical PrEP, serious adverse events were rare and similar among the women in CAPRISA-004 assigned to use tenofovir gel and those who used the placebo gel. However, women who used tenofovir gel reported a higher rate of diarrhea than placebo gel users. Investigators speculated that this could be due to local drug effect, but the mechanism remains unknown (4). A safety study of the vaginal gel applied rectally documented increased local discomfort compared to a placebo gel, probably because of glycerin being part of the vaginal gel (27). A glycerin-free rectal formulation of tenofovir gel was well-tolerated by men and women in a Phase 1 safety study (28), and Phase 2 studies are being planned for MSM. Yet, because of high levels of non-adherence in iPrEx and CAPRISA-004 and the longest duration of follow-up was 72 weeks in iPrEx (29), the “true” adverse event profile among those who routinely use PrEP remains uncertain.

What Counseling and Monitoring Should Accompany PrEP Prescription?

The Centers for Disease Control and Prevention (CDC) has published guidance for the prescription of daily oral TDF-FTC as PrEP to at-risk MSM (30). If the FDA accepts the advice of its Advisory Panel, the CDC will likely revise this guidance to extend to heterosexual discordant couples and other high-risk individuals.

The CDC recommends that providers document a negative HIV antibody test immediately before starting PrEP and test for acute HIV infection if symptoms consistent with this syndrome are present. The CDC also recommends regular, serial HIV testing during PrEP use. Individuals who acquire HIV infection during PrEP should immediately discontinue PrEP to reduce the risk of developing drug resistance and to enable initiation of a therapeutic antiretroviral regimen. Optimal frequency of HIV testing requires further study. Rapid HIV antibody testing was performed monthly in iPrEx, and no emergent drug resistance was detected in participants assigned to TDF-FTC who seroconverted (5), but monthly testing may be impractical in some clinical settings. Home HIV testing, which is currently under study, may enable patients to monitor themselves and be a useful adjunct to clinical testing. Currently, the CDC suggests HIV antibody testing every 2–3 months for MSM on daily TDF-FTC as PrEP (30).

The CDC also advises screening for sexually transmitted infections before initiating PrEP and then at least every 6 months in the absence of symptoms suggesting sexually transmitted

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infections (30). Of course, patients should be tested if symptoms suggesting infection are present and treated if infection is diagnosed.

The CDC recommends baseline screening for hepatitis B infection (30). Both tenofovir and emtricitabine have activity against hepatitis B, and clinically significant hepatitis flares have occurred in HIV-infected persons with active hepatitis B during antiviral initiation or interruption (31, 32). Completed PrEP trials have shown no evidence of increased rates of hepatic inflammation in persons using tenofovir versus placebo, including trials conducted in regions where hepatitis B prevalence is high (4, 33). The CDC suggests that providers offer hepatitis B vaccination to seronegative MSM, which is sound clinical practice for sexually active persons. For MSM with active hepatitis B, providers are advised to consider using TDF-FTC for both treatment of active hepatitis B and as PrEP, to monitor liver function carefully, and to avoid sudden drug discontinuation (30).

The CDC guidance also recommends documenting that estimated creatinine clearance is greater than 60 mL/minute before initiating TDF-FTC and repeating renal function testing at 3 months after initiation and then yearly thereafter (30).

It is possible that patients on PrEP will feel that the protection of PrEP will compensate for very high risk behaviors and that such behavior could mitigate the benefits of PrEP. Thus, in addition to monitoring for medication-related adverse effects and HIV acquisition, providers should monitor PrEP users for high-risk behaviors. Such behavior has not been observed in studies of PrEP to date (4–6, 33). Levels of risk-taking actually decreased during iPrEx, with the total number of receptive anal sexual partners decreasing over time and the percentage of sexual partners using condoms increasing to a plateau over the first 6 months of trial participation (5). However, this could be attributable to the intensive behavioral counseling that accompanied PrEP provision as part of the informed consent process, as well as participant realization that they might be assigned to placebo. The CDC suggests behavioral counseling and condom provision at least every 2–3 months during PrEP use (30). Patients and providers must understand that PrEP does not provide complete protection against HIV acquisition. Further studies of how providers can deliver effective counseling against risk compensation during PrEP use in the context of routine clinical care will be essential.

Management of HIV Acquisition during PrEP

PrEP users who acquire HIV-infection require immediate testing for antiretroviral resistance. The use of 1–2 antiretrovirals during acute infection facilitates the development of resistance by selecting for transmitted or newly-evolved resistant strains. Early detection of resistance allows for therapeutic choices that minimize additional mutations that could compromise therapeutic options. Individuals who acquired HIV after being randomized to use PrEP in iPrEx and several other PrEP trials did not exhibit drug resistance, but it is possible that many acute infections occurred in non-adherent individuals, limiting the opportunities for resistance to evolve (4–6). Four of 33 women who acquired HIV after being randomized to receive daily TDF-FTC in FEM-PrEP exhibited resistance to emtricitabine, but it is not known whether these women were infected with drug-resistant virus or if resistance emerged after infection. None of these women had detectable resistance to tenofovir (8). A modeling study concluded that PrEP use is likely to have a detectable but relatively minor impact on the development of drug resistance (34). However, assessment of drug resistance among those who become infected while using PrEP will be important as PrEP use expands beyond the clinical trial environment.

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Adherence Counseling

Clinicians will need to counsel persons who use PrEP about the importance of adherence. A case-control analysis in iPrEx showed that 9% of men who acquired HIV infection after being randomized to TDF-FTC had detectable levels of study drug compared to 51% of men who remained uninfected (5), underscoring that PrEP's effectiveness depends on adherence. Although self-reported rates of pill use in iPrEx were high (more than 89% average pill use), only 54% of those randomized to the TDF-FTC arm had detectable serum levels of study drug during random screenings, suggesting that actual adherence was lower (35).

It will be important to determine the least amount of medication that provides optimal protection and which patterns of non-daily use result in the best adherence, particularly for individuals whose risky behaviors are intermittent. Intermittent dosing could mitigate nonadherence and feasibility trials are currently underway (13, 36). However, event-driven dosing regimens may confront similar challenges to optimal adherence as regimens with more frequent schedules, as only approximately 40% of women in CAPRISA-004 reported using the gel at least 50% of the time (4).

Are At-Risk Persons interested in using PrEP…and will Clinicians Prescribe it?

Currently, awareness and utilization of PrEP are limited among at-risk persons, but interest in using PrEP exists. A national survey of U.S. MSM using a social networking website conducted 1 month after release of iPrEx results demonstrated that 19% of participants were aware of PrEP, <1% had used PrEP, and 79% expressed interest in PrEP use once they knew about it (37). Over 97% of women who participated in CAPRISA-004 found tenofovir 1% gel to be acceptable and expressed intent to use it if it was approved (4).

A survey of Massachusetts-based HIV specialists and generalist physicians suggested that many clinicians (73%) would be willing to prescribe PrEP to at-risk MSM based on the iPrEx results (38). Clearly, recommendations from public health authorities and the safety and efficacy data that emerge from clinical trials of PrEP will influence actual prescribing behavior (39).

Cost Considerations

Costs will be a substantial barrier to PrEP. A modeling study of PrEP use among MSM in the U.S. estimated that the cost to administer TDF-FTC once daily with associated monitoring and care would be $11,740 annually per person, with 91% due to drug costs (40). Models suggest that, in the absence of an increase in high risk behavior among people on PrEP, oral PrEP could be cost-effective among high-risk MSM in the U.S. (40, 41)and serodiscordant heterosexual couples (42) in South Africa. Topical PrEP is likely to be cost-effective among South African women (43). Availability of generic drugs could reduce costs for oral PrEP, but the patent for TDF-FTC (Truvada®, Gilead Sciences, Foster City, California) does not expire until 2021 (44).

It is unknown whether insurers will cover PrEP. Without insurance, out-of-pocket expenses are likely to be prohibitive for many high-risk persons. Moreover, given that nearly 3,000 Americans are on waiting lists to receive funds for treatment (45), and globally less than 1/2 of persons who need treatment are receiving it (1), issues of how best to use limited resources must be considered. Increased funding for both treatment and prevention will be crucial to minimize discord (44). Given limited resources, clinicians and policymakers will need to think carefully about which individuals are most likely to benefit from PrEP.

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Who Should Clinicians Offer PrEP?

Identifying individuals who are most likely to benefit from PrEP requires an understanding of local transmission dynamics. Generalized heterosexual epidemics predominate in some nations (e.g. South Africa), whereas concentrated epidemics, including injection drug users, sex workers, and MSM, exist in others (e.g. Thailand (46)). In the U.S., MSM are associated with the largest number of new infections (61%) (2), and the epidemic disproportionately affects African-Americans in urban areas and in smaller cities in the South (47).

The incorporation of HIV risk assessment into primary care has remained challenging since the beginning of the HIV epidemic, but will be essential to implement PrEP on a wide scale (48–50). Individual risk behaviors change over time, so serial risk assessment is necessary (51). Stigma associated with homosexuality in many cultures and criminalization of sexual practices in some nations (52) may limit the willingness of providers to ask, and patients to disclose, risky practices. Computer-assisted self-interviews may enable disclosure of risky behaviors (53). Strategies to develop provider comfort and skills around risk assessment will be important to optimize PrEP use.

HIV Serodiscordant Couples: Treating HIV-infected Partners, PrEP, or Both?

A recent study of 1763 HIV serodiscordant heterosexual couples demonstrated that early administration of ART to the HIV-infected partner (who had to have a CD4 count between 350 and 550 cells/mm^3) reduced the risk of HIV transmission to the uninfected partner by 96%, as compared to those whose ART initiation was delayed, during a median follow-up of 1.7 years (54). These results suggest that early administration of ART to HIV-infected persons offers an additional strategy for using antiretrovirals to decrease HIV transmission. Clinical events (primarily extrapulmonary tuberculosis) were less frequent among those who initiated ART sooner, suggesting that earlier treatment benefited the index participants as well as their partners. However, genotypic testing demonstrated that 11 of 39 participants who were initially uninfected acquired HIV from persons other than their primary partner during the course of the study, highlighting that treating infected partners does not completely protect their partners if they have other sexual contacts.

The efficacy of administering PrEP to the uninfected partner of a serodiscordant couple that is monogamous, in which the HIV-positive partner is on antiretroviral medications, is unknown. PrEP could potentially offer protection in this context during periods when the HIV-infected partner is viremic, such as early after initiating ART (i.e., before virologic suppression), when adherence is suboptimal, or after virologic failure. Clinicians caring for serodiscordant couples will need to discuss the relative merits of early ART for the infected partner plus or minus PrEP for the uninfected partner to determine the optimal strategies. For high-risk individuals without a single defined partner, PrEP may be the best option.

Conclusion

Primary care providers can play an important role in identifying persons who are at high-risk for HIV acquisition and helping them to make informed decisions about PrEP in combination with other prevention strategies. The efficacy of PrEP for MSM (44%), serodiscordant couples (67–75%), and heterosexual men and women in Africa (63%) is favorable when compared to other prophylactic measures, including voluntary medical male circumcision for African males (38–66%) (55) and early ART in HIV-infected members of serodiscordant couples (96%) (54, 56). Antiretrovirals can also decrease rates of mother-to-child transmission to 1–2% (57) and offer protection when administered as post-exposure

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prophylaxis (58). Similar to other prevention strategies, PrEP does not provide complete protection against HIV acquisition. Available evidence suggests that PrEP would be most effective as part of a multifaceted "prevention package." Clinicians and policymakers must tailor prevention interventions to address local epidemic dynamics (59) and individual patient preferences.

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References

1. UNAIDS Report on the Global AIDS Epidemic. Joint United Nations Programme on HIV/AIDS (UNAIDS); 2010. Accessed at http://www.unaids.org/GlobalReport/default.htm on [1 June 2012]
2. Prejean J, Song R, Hernandez A, Ziebell R, Green T, Walker F, et al. Estimated HIV Incidence in the United States, 2006–2009. PLoS One. 2011; 6(8):e17502. [PubMed: 21826193]
3. The New York Times. May 11. 2012 FDA Advisory Committee Supports Approval of Gilead's Truvada® for Reducing the Risk of Acquiring HIV.
4. Abdool Karim Q, Abdool Karim SS, Frohlich JA, Grobler AC, Baxter C, Mansoor LE, et al. Effectiveness and safety of tenofovir gel, an antiretroviral microbicide, for the prevention of HIV infection in women. Science. 2010; 329(5996):1168–74. [PubMed: 20643915]
5. Grant RM, Lama JR, Anderson PL, McMahan V, Liu AY, Vargas L, et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. N Engl J Med. 2010; 363(27):2587–99. [PubMed: 21091279]
6. Baeten, J.; Donnell, D.; Ndase, P.; Mugo, N.; Mujugira, A.; Celum, C., et al. ARV PrEP for HIV-1 Prevention among Heterosexual Men and Women [Abstract #29]. 19th Conference on Retroviruses and Opportunistic Infections; Seattle. 5–8 March 2012; Accessed at http://www.retroconference.org/2012b/Abstracts/43082.htm on
7. Thigpen, MC.; Kebaabetswe, PM.; Smith, DK.; Segolodi, TM.; Soud, FA.; Chillag, K., et al. Daily Oral Antiretroviral Use for the Prevention of HIV Infection in Heterosexually Active Young Adults in Botswana: Results from the TDF2 Study [Abstract WELBC01]. 6th International AIDS Society Conference on HIV Pathogenesis, Treatment, and Prevention; Rome. 17–20 July 2011; Accessed at http://pag.ias2011.org/abstracts.aspx?aid=4631 on
8. Van Damme, L.; Corneli, A.; Ahmed, K.; Lombaard, J.; Kagipa, S.; Grant, R., et al. The FEM-PrEP Trial of Emtricitabine/Tenofovir Disoproxil Fumarate (Truvada) among African Women [Abstract #32LB]. 19th Conference on Retroviruses and Opportunistic Infections; Seattle. 5–8 March 2012; Accessed at http://www.retroconference.org/2012b/Abstracts/45406.htm on
9. FEM-PrEP June 2011 Update. Family Health International; Apr 18. 2011 Accessed at http://www.fhi.org/en/Research/Projects/FEM-PrEP.htm on [1 June 2012]
10. Press Release: MTN Statement on Decision to Discontinue Use of Tenofovir Gel in VOICE, a Major HIV Prevention Study in Women. Microbicides Trial Network; Nov 28. 2011 Accessed at: http://www.mtnstopshiv.org/node/3909 on [1 June 2012]
11. Donnell, D.; Baeten, J.; Hendrix, C.; Bumpus, N.; Bangsberg, D.; Haberer, J., et al. Tenofovir Disoproxil Fumarate Drug Levels Indicate PrEP Use Is Strongly Correlated with HIV-1 Protective Effects: Kenya and Uganda [Abstract #30]. 19th Conference on Retroviruses and Opportunistic Infections; Seattle. 5–8 March 2012; Accessed at: http://www.retroconference.org/2012b/Abstracts/43156.htm on

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12. Follow-on African Consortium for Tenofovir Studies (FACTS) [website]. [1 June 2012] Accessed at http://www.facts-consortium.co.za/?page_id=83 on
13. AIDS Vaccine Advocacy Coalition [website]. [1 June 2012] Accessed at http://avac.org/ on
14. Kwara A, DeLong A, Rezk N, Hogan J, Burtwell H, Chapman S, et al. Antiretroviral Drug Concentrations and HIV RNA in the Genital Tract of HIV-Infected Women Receiving Long-Term Highly Active Antiretroviral Therapy. Clinical Infectious Diseases. 2008; 46(5):719–25. [PubMed: 18220480]
15. Dumond JB, Yeh RF, Patterson KB, Corbett AH, Jung BH, Rezk NL, et al. Antiretroviral drug exposure in the female genital tract: implications for oral pre- and post-exposure prophylaxis. AIDS. 2007; 21(14):1899–907. [PubMed: 17721097]
16. Nel A, Smythe S, Young K, Malcolm K, McCoy C, Rosenberg Z, et al. Safety and pharmacokinetics of dapivirine delivery from matrix and reservoir intravaginal rings to HIV-negative women. J Acquir Immune Defic Syndr. 2009; 51(4):416–23. [PubMed: 19623693]
17. Patel SM, Johnson S, Belknap SM, Chan J, Sha BE, Bennett C. Serious adverse cutaneous and hepatic toxicities associated with nevirapine use by non-HIV-infected individuals. J Acquir Immune Defic Syndr. 2004; 35(2):120–5. [PubMed: 14722442]
18. Mallal S, Nolan D, Witt C, Masel G, Martin AM, Moore C, et al. Association between presence of HLA-B*5701, HLA-DR7, and HLA-DQ3 and hypersensitivity to HIV-1 reverse-transcriptase inhibitor abacavir. Lancet. 2002; 359(9308):727–32. [PubMed: 11888582]
19. Dunkle KL, Jewkes RK, Brown HC, Gray GE, McIntryre JA, Harlow SD. Gender-based violence, relationship power, and risk of HIV infection in women attending antenatal clinics in South Africa. Lancet. 2004; 363(9419):1415–21. [PubMed: 15121402]
20. Shannon K, Csete J. Violence, Condom Negotiation, and HIV/STI Risk Among Sex Workers. JAMA. 2010; 304(5):573–4. [PubMed: 20682941]
21. Mayer KH, Maslankowski LA, Gai F, El-Sadr WM, Justman J, Kwiecien A, et al. Safety and tolerability of tenofovir vaginal gel in abstinent and sexually active HIV-infected and uninfected women. AIDS. 2006; 20(4):543–51. [PubMed: 16470118]
22. Jacobson DL, Spiegelman D, Knox TK, Wilson IB. Evolution and predictors of change in total bone mineral density over time in HIV-infected men and women in the nutrition for healthy living study. J Acquir Immune Defic Syndr. 2008; 49(3):298–308. [PubMed: 18845956]
23. Szczech LA. Renal dysfunction and tenofovir toxicity in HIV-infected patients. Top HIV Med. 2008; 16(4):122–6. [PubMed: 18838746]
24. Grohskopf, L.; Gvetadze, R.; Pathak, S.; O'Hara, B.; Mayer, K.; Liu, A., et al. Preliminary analysis of biomedical data from the phase II clinical safety trial of tenofovir disoproxil fumarate (TDF) for HIV-1 pre-exposure prophylaxis (PrEP) among U.S. men who have sex with men (MSM) [Abstract FRLBC102]. XVIII International AIDS Conference; Vienna, Austria. 18–23 July 2010; Accessed at http://pag.aids2010.org/Abstracts.aspx?AID=17777 on
25. Liu AY, Vittinghoff E, Sellmeyer DE, Irvin R, Mulligan K, Mayer K, et al. Bone Mineral Density in HIV-Negative Men Participating in a Tenofovir Pre-Exposure Prophylaxis Randomized Clinical Trial in San Francisco. PLoS One. 2011; 6(8):e23688. [PubMed: 21897852]
26. Mulligan, K.; Glidden, DV.; Gonzales, P.; Ramirez-Cardich, ME.; Liu, A.; Namwongprom, S., et al. Effects of FTC/TDF on Bone Mineral Density in Seronegative Men from 4 Continents: DEXA Results of the Global iPrEx Study [Abstract #94LB]. 18th Conference on Retroviruses and Opportunistic Infections; Boston. 27 February-2 March 2011; Accessed at http://www.retroconference.org/2011/Abstracts/42550.htm on
27. Anton, P.; Cranston, R.; Carballo-Dieguez, A.; Kashuba, A.; Khanukhova, E.; Elliott, J., et al. RMP-02/MTN-006: A Phase 1 Placebo-controlled Trial of Rectally Applied 1% Vaginal TFV Gel with Comparison to Oral TDF [Abstract #34LB]. 18th Conference on Retroviruses and Opportunistic Infections; Boston. 27 February-2 March 2011; Accessed at http://www.retroconference.org/2011/Abstracts/42556.htm on
28. McGowan, I.; Hoesley, C.; Andrew, P.; Janocko, L.; Dai, J.; Carballo-Diéguez, A., et al. MTN-007: A Phase 1 Randomized, Double-blind, Placebo-controlled Rectal Safety and Acceptability Study of Tenofovir 1% Gel [Abstract #34LB]. 19th Conference on Retroviruses and

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Opportunistic Infections; Seattle. 5–8 March 2012; Accessed at http://www.retroconference.org/2012b/Abstracts/45234.htm on

29. Grant, R.; Lama, J.; Glidden, D. iPrEx Study Team. Pre-exposure Chemprophylaxis for Prevention of HIV among Trans-women and MSM: iPREx Study [Abstract #92]. 18th Conference on Retroviruses and Opportunistic Infections; Boston. 27 February-2 March 2011; Accessed at http://www.retroconference.org/2011/Abstracts/42567.htm on
30. Interim Guidance: Preexposure Prophylaxis for the Prevention of HIV Infection in Men Who Have Sex with Men. MMWR Morb Mortal Wkly Rep. 2011; 60(3):65–8. [PubMed: 21270743]
31. Crane M, Oliver B, Matthews G, Avihingsanon A, Ubolyam S, Markovska V, et al. Immunopathogenesis of hepatic flare in HIV/hepatitis B virus (HBV)-coinfected individuals after the initiation of HBV-active antiretroviral therapy. J Infect Dis. 2009; 199(7):974–81. [PubMed: 19231993]
32. Nuesch R, Ananworanich J, Srasuebkul P, Chetchotisakd P, Prasithsirikul W, Klinbuayam W, et al. Interruptions of tenofovir/emtricitabine-based antiretroviral therapy in patients with HIV/hepatitis B virus co-infection. AIDS. 2008; 22(1):152–4. [PubMed: 18090405]
33. Peterson L, Taylor D, Roddy R, Belai G, Phillips P, Nanda K, et al. Tenofovir disoproxil fumarate for prevention of HIV infection in women: a phase 2, double-blind, randomized, placebo-controlled trial. PLoS Clin Trials. 2007; 2(5):e27. [PubMed: 17525796]
34. Abbas, U.; Glaubius, R.; Mubayi, A.; Hood, G.; Mellors, J. Predicting the Impact of ART and PrEP with Overlapping Regimens on HIV Transmission and Drug Resistance in South Africa [Abstract #98LB]. 18th Conference on Retroviruses and Opportunistic Infections; Boston. 27 February-2 March 2011; Accessed at http://www.retroconference.org/2011/Abstracts/42475.htm on
35. Amico, KR.; Liu, A.; McMahan, V.; Anderson, P.; Lama, JR.; Guanira, J., et al. Adherence Indicators and PrEP Drug Levels in the iPrEx Study [Abstract #95LB]. 18th Conference on Retroviruses and Opportunistic Infections; Boston. 27 February-2 March 2011; Accesssed at http://www.retroconference.org/2011/Abstracts/42627.htm on
36. Mutua, G.; Sanders, E.; Kamali, A.; Kibengo, F.; Mugo, P.; Anzala, O., et al. Safety and adherence to intermittent emtricitabine/tenofovir for HIV pre-exposure prophylaxis (PrEP) in Kenya and Uganda [Abstract MOPE0369]. XVIII International AIDS Conference; Vienna, Austria. 18–23 July 2010; Accessed at http://pag.aids2010.org/Abstracts.aspx?AID=2521 on
37. Krakower DS, Mimiaga MJ, Rosenberger JG, Novak DS, Mitty JA, White JM, et al. Limited Awareness and Low Immediate Uptake of Pre-Exposure Prophylaxis among Men Who Have Sex with Men Using an Internet Social Networking Site. PLoS One. 2012; 7(3):e33119. [PubMed: 22470438]
38. Mayer, K.; White, J.; Krakower, D.; Mimiaga, MJ. Evolution of Physician Attitudes, Knowledge, and Experience Regarding the Use of Antiretrovirals for HIV Prevention [Abstract 493]. 49th Annual Meeting of the Infectious Diseases Society of America; Boston. 20–23 October 2011; Accessed at http://idsa.confex.com/idsa/2011/webprogram/Paper31210.html on
39. White J, Mimiaga M, Krakower D, Mayer K. Evolution of Massachusetts Physician Attitudes, Knowledge and Experience Regarding the Use of Antiretrovirals for HIV Prevention. AIDS Patient Care and STDs. In press.
40. Desai K, Sansom SL, Ackers ML, Stewart SR, Hall HI, Hu DJ, et al. Modeling the impact of HIV chemoprophylaxis strategies among men who have sex with men in the United States: HIV infections prevented and cost-effectiveness. AIDS. 2008; 22(14):1829–39. [PubMed: 18753932]
41. Juusola JL, Brandeau ML, Owens DK, Bendavid E. The cost-effectiveness of preexposure prophylaxis for HIV prevention in the United States in men who have sex with men. Ann Intern Med. 2012; 156(8):541–50. [PubMed: 22508731]
42. Hallett TB, Baeten JM, Heffron R, Barnabas R, de Bruyn G, Cremin I, et al. Optimal Uses of Antiretrovirals for Prevention in HIV-1 Serodiscordant Heterosexual Couples in South Africa: A Modelling Study. PLoS Med. 2011; 8(11):e1001123. [PubMed: 22110407]
43. Walensky RP, Park JE, Wood R, Freedberg KA, Scott CA, Bekker LG, et al. The Cost-Effectiveness of Pre-Exposure Prophylaxis for HIV Infection in South African Women. Clin Infect Dis. 2012

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44. Summary on AVAC Think Tank on PrEP Financing in the US. AIDS Vaccine Advocacy Coalition; Jan 14. 2009 Accessed at http://www.avac.org/ht/a/GetDocumentAction/i/3529 on [1 June 2012]
45. The ADAP Watch. [1 June, 2012] National Alliance of State & Territorial AIDS Directors. May 17. 2012 Accessed at http://www.nastad.org/Docs/115231_ADAP%20Watch%20update%20-%205.18.12.pdf on
46. [1 June 2012] UNGASS Country Report: Thailand; Reporting period January 2008 – December 2009. United Nations General Assembly Special Session on HIV/AIDS. Accessed at http://data.unaids.org/pub/Report/2010/thailand_2010_country_progress_report_en.pdf on
47. El-Sadr WM, Mayer KH, Hodder SL. AIDS in America--forgotten but not gone. N Engl J Med. 2010; 362(11):967–70. [PubMed: 20147707]
48. Epstein RM, Morse DS, Frankel RM, Frarey L, Anderson K, Beckman HB. Awkward moments in patient-physician communication about HIV risk. Ann Intern Med. 1998; 128(6):435–42. [PubMed: 9499326]
49. Vergeront JM, Reiser WJ, Krchnavek KA, Druckenmiller JK, Davis JP. Meeting the challenge of early identification of HIV infection in primary care. WMJ. 1998; 97(11):52–61. [PubMed: 9894442]
50. From the Centers for Disease Control and Prevention. HIV prevention practices of primary-care physicians--United States, 1992. JAMA. 1994; 271(4):261–2. [PubMed: 8295276]
51. Dariotis JK, Sonenstein FL, Gates GJ, Capps R, Astone NM, Pleck JH, et al. Changes in sexual risk behavior as young men transition to adulthood. Perspect Sex Reprod Health. 2008; 40(4):218–25. [PubMed: 19067935]
52. Baral S, Sifakis F, Cleghorn F, Beyrer C. Elevated risk for HIV infection among men who have sex with men in low- and middle-income countries 2000–2006: a systematic review. PLoS Med. 2007; 4(12):e339. [PubMed: 18052602]
53. Metzger DS, Koblin B, Turner C, Navaline H, Valenti F, Holte S, et al. Randomized controlled trial of audio computer-assisted self-interviewing: utility and acceptability in longitudinal studies. HIVNET Vaccine Preparedness Study Protocol Team. Am J Epidemiol. 2000; 152(2):99–106. [PubMed: 10909945]
54. Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, et al. Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med. 2011; 365(6):493–505. [PubMed: 21767103]
55. Siegfried N, Muller M, Deeks JJ, Volmink J. Male circumcision for prevention of heterosexual acquisition of HIV in men. Cochrane Database Syst Rev. 2009; (2):CD003362. [PubMed: 19370585]
56. Donnell D, Baeten JM, Kiarie J, Thomas KK, Stevens W, Cohen CR, et al. Heterosexual HIV-1 transmission after initiation of antiretroviral therapy: a prospective cohort analysis. The Lancet. 2010; 375(9731):2092–8.
57. Siegfried N, van der Merwe L, Brocklehurst P, Sint TT. Antiretrovirals for reducing the risk of mother-to-child transmission of HIV infection. Cochrane Database Syst Rev. 2011; (7):CD003510. [PubMed: 21735394]
58. Cardo DM, Culver DH, Ciesielski CA, Srivastava PU, Marcus R, Abiteboul D, et al. A Case–Control Study of HIV Seroconversion in Health Care Workers after Percutaneous Exposure. New England Journal of Medicine. 1997; 337(21):1485–90. [PubMed: 9366579]
59. Kurth AE, Celum C, Baeten JM, Vermund SH, Wasserheit JN. Combination HIV Prevention: Significance, Challenges, and Opportunities. Curr HIV/AIDS Rep. 2010

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Table 1

Completed and Ongoing Efficacy Trials of HIV Antiretroviral Pre-Exposure Prophylaxis (PrEP).

Trial name	High-Risk Population	Location	Drug and Means of Administration	N	Results
iPrEx (5)	MSM and transgender females	Brazil; Ecuador; Peru; South Africa; Thailand; U.S.	Daily oral TDF-FTC	2,499	PrEP reduced HIV incidence by 44% compared to placebo. Open label extension ongoing.
CAPRISA-004 (4)	Heterosexual women	South Africa	Pericoitally-administered topical vaginal TFV	1085	PrEP decreased HIV incidence by 39% compared to placebo
FEM-PrEP (8)	Heterosexual women	Kenya; South Africa; Tanzania	Daily oral TDF-FTC	2000	Stopped at interim analyses: unable to demonstrate efficacy of PrEP
TDF-2 (7)	Heterosexual men and women	Botswana	Daily oral TDF-FTC	1200	PrEP decreased HIV incidence by 63% compared to placebo
Partners PrEP (6)	Serodiscordant heterosexual couples	Kenya; Uganda	Daily oral tenofovir or TDF-FTC	4700	PrEP decreased HIV incidence by 67% (tenofovir) and 75% (TDF-FTC) compared to placebo
Bangkok Tenofovir Study (13)	Injection drug users	Thailand	Daily oral tenofovir	2400	Enrollment completed 2010; results expected in 2012
VOICE (10)	Heterosexual women	South Africa; Uganda; Zambia; Zimbabwe	Daily oral tenofovir, TDF-FTC, or topical vaginal TFV	5000	Oral tenofovir and topical TFV arms stopped at interim analyses: unable to demonstrate efficacy. Oral TDF-FTC arm ongoing.
FACTS-001 (12)	Heterosexual women	South Africa	Pericoitally-administered topical vaginal	2200	Enrolling

PrEP = pre-exposure prophylaxis; iPrEx = Pre-Exposure Prophylaxis Initiative; MSM = men who have sex with men; TDF-FTC = Fixed-dose combination of emtricitabine and tenofovir disoproxil fumarate. CAPRISA-004 = Center for the AIDS Programme of Research in South Africa 004 trial; TFV = Tenofovir 1% gel; VOICE = Vaginal and Oral Interventions to Control the Epidemic; FACTS-001 = Follow-on African Consortium for Tenofovir Studies 001 trial.

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Table 2

Baseline and Follow-up Assessment, Testing, and Counseling that Clinicians should Provide when Prescribing HIV Antiretroviral Pre-Exposure Prophylaxis (PrEP).*

Before prescribing PrEP	Follow-Up Assessments	Frequency
Document negative HIV antibody test. Test for HIV RNA if signs/symptoms suggesting acute HIV infection are present.	Serial HIV antibody testing.	At least every 2–3 months. If HIV-infected, discontinue PrEP, obtain HIV resistance testing and link to HIV care.
Screen and treat for STDs: serologic testing for syphilis and NAATs for *Neisseria gonorrhoeae* and *Chlamydia trachomatis* from appropriate mucosal sites.	Rescreening and treatment for STDs.	With any signs/symptoms of STD; at least every 6 months if asymptomatic.
Screen for hepatitis B infection. Vaccinate against hepatitis B if susceptible. If active hepatitis B exists, document baseline aminotransferase levels and consider using TDF-FTC for hepatitis B treatment and PrEP.	Monitor for signs/symptoms of hepatic inflammation and increases in aminotransferase levels. Avoid sudden discontinuation of TDF-FTC.	At least every 2–3 months. If discontinuing TDF-FTC, consider continuing treatment of hepatitis B with appropriate regimen.
Document calculated creatinine clearance ≥ 60 mL/minute.	Repeat renal function testing.	Three months after initiation, then yearly.
Behavioral risk assessment to confirm individual is at ongoing high risk for HIV acquisition. Provide risk reduction counseling and condoms.	Repeat risk assessment, counseling and provision of condoms.	Every visit; at least every 2–3 months.
Adherence counseling	Adherence assessment. Provide counseling and support as needed.	Every visit; at least every 2–3 months.

PrEP = pre-exposure prophylaxis. RNA = ribonucleic acid. STD = Sexually transmitted disease. NAAT = Nucleic acid amplification test. TDF-FTC = Fixed-dose combination of emtricitabine and tenofovir disoproxil fumarate.

* Bone mineral density as assessed by dual energy x-ray absorptiometry was decreased in TDF-FTC users in iPrEx. Further studies are underway to determine if ongoing assessments of bone mineral density for PrEP users in community settings are warranted.

Clinical guidance

PrEP Patient Eligibility Guidelines

Men Who Have Sex With Men (MSM)

A gay, bisexual, or other man who has had sex with a man in the past 6 months

- Not in a mutually monogamous relationship with a known HIV negative partner
- AND one of the following:
  - Ongoing sex with a HIV positive partner
  - Any sex without condoms in the past 6 months
  - Any STI in the past 6 months

Heterosexual Women And Men

A woman who has had sex with a man or a man who has had sex with a woman in the past 6 months

- Not in a mutually monogamous relationship with a known HIV negative partner
- AND one of the following:
  - Ongoing sex with a HIV positive partner
  - Any sex without condoms in the past 6 months
  - Any STI in the past 6 months

People Who Inject Drugs (PWID)

A person with injection drug use not prescribed by a clinician in the past 6 months or a person with a past or current history of treatment for injection drug use

- Not in a mutually monogamous relationship with a known HIV negative partner
- AND one of the following:
  - Any sharing of injection or drug preparation equipment in the past 6 months
  - Ongoing sex with a HIV positive partner
  - Any sex without condoms in the past 6 months
  - Any STI in the past 6 months

HIV Pre-Exposure Prophylaxis Clinical Guide

Initial Visit

- Assess patient eligibility for and interest in PrEP
- Assess for acute HIV symptoms (Refer to ER/Chase Brexton for HIV PEP if high risk in last 72 hrs)
- Discuss PrEP benefits and risks
- Assess patient willingness to take PrEP daily
- Discuss HIV/STI risk reduction
- Perform or schedule laboratory tests
  - HIV test, rule out HIV infection (negative HIV test within one week of starting PrEP)
  - STI testing (syphilis, gonorrhea, chlamydia)
  - Basic metabolic panel
  - Viral hepatitis A/B/C testing
  - Urinalysis
  - Pregnancy test, as indicated
- Offer hepatitis A/B vaccination, HPV vaccination if age appropriate

Confirm negative HIV test and creatinine clearance level
Prescribe 30-day supply with no refills

Perform 2 week follow up call and assess side effects

30-Day Visit

- Assess side effects, medication adherence, and acute HIV symptoms
- Review HIV/STI risk reduction
- Perform or schedule laboratory tests
  - HIV test, rule out HIV infection
  - Pregnancy test

Prescribe 30-day supply with 1 refill

3-Month Visit

- Assess side effects, medication adherence, and acute HIV symptoms
- Review HIV/STI risk reduction
- Perform or schedule laboratory tests
  - HIV test, rule out HIV infection
  - STI testing (syphilis, gonorrhea, chlamydia, hepatitis C)
  - Serum creatinine and calculated creatinine clearance
  - Urinalysis
  - Pregnancy test, as indicated

Prescribe 90-day supply

6-Month Visit

- Review HIV/STI risk reduction
- Perform or schedule laboratory tests
  - HIV test, rule out HIV infection
  - STI testing (syphilis, gonorrhea, chlamydia, hepatitis C)
  - Pregnancy test, as indicated

Prescribe 90-day supply

Every 3 months

- Assess side effects, medication adherence, and acute HIV symptoms
- Review HIV/STI risk reduction
- Perform or schedule laboratory tests
  - HIV test, rule out HIV infection
  - STI testing (syphilis, gonorrhea, chlamydia, hepatitis C)
  - Pregnancy test, as indicated

Every 6 months

- Serum creatinine
- Urinalysis to look for proteinuria, glucosuria

Consider bone mineral density testing in clients with predisposition to low bone mineral density

Public Health
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Adapted from
http://www.cdc.gov/hiv/pdf/PrEPguidelines2014.pdf

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Pre-exposure management advice for clinicians, by clinicians:

- Medication management
- Laboratory evaluation and follow-up testing
- Transitioning from PEP to PrEP
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US Public Health Service

PREEXPOSURE PROPHYLAXIS FOR THE PREVENTION OF HIV INFECTION IN THE UNITED STATES – 2017 UPDATE

A CLINICAL PRACTICE GUIDELINE

What's New in the Preexposure Prophylaxis for the Prevention of HIV Infection in the United States - 2017 Update – A Clinical Practice Guideline?

(Published online March 2018)

The Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2014 was published in an electronic format in July 2014 so that it could be updated as relevant changes in supporting evidence became available. The Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2016: Update – A Clinical Practice Guideline includes revisions to several sections. These revisions are highlighted throughout the document and are intended solely to update the developing evidence base or to clarify specific points in clinical care. No changes were made to the graded recommendations for the use of PrEP in the US.

Evidence of the Safety and Efficacy of Antiretroviral Prophylaxis

Based on an updated systematic review of publications through June 2017, data from trials and open-label studies were added to the text summary and evidence tables.

Identifying Indications for PrEP

In Box B3 (recommended indications for PrEP use by injection drug users) we deleted whether they had been in drug treatment in the prior 6 months as this was causing confusion for many clinicians.

Laboratory Tests and other Diagnostic Procedures

We replaced the HIV test characteristic tables previously in appendices with a link to a CDC website that is more frequently updated.

The figure and text on testing by clinicians to determine HIV status for PrEP provision (including detection of acute HIV infection) was revised to include a preference for antigen/antibody testing whenever available (rather than antibody-only tests) and use of a 3,000 copies/ml cut-off for suspected false-positive viral load tests.

Additional information about hepatitis C screening associated with provision of PrEP is provided, consistent with the 2017 American Association for the Study of Liver Diseases (AASLD) and the Infectious Disease Society of America (IDSA) guidance.

Providing PrEP

Ledipasvir/sofosbuvir was added to the table (10) of drug interactions

Tenofovir alafenamide (TAF) was added to the section "What not to use"

We revised the clinical follow up schedule to include STI testing for asymptomatic MSM at high risk for recurrent STIs (e.g., those with recent STIs or multiple sex partners) at the 3 month visit in addition to testing for all symptomatic sexually-active persons. This is consistent with 2015 STD guidelines recommendation for STD screening every 3-6 months with multiple sex partners (https://www.cdc.gov/std/tg2015/tg-2015-print.pdf).

Minor revisions were also made to correct typos, add references, and update content from cited guidelines and source materials.

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For more clinical advice about PrEP guidelines:

- call the National Clinicians Consultation Center PrEPline at **855-448-7737** or
- go to their website at http://nccc.ucsf.edu/clinician-consultation/prep-pre-exposure-prophylaxis/

Table of Contents

List of Tables, Figures, and Boxes……...……6

Abbreviations (In Guideline and Clinical Provider Supplement)……..……7

Summary……,……9

Introduction……...…12

Evidence of Need for Additional HIV Prevention Methods…….....13

Evidence of the Safety and Efficacy of Antiretroviral Prophylaxis……14

Published Trials of Antiretroviral Preexposure Prophylaxis Among Men Who Have Sex with Men.....14

iPrEx (Preexposure Prophylaxis Initiative) Trial……....….14

US MSM Safety Trial……...…15

Adolescent Trials Network (ATN) 082……16

Ipergay (Intervention Préventive de l'Exposition aux Risques avec et pour les Gays) 16

Published Observational and Open-Label Studies of Antiretroviral Preexposure Prophylaxis Among Men Who Have Sex with Men……. …….....17

iPrEx Open-Label Extension (OLE) Study……...17

PROUD……...…17

Kaiser Permanente…….…...….18

Demo Project…….....18

Ipergay Open-Label Extension (OLE) Study……..……..18

Published Trials of Antiretroviral Preexposure Prophylaxis Among Heterosexual Men an Women……..…..…19

Partners PrEP Trial……..…..…19

TDF2 Trial……...…..….19

FEM-PrEP Trial……...…….….20

Phase 2 Trial of Preexposure Prophylaxis with Tenofovir Among Women in Ghana, Cameroon, and Nigeria…… ……..…21

VOICE (Vaginal and Oral Interventions to Control the Epidemic) Trial……....21

Published Trial of Antiretroviral Preexposure Prophylaxis Among Persons Who Inject Drugs..22

Bangkok Tenofovir Study (BTS)……..…22

Published Observational and Open-Label Studies of Antiretroviral Preexposure Prophylaxis Among Persons Who Inject Drugs……...…….....23

Bangkok Tenofovir Study (BTS) OLE……...…… …….…....23

Identifying Indications for PrEP……...….31

Assessing Risk of Sexual HIV Acquisition…….…..31

Assessing Risk of HIV Acquisition Through Injection Practices……..…35

Laboratory Tests and Other Diagnostic Procedures…….…..…36

HIV Testing……..….36

Acute HIV Infection……...…...37

Renal Function……..……39

Hepatitis Serology……..……..40

Testing for Sexually Transmitted Infections ……..……..42

Providing PrEP……...….42

Goals of PrEP Therapy…….…….42

Indicated Medication…….....…43

What Not to Use…….……...44

Time to achieving protection……...…...44

Managing side effects…….....45

Clinical Follow-Up and Monitoring……...…....45

Optional Assessments……...…..46

Bone Health……...46

Therapeutic Drug Monitoring……..……..46

Persons with Documented HIV Infection……..47

Discontinuing PrEP……47

Special Clinical Considerations……..48

Women Who Become Pregnant or Breastfeed While Taking PrEP Medication…….....48

Patients with Chronic Active Hepatitis B Virus Infection……..…49

Patients with Chronic Renal Failure…….….50

Adolescent Minors……....…50

Nonoccupational Postexposure Prophylaxis…….....….50

Improving Medication Adherence……...…...51

Reducing HIV Risk Behaviors……...…….54

Financial Case-Management Issues for PrEP……...……55

Decision Support, Training and Technical Assistance……...……..55

Related DHHS Guidelines……...……56

Appendices……...…….58

Appendix 1 Grading of Strength of Recommendations and Quality of Evidence…...……..…59

References……...……..61

List of Tables, Figures, and Boxes

Table 1 Summary of Guidance for PrEP Use 11

Table 2 PrEP Evidence Summary—GRADE Overall Evidence Quality RCTs 24

Table 3 PrEP Evidence Summary— HIV Incidence Findings RCTs 25

Table 4 PrEP Evidence Summary—Measures of Efficacy by Medication Adherence RCTs 26

Table 5 PrEP Evidence Summary— Safety and Toxicity RCTs 27

Table 6 PrEP Evidence Summary— HIV Resistance Findings RCTs 28

Table 7 PrEP Evidence Summary— Open-Label Studies 29

Table 8 Clinical Signs and Symptoms of Acute (Primary) HIV Infection 36

Table 9 Hepatitis Screening Serology 38

Table 10 Recommended Oral PrEP Medications 40

Table 11 PrEP Medication Drug Interactions 40

Table 12 Rating Scheme for Recommendations 54

Table 13 Criteria for Rating Quality of Scientific Evidence 55

Figure Clinician Determination of HIV Status for PrEP Provision 36

Box A Risk Behavior Assessments 30

Box A1 Risk Behavior Assessment for MSM 30

Box A2 Risk Behavior Assessment for Heterosexually Active Men and Women 31

Box A3 Risk Behavior Assessment for Injection Drug Users 33

Box B Recommended Indications for PrEP Use 33

Box B1 Recommended Indications for PrEP Use by MSM 33

Box B2 Recommended Indications for PrEP Use by Heterosexually Active Men and Women 33

Box B3 Indications for PrEP Use by Injection Drug Users 34

Box C Cockcroft-Gault Formulas 38

Box D Key Components of Medication Adherence Counseling 49

Box E Key Components of Behavioral Risk Reduction Counseling 51

Abbreviations (In Guideline and Clinical Providers' Supplement)

ACTG	AIDS Clinical Trials Group
AHRQ	Agency for Healthcare Research and Quality
AIDS	acquired immunodeficiency syndrome
BMD	bone mineral density
CDC	Centers for Disease Control and Prevention
CPT	common procedural terminology
DEXA	dual-emission X-ray absorptiometry
DHAP	Division of HIV/AIDS Prevention, CDC
DHHS	Department of Health and Human Services
eCrCl	estimated creatinine clearance rate (ml/min)
EIA	enzyme-linked immunoassay
FDA	Food and Drug Administration
FHI	Family Health International
FTC	emtricitabine (trade name Emtriva)
GEM	Guidelines Elements Model
GLIA	GuideLine Implementability Appraisal
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HBV	hepatitis B virus
HCV	hepatitis C virus
HIV	human immunodeficiency virus
HRSA	Health Resources and Services Administration
ICD	International Classification of Diseases
IDU	injection drug users (also called PWID)
IFA	indirect immunofluorescence assay
IHS	Indian Health Service
IQR	interquartile range
MSM	men who have sex with men
MTN	Microbicide Trials Network
NCHHSTP	National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention
NGC	National Guidelines Clearinghouse
NIAID	National Institute of Allergy and Infectious Diseases
NIH	National Institutes of Health
nPEP	nonoccupational postexposure prophylaxis
NSAID	non-steroidal anti-inflammatory drug
NQMC	National Quality Measures Clearinghouse
OHAP	Office of HIV/AIDS Policy, DHHS
ONAP	Office of National AIDS Policy
ONDCP	Office of National Drug Control Policy
OPA	Office of Population Affairs, DHHS

PCR	polymerase chain reaction
PEP	postexposure prophylaxis
PHS	(U.S.) Public Health Service
PWID	persons who inject drugs (also called IDU)
PrEP	preexposure prophylaxis
SAMHSA	Substance Abuse and Mental Health Services Administration
STD	sexually transmitted disease
STI	sexually transmitted infection
TB	tuberculosis
TDF	tenofovir disoproxil fumarate (trade name Viread®)
TAF	tenofovir alafenamide
TDM	therapeutic drug monitoring
UNAIDS	Joint United National Programme on HIV/AIDS
VA	Veterans Administration
WHO	World Health Organization

Summary

Preexposure Prophylaxis for HIV Prevention in the United States – 2017 Update: A Clinical Practice Guideline provides comprehensive information for the use of daily oral antiretroviral preexposure prophylaxis (PrEP) to reduce the risk of acquiring HIV infection in adults. The key messages of the guideline are as follows:

- Daily oral PrEP with the fixed-dose combination of tenofovir disoproxil fumarate (TDF) 300 mg and emtricitabine (FTC) 200 mg has been shown to be safe and effective in reducing the risk of sexual HIV acquisition in adults; therefore,
    - PrEP is recommended as one prevention option for sexually-active adult MSM (men who have sex with men) at substantial risk of HIV acquisition **(IA)**[1]
    - PrEP is recommended as one prevention option for adult heterosexually active men and women who are at substantial risk of HIV acquisition. **(IA)**
    - PrEP is recommended as one prevention option for adult persons who inject drugs (PWID) (also called injection drug users [IDU]) at substantial risk of HIV acquisition. **(IA)**
    - PrEP should be discussed with heterosexually-active women and men whose partners are known to have HIV infection (i.e., HIV-discordant couples) as one of several options to protect the uninfected partner during conception and pregnancy so that an informed decision can be made in awareness of what is known and unknown about benefits and risks of PrEP for mother and fetus **(IIB)**
- Currently the data on the efficacy and safety of PrEP for adolescents are insufficient. Therefore, the risks and benefits of PrEP for adolescents should be weighed carefully in the context of local laws and regulations about autonomy in health care decision-making by minors. **(IIIB)**
- Acute and chronic HIV infection must be excluded by symptom history and HIV testing immediately before PrEP is prescribed. **(IA)**
- The only medication regimen approved by the Food and Drug Administration and recommended for PrEP with all the populations specified in this guideline is daily TDF 300 mg co-formulated with FTC 200 mg (Truvada) **(IA)**
    - TDF alone has shown substantial efficacy and safety in trials with PWID and heterosexually active adults and can be considered as an alternative regimen for these populations, but not for MSM, among whom its efficacy has not been studied. **(IC)**
    - The use of other antiretroviral medications for PrEP, either in place of or in addition to TDF/FTC (or TDF) is not recommended. **(IIIA)**
    - The prescription of oral PrEP for coitally-timed or other noncontinuous daily use is not recommended. **(IIIA)**

[1] See Appendix 1, Grading of Strength of Recommendations and Quality of Evidence (Tables 12-13)

- HIV infection should be assessed at least every 3 months while patients are taking PrEP so that those with incident infection do not continue taking it. The 2-drug regimen of TDF/FTC is inadequate therapy for established HIV infection, and its use may engender resistance to either or both drugs. **(IA)**
- Renal function should be assessed at baseline and monitored at least every 6 months while patients are taking PrEP so that those in whom renal failure is developing do not continue to take it. **(IIIA)**
- When PrEP is prescribed, clinicians should provide access, directly or by facilitated referral, to proven effective risk-reduction services. Because high medication adherence is critical to PrEP efficacy but was not uniformly achieved by trial participants, patients should be encouraged and enabled to use PrEP in combination with other effective prevention methods. (**IIIA**)

Table 1: Summary of Guidance for PrEP Use

	Men Who Have Sex with Men	Heterosexual Women and Men	Persons Who Inject Drugs
Detecting substantial risk of acquiring HIV infection	HIV-positive sexual partner Recent bacterial STI† High number of sex partners History of inconsistent or no condom use Commercial sex work	HIV-positive sexual partner Recent bacterial STI‡ High number of sex partners History of inconsistent or no condom use Commercial sex work In high HIV prevalence area or network	HIV-positive injecting partner Sharing injection equipment
Clinically eligible	Documented negative HIV test result before prescribing PrEP No signs/symptoms of acute HIV infection Normal renal function; no contraindicated medications Documented hepatitis B virus infection and vaccination status		
Prescription	Daily, continuing, oral doses of TDF/FTC (Truvada), ≤90-day supply		
Other services	Follow-up visits at least every 3 months to provide the following: HIV test, medication adherence counseling, behavioral risk reduction support, side effect assessment, STI symptom assessment At 3 months and every 6 months thereafter, assess renal function Every 3-6 months, test for bacterial STIs		
	Do oral/rectal STI testing	For women, assess pregnancy intent Pregnancy test every 3 months	Access to clean needles/syringes and drug treatment services

STI: sexually transmitted infection

† Gonorrhea, chlamydia, syphilis for MSM including those who inject drugs
‡ Gonorrhea, syphilis for heterosexual women and men including those who inject drugs

Introduction

Recent findings from several clinical trials have demonstrated safety[1] and a substantial reduction in the rate of HIV acquisition for men who have sex with men (MSM) [2], men and women in heterosexual HIV-discordant couples[3], and heterosexual men and women recruited as individuals[4] who were prescribed daily oral antiretroviral preexposure prophylaxis (PrEP) with a fixed-dose combination of tenofovir disoproxil fumarate (TDF) and emtricitabine (FTC). In addition, one clinical trial among persons who injection drugs (PWID) (also called injection drug users [IDU][5] and one among men and women in heterosexual HIV-discordant couples[3] have demonstrated substantial efficacy and safety of daily oral PrEP with TDF alone. The demonstrated efficacy of PrEP was in addition to the effects of repeated condom provision, sexual risk-reduction counseling, and the diagnosis and treatment of sexually transmitted infection (STI), all of which were provided to trial participants, including those in the drug treatment group and those in the placebo group. In July 2012, after reviewing the available trial results, the U.S. Food and Drug Administration (FDA) approved an indication for the use of Truvada[§] (TDF/FC) "in combination with safer sex practices for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 in adults at high risk"[6,7].

On the basis of these trial results and the FDA approval, the U.S. Public Health Service recommends that clinicians evaluate their male and female patients who are sexually active or who are injecting illicit drugs and consider offering PrEP as one prevention option to those whose sexual or injection behaviors and epidemiologic context place them at substantial risk of acquiring HIV infection.

The evidence base for the 2014 recommendations were derived from a systematic search and review of published literature. To identify all PrEP safety and efficacy trials pertaining to the prevention of sexual and injection acquisition of HIV, a search of the clinical trials registry (http://www.clinicaltrials.gov) was performed by using combinations search terms (preexposure prophylaxis, pre-exposure prophylaxis, PrEP, HIV, Truvada, tenofovir, and antiretroviral). In addition, the same search terms were used to search conference abstracts for major HIV conferences (e.g., International AIDS Conference, Conference on Retroviruses and Opportunistic Infections) for the years 2009-2013. These same search terms were used to search PubMed and Web of Science databases for the years 2006-2013. Finally, a review of references from published PrEP trial data and the data summary prepared by FDA for its approval decision[8] confirmed that no additional trial results were available. For the 2017 update, the systematic review of published literature was updated through June 2017 and expanded to include the terms *chemoprophylaxis* and *chemoprevention* and searches of the MEDLINE, Embase, CINAHL, and Cochrane Library database in addition to those used in 2014. The results of this systematic review were crosschecked for completeness with the review conducted by the World Health

[§] Use of trade names and commercial sources is for identification only and does not imply endorsement by the U.S. Department of Health and Human Services.

Organization[9]. For additional information about the systematic review process, see the Clinical Providers' Supplement, Section 14 at https://www.cdc.gov/hiv/pdf/risk/prep-cdc-hiv-prep-provider-supplement-2017.pdf

Potential conflicts of interest: CDC and individual employees involved in the guideline development process are named in US government patents and patent applications related to methods for HIV prophylaxis.

This publication provides a comprehensive clinical practice guideline for the use of PrEP for the prevention of HIV infection in the United States. It incorporates and extends information provided in interim guidance for PrEP use with MSM[10], with heterosexually active adults[11], and with PWID (also called IDU)[12]. Currently, prescribing daily oral PrEP with TDF/FTC is recommended as one prevention option for MSM, heterosexual men, heterosexual women, and PWID at substantial risk of HIV acquisition. As the results of additional PrEP clinical trials and studies in these and other populations at risk of HIV acquisition become known, this guideline will be updated.

The intended users of this guideline include

- primary care clinicians who provide care to persons at risk of acquiring HIV infection
- clinicians who provide substance abuse treatment
- infectious disease and HIV treatment specialists who may provide PrEP or serve as consultants to primary care physicians about the use of antiretroviral medications
- health program policymakers.

Evidence of Need for Additional HIV Prevention Methods

Approximately 40,000 people in the United States are infected with HIV each year[13]. From 2008 through 2014, estimated annual HIV incidence declined 18% overall but progress was uneven. Although declines occurred among heterosexuals, PWID, and white MSM, no decline was observed in the estimated number of annual HIV infections among black MSM and an increase was documented among Latino MSM[13]. In 2015, 67% of the 39,513 newly diagnosed HIV infections were attributed to male-male sexual activity without injection drug use, 3% to male-male sexual activity with injection drug use, 24% to male-female sexual contact without injection drug use, and 6% to injection drug use. Among the 24% of persons with newly diagnosed HIV infection attributed to heterosexual activity, 64% were African-American women and men[14]. These data indicate a need for additional methods of HIV prevention to further reduce new HIV infections, especially (but not exclusively) among young adult and adolescent MSM of all races and Hispanic/Latino ethnicity and for African American heterosexuals (populations with higher HIV prevalence and at higher risk of HIV infection among those without HIV infection).

Evidence of the Safety and Efficacy of Antiretroviral Prophylaxis

The biological plausibility and the short-term safety of antiretroviral use to prevent HIV acquisition in other exposure situations have been demonstrated in 2 studies conducted prior to the PrEP trials. In a randomized placebo-controlled trial, perinatal transmission was reduced 68% among the HIV-infected women who received zidovudine during pregnancy and labor and whose infants received zidovudine for 6 weeks after birth[15]. That is, these infants received both preexposure and postexposure prophylaxis. In 1995, investigators used case-control surveillance data from health-care workers to demonstrate that zidovudine provided within 72 hours after percutaneous exposure to HIV-infected blood and continued for 28 days (PEP, or postexposure prophylaxis) was associated with an 81% reduction in the risk of acquiring HIV infection[16-18].

Evidence from these human studies of blood-borne and perinatal transmission as well as studies of vaginal and rectal exposure among animals suggested that PrEP (using antiretroviral drugs) could reduce the risk of acquiring HIV infection from sexual and drug-use exposures. Clinical trials were launched to evaluate the safety and efficacy of PrEP in populations at risk of HIV infection through several routes of exposure. The results of completed trials and open label or observational studies published as of June 2017 are summarized below. See also Tables 2-7. The quality of evidence in each study was assessed using GRADE criteria (http://www.gradeworkinggroup.org/FAQ/evidence_qual.htm) and the strength of evidence for all studies relevant to a specific recommendation was assessed by the method used in the DHHS antiretroviral treatment guidelines (See Appendix 1)

Published Trials of Antiretroviral Preexposure Prophylaxis Among Men Who Have Sex with Men

iPrEx (Preexposure Prophylaxis Initiative) Trial

The iPrEx study[2] was a phase 3, randomized, double-blind, placebo-controlled trial conducted in Peru, Ecuador, Brazil, Thailand, South Africa, and the United States among men and male-to-female transgender adults who reported sex with a man during the 6 months preceding enrollment. Participants were randomly assigned to receive a daily oral dose of either the fixed-dose combination of TDF and FTC or a placebo. All participants (drug and placebo groups) were seen every 4 weeks for an interview, HIV testing, counseling about risk- reduction and adherence to PrEP medication doses, pill count, and dispensing of pills and condoms. Analysis of data through May 1, 2010, revealed that after the exclusion of 58 participants (10 later determined to be HIV- infected at enrollment and 48 who did not have an HIV test after enrollment), 36 of 1,224 participants in the TDF/FTC group and 64 of 1,217 in the placebo group had acquired HIV infection. Enrollment in the TDF/FTC group was associated with a 44% reduction in the risk of HIV acquisition (95% CI, 15-63). The reduction was greater in the as-treated analysis: at the visits at which adherence was ≥50% (by self-report and pill count/dispensing), the reduction in HIV acquisition was 50% (95% CI, 18-70). The reduction in the risk of HIV acquisition was

73% at visits at which self-reported adherence was ≥90% (95% CI, 41-88) during the preceding 30 days. Among participants randomly assigned to the TDF/FTC group, plasma and intracellular drug-level testing was performed for all those who acquired HIV infection during the trial and for a matched subset who remained HIV- uninfected: a 92% reduction in the risk of HIV acquisition (95% CI, 40-99) was found in participants with detectable levels of TDF/FTC versus those with no drug detected.

Generally, TDF/FTC was well tolerated, although nausea in the first month was more common among participants taking medication than among those taking placebo (9% versus 5%). No differences in severe (grade 3) or life-threatening (grade 4) adverse laboratory events were observed between the active and placebo group, and no drug-resistant virus was found in the 100 participants infected after enrollment. Among 10 participants who were HIV-negative at enrollment but later found to have been infected before enrollment, FTC-resistant virus was detected in 2 of 2 men in the active group and 1 of 8 men in the placebo group. Compared to participant reports at baseline, over the course of the study participants in both the TDF/FTC and placebo groups reported fewer total numbers of sex partners with whom the participants had receptive anal intercourse and higher percentages of partners who used condoms.

In the original iPrEx publication[2], of 2,499 MSM, 29 identified as female (i.e., transgender women). In a subsequent subgroup analysis[19], men were categorized as transgender women (n=339) if they were born male and either identified as women (n=29), identified as transgender (n=296), or identified as male and used feminizing hormones (n=14). Using this expanded definition, among transgender women, no efficacy of PrEP was demonstrated. There were 11 infections among the PrEP group and 10 in the placebo group (HR 1.1, 95% CI: 0.5-2.7). By drug level testing (*always* versus *less than always*), compared with MSM, transgender women had less consistent PrEP use OR 0.39 (95% CI: 0.16-0.96). In the subsequent open-label extension study (see below), one transgender woman seroconverted while receiving PrEP and one seroconversion occurred in a woman who elected not to use PrEP.

US MSM Safety Trial

The US MSM Safety Trial[1] was a phase 2 randomized, double-blind, placebo-controlled study of the clinical safety and behavioral effects of TDF for HIV prevention among 400 MSM in San Francisco, Boston, and Atlanta. Participants were randomly assigned 1:1:1:1 to receive daily oral TDF or placebo immediately or after a 9- month delay. Participants were seen for follow-up visits 1 month after enrollment and quarterly thereafter. Among those without directed drug interruptions, medication adherence was high: 92% by pill count and 77% by pill bottle openings recorded by Medication Event Monitoring System (MEMS) caps. Temporary drug interruptions and the overall frequency of adverse events did not differ significantly between TDF and placebo groups. In multivariable analyses, back pain was the only adverse event associated with receipt of TDF. In a subset of men at the San Francisco site (n=184) for whom bone mineral density (BMD) was assessed, receipt of TDF was associated with small decrease in BMD (1% decrease

at the femoral neck, 0.8% decrease for total hip)[20]. TDF was not associated with reported bone fractures at any anatomical site. Among 7 seroconversions, no HIV with mutations associated with TDF resistance was detected. No HIV infections occurred while participants were being given TDF; 3 occurred in men while taking placebo, 3 occurred among men in the delayed TDF group who had not started receiving drug; 1 occurred in a man who had been randomly assigned to receive placebo and who was later determined to have had acute HIV infection at the enrollment visit.

ADOLESCENT TRIALS NETWORK (ATN) 082

ATN 082[21] was a randomized, blinded, pilot feasibility study comparing daily PrEP with TDF/FTC with and without a behavioral intervention (Many Men, Many Voices) to a third group with no pill and no behavioral intervention. Participants had study visits every 4 weeks with audio-computer assisted interviews (ACASI), blood draws, and risk-reduction counseling. The outcomes of interest were acceptability of study procedures, adherence to pill-taking, safety of TDF/FTC, and levels of sexual risk behaviors among a population of young (ages 18-22 years) MSM in Chicago. One hundred participants were to be followed for 24 weeks, but enrollment was stopped and the study was unblinded early when the iPrEx study published its efficacy result. Sixty-eight participants were enrolled. By drug level detection, adherence was modest at week 4 (62%), and declined to 20% by week 24. No HIV seroconversions were observed.

IPERGAY (INTERVENTION PRÉVENTIVE DE L'EXPOSITION AUX RISQUES AVEC ET POUR LES GAYS)

The results of a randomized, blinded, trial of non-daily dosing of TDF/FTC or placebo for HIV preexposure prophylaxis has also been published[22] and is included here for completeness, although non-daily dosing is not currently recommended by the FDA or CDC.

Four-hundred MSM in France and Canada were randomized to a complex peri-coital dosing regimen that involved taking 1) 2 pills (TDF/FTC or placebo) between 2 and 24 hours before sex, 2) 1 pill 24 hours after the first dose, 3) 1 pill 48 hours after the first dose, 4) continuing daily pills if sexual activity continues until 48 hours after the last sex. If more than a 1 week break occurred since the last pill, retreatment initiation was with 2 pills before sex or if less than a 1 week break occurred since the last pill, retreatment initiation was with 1 pill before sex. Each pre-sex dose was then followed by the 2 post-sex doses. Study visits were scheduled at 4 and 8 weeks after enrollment, and then every 8 weeks. At study visits, participants completed a computer-assisted interview, had blood drawn, received adherence and risk reduction counseling, received diagnosis and treatment of STIs as indicated, and had a pill count and a medication refill. Following an interim analysis by the data and safety monitoring board at which efficacy was determined, the placebo group was discontinued and all study participants were offered TDF/FTC. In the blinded phase of the trial, efficacy was 86% (95% CI: 40-98). By self-report,

patients took a median of 15 pills per month. By measured plasma drug levels in a subset of those randomized to TDF/FTC, 86% had TDF levels consistent with having taken the drug during the previous week.

Because of the high frequency of sex and therefore of pill-taking among those in this study population, it is not yet known whether the regimen will work if taken only a few hours or days before sex, without any buildup of the drug in rectal tissue from prior use. Studies suggest that it may take days, depending on the site of sexual exposure, for the active drug in PrEP to build up to an optimal level for preventing HIV infection. No data yet exist on how effective this regimen would be for heterosexual men and women, and persons who inject drugs, or on adherence to this relatively complex PrEP regimen outside a trial setting. IPERGAY findings, combined with other recent research, suggest that even with less than perfect daily adherence, PrEP may still offer substantial protection for MSM if taken consistently.

Daily oral PrEP with TDF/FTC is recommended as one HIV prevention option for sexually-active MSM at substantial risk of HIV acquisition because the iPrEx trial presents evidence of its safety and efficacy in this population, especially when medication adherence is high. **(IA)**

Published Observational and Open-Label Studies of Antiretroviral Preexposure Prophylaxis Among Men Who Have Sex with Men

iPrEx Open-Label Extension (OLE) Study

Persons previously enrolled in the iPrEx, ATN 082, and CDC safety PrEP clinical trials were enrolled in a 72 week open-label study and were offered PrEP free of charge[23]. Seventy-six percent of 1,603 persons (1,428 MSM and 175 transgender women) enrolled received PrEP. HIV incidence among those receiving PrEP was 1.8 per 100 person-years (py) versus 2.6 per 100 py in those concurrently not choosing PrEP (HR 0.51, 95% CI: 0.26-1.01), adjusted for baseline sexual behaviors. Among those receiving PrEP, by dried blood spot drug levels, there were no infections in persons with drug levels associated with having taken 4 or more doses per week (p<0.0001) compared with those taking < 2 doses per week.

PROUD Open-Label Extension (OLE) Study

PROUD was an open-label, randomized, wait-list controlled trial designed for MSM attending sexual health clinics in England[24]. A pilot was initiated to enroll 500 MSM, in which 275 men were randomized to receive daily oral TDF/FTC immediately, and 269 were deferred to start after 1 year. At an interim analysis, the data monitoring committee stopped the trial early for efficacy at an interim analysis and recommended that all deferred participants be offered PrEP. Follow-up was completed for 94% of those in the immediate PrEP arm and 90% of those in the deferred arm. PrEP efficacy was 86% (90% CI: 64-96).

KAISER PERMANENTE OBSERVATIONAL STUDY

An evaluation of a specialized PrEP program provided at the Kaiser Permanente San Francisco Medical Center[25] reported on a cohort of 653 MSM, 3 heterosexual women, and 1 transgender man (with male sexual partners) who initiated PrEP between July 2012 and February 2015. Of these, 20 restarted PrEP after discontinuing it during the study period. The mean duration of use was 7.2 months. No HIV diagnoses were made during 388 py of follow-up on PrEP. No medication adherence measures were reported. After 12 months of use, 50% of PrEP users had received a diagnosis of one or more STI (95% CI: 26-35). In a recent report on PrEP patients seen at this center, as of February 2017, there were no HIV infections during 5104 py of PrEP use while they were being prescribed medication[26].

DEMO PROJECT OPEN-LABEL STUDY

In this demonstration project, conducted at 3 community-based clinics in the United States[27], MSM (n = 430) and transgender women (n=5) were offered daily oral TDF/FTC free of charge for 48 weeks. All patients received HIV testing, brief counseling, clinical monitoring, and STI diagnosis and treatment at quarterly follow-up visits. A subset of men underwent drug level monitoring with dried-blood spot testing and protective levels (associated with ≥4 doses per week) were high (80.0%-85.6%) at follow-up visits across the sites. STI incidence remained high but did not increase over time. Two men became infected (HIV incidence 0.43 infections per 100 py, 95% CI: 0.05-1.54), both of whom had drug levels consistent with having taken fewer than 2 doses per week at the visit when seroconversion was detected.

IPERGAY OPEN-LABEL EXTENSION (OLE) STUDY

Findings have been reported from the open-label phase of the Ipergay trial that enrolled 361 of the original trial participants[28]. All of the open-label study participants were provided peri-coital PrEP as in the original trial. After a mean follow-up time of 18.4 months (IQR: 17.7-19.1), the HIV incidence observed was 0.19 per 100 py which, compared to the incidence in the placebo group of the original trial (6.60 per 100 py), represented a 97% (95% CI: 81-100) relative reduction in HIV incidence. The one participant who acquired HIV had not taken any PrEP in the 30 days before his reactive HIV test and was in an ongoing relationship with an HIV positive partner. Of 336 participants with plasma drug levels obtained at the 6-month visit, 71% had tenofovir detected. By self-report, PrEP was used at the prescribed dosing for the most recent sexual intercourse by 50% of participants, with suboptimal dosing by 24%, and not used by 26%. Reported condomless receptive anal sex at most recent sexual intercourse increased from 77% at baseline to 86% at the 18-month follow-up visit (p=0.0004). The incidence of a first bacterial STI in the observational study (59.0 per 100 py) was not higher than that seen in the randomized trial (49.1 per 100 py) (p=0.11).

The frequency of pill-taking in the open label study population was higher (median 18 pills per month) than that in the original trial (median 15 pills per month), Therefore it remains unclear

whether the regimen will be highly protective if taken only a few hours or days before sex, without any buildup of the drug from prior use.

Published Trials of Antiretroviral Preexposure Prophylaxis Among Heterosexual Men and Women

Partners PrEP Trial

The Partners PrEP trial[3,29] was a phase 3 randomized, double-blind, placebo-controlled study of daily oral TDF/FTC or TDF for the prevention of acquisition of HIV by the uninfected partner in 4,758 HIV-discordant heterosexual couples in Uganda and Kenya. The trial was stopped after an interim analysis in mid-2011 showed statistically significant efficacy in the medication groups (TDF/FTC or TDF) compared with the placebo group. In 48% of couples, the infected partner was male. HIV-positive partners had a median CD4 count of 495 cells/μL and were not being prescribed antiretroviral therapy because they were not eligible by local treatment guidelines. Participants had monthly follow-up visits and the study drug was discontinued among women who became pregnant during the trial.

Adherence to medication was very high: 98% by pills dispensed, 92% by pill count, and 82% by plasma drug-level testing among randomly selected participants in the TDF and TDF/FTC study groups. Rates of serious adverse events and serum creatinine or phosphorus abnormalities did not differ by study group. Modest increases in gastrointestinal symptoms and fatigue were reported in the antiretroviral medication groups compared with the placebo group, primarily in the first month of use. Among participants of both sexes combined, efficacy estimates for each of the 2 antiretroviral regimens compared with placebo were 67% (95% CI, 44-81) for TDF and 75% (95% CI, 55-87) for TDF/FTC. Among women, the estimated efficacy was 71% for TDF and 66% for TDF/FTC. Among men, the estimated efficacy was 63% for TDF and 84% for TDF/FTC. Efficacy estimates by drug regimen were not statistically different among men, women, men and women combined, or between men and women. In a Partners PrEP substudy that measured plasma TDF levels among participants randomly assigned to receive TDF/FTC, detectable drug was associated with a 90% reduction in the risk of HIV acquisition. TDF- or FTC- resistant virus was detected in 3 of 14 persons determined to have been infected when enrolled (2 of 5 in the TDF group; 1 of 3 in the TDF/FTC group)[8]. No TDF or FTC resistant virus was detected among those infected after enrollment. Among women, the pregnancy rate was high (10.3 per 100 py) and rates did not differ significantly between the study groups.

TDF2 Trial

The Botswana TDF2 Trial[4], a phase 2 randomized, double-blind, placebo-controlled study of the safety and efficacy of daily oral TDF/FTC, enrolled 1,219 heterosexual men and women in

Botswana, and follow-up has been completed. Participants were seen for monthly follow-up visits, and study drug was discontinued in women who became pregnant during the trial.

Among participants of both sexes combined, the efficacy of TDF/FTC was 62% (22%-83%). Efficacy estimates by sex did not statistically differ from each other or from the overall estimate, although the small number of endpoints in the subsets of men and women limited the statistical power to detect a difference. Compliance with study visits was low: 33.1% of participants did not complete the study per protocol. However, many were re-engaged for an exit visit, and 89.3% of enrolled participants had a final HIV test.

Among 3 participants later found to have been infected at enrollment, TDF/FTC-resistant virus was detected in 1 participant in the TDF/FTC group and a low level of TDF/FTC-resistant virus was transiently detected in 1 participant in the placebo group. No resistant virus was detected in the 33 participants who seroconverted after enrollment.

Medication adherence by pill count was 84% in both groups. Nausea, vomiting, and dizziness occurred more commonly, primarily during the first month of use, among those randomly assigned to TDF/FTC than among those assigned to placebo. The groups did not differ in rates of serious clinical or laboratory adverse events. Pregnancy rates and rates of fetal loss did not differ by study group.

FEM-PrEP Trial

The FEM-PrEP trial[30] was a phase 3 randomized, double-blind, placebo-controlled study of the HIV prevention efficacy and clinical safety of daily TDF/FTC among heterosexual women in South Africa, Kenya, and Tanzania. Participants were seen at monthly follow-up visits, and study drug was discontinued among women who became pregnant during the trial. The trial was stopped in 2011, when an interim analysis determined that the trial would be unlikely to detect a statistically significant difference in efficacy between the two study groups.

Adherence was low in this trial: study drug was detected in plasma samples of <50% of women randomly assigned to TDF/FTC. Among adverse events, only nausea and vomiting (in the first month) and transient, modest elevations in liver function test values were more common among those assigned to TDF/FTC than those assigned to placebo. No changes in renal function were seen in either group. Initial analyses of efficacy results showed 4.7 infections per 100/ person-years in the TDF/FTC group and 5.0 infections per 100 person-years in the placebo group. The hazard ratio 0.94 (95% CI, 0.59-1.52) indicated no reduction in HIV incidence associated with TDF/FTC use. Of the 68 women who acquired HIV infection during the trial, TDF or FTC resistant virus was detected in 5 women: 1 in the placebo group and 4 in the TDF/FTC group. In multivariate analyses, there was no association between pregnancy rate and study group.

PHASE 2 TRIAL OF PREEXPOSURE PROPHYLAXIS WITH TENOFOVIR AMONG WOMEN IN GHANA, CAMEROON, AND NIGERIA

A randomized, double-blind, placebo-controlled trial of oral tenofovir TDF was conducted among heterosexual women in West Africa - Ghana (n = 200), Cameroon (n = 200), and Nigeria (n = 136)[31]. The study was designed to assess the safety of TDF use and the efficacy of daily TDF in reducing the rate of HIV infection. The Cameroon and Nigeria study sites were closed prematurely because operational obstacles developed, so participant follow-up data were insufficient for the planned efficacy analysis. Analysis of trial safety data from Ghana and Cameroon found no statistically significant differences in grade 3 or 4 hepatic or renal events or in reports of clinical adverse events. Eight HIV seroconversions occurred among women in the trial: 2 among women in the TDF group (rate=0.86 per 100 person-years) and 6 among women receiving placebo (rate, 2.48 per 100 person-years), yielding a rate ratio of 0.35 (95% CI, 0.03-1.93; *p*=0.24). Blood specimens were available from 1 of the 2 participants who seroconverted while taking TDF; standard genotypic analysis revealed no evidence of drug-resistance mutations.

VOICE (VAGINAL AND ORAL INTERVENTIONS TO CONTROL THE EPIDEMIC) TRIAL

VOICE (MTN-003)[32] was a phase 2B randomized, double-blind study comparing oral (TDF or TDF/FTC) and topical vaginal (tenofovir) antiretroviral regimens against corresponding oral and topical placebos among 5,029 heterosexual women enrolled in eastern and southern Africa. Of these women, 3,019 were randomly assigned to daily oral medication (TDF/FTC, 1,003; TDF, 1,007; oral placebo, 1,009). In 2011, the trial group receiving oral TDF and the group receiving topical tenofovir were stopped after interim analyses determined futility. The group receiving oral TDF/FTC continued to the planned trial conclusion.

After the exclusion of 15 women later determined to have had acute HIV infection when enrolled in an oral medication group and 27 with no follow-up visit after baseline, 52 incident HIV infections occurred in the oral TDF group, 61 in the TDF/FTC group, and 60 in the oral placebo group. Effectiveness was not significant for either oral PrEP medication group; –49%% for TDF (hazard ratio [HR] 1.49; 95% CI, 0.97-2.29) and –4.4% for TDF/FTC (HR, 1.04; 95% CI, 0.73-1.49) in the modified-intent-to-treat analysis.

Face-to-face interview, audio computer-assisted self-interview, and pill-count medication adherence were high in all 3 groups (84%-91%). However, among 315 participants in the random cohort of the case-cohort subset for whom quarterly plasma samples were available, tenofovir was detected, on average, in 30% of samples from women randomly assigned to TDF and in 29% of samples from women randomly assigned to TDF/FTC. No drug was detected at any quarterly visit during study participation for 58% of women in the TDF group and 50% of women in the TDF/FTC group. The percentage of samples with detectable drug was less than 40% in all study drug groups and declined throughout the study. In a multivariate analysis that

adjusted for baseline confounding variables (including age, marital status), the detection of study drug was not associated with reduced risk of HIV acquisition.

The number of confirmed creatinine elevations (grade not specified) observed was higher in the oral TDF/FTC group than in the oral placebo group. However, there were no significant differences between active product and placebo groups for other safety outcomes. Of women determined after enrollment to have had acute HIV infection at baseline, two women from the TDF/FTC group had virus with the M184I/V mutation associated with FTC resistance. One woman in the TDF/FTC group who acquired HIV infection after enrollment had virus with the M184I/V mutation; No participants with HIV infection had virus with a mutation associated with tenofovir resistance.

In summary, although low adherence and operational issues precluded reliable conclusions regarding efficacy in 3 trials (VOICE, FEM-PrEP and the West African trial)[33], 2 trials (Partners PrEP and TDF2) with high medication adherence have provided substantial evidence of efficacy among heterosexual men and women. All 5 trials have found PrEP to be safe for these populations.

Daily oral PrEP with TDF/FTC is recommended as one HIV prevention option for heterosexually-active men and women at substantial risk of HIV acquisition because these trials present evidence of its safety and 2 present evidence of efficacy in these populations, especially when medication adherence is high. (IA).

Published Trial of Antiretroviral Preexposure Prophylaxis Among Persons Who Inject Drugs

Bangkok Tenofovir Study (BTS)

BTS[5] was a phase 3 randomized, double-blind, placebo-controlled study of the safety and efficacy of daily oral TDF for HIV prevention among 2,413 PWID (also called IDU) in Bangkok, Thailand[5] The study was conducted at drug treatment clinics; 22% of participants were receiving methadone treatment at baseline. At each monthly visit, participants could choose to receive either a 28-day supply of pills or to receive medication daily by directly- observed therapy. Study clinics (n=17) provided condoms, bleach (for cleaning injection equipment), methadone, primary medical care, and social services free of charge. Participants were followed for 4.6 years (mean) and received directly- observed therapy 87% of the time.

In the modified intent- to-treat analysis (excluding 2 participants with evidence of HIV infection at enrollment), efficacy of TDF was 48.9% (95% CI, 9.6-72.2; P = .01). A post-hoc modified intent-to-treat analysis was done, removing 2 additional participants in whom HIV infection was identified within 28 days of enrollment, including only participants on directly observed therapy who met pre-established criteria for high adherence (taking a pill at least 71% of days and

missing no more than two consecutive doses), and had detectable levels of tenofovir in their blood. Among this set of participants, the efficacy of TDF in plasma was associated with a 73.5% reduction in the risk for HIV acquisition (95% CI, 16.6-94.0; *P* = .03). Among participants in an unmatched case-control study that included the 50 persons with incident HIV infection and 282 participants at 4 clinics who remained HIV uninfected, detection of TDF in plasma was associated with a 70.0% reduction in the risk for acquiring HIV infection (95% CI, 2.3-90.6; *P* = .04).

Rates of nausea and vomiting were higher among TDF than among placebo recipients in the first 2 months of medication but not thereafter. The rates of adverse events, deaths, or elevated creatinine did not differ significantly between the TDF and the placebo groups. Among the 49 HIV infections for which viral RNA could be amplified (of 50 incident infections and 2 infections later determined to have been present at enrollment), no virus with mutations associated with TDF resistance were identified.

Among participants with HIV infection followed up for a maximum of 24 months, HIV plasma viral load was lower in the TDF than in the placebo group at the visit when HIV infection was detected (*P* = .01), but not thereafter (*P* = .10).

Published Open-Label Study of Antiretroviral Preexposure Prophylaxis Among Person Who Inject Drugs

Bangkok Tenofovir Study (BTS) Open-Label Extension (OLE) Study

All 1315 participants in the randomized trial (BTS) who were HIV-negative and had no renal contraindication were offered daily oral TDF for 1 year in an open label extension study[34]. Sixty-one percent (n=798) elected to take PrEP. Participants who were older (≥30 years, $p<0.0001$), injected heroin ($p=0.007$) or had been in prison ($p=0.0007$) were more likely to start PrEP than those without these characteristics. Twenty-eight percent (n=220) did not return for any follow-up visits. Those who had injected heroin ($p=0.01$) or had been in prison ($p=0.0007$) during the 3 months before the open label study returned for a follow-up visit. Overall, by diary, adherence was lower in the open label study (38.5 % of days) than in the randomized clinical trial (83.8% of days). Those who injected midazolam ($p=0.02$) or were in prison ($p<0.0001$) during the open label study were more likely to be more than 90% adherent than those without these characteristics. During a median 335 days of follow-up, one HIV infection occurred in a participant who reported not taking any doses during the 60 days before the positive test, yielding an HIV incidence of 2.1 per 1000 py (95% CI: 0.05-11.7). Among the 339 (42%) who completed a 12-month follow-up visit, injection and needle sharing did not increase during the open-label study.

Daily oral PrEP with TDF/FTC (or TDF alone) is recommended as one HIV prevention option for PWID at substantial risk of HIV acquisition because this trial presents evidence of the safety and efficacy of TDF as PrEP in this population, especially when medication adherence is high. **(IA)**

Table 2: Evidence Summary — Overall Evidence Quality of Randomized Clinical Trials (per GRADE Criteria[35])

Study	Design[a]	Participants		Limitations	Quality of Evidence (See Table 14, Appendix 2)
		Agent	Control		
Among Men Who have Sex with Men					
iPrEx Trial	Phase 3	TDF/FTC (n = 1251)	Placebo (n = 1248)	Adherence	High
US MSM Safety Trial	Phase 2	TDF (n = 201)	Placebo (n = 199)	Minimal	High
ATN 082	Pilot	TDF/FTC (n=20)	Placebo (n=19) No pill (n=19)	Small size, stopped early, limited follow-up time, low medication adherence	Low
Among Heterosexual Men and Women					
Partners PrEP	Phase 3	TDF (n = 1589) TDF/FTC (n = 1583)	Placebo (n = 1586)	Minimal	High
TDF2	Phase 2	TDF/FTC (n = 611)	Placebo (n = 608)	High loss to follow-up; modest sample size	Moderate
Among Heterosexual Women					
FEM-PrEP	Phase 3	TDF/FTC (n = 1062)	Placebo (n = 1058)	Stopped at interim analysis, limited follow-up time; very low adherence to drug regimen	Low
West African Trial	Phase 2	TDF (n = 469)	Placebo (n = 467)	Stopped early for operational concerns; small sample size; limited follow-up time on assigned drug	Low
VOICE	Phase 2B	TDF (n = 1007) TDF/FTC (n = 1003)	Placebo (n = 1009)	TDF arm stopped at interim analysis (futility); very low adherence to drug regimen in both TDF and TDF/FTC arms	Low
Among Injection Drug Users					
BTS	Phase 3	TDF (n = 1204)	Placebo (n = 1207)	Minimal	High

Note: GRADE quality ratings:
high = further research is very unlikely to change our confidence in the estimate of effect;
moderate = further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate;
low = further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate;
very low = any estimate of effect is very uncertain.

[a] All trials in this table were randomized, double-blind, prospective clinical trials

Table 3: Evidence Summary of Randomized Clinical Trials — HIV Incidence Findings

Study	Outcome Analyses— HIV incidence (mITT)		Effect — HR [Efficacy Estimate] (95% CI)		
	Agent	Control			
iPrEx (MSM)	36 infections among 1224 persons	64 infections among 1217 persons	0.56 [44%] (0.37–0.85)		
US MSM Safety Trial	3 infections among 201 persons (all 3 in delayed arm, not on TDF)	4 infections among 199 persons (1 acute infection at enrollment)	Not Reported		
Partners PrEP (heterosexual men and women)	TDF 17 infections among 1572 persons TDF/FTC 13 infections among 1568 persons	52 infections among 1568 persons		TDF	TDF/FTC
			All	0. 33 [67%] (0.19–0.56)	0.25 [75%] (0.13–0.45)
			Women	0.29 [71%] (0.13–0.63)	0.34 [66%] (0.16–0.72)
			Men	0.37 [63%] (0.17–0.80)	0.16 [84%] (0.06–0.46)
TDF2 (heterosexual men and women)	9 infections among 601 persons 1.2 infections/100 person-years	24 infections among 599 persons 3.1 infections per 100 person-years	0.38 [62%] (0.17–0.79)		
FEM-PrEP (heterosexual women)	33 infections among 1024 persons 4.7 infections per 100 person-years	35 infections among 1032 persons 5.0 infections per 100 person-years	0.94 [6%] [a] (0.59–1.52)		
West African Trial (heterosexual women)	2 infections among 427 persons 0.86 infections per 100 person-years	6 infections among 432 persons 2.48 infections per 100 person-years	0.35 [65%][a] (0.03–1.93)		
VOICE (heterosexual women)	TDF 52 infections among 993 persons 6.3 infections per 100 person-years TDF/FTC 61 infections among 985 persons 4.7 infections per 100 person-years	35 infections among 999 persons 4.2 infections per 100 person-years	TDF	TDF/FTC	
			1.49 [-50 %][a] (0.97–2.3)	1.04 [-4%][a] (0.73, 1.5)	
BTS (persons who inject drugs)	17 infections among 1204 persons 0.35 infections per 100 person-years	33 infections among 1207 persons 0.68 infections per 100 person-years	0.51 [49%] (9.6, 72.2)		

mITT: modified intent to treat analysis; HR: hazard ratio.

[a] Not statistically significant.

Table 4: Measures of Efficacy, by Medication Adherence, Percentage Reduction in HIV Incidence in Randomized Clinical Trials (95% Confidence Interval)

Study	Modified Intent-to-Treat Efficacy			Efficacy by Self-report Adherence Measures	Efficacy by Pill-count Adherence Measures	Efficacy by Blood Detection of Drug Measures[a]
iPrEx (TDF/FTC)	44% (15–63%)			>50% 50% (18–70%) >90% 73% (41–88%)		92% (40–99%)
Partners PrEP	All TDF: 67% TDF/FTC: 75%	Men TDF: 63% TDF/FTC: 84%	Women TDF: 71% TDF/FTC: 66%	NR	100% (87–100%)	TDF: 86% (67–94%) TDF/FTC: 90% (58–98%)
TDF2 (TDF/FTC)	All 63%	Men 80%	Women 49%[b]	NR	NR	TDF detected: 85%[b]
FEM-PrEP (TDF/FTC)	NR			NR	NR	NR
VOICE (TDF,TDF/FTC)	NR			NR	NR	NR
BTS (TDF)	49%			NR	56% (-19 to 86%)[c]	74% (17–94%)

NR, not reported.

[a] Tenofovir detection assays were done in subsets of persons randomly assigned to receive TDF or TDF/FTC

[b] Finding not statistically significant

[c] Among participants on directly observed therapy

Table 5: Evidence Summary of Randomized Clinical Trials — Safety and Toxicity

Study	Outcome Analyses	
	Agent	**Control**
Grade 3/4 Adverse Clinical Events[a]		
iPrEx	52 events	59 events
ATN 082	1 event	1 event
TDF2	9 events	10 events
West African Trial	NR	NR
Grade 3/4 Adverse Laboratory Events [a]		
iPrEx	59 events	48 events
ATN 082	3 events	0 events
TDF2	32 events	32 events
West African Trial	1 event	5 events
Grade 3/4 Adverse Events (Clinical and Laboratory)[a]		
Partners PrEP	TDF: 323 events TDF/FTC: 337 events	307 events
FEM-PrEP	NR	NR
US MSM Safety Trial	36 events	26 events
VOICE	NR	NR
BTS	175 events	173 events

NR, not reported.

[a] RDBPCT = randomized, double-blind, prospective clinical trial

Table 6: Evidence Summary of Randomized Clinical Trials — HIV Resistance Findings (TDF or FTC Drug Resistant Virus Detected)

Study	Outcome Analyses	
	Agent	Control
iPrEx	2 resistant viruses among 2 persons infected at baseline 0 resistant viruses among 36 persons infected after baseline	1 resistant virus among 8 persons infected at baseline 0 resistant viruses among 64 persons infected after baseline
US MSM Safety Trial	0 resistant viruses among 3 persons infected after baseline (in delayed arm before starting drug)	1 resistant virus among 1 person infected at baseline 0 resistant viruses among 3 persons infected after baseline
Partners PrEP	2 resistant viruses among 5 persons infected at baseline and randomly assigned to TDF 1 resistant virus among 3 persons infected at baseline and randomly assigned to TDF/FTC 0 resistant viruses among 27 persons infected after baseline	0 resistant viruses among 6 persons infected at baseline 0 resistant viruses among 51 persons infected after baseline
TDF2	1 resistant virus in 1 person infected at baseline 0 resistant viruses among 9 persons infected after baseline	1 resistant virus in 1 person infected at baseline (very low frequency and transient detection) 0 resistant viruses among 24 persons infected after baseline
FEM-PrEP	4 resistant viruses among 33 persons infected after baseline	1 resistant virus in 35 persons infected after baseline
West African Trial	0 resistant viruses among 2 persons infected while on TDF	NR
VOICE	NR	—
BTS	0 resistant viruses among 49 persons infected after baseline	

NR, not reported.

Table 7. Evidence Summary of Open-Label Studies (daily oral TDF/FTC)

Study	Design	Population	Effect HR [Efficacy Estimate]	Efficacy by Blood Detection of Drug Measure	Resistance
PROUD	Wait-list Control	MSM	[86%] [90% CI: 64%-96%] comparing immediate vs. deferred group	Not reported	• 2 resistant viruses among 3 persons infected at baseline • 0 resistant viruses among 23 persons infected after baseline
iPrEx OLE[a]	RCT Open-Label Extension	MSM	0.51 [49%] (95% CI: 0.26-1.01) comparing those electing to use PrEP with those who did not , adjusted for baseline sexual risk behavior	Compared with being off PrEP, HRs for seroconversion stratified by weekly dosing inferred from blood drug levels: <2 doses/week 0.56 [44%](0.23-1.31) 2-3 doses/week 0.16 [84%] (0.01-0.79) 4-6 doses/week 0.0 [100%] (0.0-0.21) 7 doses/week 0.0 [100%] (0.0-0.43)	• 0 resistant viruses among 2 persons infected at baseline (not started on PrEP) • 1 resistant virus among 28 persons infected after baseline started on PrEP • 0 resistant viruses among 13 persons infected after baseline not started on PrEP
Demo Project	Clinical Cohort	MSM[b]	HIV incidence 0.43 per 100 py (no comparison group) in a population with an STI incidence of 90 per 100 py observed during follow-up.[b]	Both seroconverters had blood drug levels associated with <2 doses/week	• 1 resistant virus among 3 persons infected at enrollment and started on PrEP • 0 resistant viruses among 2 persons infected after baseline started on PrEP
Kaiser Permanente	Clinical Cohort	MSM	0 HIV diagnoses in 5104 py of follow-up	Not reported	Not applicable

[a] included men who had participated in the iPrEx, CDC Safety, and Adolescent Trials Network 082 PrEP trials
[b] 653 MSM, 3 heterosexual women, 1 transgender man who has sex with men

Identifying Indications for PrEP

Taking a sexual history is recommended for all adult and adolescent patients as part of ongoing primary care, but the sexual history is often deferred because of urgent care issues, provider discomfort, or anticipated patient discomfort. This deferral is common among providers of primary care[36], STI care[37], and HIV care[38-40].

Routinely taking a sexual history is a necessary first step to identify which patients in a clinical practice are having sex with same-sex partners, which are having sex with opposite-sex partners, and what specific sexual behaviors may place them at risk for, or protect them from, HIV acquisition. To identify the sexual health needs of all their patients, clinicians should not limit sexual history assessments to only selected patients (e.g., young, unmarried persons or women seeking contraception), because new HIV infections and STIs are occurring in all adult and adolescent age groups, both sexes, and both married and unmarried persons. The clinician can introduce this topic by stating that taking a brief sexual history is routine practice, go on to explain that the information is necessary to the provision of individually appropriate sexual health care, and close by reaffirming the confidentiality of patient information.

Transgender persons are those whose sex at birth differs from their self-identified gender. Although the effectiveness of PrEP for transgender women has not yet been definitively proven in trials[19], and trials have not been conducted among transgender men, PrEP has been shown to reduce the risk for HIV acquisition during anal sex and penile-vaginal sex. Therefore, its use may be considered in all persons at risk of acquiring HIV sexually.

Assessing Risk of Sexual HIV Acquisition

Because offering PrEP is currently indicated for MSM at substantial risk of HIV acquisition, it is important to consider that although 76% of MSM surveyed in 2008 in 21 US cities reported a health care visit during the past year[41], other studies reported that health care providers do not ask about, and patients often do not disclose, same-sex behaviors[42]. Box A1 contains a set of brief questions designed to identify men who are currently having sex with men and to assess a key set of sexual practices that are associated with the risk of HIV acquisition. In studies to develop scored risk indexes predictive of incident HIV infection among MSM[43,44] (see Clinical Providers' Supplement, Section 6), several critical factors were identified.

BOX A1: RISK BEHAVIOR ASSESSMENT FOR MSM[44]

In the past 6 months:

- Have you had sex with men, women, or both?
- *(if men or both sexes)* How many men have you had sex with?
- How many times did you have receptive anal sex (you were the bottom) with a man who was not wearing a condom?
- How many of your male sex partners were HIV-positive?
- *(if any positive)* With these HIV-positive male partners, how many times did you have insertive anal sex (you were the top) without you wearing a condom?
- Have you used methamphetamines (such as crystal or speed)?

Box A2 contains a set of brief questions designed to identify women and men who are currently having sex with opposite-sex partners (heterosexually active) and to assess a key set of sexual practices that are associated with the risk of HIV acquisition as identified both in PrEP trials and epidemiologic studies[45-48].

BOX A2: RISK BEHAVIOR ASSESSMENT FOR HETEROSEXUAL MEN AND WOMEN

In the past 6 months:

- Have you had sex with men, women, or both?
- *(if opposite sex or both sexes)* How many men/women have you had sex with?
- How many times did you have vaginal or anal sex when neither you nor your partner wore a condom?
- How many of your sex partners were HIV-positive?
- *(if any positive)* With these HIV-positive partners, how many times did you have vaginal or anal sex without a condom?

In addition, for all sexually active patients, clinicians may want to consider reports of diagnoses of bacterial STIs (chlamydia, syphilis, gonorrhea) during the past 6 months as evidence of sexual activity that could result in HIV exposure. For heterosexual women and men, sex without a condom (or its correct use) may also be indicated by recent pregnancy of a female patient or sexual partner of a male patient.

Clinicians should also briefly screen all patients for alcohol abuse[49] (especially before sexual activity) and the use of illicit non-injection drugs (e.g., amyl nitrite, stimulants) [50,51]. The use of these substances may affect sexual risk behavior[52], hepatic or renal health, or medication adherence, any of which may affect decisions about the appropriateness of prescribing PrEP medication. In addition, if substance abuse is reported, the clinician should provide referral for appropriate treatment or harm-reduction services acceptable to the patient.

Lastly, clinicians should consider the epidemiologic context of the sexual practices reported by the patient. The risk of HIV acquisition is determined by both the frequency of specific sexual practices

(e.g., unprotected anal intercourse) and the likelihood that a sex partner has HIV infection. The same behaviors when reported as occurring in communities and demographic populations with high HIV prevalence or occurring with partners known to have HIV infection, are more likely to result in exposure to HIV and so will indicate greater need for intensive risk-reduction methods (PrEP, multisession behavioral counseling) than when they occur in a community or population with low HIV prevalence (see http://www.AIDSvu.org or http://www.cdc.gov/nchhstp/atlas/).

After assessing the risk of HIV acquisition, clinicians should discuss with the patient which of several effective prevention methods (e.g., PrEP, behavioral interventions) will be pursued (see CDC HIV risk reduction tool at https://wwwn.cdc.gov/hivrisk/estimator.html#). When supporting consistent and correct condom use is feasible and the patient is motivated to achieve it, high levels of protection against both HIV and several STIs[48] are afforded without the side effects or cost of medication. A clinician can support consistent condom use by providing brief clinical counseling (see Clinical Providers' Supplement, Section 11), by referring the patient to behavioral medicine or health education staff in the clinical setting, or by referring the patient to community-based or local health department counseling and support services.

Reported consistent ("always") condom use is associated with an 80% reduction in HIV acquisition among heterosexual couples[53] and 70% among MSM[57]. However, inconsistent condom use is less effective[45,55], and studies have reported low rates of recent consistent condom use among MSM[57,59] and other sexually active adults[57]. Especially low rates have been reported when condom use was measured over several months rather than during most recent sex or the past 30 days[58]. Therefore, unless the patient reports confidence that consistent condom use can be achieved, additional HIV prevention methods, including the consideration of PrEP should be provided while continuing to support condom.

A patient who reports that 1 or more regular sex partners is of unknown HIV status should be offered HIV testing for those partners, either in the clinician's practice or at a confidential testing site (see zip code lookup at http://www.hivtest.org/).

Lastly, for any regular sex partner reported to be HIV-positive, clinician should determine whether the HIV-negative patient knows if the HIV-positive partner is receiving antiretroviral therapy and whether a recent evaluation indicates an undetectable viral load. In addition to the known health benefits of viral load suppression by antiretroviral therapy, a recent clinical trial (HPTN 052[59]) demonstrated that antiretroviral therapy also substantially protects against HIV transmission to a heterosexual partner. Among 1,753 HIV discordant couples where the infected partner was treated, transmission risk was reduced 93%. All documented infections where viral genetic linkage was confirmed occurred in the context of an unsuppressed viral load in the partner initially infected with HIV. Another study included 548 HET and 340 MSM HIV-discordant couples where the partner with HIV infection was virally suppressed with antiretroviral treatment[60,61]. This study observed no HIV transmissions to the uninfected partner despite approximately 58,000 reported episodes of condomless vaginal or anal intercourse during 1,200 couple/years of observation substantial protection (100%). However, some persons who know they have HIV infection may not be in care, may not be receiving antiretroviral

therapy, may not be receiving highly effective regimens, may not be adherent to their medications, or for other reasons may not have viral loads that are associated with the least risk of transmission to an uninfected sex partner[62,63]. In addition, clinicians providing care to the HIV-negative patient may not have access to the medical records of the HIV-positive partner to document their recent viral load status and over time.

Box B1: Recommended Indications for PrEP Use by MSM[2]

- Adult man
- Without acute or established HIV infection
- Any male sex partners in past 6 months (if also has sex with women, see Box B2)
- Not in a monogamous partnership with a recently tested, HIV-negative man

AND at least one of the following

- Any anal sex without condoms (receptive or insertive) in past 6 months
- A bacterial STI (syphilis, gonorrhea, or chlamydia) diagnosed or reported in past 6 months

Box B2: Recommended Indications for PrEP Use by Heterosexually Active Men and Women

- Adult person
- Without acute or established HIV infection
- Any sex with opposite sex partners in past 6 months
- Not in a monogamous partnership with a recently tested HIV-negative partner

AND at least one of the following

- Is a man who has sex with both women and men (behaviorally bisexual) [also evaluate indications for PrEP use by Box B1 criteria]
- Infrequently uses condoms during sex with 1 or more partners of unknown HIV status who are known to be at substantial risk of HIV infection (PWID or bisexual male partner)
- Is in an ongoing sexual relationship with an HIV-positive partner
- A bacterial STI (syphilis, gonorrhea in women or men) diagnosed or reported in past 6 months

Assessing Risk of HIV Acquisition Through Injection Practices

Although the annual number of new HIV infections among PWID in the United States has declined, a sizable number occur each year. In 2010, PWID accounted for 8% of estimated incident HIV infections[13]. According to the National HIV Behavioral Surveillance System (NHBS)[64] substantial proportions of PWID report sharing syringes (34%) and sharing injection equipment (58%). In addition, in NHBS and epidemiologic studies conducted with PWID, most PWID report sexual behaviors that also confer risk of HIV acquisition[65]. Because of the efficacy and safety demonstrated in the PrEP trial with PWID, providing PrEP to those who report injection behaviors that place them at substantial risk of acquiring HIV infection could contribute to HIV prevention for PWID at both the individual and the population level.

Although current evidence is insufficient for a recommendation that all patients be screened for injection or other illicit drug use, the US Preventive Services Task Force recommends that clinicians be alert to the signs and symptoms of illicit drug use in patients[66]. Clinicians should determine whether patients who are currently using illicit drugs are in (or want to enter) behavioral, medication-assisted, or in-patient drug treatment. For persons with a history of injecting illicit drugs but who are currently not injecting, clinicians should assess the risk of relapse along with the patients' use of relapse prevention services (e.g., a drug-related behavioral support program, use of mental health services, 12-step program).

Box A3 contains a set of brief questions that may help identify persons who are injecting illicit drugs, and to assess a key set of injection practices that are associated with the risk of HIV acquisition as identified in the PrEP trial with PWID[5] and in epidemiologic studies[64,67] (for a scored risk index predictive of incident HIV infection among PWID[63], see the Clinical Providers' Supplement, Section 7)

Box A3: Risk Behavior Assessment for Persons Who Inject Drugs[68]

- Have you ever injected drugs that were not prescribed to you by a clinician?
- *(if yes),* When did you last inject unprescribed drugs?
- In the past 6 months, have you injected by using needles, syringes, or other drug preparation equipment that had already been used by another person?
- In the past 6 months, have you been in a methadone or other medication-based drug treatment program?

BOX B3: RECOMMENDED INDICATIONS FOR PREP USE BY PERSONS WHO INJECT DRUGS

- Adult person
- Without acute or established HIV infection
- Any injection of drugs not prescribed by a clinician in past 6 months

AND at least one of the following

- Any sharing of injection or drug preparation equipment in past 6 months
- Risk of sexual acquisition (also evaluate by criteria in Box B1 or B2)

PrEP or other HIV prevention should be integrated with prevention and clinical care services for the many health threats PWID may face (e.g., hepatitis B and C infection, abscesses, septicemia, endocarditis, overdose)[69] In addition, referrals for drug treatment, mental health services, and social services may be indicated.

LABORATORY TESTS AND OTHER DIAGNOSTIC PROCEDURES

All patients whose sexual or drug injection history indicates consideration of PrEP and who are interested in taking PrEP must undergo laboratory testing to identify those for whom this intervention would be harmful or for whom it would present specific health risks that would require close monitoring.

HIV TESTING

HIV testing and the documentation of results are required to confirm that patients do not have HIV infection when they start taking PrEP medications. For patient safety, HIV testing and should be repeated at least every 3 months (before prescriptions are refilled or reissued). This requirement should be explained to patients during the discussion about whether PrEP is appropriate for them.

The Centers for Disease Control and Prevention (CDC) and the US Preventive Services Task Force recommends that MSM, PWID, patients with a sex partner who has HIV infection, and others at substantial risk of HIV acquisition undergo an HIV test at least annually or for those with additional risk factors, every 3-6 months[70,71]. However, outside the context of PrEP delivery, testing is often not done as frequently as recommended[72].

Clinicians should document a negative antibody test result within the week before initiating (or reinitiating) PrEP medications, ideally with an antigen/antibody test conducted by a laboratory. The required HIV testing can be accomplished by (1) drawing blood (serum) and sending the specimen to a laboratory for an antigen/antibody test or and antibody-only test or (2) performing a rapid, point-of-care, FDA-approved, fingerstick blood test. Rapid tests that use oral fluid should not be used to screen for HIV infection when considering PrEP use because they can be less sensitive than blood tests[73]. Clinicians should not accept patient-reported test results or documented anonymous test results. A

preliminary positive HIV antibody test must be confirmed according to the local laboratory standard practice[74] and viral load and CD4 lymphocyte tests should be ordered to assist in future treatment decisions.

See http://www.cdc.gov/hiv/testing/laboratorytests.html for FDA-approved HIV tests, specimen requirements, and time to detection of HIV infection.

ACUTE HIV INFECTION

In the iPrEx trial, drug-resistant virus developed in 2 persons with unrecognized acute HIV infection at enrollment and for whom TDF/FTC had been dispensed. These participants had negative antibody test results before they started taking PrEP, tested positive at a later study visit, and PCR (polymerase chain reaction) on stored specimens from the initial visit detected the presence of virus. When questioned, most of the 10 acutely infected participants (8 of whom had been randomly assigned the placebo group) reported signs and symptoms consistent with a viral syndrome[2]. Both acutely infected patients to whom TDF/FTC had been dispensed had the M184V/I mutation associated with emtricitabine resistance, but not the K65R mutation associated with tenofovir resistance[2]. Among participants who were dispensed PrEP medication in the US MSM Safety Trial and in the Partners PrEP, TDF2, and VOICE trials (see Table 6), the M184V mutation, developed in several persons who were enrolled and had started taking medication with unrecognized acute HIV infection but K65R developed in only one (in the TDF2 study). However, no mutations emerged in persons who acquired infection after baseline. In the one trial with very low medication adherence that has published its resistance testing results, the emtricitabine resistance mutation, but not the K65R mutation was found in a few persons with incident infection after baseline (4 persons in the FEM-PrEP trial).

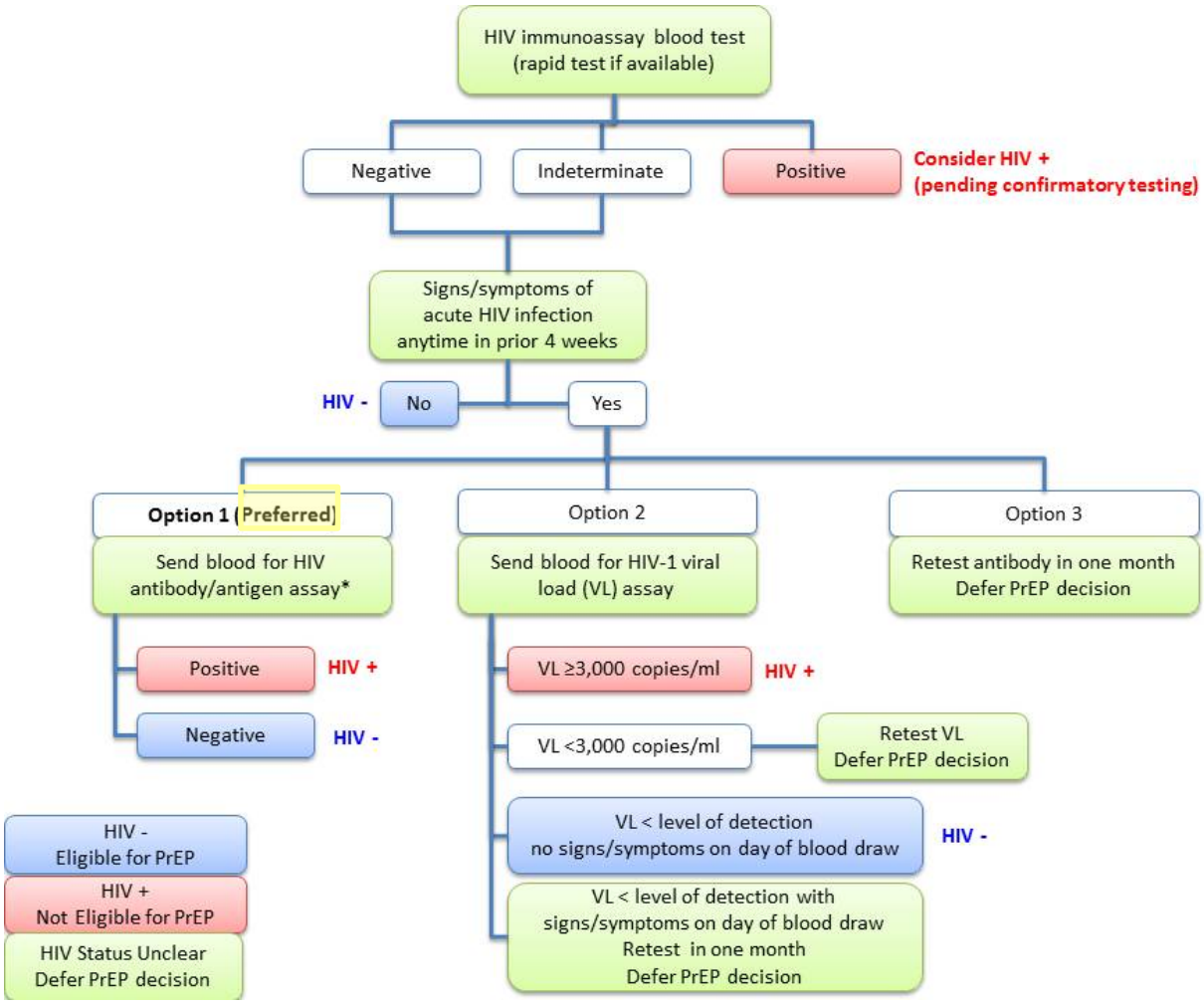
PrEP is indicated for MSM, heterosexual men and women, and PWID who report injection or sexual behaviors that place them at substantial risk of HIV acquisition. Therefore clinicians should suspect acute HIV infection in persons known to have been exposed recently (e.g., a condom broke during sex with an HIV-infected partner, relapse to injection drug use with shared injection equipment). In addition, clinicians should solicit a history of nonspecific signs or symptoms of viral infection during the preceding month or on the day of evaluation (see Table 8) in all PrEP candidates with a negative or an indeterminate result on an HIV antigen/antibody or antibody-only test.

Table 8: Clinical Signs and Symptoms of Acute (Primary) HIV Infection[75]

Features	Overall (n = 375) %	Sex		Route of transmission	
		Male (n = 355) %	Female (n = 23) %	Sexual (n = 324) %	Injection Drug Use (n = 34) %
Fever	75	74	83	77	50
Fatigue	68	67	78	71	50
Myalgia	49	50	26	52	29
Skin rash	48	48	48	51	21
Headache	45	45	44	47	30
Pharyngitis	40	40	48	43	18
Cervical adenopathy	39	39	39	41	27
Arthralgia	30	30	26	28	26
Night sweats	28	28	22	30	27
Diarrhea	27	27	21	28	23

The figure below illustrates the recommended clinical testing algorithm to establish HIV infection status before the initiation of PrEP or its re-initiation after more than a week off PrEP medication. . Laboratory antigen/antibody tests (option 1) are preferred because they have the highest sensitivity for detecting acute HIV infection which is associated with high viral loads. While viral load testing is sensitive (option 2), healthcare providers should be aware that available assays might yield false-positive low viral load results (e.g., <3,000 copies/mL) among persons without HIV infection. Without confirmatory tests, such false-positive results can lead to misdiagnosis of HIV infection.[76,.77] Repeat antibody testing (option 3) is least preferred because it delays determination of true HIV status and uninfected patients may have additional exposures and become infected without PrEP while waiting to retest. When clinicians prescribe PrEP based solely on the results of antibody-only or rapid tests, ordering a laboratory antigen/antibody test at the time baseline labs are drawn is recommended. This will increase the likelihood of detecting unrecognized acute infection so that PrEP can be stopped and the patient started on antiretroviral treatment in a timely manner.

Figure Clinician Determination of HIV Status for PrEP Provision



RENAL FUNCTION

In addition to confirming that any person starting PrEP medication is not infected with HIV, a clinician should determine renal function and test for infection with hepatitis B virus (HBV) because both decreased renal function and active HBV infection are potential safety issues for the use of TDF/FTC as PrEP.

TDF is widely used in combination antiretroviral regimens for the treatment of HIV infection[78]. Among HIV-infected persons prescribed TDF-containing regimens, decreases in renal function (as measured by estimated creatinine clearance [eCrCl]) have been documented, and occasional cases of acute renal failure, including Fanconi's syndrome, have occurred [79-81].

In the PrEP trials among otherwise healthy, HIV-uninfected adults, an eCrCl of ≥60 ml/min was an eligibility criterion. Safety data for TDF/FTC prescribed to persons with reduced renal function are not available. Therefore, for all persons considered for PrEP, a serum creatinine test should be done, and

an eCrCL should be calculated by using the Cockcroft-Gault formula (see Box C). Any person with an eCrCl of <60 ml/min should not be prescribed PrEP with TDF/FTC.

BOX C COCKCROFT-GAULT FORMULAS

Basic Formula[82]

$eCrCl_{CG}$ = [[(140 - age) × IBW × 0.85 for females] ÷ (serum creatinine × 72)]

IBW = ideal body weight Males: IBW = 50 kg + 2.3 kg for each inch over 5 feet
Females: IBW = 45.5 kg + 2.3 kg for each inch over 5 feet

Age in years, weight in kg, and serum creatinine in mg/100mL

Optional adjustment for low actual body weight[83]
If the actual body weight is less than the IBW (ideal body weight) use the actual body weight for calculating the eCrCl.

Optional adjustment of high actual body weight[83]
Used only if the actual body weight is 30% greater than the IBW. Otherwise, the IBW is used.

eCrCl = [[(140 - age) × AjBW] ÷ (serum creatinine × 72)] (× 0.85 for females)

AjBW = IBW + 0.3(ABW - IBW)
AjBW = adjusted body weight ABW = actual body weight

Optional adjustment for body surface area (BSA)[84]
Can be used if actual body weight is greater or less than IBW

$eCrCl_{BSAadj}$ =1.73m^2 × $eCrCl_{CG}$ (ml/min) ÷ BSA of the patient (m^2)

BSA (DuBois and DuBois formula[74]) = (height (m)$^{0.725}$ × weight (kg)$^{0.425}$) ÷ 139.2

HEPATITIS SEROLOGY

Sexually active adults (especially MSM), and persons who inject illicit drugs, are at risk of acquiring HBV infection[85] and hepatitis C virus (HCV) infection[86].

Vaccination against HBV is recommended for all adolescents and adults at substantial risk for HIV infection, especially for MSM. Therefore, HBV infection status should be documented by screening serology before TDF/FTC is prescribed as PrEP (see Table 9). Those patients determined to be susceptible to HBV infection should be vaccinated. Those patients found to be HBsAg positive should

be evaluated for possible treatment either by the clinician providing PrEP care or by linkage to an experienced HBV care provider.

HBV infection is not a contraindication to PrEP use. Both TDF and FTC are active against HBV[87]. HBV-monoinfected patients taking TDF or FTC, whether as PrEP or to treat HBV infection, who then stop these medications must have their liver function closely monitored for reactivation of HBV replication that can result in hepatic damage[6].

Table 9: Hepatitis B Screening Serology

HBsAg	Total anti-HBc	IgM anti-HBc	anti-HBs	Interpretation	Action
Negative	Negative	—	Negative	Susceptible	Vaccinate
Negative	Positive	—	Positive*	Immune (natural infection)	Document
Negative	Negative	—	Positive*	Immune (prior vaccination)	Document
Positive	Positive	Negative	Negative	Chronic HBV infection	Evaluate for treatment
Positive	Positive	Positive	Negative	Acute HBV infection	Follow and evaluate for treatment
Negative	Positive	—	Negative	Unclear—could be: • Resolved infection (most common) • False-positive anti-HBc; susceptible • "low level" chronic infection • Resolving acute infection	Case-by-case evaluation

*= seroprotective levels of >10 mIU/mL

For additional guidance about the management of PrEP in persons with chronic active HBV infection see the section Special Clinical Considerations.

Serologic testing for HCV is recommended for persons who have ever injected drugs[88]. MSM at substantial risk for HIV infection being started on PrEP have been shown to have a high prevalence of HCV infection [89,9091]. Therefore, MSM starting PrEP should be tested for HCV infection as a part of baseline laboratory assessment. HCV testing for all sexually active persons starting PrEP is a recommended consideration by guidance from the American Association for the Study of Liver Diseases (AASLD) and the Infectious Disease Society of America (IDSA)[92]. In addition, persons born during 1945 through 1965 should be tested for HCV at least once in a lifetime (without prior ascertainment of HCV risk factors). Guidance from AASLD-IDSA recommends annual HCV retesting

for PWID, and clinicians can consider annual retesting for other persons with ongoing risk of HCV exposure[92].

Patients with active HCV infection (HCV RNA+ with or without anti-HCV seropositivity) should be evaluated for possible treatment because TDF/FTC does not treat HCV infection. When the clinician providing PrEP care is not able to provide HCV care, the patient should be linked to an experienced HCV care provider

TESTING FOR SEXUALLY TRANSMITTED INFECTIONS

Tests to screen for syphilis are recommended for all adults prescribed PrEP, both at screening and at semi-annual visits. See the 2015 STD guidelines for recommended assays[93].

Tests to screen for gonorrhea are recommended for all sexually active adults prescribed PrEP, both at screening and at semi-annual visits. Tests to screen for chlamydia are recommended for all sexually active MSM prescribed PrEP, both at screening prior to initiation and at semi-annual visits.

Because chlamydia is very common, especially in young women[94] and does not strongly correlate with risk of HIV acquisition[61], regular screening for chlamydia is not recommended for all sexually active women as a component of PrEP care. However, clinicians should refer to the 2015 STD guidelines for recommendations about chlamydia testing frequency for women regardless of PrEP use[93].

For gonorrhea and chlamydia testing in MSM, NAAT tests are preferred because of their sensitivity. Pharyngeal, rectal, and urine specimens should be collected ("3-site testing") to maximize the identification of infection, which may occur at any of these sites of exposure during sex. Self-collected samples have equivalent performance as clinician-obtained samples [95-97] and can help streamline patient visit flow.

For gonorrhea testing in women, vaginal specimens for NAAT tests are preferred. They may also be self-collected. For women who report engaging in anal sex, rectal specimens for gonorrhea and chlamydia testing should be collected in addition to vaginal specimens[98-100]. Studies have estimated that 29% of HIV infections in women are linked to sex with MSM (i.e., bisexual men)[101,102], and that more than 1/3 of women report having had anal sex[103]. In the HPTN 064 trial that recruited women at high risk of HIV acquisition, 38% reported condomless anal sex in the 6 months prior to enrollment[104]. Identifying asymptomatic rectal gonorrhea in women at substantial risk for HIV infection and providing treatment can provide benefits to the woman's health and help reduce the burden of infection in her sexual networks as well[105,106], especially when accompanied by partner services[107] or expedited partner therapy[108-110].

Providing PrEP

Goals of PrEP Therapy

The ultimate goal of PrEP is to reduce the acquisition of HIV infection with its resulting morbidity, mortality, and cost to individuals and society. Therefore clinicians initiating the provision of PrEP should

- Prescribe medication regimens that are proven safe and effective for uninfected persons who meet recommended criteria to reduce their risk of HIV acquisition
- Educate patients about the medications and the regimen to maximize their safe use
- Provide support for medication-adherence to help patients achieve and maintain protective levels of medication in their bodies
- Provide HIV risk-reduction support and prevention services or service referrals to help patients minimize their exposure to HIV
- Provide effective contraception to women who are taking PrEP and who do not wish to become pregnant
- Monitor patients to detect HIV infection, medication toxicities, and levels of risk behavior in order to make indicated changes in strategies to support patients' long-term health

Indicated Medication

The medication proven safe and effective, and currently approved by FDA for PrEP in healthy adults at risk of acquiring HIV infection, is the fixed-dose combination of TDF and FTC in a single daily dose (see Table 10). Therefore, TDF/FTC is the recommended medication that should be prescribed for PrEP for MSM, heterosexually active men and women, and PWID who meet recommended criteria. Because TDF alone has been proven effective in trials with PWID and heterosexually active men and women, it can be considered as an alternative regimen for these specific populations. As PrEP for MSM, TDF alone is not recommended because no trials have been done, so the efficacy of TDF alone for MSM is unknown.

Table 10: Recommended Oral PrEP Medications

Generic Name	Trade Name	Dose	Frequency	Common Side Effects[73]
Tenofovir disoproxil fumarate (TDF)	Viread	300 mg	Once a day	Nausea, flatulence
Emtricitabine (FTC)[a]	Emtriva	200 mg	Once a day	Rash, headache
TDF + FTC	Truvada	300mg/200 mg	Once a day	—

[a] Not recommended alone; only for use in combination with TDF.

In addition to the safety data obtained in PrEP clinical trials, data on drug interactions and longer-term toxicities have been obtained by studying the component drugs individually for their use in treatment of HIV-infected persons. Studies have also been done in small numbers of HIV-uninfected, healthy adults (see Table 11).

Table 11: PrEP Medication Drug Interactions [6,80]

	TDF	FTC
Buprenorphine	No significant effect. No dosage adjustment necessary.	No data
Methadone	No significant effect. No dosage adjustment necessary.	No data
Oral contraceptives	No significant effect. No dosage adjustment necessary.	No data
Acyclovir, valacyclovir, cidofovir, ganciclovir, valganciclovir, aminoglycosides, high-dose or multiple NSAIDS or other drugs that reduce renal function or compete for active renal tubular secretion	Serum concentrations of these drugs and/or TDF may be increased. Monitor for dose-related renal toxicities.	No data
Ledipasvir/sofosbuvir	Serum concentrations of TDF may be increased. Monitor for toxicities.	No significant effect

WHAT NOT TO USE

No antiretroviral regimens should be used for PrEP other than a daily oral dose of TDF/FTC, or a daily dose of TDF alone as an alternative only for PWID and heterosexually active adults.

Other medications and other dosing schedules have not yet been shown to be safe or effective in preventing HIV acquisition among otherwise healthy adults and are not approved by FDA for PrEP.

- Do not use other antiretroviral medications (e.g., 3TC, TAF [tenofovir alafenamide]), either in place of, or in addition to, TDF/FTC or TDF.
- Do not use other than daily dosing (e.g., intermittent, episodic [pre/post sex only], or other discontinuous dosing)
- Do not provide PrEP as expedited partner therapy (i.e., do not prescribe for an uninfected person not in your care).

TIME TO ACHIEVING PROTECTION

The time from initiation of daily oral doses of TDF/FTC to maximal protection against HIV infection is unknown. There is not scientific consensus on what intracellular concentrations are protective for either drug or the protective contribution of each drug in specific body tissues. It has been shown that the pharmacokinetics of TDF and FTC vary by tissue[111].

Data from exploratory pharmacokinetic studies conducted with HIV-uninfected men and women does provide preliminary data on the lead-time required to achieve steady state levels of tenofovir diphosphate (TFV-DP, the activated form of the medication) in blood (PBMCs [peripheral blood mononuclear cells]), rectal, and vaginal tissues[112,113]. These data suggest that maximum intracellular

concentrations of TFV-DP are reached in blood after approximately 20 days of daily oral dosing, in rectal tissue at approximately 7 days, and in cervicovaginal tissues at approximately 20 days. No data are yet available about intracellular drug concentrations in penile tissues susceptible to HIV infection to inform considerations of protection for male insertive sex partners.

MANAGING SIDE EFFECTS

Patients taking PrEP should be informed of side effects among HIV-uninfected participants in clinical trials (see Table 5). In these trials, side effects were uncommon and usually resolved within the first month of taking PrEP ("start-up syndrome"). Clinicians should discuss the use of over-the-counter medications for headache, nausea, and flatulence should they occur. Patients should also be counseled about signs or symptoms that indicate a need for urgent evaluation (e.g., those suggesting possible acute renal injury or acute HIV infection).

CLINICAL FOLLOW-UP AND MONITORING

Once PrEP is initiated, patients should return for follow-up approximately every 3 months. Clinicians may wish to see patients more frequently at the beginning of PrEP (e.g., 1 month after initiation, to assess and confirm HIV-negative test status, assess for early side effects, discuss any difficulties with medication adherence, and answer questions.

All patients receiving PrEP should be seen as follows:

- **At least every 3 months to**
  - Repeat HIV testing and assess for signs or symptoms of acute infection to document that patients are still HIV negative (see Figure)
  - Repeat pregnancy testing for women who may become pregnant
  - Provide a prescription or refill authorization of daily TDF/FTC for no more than 90 days (until the next HIV test)
  - Assess side effects, adherence, and HIV acquisition risk behaviors
  - Provide support for medication adherence and risk-reduction behaviors
  - Respond to new questions and provide any new information about PrEP use
  - Conduct STI testing for sexually active persons with signs or symptoms of infection and screening for asymptomatic MSM at high risk for recurrent bacterial STIs (e.g., those with syphilis, gonorrhea, or chlamydia at prior visits or multiple sex partners)
- **At least every 6 months to**
  - Monitor eCrCl
    - If other threats to renal safety are present (e.g., hypertension, diabetes), renal function may require more frequent monitoring or may need to include additional tests (e.g., urinalysis for proteinuria)
    - A rise in serum creatinine is not a reason to withhold treatment if eCrCl remains ≥60 ml/min.

        - If eCrCl is declining steadily (but still ≥60 ml/min), consultation with a nephrologist or other evaluation of possible threats to renal health may be indicated.
    - Conduct STI screening for sexually active adolescents and adults (i.e., syphilis and gonorrhea for both men and women, chlamydia for MSM) even if asymptomatic
- **At least every 12 months to**
    - Evaluate the need to continue PrEP as a component of HIV prevention

Optional Assessments

Bone Health

Decreases in bone mineral density (BMD) have been observed in HIV-infected persons treated with combination antiretroviral therapy (including TDF-containing regimes)[114,115]. However, it is unclear whether this 3%-4% decline would be seen in HIV-uninfected persons taking fewer antiretroviral medications for PrEP. The iPrEx trial (TDF/FTC) and the CDC PrEP safety trial in MSM (TDF) conducted serial dual-emission x-ray absorptiometry (DEXA) scans on a subset of MSM in the trials and determined that a small (~1%) decline in BMD that occurred during the first few months of PrEP either stabilized or returned to normal[23,116]. There was no increase in fragility (atraumatic) fractures over the 1-2 years of observation in these studies comparing those persons randomized to receive PrEP medication and those randomized to receive placebo[117].

Therefore, DEXA scans or other assessments of bone health are not recommended before the initiation of PrEP or for the monitoring of persons while taking PrEP. However, any person being considered for PrEP who has a history of pathologic or fragility bone fractures or who has significant risk factors for osteoporosis should be referred for appropriate consultation and management.

Therapeutic drug monitoring

Similar to the limited use of therapeutic drug monitoring (TDM) in the treatment of HIV infection[80], several factors mitigate against the routine use of TDM during PrEP. These factors include (1) a lack of established concentrations in blood associated with robust efficacy of TDF or FTC for the prevention of HIV acquisition in adults after exposure during penile-rectal or penile-vaginal intercourse[118] and (2) the limited but growing availability of clinical laboratories that perform quantitation of antiretroviral medicine concentrations under rigorous quality assurance and quality control standards.

However, some clinicians may want to use TDM periodically to assess adherence to PrEP medication. If so, a key limitation should be recognized. The levels of medication in serum or plasma reflect only very recent doses, so they are not valid estimates of consistent adherence[118]. However, if medication is not detected or is detected at a very low level, support to reinforce medication adherence would be indicated.

Persons with Documented HIV Infection

All persons with HIV-positive test results whether at screening or while taking TDF/FTC or TDF alone as PrEP should be provided the following services[80].

- Laboratory confirmation of HIV status (see Figure)
- Determination of CD4 lymphocyte count and viral load to guide therapeutic decisions
- Documentation of results of genotypic HIV viral resistance testing to guide future treatment decisions
- If on PrEP, conversion of the PrEP regimen to an HIV treatment regimen recommended by the DHHS Panel on Antiretroviral Guidelines for Adults and Adolescents[80] without waiting for additional laboratory test results. See Clinical Providers' Supplement Section 8.
- Provision of, or referral to, an experienced provider for the ongoing medical management of HIV infection
- Counseling about their HIV status and steps they should take to prevent HIV transmission to others and to improve their own health
- Assistance with, or referral to, the local health department for the identification of sex partners who may have been recently exposed to HIV so that they can be tested for HIV infection, considered for nonoccupational postexposure prophylaxis (nPEP)[119], and counseled about their risk-reduction practices

In addition, a confidential report of new HIV infection should be provided to the local health department.

Discontinuing PrEP

Patients may discontinue PrEP medication for several reasons, including personal choice, changed life situations resulting in lowered risk of HIV acquisition, intolerable toxicities, chronic nonadherence to the prescribed dosing regimen despite efforts to improve daily pill-taking, or acquisition of HIV infection. How to safely discontinue and restart PrEP use should be discussed with patients both when starting PrEP and when discontinuing PrEP. Protection from HIV infection will wane over 7-10 days after ceasing daily PrEP use[120-122]. Because some patients have acquired HIV infection soon after stopping PrEP use[29], alternative methods to reduce risk for HIV acquisition should be discussed, including indications for PEP and how to access it quickly if needed.

Upon discontinuation for any reason, the following should be documented in the health record:

- HIV status at the time of discontinuation
- Reason for PrEP discontinuation
- Recent medication adherence and reported sexual risk behavior

For persons with incident HIV infection, see Persons with Documented HIV Infection. See also Clinical Providers' Supplement Section 8 for a suggested management protocol.

For persons with active hepatitis B infection, see Special Clinical Considerations.

Any person who wishes to resume taking PrEP medications after having stopped should undergo all the same pre-prescription evaluation as a person being newly prescribed PrEP, including an HIV test to establish that they are still without HIV infection. In addition, a frank discussion should clarify the changed circumstances since discontinuing medication that indicate the need to resume medication, and the commitment to take it.

Special Clinical Considerations

The patient with certain clinical conditions requires special attention and follow-up by the clinician.

Women who become pregnant or breastfeed while taking PrEP medication

Women without HIV infection who have sex partners with documented HIV infection may be at risk of HIV acquisition during attempts to conceive (i.e., sex without a condom). Pregnancy is associated with an increased risk of HIV acquisition[123]. Risk is substantial for women whose partners are not taking antiretroviral treatment medication or women whose partners are treated but not virally suppressed. Women whose partners have documented sustained viral load suppression are at effectively no risk of sexual acquisition of HIV infection (see page 32 above). The extent to which PrEP use further decreases risk of HIV acquisition when the male partner has a documented recent undetectable viral load is unknown.

However, clinicians providing pre-conception and pregnancy care to women who report their partners have HIV infection, may not be providing care to the male partner and so may not have access to their medical records documenting the recent viral load status of the partner with HIV infection[65]. When the HIV status of the male partner is unknown, the clinician should offer HIV testing for the partner. When the male partner is reported to have HIV infection but his recent viral load status is not known, is reported detectable, or cannot be documented as undetectable, PrEP use during the preconception period and pregnancy by the uninfected woman offers an additional tool to reduce the risk of sexual HIV acquisition. Both the FDA labeling information[6] and the perinatal antiretroviral treatment guidelines[124] permit off-label use in pregnancy. However, data directly related to the safety of PrEP use for a developing fetus are limited. Providers should discuss available information about potential risks and benefits of beginning or continuing PrEP during pregnancy so that an informed decision can be made. (See Clinical Providers' Supplement, Section 5 at https://www.cdc.gov/hiv/pdf/risk/prep-cdc-hiv-prep-provider-supplement-2017.pdf

In the PrEP trials with heterosexual women, medication was promptly discontinued for those who became pregnant, so the safety for exposed fetuses could not be adequately assessed. A single small study of periconception use of TDF in 46 uninfected women in HIV-discordant couples found no ill effects on the pregnancy and no HIV infections[125]. Additionally, TDF and FTC are widely used for the treatment of HIV infection and continued during pregnancies that occur[126-128]. The data on pregnancy outcomes in the Antiretroviral Pregnancy Registry provide no evidence of adverse effects among fetuses exposed to these medications[129].

Providers should educate HIV-discordant couples who wish to become pregnant about the potential risks and benefits of all available alternatives for safer conception[130,131] and if indicated make referrals for assisted reproduction therapies. Whether or not PrEP is elected, the HIV-infected partner should be prescribed effective antiretroviral therapy before conception attempts[124,132]: if the infected partner is male, to reduce the risk of transmission-related viral load in semen; and in both sexes, for the benefit of their own health[133].

In addition, health care providers are strongly encouraged to prospectively and anonymously submit information about any pregnancies in which PrEP is used to the Antiretroviral Pregnancy Registry at http://www.apregistry.com/.

The safety of PrEP with TDF/FTC or TDF alone for infants exposed during lactation has not been adequately studied. However, data from studies of infants born to HIV-infected mothers and exposed to TDF or FTC through breast milk suggest limited drug exposure.[134,135] Additionally, the World Health Organization has recommended the use of TDF/FTC or 3TC/efavirenz for all pregnant and breastfeeding women for the prevention of perinatal and postpartum mother-to-child transmission of HIV[136]. Therefore, providers should discuss current evidence about the potential risks and benefits of beginning or continuing PrEP during breastfeeding so that an informed decision can be made[11]. (See Clinical Providers' Supplement, Section 5 at https://www.cdc.gov/hiv/pdf/risk/prep-cdc-hiv-prep-provider-supplement-2017.pdf

Patients with Chronic Active Hepatitis B Virus Infection

TDF and FTC are each active against both HIV infection and HBV infection and thus may prevent the development of significant liver disease by suppressing the replication of HBV. Only TDF, however, is currently FDA-approved for this use. Therefore, in persons with substantial risk of both HIV acquisition and active HBV infection, daily doses of TDF/FTC may be especially indicated.

All persons screened for PrEP who test positive for hepatitis B surface antigen (HBsAg) should be evaluated by a clinician experienced in the treatment of HBV infection. For clinicians without this experience, co-management with an infectious disease or a hepatic disease specialist should be considered. Patients should be tested for HBV DNA by the use of a quantitative assay to determine the level of HBV replication[137] before PrEP is prescribed and every 6-12 months while taking PrEP.

TDF presents a very high barrier to the development of HBV resistance. However, it is important to reinforce the need for consistent adherence to the daily doses of TDF/FTC to prevent reactivation of

[11]Although the DHHS Perinatal HIV Guidelines state that "pregnancy and breastfeeding are not contraindications for PrEP"[9], the FDA-approved package insert[6] says "If an uninfected individual becomes pregnant while taking TRUVADA for a PrEP indication, careful consideration should be given to whether use of TRUVADA should be continued, taking into account the potential increased risk of HIV-1 infection during pregnancy" and "mothers should be instructed not to breastfeed if they are receiving TRUVADA, whether they are taking TRUVADA for treatment or to reduce the risk of acquiring HIV-1.". Therefore both are currently off-label uses of Truvada.

HBV infection with the attendant risk of hepatic injury, and to minimize the possible risk of developing TDF-resistant HBV infection[138].

If PrEP is no longer needed to prevent HIV infection, a separate determination should be made to about whether to continue TDF/FTC as a means of providing TDF to treat HBV infection. Acute flares resulting from the reactivation of HBV infection have been seen in HIV-infected persons after the cessation of TDF and other medications used to treat HBV infection. Such flares have not yet been seen in HIV-uninfected persons with chronic active HBV infection who have stopped taking TDF-containing PrEP regimens. Nonetheless, when such patients discontinue PrEP, they should continue to receive care from a clinician experienced in the management of HBV infection so that if flares occur, they can be detected promptly and treated appropriately.

Patients with Chronic Renal Failure

HIV-uninfected patients with chronic renal failure, as evidenced by an eCrCl of <60 ml/min, should not take PrEP because the safety of TDF/FTC for such persons was not evaluated in the clinical trials. TDF is associated with modestly reduced renal function when used as part of an antiretroviral treatment regimen in persons with HIV infection (which itself can affect renal function). Because other HIV prevention options are available, the only PrEP regimen proven effective to date (TDF/FTC) and approved by FDA for PrEP is not indicated for persons with chronic renal failure.[6]

Adolescent Minors

As a part of primary health care, HIV screening should be discussed with all adolescents who are sexually active or have a history of injection drug use. Parental/guardian involvement in an adolescent's health care is often desirable but is sometimes contraindicated for the safety of the adolescent. However, laws and regulations that may be relevant for PrEP-related services (including HIV testing), such as those concerning consent, confidentiality, parental disclosure, and circumstances requiring reporting to local agencies, differ by jurisdiction. Clinicians considering providing PrEP to a person under the age of legal adulthood (a minor) should be aware of local laws, regulations, and policies that may apply[1139].

Although the FDA labeling information specifies PrEP indications for "adults," an age above which an adolescent is considered an adult is not provided.[6] None of the completed PrEP trials have included persons under the age of 18. Therefore, clinicians should consider carefully the lack of data on safety and effectiveness of PrEP taken by persons under 18 years of age, the possibility of bone or other toxicities among youth who are still growing, and the safety evidence available when TDF/FTC is used in treatment regimens for HIV-infected youth[140,141]. These factors should be weighed against the potential benefit of providing PrEP for an individual adolescent at substantial risk of HIV acquisition.

Nonoccupational Postexposure Prophylaxis

Persons not receiving PrEP who seek care within 72 hours after an isolated sexual or injection-related HIV exposure should be evaluated for the potential need for nPEP[119]. If the exposure is isolated (e.g., sexual assault, infrequent condom failure), nPEP should be prescribed, but PrEP or other continued antiretroviral medication is not indicated after completion of the 28-day PEP course.

Persons who repeatedly seek nPEP or who are at risk for ongoing HIV exposures should be evaluated for possible PrEP use after confirming they have not acquired HIV infection[142]. Because HIV infection has been reported in association with exposures soon after completing an nPEP course, daily PrEP may be more protective than repeated intermittent episodes of nPEP. Persons who engage in behaviors that result in frequent, recurrent exposures that would require sequential or near-continuous courses of nPEP should be offered PrEP at the conclusion of their 28-day nPEP medication course. Because no definitive evidence exists that prophylactic antiretroviral use delays seroconversion, and nPEP is highly effective when taken as prescribed, a gap is unnecessary between ending nPEP and beginning PrEP. Upon documenting HIV-negative status, preferably by using a laboratory-based Ag/Ab test, daily use of the fixed dose combination of TDF (300mg) and FTC (200 mg) can begin immediately for patients for whom PrEP is indicated. See Clinical Providers' Supplement Section 9 for a recommended transition management strategy.

In contrast, patients fully adhering to a daily PrEP regimen do not need nPEP if they experience a potential HIV exposure while on PrEP. PrEP is highly effective when taken daily or near daily. For patients who report taking their PrEP medication sporadically, and those who did not take it within the week before the recent exposure, initiating a 28-day course of nPEP might be indicated. In that instance, all nPEP baseline and follow-up laboratory evaluations should be conducted. After the 28-day nPEP regimen is completed, if confirmed to be HIV uninfected, the previously experienced barriers to PrEP adherence should be evaluated and if addressed, daily PrEP regimen can be reinitiated.

Improving Medication Adherence

Data from the published studies of daily oral PrEP indicate that medication adherence is critical to achieving the maximum prevention benefit (see Table 4) and reducing the risk of selecting for a drug-resistant virus if non-adherence leads to HIV acquisition[143-145]. Three additional studies reinforce the need to prescribe, and support adherence to uninterrupted daily doses of TDF/FTC.

A study of the pharmacokinetics of directly observed TDF dosing in MSM in the STRAND trial found that the intracellular levels of the active form of TDF (tenofovir diphosphate), when applied to the drug detection-efficacy statistical model with iPrEx participants, corresponded to an HIV risk reduction efficacy of 99% for 7 doses per week, 96% for 4 doses per week, and 76% for 2 doses per week143. This finding adds to the evidence that despite some "forgiveness" for occasional missed doses for MSM, a high level of prevention efficacy requires a high level of adherence to daily medication. However, a laboratory study comparing vaginal and colorectal tissue levels of active metabolites of TDF and FTC found that drug levels associated with significant protection against HIV infection

required 6-7 doses per week (~85% adherence) for lower vaginal tract tissues but only 2 doses per week (28% adherence) for colorectal tissures146. This strongly suggests that there is less "forgiveness" for missed doses among women than among MSM.

A pilot study of daily TDF/FTC as PrEP with young MSM was stopped when the iPrEx trial results were reported.[147] Among the 68 men enrolled (mean age, 20 years; 53% African American; 40% Hispanic/Latino) plasma specimens were tested to objectively measure medication adherence. At week 4, 63% had detectable levels of tenofovir, but at week 24, only 20% had detectable levels of tenofovir. Two open-label safety studies with 243 young MSM (median age 19, 46% African American, 32% Latino/Hispanic) similarly found lower adherence in young adult men than has been reported in older adult men taking PrEP, and lower adherence with quarterly visits than with monthly visits[148].

In addition, a study with MSM and commercial sex workers in Kenya evaluated adherence to daily, fixed-interval (Mondays and Fridays), and coitally-timed (single post-coital) TDF/FTC dosing schedules by the use of pill bottles with caps monitored by an electronic medication event monitoring system (MEMS) and monthly interviews about sexual behavior[149]. Among the 67 men and 5 women in this study, 83% adhered to daily dosing, 55% to fixed-interval dosing, and 26% to post-coital dosing regimens. These findings suggest that adherence is better with daily dosing, as currently recommended, than with non-daily regimens (not yet proven effective as PrEP). These data confirm that medication education and adherence counseling (also called medication self-management) will need to be provided to support daily PrEP use.

A recent review of the antiretroviral treatment adherence studies over the past 15 years and adherence data from the completed PrEP trials suggests various approaches to effectively support medication adherence[150]. These approaches include educating patients about their medications; helping them anticipate and manage side effects; helping them establish dosing routines that mesh with their work and social schedules; providing reminder systems and tools; addressing financial, substance abuse, or mental health needs that may impede adherence; and facilitating social support.

Although many published articles address antiretroviral medication adherence among persons being treated for HIV infection, these findings may be only partially applicable to PrEP users. HIV treatment regimens include more than 2 drugs (commonly including more than 1 pill per day), resulting in an increased pill burden, and the possibility of side effects and toxicities with 3 or more drugs may occur that would not occur with TDF/FTC alone. The motivations of persons being treated for HIV infection and persons trying to prevent HIV infection may differ. Because PrEP will be used in otherwise healthy adults, studies of the use of medications in asymptomatic adults for the prevention of potential serious future health outcomes may also be informative for enhancing adherence to PrEP medications. The most cost-effective interventions for improving adherence to antihypertensive and lipid-lowering medications were initiated soon after the patients started taking medication and involved personalized, regularly scheduled education and symptom management (patients were aware that adherence was being monitored)[151]. Patients with chronic diseases reported that the most important factors in adherence to medications were incorporating medication into their daily routines, knowing that the

medications work, believing that the benefits outweigh the risks, knowing how to manage side effects, and low out-of pocket costs[152,153].

When initiating a PrEP regimen, clinicians must educate patients so that they understand clearly how to take their medications (i.e., when to take them, how many pills to take at each dose) and what to do if they experience problems (e.g., what constitutes a missed dose [number of hours after the failure to take a scheduled dose], what to do if they miss a dose). Patients should be told to take a single missed dose as soon as they remember it, unless it is almost time for the next dose. If it is almost time for the next dose, patients should skip the missed dose and continue with the regular dosing schedule.

Side effects can lead to non-adherence, so clinicians need a plan for addressing them. Clinicians should tell patients about the most common side effects and should work with patients to develop a specific plan for handling them, including the use of specific over-the-counter medications that can mitigate symptoms. The importance of using condoms during sex, especially for patients who decide to stop taking their medications, should be reinforced.

Box D: Key Components of Medication Adherence Counseling

Establish trust and bidirectional communication

Provide simple explanations and education

- Medication dosage and schedule
- Management of common side effects
- Relationship of adherence to the efficacy of PrEP
- Signs and symptoms of acute HIV infection and recommended actions

Support adherence

- Tailor daily dose to patient's daily routine
- Identify reminders and devices to minimize forgetting doses
- Identify and address barriers to adherence

Monitor medication adherence in a non-judgmental manner

- Normalize occasional missed doses, while ensuring patient understands importance of daily dosing for optimal protection
- Reinforce success
- Identify factors interfering with adherence and plan with patient to address them
- Assess side effects and plan how to manage them

Using a broad array of a health care professionals (e.g., physicians, nurses, case-managers, physician assistants, clinic-based and community pharmacists) that work together on a health care team to influence and reinforce adherence instructions[154] significantly improves medication adherence and may alleviate the time constraints of individual providers[155,156]. This broad-team approach may also provide a larger number of providers to counsel patients about self-management of behavioral risks.

For additional information on adherence counseling, see the Clinical Providers' Supplement, Section 10 at https://www.cdc.gov/hiv/pdf/risk/prep-cdc-hiv-prep-provider-supplement-2017.pdf.

Reducing HIV Risk Behaviors

The adoption and the maintenance of safer behaviors (sexual, injection, and other substance abuse) are critical for the lifelong prevention of HIV infection and are important for the clinical management of persons prescribed PrEP.

Video-based interventions such as Safe in the City, which make use of waiting-room time rather than clinician time[150,157], have reduced STI incidence in a general clinic population. However, they take a general approach, so they do not allow tailoring to the sexual risk-reduction needs of individual patients (e.g., as partners change, PrEP is initiated or discontinued).

Interactive, client-centered counseling (in which content is tailored to a patient's sexual risk behaviors and the situations in which risks occur), in conjunction with goal-setting strategies is effective in HIV prevention[142,158-160]. An example of this method is Project Respect: although this counseling protocol alone did not reduce HIV incidence significantly, 20-minute clinical counseling sessions to develop and review patient-specific, incremental risk-reduction plans led to reduced incidence of STIs in a heterosexual population,[161] . Project Aware included MSM and heterosexuals attending STD clinics and provided a single brief counseling session (using the Respect-2 protocol) while conducting rapid HIV testing. There was no reduction in the incidence of STIs attributed to counseling[162]. However, in the context of PrEP delivery, brief, repeated counseling sessions can take advantage of multiple visits for follow-up care[163] while addressing the limited time available for individual visits[157] and the multiple prevention[155,156] and treatment topics that busy practitioners need to address.

Reducing or eliminating injection risk practices can be achieved by providing access to drug treatment and relapse prevention services (e.g., methadone, buprenorphine for opiate users) for persons who are willing to participate[164]. For persons not able (e.g., on a waiting list or lacking insurance) or not motivated to engage in drug treatment, providing access to unused injection equipment through syringe service programs (where available), prescriptions for syringes or purchase from pharmacies without a prescription (where legal) can reduce HIV exposure. In addition, providing or referring for cognitive or behavioral counseling and any indicated mental health or social services may help reduce risky injection practices. See the Substance Abuse Treatment and Mental Health Treatment Locators at http://findtreatment.samhsa.gov/.

For additional information on risk reduction interventions, see Clinical Providers' Supplement, Section 11 at https://www.cdc.gov/hiv/pdf/risk/prep-cdc-hiv-prep-provider-supplement-2017.pdf.

Box E: Key Components of Behavioral Risk-Reduction Counseling

Establish trust and 2-way communication

Provide feedback on HIV risk factors identified during sexual and substance use history taking

- Elicit barriers to, and facilitators of, consistent condom use
- Elicit barriers to, and facilitators of, reducing substance abuse

Support risk-reduction efforts

- Assist patient to identify 1 or 2 feasible, acceptable, incremental steps toward risk reduction
- Identify and address anticipated barriers to accomplishing planned actions to reduce risk

Monitor behavioral adherence in a non-judgmental manner

- Acknowledge the effort required for behavior change
- Reinforce success
- If not fully successful, assess factors interfering with completion of planned actions and assist patient to identify next steps

Financial Case-Management Issues for PrEP

One critical component in providing PrEP medications and related clinical and counseling services is identifying insurance and other reimbursement sources. Although some commercial insurance and employee benefits programs have defined policies for the coverage of PrEP, others have not yet done so. Similarly, public insurance sources vary in their coverage policy. Most public and private insurers cover PrEP but co-pay, co-insurance, and prior authorization policies differ.

For patients who do not have health insurance, whose insurance does not cover PrEP medication, and whose personal resources are inadequate to pay out-of-pocket, Gilead Sciences has established a PrEP medication assistance program. In addition to providing Truvada to providers for eligible patients and access to free HIV testing, the program provides co-pay assistance for medication and free condoms to patients on request[165]. Providers may obtain applications for their patients at https://start.truvada.com/. In addition, a few states and cities have PrEP-specific financial assistance programs (check with your local health department).

Decision Support, Training and Technical Assistance

Decision support systems (electronic and paper), flow sheets, checklists (see Clinical Providers' Supplement, Section 1 for a PrEP provider/patient checklist at https://www.cdc.gov/hiv/pdf/risk/prep-cdc-hiv-prep-provider-supplement-2017.pdf, feedback reminders, and involvement of nurse clinicians and pharmacists will be helpful in managing the many steps indicated for the safe use of PrEP and to increase the likelihood that patients will follow them. Often these systems are locally developed but may become available from various sources including training centers and Web sites funded by government agencies; professional associations, or interested private companies. Examples include downloadable applications (widgets) to support the delivery of nPEP or locate nearby sites for

confidential HIV tests (http://www.hivtest.org); and confidential commercial services to electronically monitor medication-taking, send text message reminders, or provide telephone assistance to help patients with problems concerning medication adherence.

Training and technical assistance in providing components of PrEP-related services, medications, and counseling are available at the following Web sites:

- PrEPline: National Clinician's Consultation Center (http://nccc.ucsf.edu/clinical-resources/prep-guidelines-and-resources/)
- National PrEP Clinician Locator (https://preplocator.org/)
- AIDS Info (http://www.aidsinfo.nih.gov, http://www.aids.gov)
- The National Network of STD/HIV Prevention Training Centers (http://nnptc.org/)
- The AIDS Education Training Centers National Resource Center (http://www.aids-ed.org)
- The Addiction Technology Transfer Center Network (http://www.attcnetwork.org)

Related Guidelines

This document is consistent with several other guidelines from several organizations related to sexual health, HIV prevention, and the use of antiretroviral medications. Clinicians should refer to these other documents for detailed guidance in their respective areas of care.

- Screening For HIV: Current Recommendations USPSTF, 2013[167]
- Revised Recommendations for HIV Testing of Adults, Adolescents, and Pregnant Women in Health-Care Settings[73]
- Recommendations for HIV Screening of Gay, Bisexual, and Other Men Who Have Sex with Men — United States, 2017[169]
- Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents[80]
- Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States[74]
- Updated Guidelines for Antiretroviral Postexposure Prophylaxis After Sexual, Injection Drug Use, or Other Non-occupational Exposure to HIV -United States, 2017[119]
- Sexually Transmitted Diseases Treatment Guidelines, 2015[93]
- Recommendations for Partner Services Programs for HIV Infection, Syphilis, Gonorrhea, and Chlamydial Infection[107]
- Expedited Partner Therapy in the Management of Sexually Transmitted Diseases, 2006[110]
- Guidance on the Use of Expedited Partner Therapy in the Treatment of Gonorrhea. 2016[109]
- Behavioral counseling to prevent sexually transmitted infections: U.S. Preventive Services Task Force recommendation statement[159]
- Recommendations for Identification and Public Health Management of Persons with Chronic Hepatitis B Virus Infection[168]
- Hepatitis C guidance: AASLD-I DSA recommendations for testing, managing, and treating adults infected with hepatitis C virus[92]

- Integrated prevention services for HIV infection, viral hepatitis, sexually transmitted diseases, and tuberculosis for persons who use drugs illicitly: summary guidance from CDC and the U.S. Department of Health and Human Services[72]

Appendices

APPENDIX 1 GRADING OF STRENGTH OF RECOMMENDATIONS AND QUALITY OF EVIDENCE

Key recommendations in this guideline are based on the review of published scientific evidence and expert opinions. For details on the guidelines development process used, see the Clinical Providers' Supplement, Section 14 at https://www.cdc.gov/hiv/pdf/risk/prep-cdc-hiv-prep-provider-supplement-2017.pdf.

Using the same grading system as the DHHS antiretroviral treatment guidelines[80], these key recommendations are rated with a letter to indicate the strength of the recommendation and with a numeral to indicate the quality of the combined evidence supporting each recommendation.

Table 12: Rating Scheme for Recommendations

A. Strong recommendation for the statement	**I.** One or more well-executed randomized, controlled trials with clinical outcomes, validated laboratory endpoints, or both
B. Moderate recommendation for the statement	**II.** One or more well-executed, nonrandomized trials or observational cohort studies with clinical outcomes
C. Optional recommendation for the statement	**III.** Expert opinion

The quality of scientific evidence ratings in Table 2 are based on the GRADE rating system.[38]

Table 13: Criteria for rating quality of scientific evidence

Type of evidence	Randomized trial = high Observational study = low Any other evidence = very low
Decrease grade if[a]	▪ Serious or very serious limitation to study quality ▪ Important inconsistency ▪ Some or major uncertainty about directness ▪ Imprecise or sparse data ▪ High probability of reporting bias
Increase grade if[a]	▪ Strong evidence of association – significant relative risk >2 (<0.5) based on consistent evidence from 2 or more observational studies, with no plausible confounders (+1) ▪ Very strong evidence of association – significant relative risk of >5 (<0.2) based on direct evidence with no major threats to validity (+2) ▪ Evidence of a dose-response gradient (+1) ▪ All plausible confounders would have reduced the effect (+1)
Range	High-quality evidence Moderate-quality evidence Low-quality evidence Very-low quality evidence

[a] Each quality criterion can reduce or increase the quality by 1 or, if very significant, by 2 levels.
Source: http://www.gradeworkinggroup.org/FAQ/evidence_qual.htm

References

1. Grohskopf LA, Chillag KL, Gvetadze R, et al. Randomized trial of clinical safety of daily oral tenofovir disoproxil fumarate among HIV-uninfected men who have sex with men in the United States. *J Acquir Immune Defic Syndr.* 2013;64(1):79-86.

2. 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.

3. 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.

4. 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.

5. 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.

6. Gilead Sciences. Truvada Package Insert. 2017. http://gilead.com/~/media/files/pdfs/medicines/hiv/truvada/truvada_pi.pdf. Accessed July 26, 2017.

7. Food and Drug Administration. Truvada approved to reduce the risk of sexually transmitted HIV in people who are not infected with the virus. 2012; http://www.fda.gov/ForConsumers/ByAudience/ForPatientAdvocates/HIVandAIDSActivities/ucm312264.htm. Accessed 6 August 2012.

8. Food and Drug Administration. Background package for NDA 21-752/Supplement 30. 2012. http://www.fda.gov/downloads/AdvisoryCommittees/CommitteeMeetingMaterials/Drugs/AntiviralDrugsAdvisoryCommittee/UCM303213.pdf. Accessed February 18, 2014.

9. Fonner VA, Dalglish SL, Kennedy CE, et al. Effectiveness and safety of oral HIV pre-exposure prophylaxis (PrEP) for all populations: A systematic review and meta-analysis. *AIDS*. 2016;30-(12):1973-1983.

10. Centers for Disease C, Prevention. Interim guidance: preexposure prophylaxis for the prevention of HIV infection in men who have sex with men. *MMWR. Morbidity and mortality weekly report.* 2011;60(3):65-68.

11. Centers for Disease Control, Prevention. Interim guidance for clinicians considering the use of preexposure prophylaxis for the prevention of HIV infection in heterosexually active adults. *MMWR. Morbidity and mortality weekly report.* 2012;61(31):586-589.

12. Centers for Disease Control, Prevention. Update to interim guidance for preexposure prophylaxis (PrEP) for the prevention of HIV infection: PrEP for injecting drug users. *MMWR. Morbidity and mortality weekly report.* 2013;62(23):463-465.

13. Centers for Disease Control and Prevention. Fact sheet: HIV incidence: Estimated annual infections in the U.S., 2008-2014-Overall and by transmission route. https://www.cdc.gov/nchhstp/newsroom/docs/factsheets/hiv-incidence-fact-sheet_508.pdf Accessed 27 Feb 2017.

14. Centers for Disease Control and Prevention. *HIV Surveillance Report,* 2015; vol 27. https://www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-surveillance-report-2015-vol-27.pdf Accessed 27 Feb 2017.

15. Connor EM, Sperling RS, Gelber R, et al. Reduction of maternal-infant transmission of human-immunodeficiency-virus Type-1 with zidovudine treatment. *N Engl J Med.* 1994;331(18):1173-1180.

16. Centers for Disease Control and Prevention. Update: provisional Public Health Service recommendations for chemoprophylaxis after occupational exposure to HIV. *Morbidity and Mortality Weekly Reports.* 1996;45(22):468-472.

17. Centers for Disease Control and Prevention. Public Health Service guidelines for the management of health-care worker exposures to HIV and recommendations for postexposure prophylaxis. *Morbidity and Mortality Reports and Recommendations.* 1998;47(RR-7):1-34.

18. Cardo DM, Culver DH, Ciesielski CA, et al. A case-control study of HIV seroconversion in health care workers after percutaneous exposure. *N Engl J Med.* 1997;337(21):1485-1490.

19. Deutsch MB, Glidden DV, Sevelius J, et al. HIV pre-exposure prophylaxis in transgender women: A subgroup analysis of the iPrEx trial. *Lancet HIV.* 2015;2(12):e512-e519.

20. Liu AY, Vittinghoff E, Sellmeyer DE, et al. Bone mineral density in HIV-negative men participating in a tenofovir pre-exposure prophylaxis randomized clinical trial in San Francisco. *PloS One.* 2011;6(8):e23688.

21. Hosek SG, Siberry G, Bell M, et al. The acceptability and feasibility of an HIV preexposure prophylaxis (PrEP) trial with young men who have sex with men. *J Acquir Immune Defic Syndr.* 2013;62(4):447-456.

22. Molina JM, Capitant C, Spire B, et al. On-demand preexposure prophylaxis in men at high risk for HIV-1 infection. *N Engl J Med.* 2015;373(23):2237-2246.

23. Grant RM, Anderson PL, McMahan V, et al. Uptake of pre-exposure prophylaxis, sexual practices, and HIV incidence in men and transgender women who have sex with men: a cohort study. *Lancet Infect Dis.* 2014;14(9):820-829.

24. McCormack S, Dunn DT, Desai M, et al. Pre-exposure prophylaxis to prevent the acquisition of HIV-1 infection (PROUD): effectiveness results from the pilot phase of a pragmatic open-label randomised trial. *Lancet.* 2016;387 North American Edition(10013):53-60.

25. Volk JE, Marcus JL, Phengrasamy T, et al. No new HIV infections with increasing use of HIV preexposure prophylaxis in a clinical practice setting. *Clin Infect Dis.* 2015;61(10):1601-1603.

26. Marcus JL, Hurley LB, Nguyen DP, Silverberg MJ, Volk JE. Redefining HIV Preexposure Prophylaxis Failures. *Clin Infect Dis.* 2017:cix593.

27. Liu AY, Cohen SE, Vittinghoff E, et al. Preexposure prophylaxis for HIV infection integrated with municipal-and community-based sexual health services. *JAMA Internal Medicine.* 2016;176(1):75-84.

28. Molina JM, Charreau I, Spire B, et al. Efficacy, safety, and effect on sexual behaviour of on-demand pre-exposure prophylaxis for HIV in men who have sex with men: an observational cohort study. *Lancet HIV.* 2017: online first: available at : http://dx.doi.org/10.1016/S2352-3018(17)30089-9

29. Murnane PM, Celum C, Mugo N, et al. Efficacy of preexposure prophylaxis for HIV-1 prevention among high-risk heterosexuals: subgroup analyses from a randomized trial. *AIDS.* 2013;27(13):2155-2160.

30. 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.

31. Peterson L, Taylor D, Roddy R, et al. Tenofovir disoproxil fumarate for prevention of HIV infection in women: A phase 2, double-blind, randomized, placebo-controlled trial. *PLoS Clin Trial.* 2007;2(5):e27.

32. Marrazzo JM, Ramjee G, al . Tenofovir-based preexposure prophylaxis for HIV infection among African women. *N Engl J Med.* 2015; 372(6):509-18.

33. Baeten J. What Can the twisted tale of PrEP results teach us? *Conference on Retroviruses and Opportunistic Infections* 2012; http://www.retroconference.org/2012b/Abstracts/45269.htm. Accessed 21 April 2012.

34. Martin M, Vanichseni S, Suntharasamai P, et al. Factors associated with the uptake of and adherence to HIV pre-exposure prophylaxis in people who have injected drugs: an

observational, open-label extension of the Bangkok Tenofovir Study. *Lancet HIV.* 2017; 4(2): e59-e65.

35. Guyatt G, Oxman AD, Akl EA, et al. GRADE guidelines: 1. Introduction--GRADE evidence profiles and summary of findings tables. *J Clin Epidemiology.* 2011;64(4):383-394.

36. Wimberly YH, Hogben M, Moore-Ruffin J, Moore SE, Fry-Johnson Y. Sexual history-taking among primary care physicians. *J Natl Med Assoc.* 2006;98(12):1924-1929.

37. Kurth AE, Holmes KK, Hawkins R, Golden MR. A national survey of clinic sexual histories for sexually transmitted infection and HIV screening. *Sexually Transmitted Diseases* 2005;32(6):370-376.

38. Laws MB, Bradshaw YS, Safren SA, et al. Discussion of sexual risk behavior in HIV care is infrequent and appears ineffectual: A Mixed Methods Study. *AIDS Behav.* 2011;15(4):812-822.

39. Metsch LR, Pereyra M, del Rio C, et al. Delivery of HIV prevention counseling by physicians at HIV medical care settings in 4 US cities. *Am J Public Health.* 2004;94(7):1186-1192.

40. Duffus WA, Barragan M, Metsch L, et al. Effect of physician specialty on counseling practices and medical referral patterns among physicians caring for disadvantaged human immunodeficiency virus-infected populations. *Clin Infect Dis.* 2003;36(12):1577-1584.

41. Smith A, Le B, Finlayson T, Oster A, DiNenno E. Prevalence and awareness of HIV infection among men who have sex with men-21 cities, United States, 2008. *Morbidity and Mortality Weekly Report.* 2010;59(37):1201-1207.

42. Bernstein KT, Liu KL, Begier EM, Koblin B, Karpati A, Murrill C. Same-sex attraction disclosure to health care providers among New York City men who have sex with men: implications for HIV testing approaches. *Arch Intern Med.* 2008;168(13):1458-1464.

43. Menza TW, Hughes JP, Celum CL, Golden MR. Prediction of HIV acquisitiona men who have sex with men. *Sexually Transmitted Diseases.* 2009;36(9):547-555.

44. Smith DK, Pals SL, Herbst JH, Shinde S, Carey JW. Development of a clinical screening index predictive of incident HIV infection among men who have sex with men in the United States. *J Acquir Immune Defic Syndr.* 2012;60(4):421-427.

45. Pinkerton SD, Abramson PR. Effectiveness of condoms in preventing HIV transmission. *Soc Sci Med.* 1997;44(9):1303-1312.

46. Jenness SM, Neaigus Alan, Murrill CS, Wendel T, Forgione L, Hagan H. Estimated HIV incidence among high-risk in New York City, 2007. *J Acquir Immune Defic Syndr.* 2011;56(2):193-197.

47. LaLota M, Beck D, Metsch L, et al. HIV seropositivity and correlates of infection among heterosexually active adults in high-risk areas in South Florida. *AIDS Behav.* 2011;15(6):1259-1263.

48. Neaigus A, Miller M, Gyarmathy VA, Friedman SR. HIV heterosexual sexual risk from injecting drug users among HIV-seronegative noninjecting heroin users. *Substance Use & Misuse.* 2011;46(2-3):208-217.

49. Chan AW, Pristach EA, Welte JW. Detection by the CAGE of alcoholism or heavy drinking in primary care outpatients and the general population. *Journal of substance abuse.* 1994;6(2):123-135.

50. Bastiaens L, Riccardi K, Sakhrani D. The RAFFT as a screening tool for adult substance use disorders. *The American journal of drug and alcohol abuse.* 2002;28(4):681-691.

51. Knight JR, Sherritt L, Shrier LA, Harris SK, Chang G. Validity of the CRAFFT substance abuse screening test among adolescent clinic patients. *Archives of pediatrics & adolescent medicine.* 2002;156(6):607-614.

52. Halkitis PN, Pollock JA, Pappas MK, et al. Substance use in the MSM population of New York City during the era of HIV/AIDS. *Substance Use & Misuse.* 2011;46(2-3):264-273.

53. Weller S, Davis K. Condom effectiveness in reducing heterosexual HIV transmission. *Cochrane Database Syst Rev.* 2002(1):CD003255.

54. Smith DK, Herbst JH, Zhang X, Rose CE. Condom effectiveness for HIV prevention by consistency of use among men who have sex with men in the United States. *J Acquir Immune Defic Syndr.* 2015;68(3):337-344.

55. Ahmed S, Lutalo T, Wawer M, et al. HIV incidence and sexually transmitted disease prevalence associated with condom use: a population study in Rakai, Uganda. *AIDS.* 2001;15(16):2171-2179.

56. Koblin B, Chesney M, Coates T, Team ES. Effects of a behavioural intervention to reduce acquisition of HIV infection among men who have sex with men: the EXPLORE randomised controlled study. *Lancet.* 2004;364(9428):41-50.

57. Reece M, Herbenick D, Schick V, Sanders SA, Dodge B, Fortenberry JD. Condom use rates in a national probability sample of males and females ages 14 to 94 in the United States. *The Journal of Sexual Medicine.* 2010;7:266-276.

58. Peterman TA, Tian LH, Warner L, et al. Condom use in the year following a sexually transmitted disease clinic visit. *International journal of STD & AIDS.* 2009;20(1):9-13.

59. Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, Hakim JG, Kumwenda J, Grinsztejn B, Pilotto JH, Godbole SV. Antiretroviral therapy for the prevention of HIV-1 transmission. *N Engl J Med.* 2016;;375(9):830-9.

60. Rodger AJ, Cambiano V, Bruun T, et al.; PARTNER Study Group. Sexual activity without condoms and risk of HIV transmission in serodifferent couples when the HIV-positive partner is using suppressive antiretroviral therapy. *JAMA.* 2016;316:171–81.

61. Centers for Disease Control and Prevention. Dear Colleague: National Gay Men's HIV/AIDS Awareness Day (NGMHAAD) -- September 27, 2017. 2017; https://www.cdc.gov/hiv/library/dcl/dcl/092717.html. Accessed October 3, 2017.

62. Crepaz N, Tang T, Marks G, Hall H. VIral suppression patterns among persons in the United States with diagnosed HIV infection in 2014. *Ann Intern Med.* 2017;167(6):446-447.

63. Gardner EM, McLees MP, Steiner JF, Del Rio C, Burman WJ. The spectrum of engagement in HIV care and its relevance to test-and-treat strategies for prevention of HIV infection. *Clin Infect Dis.* 2011;52(6):793-800.

64. Centers for Disease C, Prevention. HIV infection and HIV-associated behaviors among injecting drug users - 20 cities, United States, 2009. *MMWR. Morbidity and mortality weekly report.* 2012;61(8):133-138.

65. Strathdee SA, Stockman JK. Epidemiology of HIV among injecting and non-injecting drug users: current trends and implications for interventions. *Curr HIV/AIDS Rep.* 2010;7(2):99-106.

66. U.S. Preventive Services Task Force. Screening for Illicit Drug Use. 2012; http://www.uspreventiveservicestaskforce.org/uspstf08/druguse/drugrs.htm#summary. Accessed August 20, 2013.

67. Boileau C, Bruneau J, Al-Nachawati H, Lamothe F, Vincelette J. A prognostic model for HIV seroconversion among injection drug users as a tool for stratification in clinical trials. *J Acquir Immune Defic Syndr.* 2005;39(4):489-495.

68. Smith DK, Pan Y, Rose CE, et al. A brief screening tool to assess the risk of contracting HIV infection among active injection drug users. *Journal of addiction medicine.* 2014;9(3):226-232.

69. Centers for Disease C, Prevention. Integrated prevention services for HIV infection, viral hepatitis, sexually transmitted diseases, and tuberculosis for persons who use drugs illicitly: summary guidance from CDC and the U.S. Department of Health and Human Services. *MMWR Recomm Rep.* 2012;61(RR-5):1-40.

70. Centers for Disease Control and Prevention, Branson BM, Handsfield HH, et al. Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings. *Morbidity and Mortality Reports and Recommendations.* 2006;September 22, 2006 / 55(RR14);1-17.

71. DiNenno EA. Recommendations for HIV Screening of Gay, Bisexual, and Other Men Who Have Sex with Men—United States, 2017. *MMWR. Morbidity and mortality weekly report*. 2017;66.

72. Mimiaga MJ, Reisner SL, Bland S, et al. Health system and personal barriers resulting in decreased utilization of HIV and STD testing services among at-risk black men who have sex with men in Massachusetts. *AIDS patient care and STDs.* 2009;23(10):825-835.

73. Stekler JD, Ure G, O'Neal JD, et al. Performance of Determine Combo and other point-of-care HIV tests among Seattle MSM. *J Clin Virol.* 2016;76:8-13.

74. Centers for Disease Control and Prevention and Association of Public Health Laboratories. Laboratory testing for the diagnosis of HIV infection: Updated recommendations. 2014; http://dx.doi.org/10.15620/cdc.23447. Accessed August 8, 2016.

75. Daar ES, Pilcher CD, Hecht FM. Clinical presentation and diagnosis of primary HIV-1 infection. *Curr Opin HIV AIDS.* 2008;3(1):10-15.

76. Rich JD, Mylonakis E, Flanigan TP. Misdiagnosis of HIV infection - Response. *Ann Intern Med.* 1999;131(7):547-548.

77. Wu H, Cohen SE, Westheimer E, Gay CL, Hall L, Rose C, Hightow-Weidman LB, Gose S, Fu J, Peters PJ. Diagnosing acute HIV infection: The performance of quantitative HIV-1 RNA testing (viral load) in the 2014 laboratory testing algorithm. *J Clin Virol*. 2017;93:85-6.

78. DHHS Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. 2017. http://aidsinfo.nih.gov/contentfiles/AdultandAdolescentGL.pdf. Accessed July 26, 2017.

79. Cooper RD, Wiebe N, Smith N, Keiser P, Naicker S, Tonelli M. systematic review and meta-analysis: Renal safety of tenofovir disoproxil fumarate in HIV-infected patients. *Clin Infect Dis.* 2010;51(5):496-505.

80. Hall AM, Hendry BM, Nitsch D, Connolly JO. Tenofovir-associatedk toxicity in HIV-infected patients: A review of the evidence. *American Journal of Kidney Diseases.* 2011;57(5):773-780.

81. Phair J, Palella F. Renal disease in HIV-infected individuals. *Curr Opin HIV AIDS.* 2011;6(4):285-289.

82. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron.* 1976;16(1):31-41.

83. Wargo KA, Eiland EH, 3rd, Hamm W, English TM, Phillippe HM. Comparison of the modification of diet in renal disease and Cockcroft-Gault equations for antimicrobial dosage adjustments. *Ann Pharmacother.* 2006;40(7-8):1248-1253.

84. Rostoker G, Andrivet P, Pham I, Griuncelli M, Adnot S. Accuracy and limitations of equations for predicting the glomerular filtration rate during follow-up of patients with non-diabetic nephropathies. *BMC nephrology.* 2009;10:16.

85. Wolitski RJ, Fenton KA. Sexual health, HIV, and sexually transmitted infections among gay, bisexual, and other men who have sex with men in the United States. *AIDS Behav.* 2011;15 Suppl 1:S9-17.

86. van der Helm JJ, Prins M, del Amo J, et al. The hepatitis C epidemic among HIV-positive MSM: incidence estimates from 1990 to 2007. *AIDS.* 2011;25(8):1083-1091.

87. Gatanaga H, Hayashida T, Tanuma J, Oka S. Prophylactic effect of antiretroviral therapy on hepatitis B virus infection. *Clin Infect Dis.* 2013;56(12):1812-1819.

88. Moyer VA. Screening for hepatitis C virus infection in adults: US Preventive Services Task Force recommendation statement. *Ann Intern Med.* 2013;159(5):349-357.

89. Hoornenborg E, Achterbergh RCA, Schim van der Loeff MF, et al. MSM starting preexposure prophylaxis are at risk of hepatitis C virus infection. *AIDS.* 2017;31(11):1603-1610.

90. Charre C, Cotte L, Kramer R, Miailhes P, Godinot M, Koffi J, Scholtès C, Ramière C. Hepatitis C virus spread from HIV-positive to HIV-negative men who have sex with men. *PloS One*. 2018;13(1):e0190340.

91. Volk JE, Marcus JL, Phengrasamy T, Hare CB. Incident hepatitis C virus infections among users of HIV preexposure prophylaxis in a clinical practice setting. *Clin Infect Dis*. 2015;60(11):1728-9.

92. AASLD-IDSA. HCV testing and linkage to care. Recommendations for testing, managing, and treating hepatitis C. http://www.hcvguidelines.org/full-report/hcv-testing-and-linkage-care. Accessed February 20, 2018.

93. Workowski KA, Bolan GA. Sexually transmitted diseases treatment guidelines (2015). *Morbidity and Mortality Recommendations and Reports.* 2015;64(RR3):1-137.

94. Centers for Disease Control and Prevention. 2016 Sexually Transmitted Disease Surveillance; National Profile-Overview: Chlamydia. 2017; https://www.cdc.gov/std/stats16/chlamydia.htm. Accessed October 13, 2017.

95. Barbee LA, Tat S, Dhanireddy S, Marrazzo JM. Implementation and operational research: effectiveness and patient acceptability of a sexually transmitted infection self-testing program in an HIV care setting. *J Acquir Immune Defic Syndr*. 2016;72(2):e26-e31.

96. Freeman AH, Bernstein KT, Kohn RP, Philip S, Rauch LM, Klausner JD. Evaluation of self-collected versus clinician-collected swabs for the detection of Chlamydia trachomatis and Neisseria gonorrhoeae pharyngeal infection among men who have sex with men. *Sexually transmitted diseases*. 2011;38(11):1036-1039.

97. Lunny C, Taylor D, Hoang L, et al. Self-collected versus clinician-collected sampling for Chlamydia and Gonorrhea screening: a systemic review and meta-analysis. *PloS One*. 2015;10(7):e0132776.

98. Hunte T, Alcaide M, Castro J. Rectal infections with chlamydia and gonorrhoea in women attending a multiethnic sexually transmitted diseases urban clinic. *International journal of STD & AIDS.* 2010;21(12):819-822.

99. Trebach JD, Chaulk CP, Page KR, Tuddenham S, Ghanem KG. Neisseria gonorrhoeae and Chlamydia trachomatis among women reporting extragenital exposures. *Sexually transmitted diseases*. 2015;42(5):233.

100. Danby CS, Cosentino LA, Rabe LK, et al. Patterns of extragenital chlamydia and gonorrhea in women and men who have sex with men reporting a history of receptive anal intercourse. *Sexually transmitted diseases.* 2016;43(2):105-109.

101. Oster AM, Wertheim JO, Hernandez AL, Ocfemia MC, Saduvala N, Hall HI. Using Molecular HIV Surveillance Data to Understand Transmission Between Subpopulations in the United States. *J Acquir Immune Defic Syndr.* 2015;70(4):444-451.

102. Hurt CB, Beagle S, Leone PA, et al. Investigating a sexual network of black men who have sex with men: implications for transmission and prevention of HIV infection in the United States. *J Acquir Immune Defic Syndr*. 2012;61(4):515.

103. Copen CE, Chandra A, Febo-Vazquez I. Sexual behavior, sexual attraction, and sexual orientation among adults Aged 18-44 in the United States: Data From the 20113 National Survey of Family Growth. *National Health Statistics Reports.* 2016(88):1-14.

104. Justman J, Befus M, Hughes J, et al. Sexual behaviors of US women at risk of HIV acquisition: a longitudinal analysis of findings from HPTN 064. *AIDS Behav.* 2015;19(7):1327-1337.

105. Dombrowski JC. Do women need screening for extragenital gonococcal and chlamydial infections? *Sexually Transmitted Diseases.* 2015;42(5):240-241.

106. Tao G, Hoover KW, Nye MB, Peters PJ, Gift TL, Body BA. Infrequent testing of women for rectal chlamydia and gonorrhea in the United States. *Clin Infect Dis.* 2017.

107. Centers for Disease Control and Prevention. Recommendations for partner services programs for HIV infection, syphilis, gonorrhea, and chlamydial infection. *Morbidity and Mortality Reports and Recommendations.* 2008;57(RR09):1-63.

108. American College of Obstetrics and Gynecology. Committee Opinion: Expedited Partner Therapy in the Management of Gonorrhea and Chlamydial Infection. 2015; https://www.acog.org/Resources-And-Publications/Committee-Opinions/Committee-on-Gynecologic-Practice/Expedited-Partner-Therapy-in-the-Management-of-Gonorrhea-and-Chlamydial-Infection. Accessed 12 October 2017.

109. Centers for Disease Control and Prevention. Guidance on the Use of Expedited Partner Therapy in the Treatment of Gonorrhea. 2016; https://www.cdc.gov/std/ept/gc-guidance.htm. Accessed 12 October 2017.

110. Centers for Disease Control and Prevention. Expedited partner therapy in the management of sexually transmitted diseases. 2006; https://www.cdc.gov/std/treatment/eptfinalreport2006.pdf. Accessed October 12, 2017

111 Patterson KB, Prince HA, Kraft E, et al. Penetration of tenofovir and emtricitabine in mucosal tissues: implications for prevention of HIV-1 transmission. *Science Transl Med.* 2011;3(112):112-114.

112. Anderson PL, Kiser JJ, Gardner EM, Rower JE, Meditz A, Grant RM. Pharmacological considerations for tenofovir and emtricitabine to prevent HIV infection. *Journal of Antimicrobial Chemotherapy.* 2011;66(2):240-250.

113. Anderson PL. Pharmacology Considerations for HIV Prevention. 13th International Workshop on Clinical Pharmacology of HIV 2012; Barcelona, Spain.

114. McComsey GA, Tebas P, Shane E, et al. Bone disease in HIV infection: A practical review and recommendations for HIV care providers. *Clin Infect Dis.* 2010;51(8):937-946.

115. Yin MT, Overton ET. Increasing clarity on bone loss associated with antiretroviral initiation. *J Infect Dis.* 2011;203(12):1705-1707.

116. Mulligan K, Glidden D, Gonzales P, et al. Effects of emtricitabine/tenofovir on bone mineral density in seronegative men from 4 continents: DEXA results of the global iPrEx study. Paper presented at: Boston: 18th Conference on Retroviruses and Opportunistic Infections. 2011.

117. Kasonde M, Niska RW, Rose C, et al. Bone Mineral Density Changes among HIV-Uninfected Young Adults in a Randomised Trial of Pre-Exposure Prophylaxis with Tenofovir-Emtricitabine or Placebo in Botswana. *PloS One.* 2014;9(3):e90111.

118. Anderson P LJ, Buchbinder S, Guanira J, Montoya O, Casapia M, Bargg L, Bushman L, Glidden D, Grant R, and the iPrEx study team. Interpreting detection rates of intracellular FTC-TP and TFV-DP: The iPrEx trial. 18th Conference on Retroviruses and Opportunistic Infections; 2011; Boston, Massachusetts.

119. Centers for Disease Control and Prevention. Updated guidelines for antiretroviral postexposure pophylaxis after sexual, injection drug use, or other nonoccupational exposure to HIV—United States, 2016. 2016. http://www.cdc.gov/hiv/pdf/programresources/cdc-hiv-npep-guidelines.pdf. Accessed November 1, 2017.

120. Seifert SM, Glidden DV, Meditz AL, et al. Dose response for starting and stopping HIV preexposure prophylaxis for men who have sex with men. *Clin Infect Dis.* 2015;60(5):804-810.

121. Seifert SM, Chen X, Meditz AL, et al. Intracellular tenofovir and emtricitabine anabolites in genital, rectal, and blood compartments from first dose to steady state. *AIDS Res Hum Retroviruses*. 2016;32(10-11):981-991.

122. Hendrix CW, Andrade A, Bumpus NN, et al. Dose frequency ranging pharmacokinetic study of tenofovir-emtricitabine after directly observed dosing in healthy volunteers to establish adherence benchmarks (HPTN 066). *AIDS Res Hum Retroviruses*. 2016;32(1):32-43.

123. Mugo NR, Heffron R, Donnell D, et al. Increased risk of HIV-1 transmission in pregnancy: a prospective study among African HIV-1-serodiscordant couples. *AIDS.* 2011;25(15):1887-1895.

124. Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission. Recommendations for use of antiretroviral drugs in pregnant HIV-1-infected women for maternal health and interventions to reduce perinatal HIV transmission in the United States. 2016. http://aidsinfo.nih.gov/contentfiles/lvguidelines/PerinatalGL.pdf. Accessed July 26, 2017.

125. Vernazza PL, Graf I, Sonnenberg-Schwan U, Geit M, Meurer A. Preexposure prophylaxis and timed intercourse for HIV-discordant couples willing to conceive a child. *AIDS.* 2011;25(16):2005-2008.

126. Siberry GK, Williams PL, Mendez H, et al. Safety of tenofovir use during pregnancy: early growth outcomes in HIV-exposed uninfected infants. *AIDS.* 2012;26(9):1151-1159.

127. Gibb DM, Kizito H, Russell EC, et al. Pregnancy and infant outcomes among HIV-infected women taking long-term ART with and without tenofovir in the DART trial. *PloS Med.* 2012;9(5):e1001217.

128. Mirochnick M, Best BM, Clarke DF. Antiretroviral pharmacology: special issues regarding pregnant women and neonates. *Clinics in perinatology.* 2010;37(4):907-927.

129. The Antiretroviral Pregnancy Registry. Interim Report: 1 January 1989 through 31 January 2017. 2017; http://www.apregistry.com/forms/interim_report.pdf. Accessed July 26, 2017.

130. Lampe MA, Smith DK, Anderson GJE, Edwards AE, Nesheim SR. Achieving safe conception in HIV-discordant couples: the potential role of oral preexposure prophylaxis (PrEP) in the United States. *Am J Obstet Gynecol.* 2011;204(6).

131. Brooks JT, Kawwass JF, Smith DK, et al. Effects of antiretroviral therapy to prevent HIV transmission to women in couples attempting conception when the man has HIV infection — United States, 2017. *MMWR Morb Mort Wkly Rep.* 2017;66:859-860.

132. Attia S, Egger M, Muller M, Zwahlen M, Low N. Sexual transmission of HIV according to viral load and antiretroviral therapy: systematic review and meta-analysis. *AIDS.* 2009;23(11):1397-1404.

133. Cohen MS, McCauley M, Gamble TR. HIV treatment as prevention and HPTN 052. *Curr Opin HIV AIDS.* 2012;7(2):99-105.

134. Mugwanya KK, Hendrix CW, Mugo NR, et al. Pre-exposure Prophylaxis Use by Breastfeeding HIV-Uninfected Women: A Prospective Short-Term Study of Antiretroviral Excretion in Breast Milk and Infant Absorption. *PloS Med.* 2016;13(9):e1002132.

135. Benaboud S, Pruvost A, Coffie PA, et al. Concentrations of tenofovir and emtricitabine in breast milk of HIV-1-infected women in Abidjan, Cote d'Ivoire, in the ANRS 12109 TEmAA Study, Step 2. *Antimicrobial agents and chemotherapy.* 2011;55(3):1315-1317.

136. World Health Organization. Programmatic Update: Use of antiretroviral drugs for treating pregnant women and preventing HIV infection in infants. 2012. http://aidsdatahub.org/dmdocuments/Use_of_Antiretroviral_Drugs__for_Treating_Pregnant_Women.pdf . Accessed 16 August 2013.

137. Liaw Y-F, Chu C-M. Hepatitis B virus infection. *Lancet.* 2009;373(9663):582-592.

137. Hongthanakorn C, Chotiyaputta W, Oberhelman K, et al. Virological breakthrough and resistance in patients with chronic hepatitis B receiving nucleos(t)ide analogues in clinical practice. *Hepatology.* 2011;53(6):1854-1863.

139. Culp L, Caucci L. State adolescent consent laws and implications for HIV pre-exposure prophylaxis. *Am J Prev Med.* 2013;44(1 Suppl 2):S119-124.

140. Della Negra M, de Carvalho AP, de Aquino MZ, et al. A randomized study of tenofovir disoproxil fumarate in treatment-experienced HIV-1 infected adolescents. *Ped Infect Dis J.* 2012;31(5):469-473.

141. Purswani M, Patel K, Kopp JB, et al. Tenofovir Treatment Duration Predicts Proteinuria in a Multiethnic United States Cohort of Children and Adolescents With Perinatal HIV-1 Infection. *Ped Infect Dis J.* 2013;32(5):495-500.

142. Roland ME, Neilands TB, Krone MR, et al. A Randomized Noninferiority Trial of Standard Versus Enhanced Risk Reduction and Adherence Counseling for Individuals Receiving Post-Exposure Prophylaxis Following Sexual Exposures to HIV. *Clin Infect Dis.* 2011;53(1):76-83.

143. Abbas UL, Glaubius R, Mubayi A, Hood G, Mellors JW. Antiretroviral therapy and pre-exposure prophylaxis: Combined impact on HIV transmission and drug resistance in South Africa. *J Infect Dis.* 2013;208(2):224-234.

144. Celum C, Hallett TB, Baeten JM. HIV-1 prevention With ART and PrEP: Mathematical modeling insights into resistance, effectiveness, and public health impact. *J Infect Dis.* 2013;208(2):189-191.

145. Anderson PL, Glidden DV, Liu A, et al. Emtricitabine-tenofovir concentrations and pre-exposure prophylaxis efficacy in men who have sex with men. *Sci Transl Med.* 2012;4(151):151ra125.

146. Cottrell ML, Yang KH, Prince HMA, et al. A Translational Pharmacology Approach to Predicting Outcomes of Preexposure Prophylaxis Against HIV in Men and Women Using Tenofovir Disoproxil Fumarate With or Without Emtricitabine. *J Infect Dis*. 2016;214(1):55-64.

147. Hosek S, Siberry G, Bell M, et al. The acceptability and feasibility of an HIV pre-exposure prophylaxis (PrEP) trial with young men who have sex with men (YMSM). *J Acquir Immune Defic Syndr.* 2012;62(4):447-456.

148. Koss CA, Hosek SG, Bacchetti P, et al. Comparison of Measures of Adherence to Human Immunodeficiency Virus Preexposure Prophylaxis Among Adolescent and Young Men Who Have Sex With Men in the United States. *Clin Infect Dis.* 2017:cix755-cix755.

149. Mutua G, Sanders E, Mugo P, et al. Safety and adherence to intermittent pre-exposure prophylaxis (PrEP) for HIV-1 in African men who have sex with men and female sex workers. *PloS One.* 2012;7(4):e33103..

150. Koenig LJ, Lyles C, Smith DK. Adherence to antiretroviral medications for HIV pre-exposure prophylaxis: lessons learned from trials and treatment studies. *Am J Prev Med.* 2013;44(1 Suppl 2):S91-98.

151. Chapman RH, Ferrufino CP, Kowal SL, Classi P, Roberts CS. The cost and effectiveness of adherence-improving interventions for antihypertensive and lipid-lowering drugs*. *Int J Clin Pract.* 2010;64(2):169-181.

152. Morello CM, Chynoweth M, Kim H, Singh RF, Hirsch JD. Strategies to improve medication adherence reported by diabetes patients and caregivers: Results of a taking control of your diabetes survey. *Ann Pharmacother.* 2011;45(2):145-153.

153. McHorney CA. The Adherence Estimator: a brief, proximal screener for patient propensity to adhere to prescription medications for chronic disease. *Curr Med Res Opin.* 2009;25(1):215-238.

154. Golub SA, Operario D, Gorbach PM. Pre-exposure prophylaxis state of the science: empirical analogies for research and implementation. *Curr HIV/AIDS Rep.* 2010;7(4):201-209.

155. Fiscella K, Epstein RM. So much to do, so little time: Care for the socially disadvantaged and the 15-minute visit. *Arch Intern Med.* 2008;168(17):1843-1852.

156. Yarnall KSH, Pollak KI, Ostbye T, Krause KM, Michener JL. Primary care: Is there enough time for prevention? *Am J Public Health.* 2003;93(4):635-641.

157. Warner L, Klausner JD, Rietmeijer CA, et al. Effect of a brief video intervention on incident infection among patients attending sexually transmitted disease clinics. *PloS Med.* 2008;5(6):919-927.

158. Lin JS, Whitlock E, O'Connor E, Bauer V. Behavioral counseling to prevent sexually transmitted infections: A systematic review for the U.S. Preventive Services Task Force. *Ann Intern Med.* 2008;149(7):497-499.

159. U.S. Preventive Services Task Force. Behavioral counseling to prevent sexually transmitted infections: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med.* 2008;149(7):491-496, W495.

160. Malotte CK. Brief risk-reduction counseling in clinical settings for HIV pre-exposure prophylaxis. *Am J Preventive Med.* 2013;44(1):S112-S118.

161. Kamb ML, Fishbein M, Douglas JM, Jr., et al. Efficacy of risk-reduction counseling to prevent human immunodeficiency virus and sexually transmitted diseases: a randomized controlled trial. Project RESPECT Study Group. *JAMA.* 1998;280(13):1161-1167.

162. Metsch LR, Feaster DJ, Gooden L, et al. Effect of risk-reduction counseling with rapid HIV testing on risk of acquiring sexually transmitted infections: the AWARE randomized clinical trial. *JAMA.* 2013;310(16):1701-1710.

163. Thrun MW. Provider-initiated HIV-risk behavior counseling in the context of HIV pre-exposure prophylaxis. *Am J Preventive Med.* 2013;44(1 Suppl 2):S108-111.

164. National Institute on Drug Abuse. Principles of drug addiction treatment: a Research-based guide. Third ed 2012: http://www.drugabuse.gov/publications/principles-drug-addiction-treatment. Accessed 20 August 2013.

165. National Alliance of State and Territorial AIDS Directors. Fact Sheet: Pharmaceutical company patient assistance programs and co-payment assistance programs for pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP). 2013; https://www.nastad.org/sites/default/files/PrEP-and-PEP-PAP-fact-sheet.pdf. Accessed 28 September 2013.

166. Centers for Disease Control and Prevention. Expedited partner therapy in the management of sexually transmitted diseases. 2006:1-52. http://www.cdc.gov/std/treatment/EPTFinalReport2006.pdf. Accessed 5 July 2011.

167. US Preventive Services Task Force. Screening For HIV: Current recommendations, U.S. Preventive Services Task Force. 2013. http://www.uspreventiveservicestaskforce.org/uspstf/uspshivi.htm. Accessed July 26, 2017.

168. Weinbaum CM, Williams I, Mast EE, et al. Recommendations for identification and public health management of persons with chronic hepatitis B virus infection. *MMWR Recomm Rep.* 2008;57(RR-8):1-20.

169. DiNenno EA, Prejean J, Irwin K, et al. Recommendations for HIV Screening of Gay, Bisexual, and Other Men Who Have Sex with Men — United States, 2017. *MMWR Morb Mortal Wkly Rep.* 2017;66:830–832.

US PUBLIC HEALTH SERVICE

PREEXPOSURE PROPHYLAXIS FOR THE PREVENTION OF HIV INFECTION IN THE UNITED STATES –2017 UPDATE

CLINICAL PROVIDERS' SUPPLEMENT

What's New in the Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2017 Update – Clinical Providers' Supplement?

(Published Online March 2018)

The Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2014 Clinical Providers' Supplement was published in an electronic format in July 2014 so that it could be updated as relevant changes in supporting evidence became available. The Preexposure Prophylaxis for the Prevention of HIV Infection in the United States - 2016 Update – Clinical Providers' Supplement includes revisions to several sections. These revisions are highlighted throughout the document and are intended solely to update the developing evidence base and to clarify specific points in clinical care. No changes were made to the graded recommendations for the use of PrEP in the US.

New: Section 7 HIV Incidence Risk Index for Injection Drug Users

Added recently published validated risk screening tool

New: Section 8 Management of Patients Who Acquire HIV While On PrEP

Added additional detail about recommended steps in the clinical management at visits when seroconversion is detected in patients being prescribed PrEP

New: Section 9 Transition of Patients From nPEP to PrEP

Added additional detail about recommended steps in the clinical management of patients who are concluding a course of nPEP and transitioning directly to PrEP

Section 12 PrEP-related ICD, CPT, and LOINC Codes

Deleted ICD-9 codes since they no longer in use

Section 13 Potential PrEP Quality Practice Measures

Revised measure of medication prescription to measure medication adherence assessment

Section 14 Methods for Developing the PrEP Clinical Practice Guideline

Consolidated all information about the guidelines development and update process into this section and provided details about the systematic literature review methods.

Minor revisions were also made to correct typos, add references, and update content from cited guidelines and source materials.

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For more clinical advice about PrEP guidelines:

- call the National Clinicians Consultation Center PrEPline at **855-448-7737** or
- go to their website at http://nccc.ucsf.edu/clinician-consultation/prep-pre-exposure-prophylaxis/

Supplementary Materials:

Contents

Introduction 4

Section 1 Patient/Provider Checklist....6

Section 2 Patient Information Sheet – PrEP....8

Section 3 Patient Information Sheet – Truvada....11

Section 4 Patient Information Sheet – Acute HIV Infection and PrEP 14

Section 5 Provider Information Sheet – PrEP During Conception, Pregnancy, and Breastfeeding 16

Section 6 HIV Incidence Risk Index for Men Who Have Sex With Men 22

Section 7 HIV Incidence Risk Index for Persons Who Inject Drugs 24

Section 8 Management of Patients Who Acquire HIV While on PrEP 27

Section 9 Transition of Patients from nPEP to PrEP....29

Section 10 Supplemental Counseling Information—Medication Adherence....31

Section 11 Supplemental Counseling Information—HIV Risk Reduction 36

Section 12 PrEP-related ICD, CPT and LOINC Codes 38

Section 13 Potential PrEP Practice Quality Measures....42

Section 14 Methods for Developing the PrEP Clinical Practice Guideline 43

References 51

Introduction

Recent findings from several clinical trials have demonstrated safety[1] and a substantial reduction in the rate of HIV acquisition for men who have sex with men (MSM)[2], men and women in heterosexual discordant couples[3], and heterosexual men and women recruited as individuals[4] who were prescribed daily oral antiretroviral preexposure prophylaxis (PrEP) with a fixed-dose combination of tenofovir disoproxil fumarate (TDF) and emtricitabine (FTC). The demonstrated efficacy of PrEP was in addition to the effects of repeated condom provision, sexual risk-reduction counseling, and the diagnosis and treatment of sexually transmitted infection (STI) that were provided to all trial participants. In July 2012, after reviewing these trial results, the U.S. Food and Drug Administration (FDA) approved an indication for the use of Truvada® (TDF/FTC) "in combination with safer sex practices for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 in adults at high risk" [5,6]. In July 2013, an additional clinical trial found that daily oral TDF reduced the rate of HIV acquisition for persons who inject drugs (PWID) (also called injection drug users [IDU]) [7].

On the basis of these trial results and the FDA approval, the U.S. Public Health Service has published a comprehensive clinical practice guideline for the use of PrEP for the prevention of HIV infection in the United States and updated it in 2017. https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf

This supplement to the PHS PrEP Clinical Practice Guidelines is intended to provide additional information that may be useful to clinicians providing PrEP. As additional materials become available, this document will be updated.

Section 1	Contains a template checklist that clinicians can complete and share with patients to document the services provided to PrEP patients and the actions expected from patients to maximize the efficacy and safety of PrEP.
Sections 2-4	Contain templates for informational handouts that can be provided to patients
Section 5	Contains an information sheet for providers counseling patients about PrEP use during conception, pregnancy and breastfeeding.
Section 6	Contains the HIV incidence Risk Index for MSM, a tool that clinicians may use to quickly and systematically determine which men are at especially high risk for acquiring HIV infection, for whom PrEP may be indicated.
Section 7	Contains the HIV incidence Risk Index for PWID, a tool that clinicians may use to quickly determine which persons who inject drugs are at especially high risk for acquiring HIV infection, for whom PrEP may be indicated.
Section 8	Contains more detailed information about the clinical management of patients who acquire HIV infection while on PrEP.
Section 9	Contains more detailed information about the clinical management of transitioning patients from nPEP to PrEP.
Sections 10-11	Contain more detailed information than that included in the guidelines about methods and resources for counseling patients receiving PrEP about medication adherence and HIV risk reduction behaviors.

Sections 12	Contains information relevant to administrative and billing codes for PrEP related services.
Section 13	Contains potential practice quality practice measures.
Section 14	Documents the methods used to develop the PHS PrEP Clinical Practice Guidelines.

Section 1 Patient/Provider Checklist

Organization/Clinic Name

CHECKLIST FOR INITIATING PREEXPOSURE PROPHYLAXIS (PrEP)

_____ _____

Print name of provider Print name of patient

_____

Today's date (month/day/year)

Provider Section

I have provided this patient with the following: (check all as completed):

- ☐ Assessment for possible acute HIV infection
- ☐ Indicated laboratory screening to determine indications for these medications
- ☐ An HIV risk assessment to determine whether PrEP is indicated for this patient
- ☐ A medication fact sheet listing dosing instructions and side effects
- ☐ Counseling or a referral for counseling on condom use and any other HIV risk-reduction methods this patient may need
- ☐ Advice on methods to help the patient to take medication daily as prescribed
- ☐ Information about PrEP use during conception and pregnancy (when indicated)
- ☐ A prescription for Truvada (300 mg tenofovir disoproxil fumarate, 200 mg emtricitabine)
- ☐ A follow-up appointment date

As the provider, I will:

- Limit refill periods to recommended intervals for repeat HIV testing (at least every 3 months)
- Conduct follow-up visits at least every 3 months that include the following:
  - Assessment of HIV status (including signs or symptoms of acute HIV infection)
  - Assessment of side effects and advice on how to manage them
  - Assessment of medication adherence and counseling to support adherence
  - Assessment of STI symptoms, HIV risk behavior and counseling support for risk-reduction practices
- Inform the patient of any new information about PrEP and respond to questions

Patient Section

It has been explained to me that:

- Taking a dose of PrEP medication every day may lower my risk of getting HIV infection
- This medicine does not completely eliminate my risk of getting HIV infection, so I need to use condoms during sex
- This medicine may cause side effects so I should contact my provider for advice by calling _____ if I have any health problems
- It is important for my health to find out quickly if I get HIV infection while I'm taking this medication, so
    - I will contact my provider right away if I have symptoms of possible HIV infection (fever with sore throat, rash, headache, or swollen glands)
- My provider will test for HIV infection at least once every 3 months

Therefore, I will:

- Try my best to take the medication my provider has prescribed every day
- Talk to my provider about any problems I have in taking the medication every day
- Not share the medication with any other person
- Attend all my scheduled appointments
- Call _____ to reschedule any appointments I cannot attend

Give one copy to patient

Section 2 PrEP Information Sheet

Pre-exposure Prophylaxis (PrEP) for HIV Prevention

Frequently Asked Questions

What is PrEP?

"PrEP" stands for **pre**exposure **p**rophylaxis. The word "prophylaxis" (pronounced pro fil ak sis) means to prevent or control the spread of an infection or disease. The goal of PrEP is to prevent HIV infection from taking hold if you are exposed to the virus. This is done by taking a pill that contains 2 HIV medications every day. These are the same medicines used to stop the virus from growing in people who are already infected.

Why take PrEP?

The HIV epidemic in the United States is growing. About 50,000 people get infected with HIV each year. More of these infections are happening in some groups of people and some areas of the country than in others.

Is PrEP a vaccine?

No. PrEP medication does not work the same way as a vaccine. When you take a vaccine, it trains the body's immune system to fight off infection for years. You will need to take a pill every day by mouth for PrEP medications to protect you from infection. PrEP does not work after you stop taking it. The medication that was shown to be safe and to help block HIV infection is called "Truvada" (pronounced tru va duh). Truvada is a combination of 2 drugs (tenofovir and emtricitabine). These medicines work by blocking important pathways that the HIV virus uses to set up an infection. If you take Truvada as PrEP daily, the presence of the medication in your bloodstream can often stop the HIV virus from establishing itself and spreading in your body. If you do not take the Truvada pills every day, there may not be enough medicine in your blood stream to block the virus.

Should I consider taking PrEP?

PrEP is not for everyone. Doctors prescribe PrEP for some patients who have a very high risk of coming in contact with HIV by not using a condom when they have sex with a person who has HIV infection. You should consider PrEP if you are a man or woman who sometimes has sex without using a condom, especially if you have a sex partner who you know has HIV infection. You should also consider PrEP if you don't know whether your partner has HIV infection but you know that your partner is at risk (for example, your partner inject drugs or is having sex with other people in addition to you) or if you have recently been told by a health care provider that you had a sexually transmitted infection. If your partner has HIV infection, PrEP may be an option to help protect you from getting HIV infection while you try to get pregnant, during pregnancy, or while breastfeeding.

How well does PrEP work?

PrEP was tested in several large studies with men who have sex with men, men who have sex with women, and women who have sex with men. All people in these studies (1) were tested at the beginning of the trial to be sure that they did not have HIV infection, (2) agreed to take an oral PrEP tablet daily,

(3) received intensive counseling on safer-sex behavior, (4) were tested regularly for sexually transmitted infections, and (5) were given a regular supply of condoms.

Several studies showed that PrEP reduced the risk of getting HIV infection.

- Men who have sex with men who were given PrEP medication to take, were 44% less likely to get HIV infection than were those men who took a pill without any PrEP medicine in it (a placebo). Forty-four percent was an average that included men who didn't take the medicine every day and those who did. Among the men who said they took most of their daily doses, PrEP reduced the risk of HIV infection by 73% or more, up to 92% for some.
- Among men and women in couples in which one partner had HIV infection and the other partner initially did not ("HIV-discordant" couples), those who received PrEP medication were 75% less likely to become infected than those who took a pill without any medicine in it (a placebo). Among those who said they took most of their daily doses, PrEP reduced the risk of HIV infection by up to 90%.
- In one study of men and women who entered the study as individuals (not as a couple), PrEP worked for both men and women in one study: those who received the medication were 62% less likely to get HIV infection; those who said they took most of their daily doses, were 85% less likely to get HIV infection. But in another study, only about 1 in 4 women (<26%) had PrEP medication found in their blood when it was checked. This indicated that few women were actually taking their medication and that study found no protection against HIV infection.

More information on the details of these studies can be found at http://www.cdc.gov/hiv/prep.

Is PrEP safe?

The clinical trials also provided safety information on PrEP. Some people in the trials had early side effects such as an upset stomach or loss of appetite but these were mild and usually went away within the first month. Some people also had a mild headache. No serious side effects were observed. You should tell your doctor if these or other symptoms become severe or do not go away.

How can I start PrEP?

If you think you may be at high risk for HIV, talk to your doctor about PrEP. If you and your doctor agree that PrEP might reduce your risk of getting HIV infection, you will need to come in for a general health physical, blood tests for HIV, and tests for other infections that you can get from sex partners. Your blood will also be tested to see if your kidneys and liver are functioning well. If these tests show that PrEP medicines are likely to be safe for you to take and that you might benefit from PrEP, your doctor may give you a prescription after discussing it with you.

Taking PrEP medicines will require you to follow-up regularly with your doctor. You will receive counseling on sexual behaviors and blood tests for HIV infection and to see if your body is reacting well to Truvada. You should take your medicine every day as prescribed, and your doctor will advise you about ways to help you take it regularly so that it stands the best chance to help you avoid HIV infection. Tell your doctor if you are having trouble remembering to take your medicine or if you want to stop PrEP.

If I take PrEP can I stop using condoms when I have sex?

You should not stop using condoms because you are taking PrEP. If PrEP is taken daily, it offers a lot of protection against HIV infection, but not 100%. Condoms also offer a lot of protection against HIV infection if they are used correctly every time you have sex, but not 100%. PrEP medications don't give you any protection from other infections you can get during sex, but condoms do. So you will get the most protection from HIV and other sexual infections if you consistently take PrEP medication and consistently use condoms during sex.

How long do I need to take PrEP?

You should discuss this with your doctor. There are several reasons that people stop taking PrEP. If your risk of getting HIV infections becomes low because of changes that occur in your life, you may want to stop taking PrEP. If you find you don't want to take a pill every day or often forget to take your pills, other ways of protecting yourself from HIV infection may work better for you. If you have side effects from the medication that are interfering with your life or if blood tests show that your body is reacting to PrEP in unsafe ways, your doctor may stop prescribing PrEP for you.

Section 3 Truvada Medication Information Sheet

Truvada Medication Information Sheet for Patients

Brand name: Truvada (tru va duh)

Generic name: tenofovir disoproxil fumarate and emtricitabine

Why is this medication prescribed?

- Truvada is one of several medications that are currently used to treat human immunodeficiency virus (HIV) and hepatitis B virus infection.
- Truvada is now being used to *prevent* HIV infection.
- Truvada is sometimes prescribed to some people who do not have HIV infection (for example, those who do not always use condoms or who have a sex partner that has HIV infection) to help reduce their chances of getting HIV infection
- When you take Truvada to prevent HIV infection, doctors refer to this use as "pre-exposure prophylaxis" or "PrEP".

How does Truvada (PrEP) help prevent HIV infection?

- HIV is a virus that attacks your body's immune cells (the cells that work to fight infections).
- The 2 medications that make up Truvada (tenofovir and emtricitabine) block important pathways that viruses use to set up infection.
- If you take Truvada as PrEP daily, the presence of the medication in your bloodstream can sometimes stop the virus from establishing itself and slow the spread of HIV in your body.
- By itself, PrEP with Truvada does not work all the time so you should also use condoms during sex for the most protection from HIV infection.

How should this medicine be used?

- You must take one tablet of Truvada by mouth every day.
- Follow the directions on your prescription label carefully, and ask your doctor or pharmacist to explain any part you do not understand.
- Do not stop taking Truvada without talking to your doctor. When your supply of Truvada starts to run low, contact your doctor or pharmacist to get more.
- You may be at higher risk of becoming infected with HIV if you miss doses or stop taking Truvada than if you take it every day.

What special precautions should I follow?

Before taking Truvada (tenofovir and emtricitabine) you must do the following:

- Tell your doctor and pharmacist if you are allergic to tenofovir, emtricitabine, or any other medications.
- Tell your doctor and pharmacist about all prescription and nonprescription medications, (vitamins, nutritional supplements, and herbal products) you are taking. Your doctor may need to change the doses of your medications or monitor you carefully for side effects.
- Tell your doctor if you have or have ever had kidney or liver disease.
- Tell your doctor if you become pregnant or if you are breastfeeding.

What special dietary instructions should I follow?

- Continue your normal diet unless your doctor tells you otherwise.

What should I do if I forget a dose?

- Take the missed dose as soon as you remember it. However, if it is almost time for the next dose, skip the missed dose and continue your regular dosing schedule.
- Do not take a double dose to make up for a missed one.

What side effects can this medication cause?

You may experience the following side effects while taking Truvada:

- upset stomach
- headache
- vomiting
- loss of appetite

These side effects usually fade during the first month of taking Truvada for PrEP. Tell your doctor if any of these symptoms are severe or do not go away.

Truvada may cause other side effects. Some side effects can be serious. Call your doctor immediately if you have any unusual problems while taking this medication or if you have any of the following:

- fever or chills especially with
- sore throat, cough, rash or other signs of infection

If you experience a serious side effect, you or your doctor may send a report to the Food and Drug Administration's (FDA) MedWatch Adverse Event Reporting program online (at http://www.fda.gov/Safety/MedWatch) or by phone (1-800-332-1088).

How should I store Truvada in my home?

- You should keep Truvada in the container it came in, tightly closed, and out of reach of children.
- You must store it at room temperature and away from excessive heat and moisture.
- Throw away any medication that is outdated or no longer needed. Talk to your pharmacist about the proper disposal of your medication.

What should I do in case of emergency/overdose?

- In case of overdose, call your local poison control center at 1-800-222-1222. If the person has collapsed or is not breathing, call local emergency services at 911.

What other information should I know?

- Do not let anyone else take your medication.
- Ask your pharmacist if you have any questions about refilling your prescription.
- Write a list of all of your prescription and over-the-counter medicines, as well as any vitamins, minerals, or other dietary supplements that you take.
- Bring your medication list with you each time you visit a doctor or if you are admitted to a hospital. Keep it with you always in case of emergencies.

Section 4 Patient Information Sheet – Acute HIV Infection

Information about Acute HIV Infection and PrEP

What is acute HIV Infection?

HIV stands for human immunodeficiency virus. This is the virus that causes AIDS.

Acute HIV infection is a name for the earliest stage of HIV infection, when you first get infected with the HIV virus. It is sometimes also called primary HIV infection. Many people with acute HIV infection have the following:

- A fever
- A tired feeling
- Swollen lymph nodes (also called lymph glands)
- Swollen tonsils (also called tonsillitis)
- A sore throat
- Joint and muscle aches
- Diarrhea
- A rash

These signs and symptoms of acute HIV infection can begin a few days after you are exposed to HIV and usually last for about 14 days. They could last for just a few days, or they could last for several months.

You might not realize your illness is acute HIV infection. For one thing, you may not have known that the person you had sex with had HIV infection. And the signs and symptoms of HIV infection may feel just like other common virus infections like flu, a cold, sore throat, or mononucleosis (mono).

What tests can show that I have acute HIV infection?

When HIV enters your body, it moves inside white blood cells called CD4 lymphocytes. HIV takes over the CD4 cells and makes billions of copies of the virus each day. The virus spread through your body.

Your body tries to defend itself against HIV by making antibodies (these antibodies try to block the virus from spreading in your body). Most HIV tests check to see if antibodies against HIV are in your blood. But it takes a few weeks before your body makes enough antibodies for the usual HIV tests to see them.

However, when you have acute HIV infection, you have a high amount of the HIV virus in your blood. Special tests can measure the amount of HIV in your blood. At the time you have acute HIV infection, you probably won't have enough HIV antibodies in your blood to measure, but you will have enough virus to measure. So if the blood tests do not find any antibody but do see the virus, your doctor will know that you're feeling sick because you have acute HIV infection.

How does it help to find out I have HIV at an early stage?

First, PrEP is used to help lower your chances of getting HIV infection. If you already have acute HIV infection you should not take PrEP.

Second, while PrEP helps protect people, especially when they take their doses every day, it is still possible to get HIV infection. So if you are taking PrEP and have the signs and symptoms mentioned above, it is important to see your doctor to be checked. If you have some other infection, like the flu, you should continue your PrEP medicines but if it is discovered that you have acute HIV infection, you should stop taking PrEP as soon as your tests show that you have HIV infection

Third, people who take PrEP for more than a couple of weeks while they have HIV infection can easily develop virus that can't be treated with those same drugs (resistant virus). So finding out quickly that you have HIV infection and stopping PrEP can protect your long term health and keep your treatment options open.

And fourth, when people have lots of virus in their body during acute HIV infection, they are more likely to pass the virus on to people they have sex with, especially since they may not know yet that they have gotten infected. For example, if your last HIV test result was negative and your partner also had a recent negative HIV test result, you might choose to have sex without a condom just at the time when it's very likely you would pass the virus on. So the sooner you know you have become infected, the more careful you can be to protect others from getting HIV infection.

How is HIV treated?

People who have HIV infection are treated with combinations of 3 or more medicines that fight HIV. Some doctors start people on treatment medications as soon as they become infected; other doctors wait for a while because the greatest benefits to a person's health are seen after they have been infected a while. Early treatment also reduces the chances that a person with HIV infection will pass the virus on to their sex partners.

What do I do if I suspect I might have acute HIV infection?

First, contact your doctor's office and arrange to be examined and have the right blood tests.

Second, discuss with your doctor whether to stop your PrEP medications or continue them until your test results are back.

Third, be especially careful to use condoms and take other safer sex measures to protect your partner(s).

Section 5 Provider Information Sheet – PrEP during Conception, Pregnancy, and Breastfeeding

Information for Clinicians
Counseling Patients about PrEP Use During Conception, Pregnancy, and Breastfeeding

PrEP use may be one of several options to help protect the HIV-negative male or female partner in a heterosexual HIV-discordant couple during attempts to conceive[8-10]. Pregnancy care providers may not have access to the medical records of the partner with HIV infection to document their viral load status. The extent to which PrEP use further decreases risk of HIV acquisition when the partner with HIV infection has a documented current undetectable viral load is unknown.

Based on

DHHS Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission[9]

Panel's Recommendations on Reproductive Options for HIV-Concordant and Serodiscordant Couples

For Couples who Want to Conceive

For Concordant (Both Partners are HIV-Infected) and Discordant Couples:

- Expert consultation is recommended so that approaches can be tailored to couples specific needs **(AIII)**.
- Partners should be screened and treated for genital tract infections before attempting to conceive **(AII)**.
- The HIV-infected partner(s) should attain maximum viral suppression before attempting conception **(AIII)**.

For Discordant Couples:

- The HIV-infected partner should be receiving combination antiretroviral therapy and demonstrate sustained suppression of plasma viral load below the limits of detection (AI).
- Administration of antiretroviral pre-exposure prophylaxis (PrEP) for 30 days before attempting conception and for 30 days after conception is achieved for HIV-uninfected partners may offer an additional tool to reduce the risk of sexual transmission, particularly if the HIV-infected partner's plasma viral load is unknown or detectable **(CIII)**. It is not known whether PrEP for the uninfected partner confers additional benefit when the infected partner receiving antiretroviral therapy has documented sustained viral suppression.

Discordant Couples with HIV-Infected Women:

- The safest conception option is assisted insemination, at home or in a clinician's office with a partner's sperm during the peri-ovulatory period **(AIII)**.

Discordant Couples with HIV-Infected Men:

- The use of donor sperm from an HIV-uninfected man with artificial insemination is the safest option **(AIII).**
- When the use of donor sperm is unacceptable, the use of sperm preparation techniques coupled with either intrauterine insemination or *in vitro* fertilization should be considered **(BII)**.

Based on

DHHS Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission[9]

Panel's Recommendations on Reproductive Options for HIV-Concordant and Serodiscordant Couples
• Semen analysis is recommended for HIV-infected men before conception is attempted to prevent unnecessary exposure to infectious genital fluid. Semen abnormalities appear to be more common among HIV-infected men than HIV-uninfected men (**AIII**).
Rating of Recommendations*: A = Strong; B = Moderate; C = Optional* ***Rating of Evidence****: I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

The following information is provided to help you inform your patients of current information about potential risks and benefits of PrEP use so that you and your patients can make an informed decision.

Key Points

- Provide education about PrEP and other methods of conception that minimize the risk of HIV transmission to both members of an HIV-discordant couple whenever possible.
- During counseling, include discussion of what is currently known and unknown about
  - Potential benefits
  - Potential risks
- If you prescribe PrEP, include the following in counseling:
  - Importance of adherence to daily doses of medication
  - Importance of continuing condom use after conception to protect against sexually transmitted infections and to add protection against HIV infection
- Signs and symptoms of acute HIV infection and the need for urgent HIV testing if HIV infection is suspected

FOR AN HIV-NEGATIVE MAN PLANNING PREGNANCY WITH AN HIV-POSITIVE FEMALE PARTNER

Options

Reducing the risk of HIV acquisition by an HIV-negative man during conception can be achieved by use of the following, singly or ideally in combination[10-13]:

- Antiretroviral treatment of the HIV-positive female partner to achieve an undetectable viral load[13]
- STI diagnosis and any indicated treatment for both partners before conception attempts
- Daily, oral doses of TDF/FTC beginning 1 month before a conception attempt and continuing for 1 month after a conception attempt. PrEP may be indicated when the partners recent viral load is unknown, reported to be detectable, or cannot be documented as undetectable[14].

AND EITHER

- Limit sex without a condom (natural conception) to peak fertility times identified by home or laboratory tests for ovulation[15.]

OR

- Intravaginal insemination[13] (either at home or in the clinic) with a fresh semen sample

Potential Benefits of PrEP use

In clinical trials with heterosexually active adults, daily oral PrEP with TDF/FTC was safe and reduced the risk of HIV acquisition by an average of 63%-75%. Higher levels of protection (≥90%) were found among persons whose drug levels in their blood indicated that they had consistently taken the medication[3,4].

Potential Risks of PrEP use

In PrEP trials, follow-up with persons taking medication has been conducted for an average of 1-4 years. Although no serious health risks were associated with PrEP use by HIV-uninfected adults, the long-term safety of PrEP has not yet been determined.

FOR AN HIV-NEGATIVE WOMAN PLANNING PREGNANCY WITH AN HIV-POSITIVE MALE PARTNER

Options

Reducing the risk of HIV acquisition by an HIV-negative woman during conception can be achieved by use of the following, singly or ideally in combination[10,13]:

- Antiretroviral treatment of the HIV-positive male partner to achieve an undetectable viral load[13]
- STI diagnosis and any indicated treatment for both partners before conception attempts
- Daily, oral doses of TDF/FTC beginning 1 month before a conception attempt and continuing for 1 month after a conception attempt. PrEP may be indicated when the partners recent viral load is unknown, reported to be detectable, or cannot be documented as undetectable[14].

AND EITHER

- Limit sex without a condom (natural conception) to peak fertility times identified by home or laboratory tests for ovulation in the female partner[15].

OR

- Intravaginal[16] or intrauterine insemination, or intracytoplasmic sperm injection with a semen sample processed by "sperm washing" and confirmed to have a negative test result for the presence of remnant HIV[16-17]. This option may be indicated for couples with fertility problems.

Potential Benefits of PrEP use

In clinical trials with heterosexually active adults, daily oral PrEP with TDF/FTC was safe and reduced the risk of HIV acquisition by an average of 63%-75%. Higher levels of protection (≥90%) were found among persons whose drug levels in their blood indicated that they had consistently taken the medication[3,4].

The risk of HIV acquisition increases during pregnancy[19], as does the risk of HIV transmission to an infant born to a mother who becomes infected during pregnancy or breastfeeding[20] Therefore, an HIV-negative woman whose sexual partner/spouse has HIV infection may benefit from continuing PrEP use throughout her pregnancy and breastfeeding to protect herself and her infant[a]

Potential Risks of PrEP use

In PrEP trials, follow-up with persons taking medication has been conducted for an average of 1-4 years. Although no serious health risks were associated with PrEP use by HIV-uninfected adults, the long-term safety of PrEP has not yet been determined.

In PrEP trials women were taken off medication as soon as pregnancy was detected. During these trials, no health problems have been associated with PrEP use by women in early pregnancy or for their offspring. However, the long-term safety of PrEP taken by HIV-uninfected women after fetal (during pregnancy) or infant (during breastfeeding) exposure is not yet determined.

No adverse effects have been found among infants exposed to TDF/FTC when the medications were taken as part of a treatment regimen for HIV-infected women during pregnancy[21-23] or during breastfeeding (for which data suggest limited drug exposure [24-27]).

If you prescribe PrEP to a woman while pregnant, you are encouraged to prospectively and anonymously submit information about the pregnancy to the Antiretroviral Use in Pregnancy Registry (http://www.apregistry.com/).

[a] Although the DHHS Perinatal HIV Guidelines state that "pregnancy and breastfeeding are not contraindications for PrEP"[9], the FDA-approved package insert[6] says, "If an uninfected individual becomes pregnant while taking TRUVADA for a PrEP indication, careful consideration should be given to whether use of TRUVADA should be continued, taking into account the potential increased risk of HIV-1 infection during pregnancy" and "mothers should be instructed not to breastfeed if they are receiving TRUVADA, whether they are taking TRUVADA for treatment or to reduce the risk of acquiring HIV-1.". Therefore both are currently off-label uses of Truvada.

References

1. Grohskopf LA, Chillag KL, Gvetadze R, et al. Randomized trial of clinical safety of daily oral tenofovir disoproxil fumarate among HIV-uninfected men who have sex with men in the United States. *J Acquir Immune Defic Syndr*. 2013;64(1):79-86.

2. 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.

3. 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.

4. 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.

5. Food and Drug Administration. Truvada approved to reduce the risk of sexually transmitted HIV in people who are not infected with the virus. 2012; http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm311821.htm . Accessed February 6, 2017.

6. Gilead Sciences. Truvada Package Insert. 2017. http://gilead.com/~/media/files/pdfs/medicines/hiv/truvada/truvada_pi.pdf. Accessed July 26, 2017

7. 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.

8. Centers for Disease C, Prevention. Interim guidance for clinicians considering the use of preexposure prophylaxis for the prevention of HIV infection in heterosexually active adults. *MMWR. Morbidity and Mortality Weekly Report.* 2012;61(31):586-589.

9. Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission. Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States. 2017. http://aidsinfo.nih.gov/contentfiles/lvguidelines/PerinatalGL.pdf. Accessed November 1, 2017.

10. Brooks JT, Kawwass JF, Smith DK, et al. Effects of antiretroviral therapy to prevent HIV transmission to women in couples attempting conception when the man has HIV infection — United States, 2017. *MMWR Morb Mort Wkly Rep.* 2017;66:859-860.

11. Lampe MA, Smith DK, Anderson GJE, Edwards AE, Nesheim SR. Achieving safe conception in HIV-discordant couples: the potential role of oral preexposure prophylaxis (PrEP) in the United States. *Am J Obstet Gynecol.* 2011;204(6).

12. Matthews LT, Smit JA, Cu-Uvin S, Cohan D. Antiretrovirals and safer conception for HIV-serodiscordant couples. *Curr Op HIV/AIDS.* 2012;7(6):569-578.

13. Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med.* 2011;365(6):493-505.

14. Crepaz N, Tang T, Marks G, Hall H. Viral suppression patterns among persons in the United States with diagnosed HIV infection in 2014. *Ann Intern Med*. 2017;167(6):446-447.

15. Vernazza PL, Graf I, Sonnenberg-Schwan U, et al. Preexposure prophylaxis and timed intercourse for HIV-discordant couples willing to conceive a child. *AIDS.* 2011;25(16):2005-2008.

16. Mmeje O, Cohen CR, Cohan D. Evaluating safer conception options for HIV-serodiscordant couples (HIV-infected female/HIV-uninfected male): a closer look at vaginal insemination. *Infect Dis Obstet Gynecol.* 2012;2012.

17. Kawwass JF, Smith DK, Kissin DM, et al. Strategies for preventing HIV infection among HIV-uninfected women attempting conception with HIV-infected men—United States. *MMWR. Morbidity and Mortality Weekly Report*. 2017;66: 554–557.

18. Semprini AE, Macaluso M, Hollander L, et al. Safe conception for HIV-discordant couples: insemination with processed semen from the HIV-infected partner. *Am J Obstet Gynecol.* 2013;208(5):402.e401-402.e409.

19. Mugo NR, Heffron R, Donnell D, et al. Increased risk of HIV-1 transmission in pregnancy: a prospective study among African HIV-1-serodiscordant couples. *AIDS.* 2011;25(15):1887-1895.

20. Johnson LF, Stinson K, Newell M-L, et al. The contribution of maternal HIV seroconversion during late pregnancy and breastfeeding to mother-to-child transmission of HIV. *J Acquir Immune Defic Syndr (1999).* 2012;59(4):417.

21. Foster C, Lyall H, Olmscheid B, et al. Tenofovir disoproxil fumarate in pregnancy and prevention of mother-to-child transmission of HIV-1: is it time to move on from zidovudine? *HIV Med.* 2009;10(7):397-406.

22. Gibb DM, Kizito H, Russell EC, et al. Pregnancy and infant outcomes among HIV-infected women taking long-term ART with and without tenofovir in the DART trial. *PloS Med.* 2012;9(5):e1001217.

23. Nachega JB, Uthman OA, Mofenson LM, et al. Safety of tenofovir disoproxil fumarate-based antiretroviral therapy regimens in pregnancy for HIV-infected women and their infants: a systematic review and meta-analysis. *J Acquir Immune Defic Syndr*. 2017;76(1):1-12.

24. The Antiretroviral Pregnancy Registry. Interim Report: 1 January 1989 through 31 January 2017. 2017; http://www.apregistry.com/forms/interim_report.pdf. Accessed July 26, 2017.

25. Benaboud S, Pruvost A, Coffie PA, et al. Concentrations of tenofovir and emtricitabine in breast milk of HIV-1-infected women in Abidjan, Cote d'Ivoire, in the ANRS 12109 TEmAA Study, Step 2. *Antimicrobial Agents and Chemotherapy.* 2011;55(3):1315-1317.

26. Mirochnick M, Best BM, Clarke DF. Antiretroviral pharmacology: special issues regarding pregnant women and neonates. *Clinics in Perinatology.* 2010;37(4):907-927.

27. Mugwanya KK, Hendrix CW, Mugo NR, et al. Pre-exposure prophylaxis use by breastfeeding HIV-uninfected women: a prospective short-term study of antiretroviral excretion in breast milk and infant absorption. *PLoS Med.* 2016;13(9):e1002132.

Section 6 MSM Risk Index

Epidemiologic studies have identified a wide range or personal, relationship, partner, social, cultural, network, and community factors that may be associated with the presence of HIV infection. However, to provide PrEP (or other intensive HIV prevention services), it is necessary to briefly and systematically screen for key information about those factors that are predictive of very high risk of acquiring HIV infection.

This section contains a tool that clinicians may use to quickly and systematically determine which MSM are at especially high risk of acquiring HIV infection, and for whom PrEP may be indicated.

	MSM Risk Index [28]		
1	How old are you today?	If <18 years, score 0 If 18-28 years, score 8 If 29-40 years, score 5 If 41-48 years, score 2 If 49 years or more, score 0	_____
2	In the last 6 months, how many men have you had sex with?	If >10 male partners, score 7 If 6-10 male partners, score 4 If 0-5 male partners, score 0	_____
3	In the last 6 months, how many times did you have receptive anal sex (you were the bottom) with a man when he did not use a condom?	If 1 or more times, score 10 If 0 times, score 0	_____
4	In the last 6 months, how many of your male sex partners were HIV-positive?	If >1 positive partner, score 8 If 1 positive partner, score 4 If <1 positive partner, score 0	_____
5	In the last 6 months, how many times did you have insertive anal sex (you were the top) with a man who was HIV- positive when you did not use a condom?	If 5 or more times, score 6 If 0-4 times, score 0	_____
6	In the last 6 months, have you used methamphetamines such as crystal or speed?	If yes, score 6 If no, score 0	_____
		Add down entries in right column to calculate total score	_____ TOTAL SCORE*

* If score is 10 or greater, evaluate for intensive HIV prevention services including PrEP.
If score is below 10, provide indicated standard HIV prevention services.

Section 7 PWID (IDU) Risk Index

Epidemiologic studies have identified a wide range or personal, relationship, partner, social, cultural, network, and community factors that may be associated with the presence of HIV infection. However, to provide PrEP (or other intensive HIV prevention services), it is necessary to briefly and systematically screen for key information about those factors that are predictive of very high risk of acquiring HIV infection.

This section contains a tool that clinicians can use to quickly and systematically determine which persons who inject drugs (PWID) (also called injection drug users [IDU]) are at especially high risk for acquiring HIV infection, and for whom PrEP may be indicated.

PWID (IDU) Risk Index [29]				
1	How old are you today (in years)?	If <30 years, score 38 If 30- 39 years, score 24 If 40-49 years, score 7 If ≥50 years, score 0		_____
2	In the last 6 months, were you in a methadone maintenance program?	If yes, score 0 If no, score 31		_____
3	In the last 6 months, how often did you inject heroin?	If 1 or more times, If 0 times,	Injection sub-score 1 Injection sub-score 0	_____
	In the last 6 months, how often did you inject cocaine?	If 1 or more times, If 0 times,	Injection sub-score 1 Injection sub-score 0	_____
	In the last 6 months, how often did you share a cooker?	If 1 or more times, If 0 times,	Injection sub-score 1 Injection sub-score 0	_____
	In the last 6 months, how often did you share needles?	If 1 or more times, If 0 times,	Injection sub-score 1 Injection sub-score 0	_____
	In the last 6 months, how often did you visit a shooting gallery?	If 1 or more times, If 0 times,	Injection sub-score 1 Injection sub-score 0	_____
Add the five injection subscores to obtain a Composite Injection Subscore		If sum of five injection subscores is; then Composite Injection Score is: 0 0 1 7 2 21 3 24 4 24 5 31		_____
Add the scores for age and methadone use to the Composite Injection Subscore to yield a Total Score				_____ Total Score*

* If the total score is 46 or greater, evaluate for PrEP or other intensive HIV prevention services for PWID. If score is 45 or less, provide indicated standard HIV prevention services for PWID. To identify active PWID in a clinician's practice, we recommend asking all their patients a routine question: "Have you ever injected drugs that were not prescribed for you by a physician?" If yes, ask, "When was the last time you injected any drugs?" Only complete PWID risk index if they have injected any nonprescription drug during the past 6 months.

Section 8 Management of Patients Who Acquire HIV While on PrEP

Patients who are being prescribed PrEP might acquire HIV infection for several reasons. When HIV infection is detected at the first follow-up visit after PrEP initiation, it can indicate that the patient had undetected acute infection when PrEP was initiated. When infection is detected at later follow-up visits, as it most commonly occurs, it might be because patients have stopped taking PrEP, have been taking it infrequently, or have been stopping and restarting it without retesting for HIV infection before restarting. Rarely, despite high adherence to continuous daily dosing, patients taking PrEP have acquired HIV infection. This can occur because of exposure to a drug-resistant viral strain[30] or simply because, even with daily use, PrEP protection is high but not 100%[31].

In all cases, when an HIV test during a follow-up visit indicates possible infection in a PrEP patient, the following steps should be taken:

- Counsel the patient about their HIV status and the resulting management plan:
    - If a single rapid antibody blood test was positive, explain the need to confirm presumptive HIV-positive status with laboratory testing.
    - If a rapid 4th generation (antigen/antibody) blood test was positive, explain high likelihood of HIV infection that will need to be confirmed with additional laboratory testing.
    - If a positive HIV test was based on laboratory testing with confirmatory results already known, explain certainty of HIV diagnosis.
    - Ask about signs and symptoms of acute infection since last clinic visit as well as PrEP medication adherence history.
- Conduct confirmatory HIV testing (if not completed already) and supplemental tests, if indicated:
    - If one or more rapid tests were positive, draw blood for confirmatory laboratory-based HIV testing with adequate blood for reflex HIV viral load testing if confirmed to be HIV infected.
    - If laboratory-based testing was positive, draw blood for HIV viral load, CD4 cell count, and HIV resistance testing.
    - For persons with confirmed HIV infection, conduct the following supplemental testing indicated for initiation of HIV treatment, including but not necessarily limited to the following[32]:
        - Chemistry screen, ALT, AST, bilirubin, CBC with differential, urinalysis, and pregnancy test (if female).
        - Fasting lipid profile, glucose, and hemoglobin A1c are also indicated, on the day that seroconversion is detected, if possible.
- Convert the PrEP regimen to an HIV treatment regimen recommended by the DHHS Panel on Antiretroviral Guidelines for Adults and Adolescents[32].
    - It is not necessary to stop antiretrovirals entirely while waiting for additional laboratory test results. In the most likely event that the patient has HIV infection, immediate initiation of HIV treatment is indicated. The following regimens are recommended as of July 14, 2016 but the treatment guidelines should be consulted for updates[32]:
    - Continue the prescription of Truvada (TDF 300 mg/FTC 200 mg) once daily pending results of resistance tests
    - Add either:

- Dolutegravir (Tivicay) 50 mg once daily

  OR

- Darunavir (Prezista) 800 mg with Ritonavir (Norvir) 100 mg once daily.

In cases where a viral strain with significant resistance to tenofovir is later identified, the regimen can then be optimized. In cases where HIV infection is not confirmed, return to the PrEP regimen can be accomplished by dropping the additional treatment medication.

- Provide client education about time to viral load suppression:
  - Reinforce the importance of medication adherence for the patient's long-term health.
  - Discuss the importance of condom use to protect sexual partners and provide condoms.
  - Offer HIV testing for sex and drug injection partners and assistance with disclosure, if desired.
  - Ask if the patient had condomless sex or shared injection equipment during the past 72 hours, and if yes, offer nPEP for exposed partners.

- Consult with and transfer care to an experienced HIV care provider, if necessary.
  - Clinicians can call the National Clinical Consultation Center toll-free at (800) 933-3413.

- Discuss or complete insurance paperwork necessary for coverage of treatment medication.
  - Patients who are receiving medication through PrEP-specific medication assistance programs will need to switch to an HIV treatment assistance program.
  - Public or private insurance plans will generally not require additional paperwork but prior authorizations for PrEP may raise questions when switching to a prescription for a treatment regimen.

- Schedule follow-up visits (including social services, if required).

- Complete an HIV case report for the health department (completion of fields related to PrEP use at the time of seroconversion are highlighted in red below).

HIV Antiretroviral Use History (record all dates as mm/dd/yyyy)

Main source of antiretroviral (ARV) use information (select one)
_ Patient Interview _ Medical Record Review _ Provider Report _ NHM&E _ Other

Date patient reported information __ __ / __ __ / __ __ __ __

Ever taken any ARVs? _ Yes _ No _ Unknown

If yes, reason for ARV use (select all that apply)

_ HIV Tx	ARV medications		Date began __ __ / __ __ / __ __ __ __	Date of last use __ __ / __ __ / __ __ __ __
_ PrEP	ARV medications	Truvada	Date began __ __ / __ __ / __ __ __ __	Date of last use __ __ / __ __ / __ __ __ __
_ PEP	ARV medications		Date began __ __ / __ __ / __ __ __ __	Date of last use __ __ / __ __ / __ __ __ __
_ PMTCT	ARV medications		Date began __ __ / __ __ / __ __ __ __	Date of last use __ __ / __ __ / __ __ __ __
_ HBV Tx	ARV medications		Date began __ __ / __ __ / __ __ __ __	Date of last use __ __ / __ __ / __ __ __ __
_ Other	ARV medications		Date began __ __ / __ __ / __ __ __ __	Date of last use __ __ / __ __ / __ __ __ __

HIV Testing History (record all dates as mm/dd/yyyy)

Main source of testing history information (select one)
_ Patient Interview _ Medical Record Review _ Provider Report _ NHM&E _ Other

Date patient reported information __ __ / __ __ / __ __ __ __

Ever had previous positive HIV test? _ Yes _ No _ Unknown — Date of first positive HIV test __ __ / __ __ / __ __ __ __

Ever had a negative HIV test? _ Yes _ No _ Unknown — Date of last negative HIV test *(If date is from a lab test with test type, enter in Lab Data section)* __ __ / __ __ / __ __ __ __

Number of negative HIV tests within 24 months before first positive test (# _____) _ Unknown

Section 9 Transition of Patients From Nonoccupational Postexposure Prophylaxis (nPEP) to Preexposure Prophylaxis (PrEP)

Two types of patients may be considered candidates for PrEP use after a course of nonoccupational postexposure prophylaxis (nPEP):

- Patients who request PrEP and also have had a possible sexual or injection drug-related HIV exposure in the prior 72 hours (i.e., are within the recommended window to start nPEP)
- Patients who request repeated courses of nPEP, particularly over a relatively recent period (e.g., more than twice during the past 6 months)

If evaluation demonstrates nPEP is clinically indicated and that the patient is also eligible for PrEP (e.g., behavioral risk for repeated HIV exposure, recent bacterial STI diagnosis in a sexually active person), then these patients should both be provided a 28-day course of nPEP and be evaluated for transition to PrEP at the conclusion of their nPEP course.

TRANSITIONING IMMEDIATELY FROM NPEP TO PREP

Transitioning from nPEP to PrEP without interruption at the completion of the 28-day nPEP course has the advantages of (1) maintaining satisfactory antiretroviral drug levels for PrEP (if nPEP adherence has been good); and (2) maximizing continuous prevention measures through continuity of nPEP to PrEP care. Essential steps include:

- At conclusion of 28 days of nPEP:
    - Repeat a rapid HIV test (ideally with a fourth-generation antigen/antibody assay) and assess for signs and symptoms of acute HIV infection.
    - If the rapid HIV test is positive or suspicion exists of possible acute HIV infection, draw blood for confirmatory testing and continue a 3-drug nPEP regimen pending confirmation of HIV status.
    - If HIV infection is confirmed, see Section 8 of Clinical Providers' Supplement for indicated next steps.
    - If the rapid HIV test is negative and no signs or symptoms of acute infection exist:
        - Stop the third medication in nPEP regimen and continue TDF/FTC daily as PrEP.
        - Complete any PrEP baseline laboratory testing not already performed as part of nPEP testing.
        - Provide medication adherence and risk-reduction support counseling.

- Complete any insurance/medication assistance paperwork required to cover PrEP medications (might be different than nPEP medications).
- Schedule follow-up visits for HIV, STI, and other laboratory testing as well as medication refills on the basis of standard PrEP clinical practice guidelines recommendations.

INITIATING PREP AT A LATER TIME

Deferring initiation of PrEP use can increase the period of risk for HIV acquisition because patients are left without the benefit of protective antiretroviral use. However, for some patients concluding a course of nPEP, additional time is needed to (1) make a decision about PrEP use; (2) perform additional clinical assessment and engage the patient in shared decision making in special medical circumstances, such as renal or liver impairment, pregnancy or breastfeeding; or (3) arrange and ensure coverage of medication costs, availability of continuity of PrEP care, or other logistic factors. Essential steps with this approach include:

- Reinforce the critical nature of safer sexual or injection drug use strategies while pending PrEP initiation
- Obtain baseline testing per PrEP guidelines
- Initiate PrEP, when possible

Consultation

Consultation with local or regional experts in nPEP and PrEP, or with the toll-free national PrEPline at 855-448-7737 or PEPline at 888-448-4911, can be sought for clinical scenarios requiring additional information or management options.

Section 10 Supplemental Counseling Information – Medication Adherence

MEDICATION EDUCATION AND ADHERENCE SUPPORT

Understanding what patients know about PrEP and why they are considering taking it can reveal important information about potential adherence facilitators or barriers. You may wish to begin discussion through a conversation (e.g., "Let's talk. Tell me what you know about PrEP" or "Why do you want to take PrEP?") that can help clarify whether the patient understands the risks and benefits of PrEP given their current sexual behavior and protection strategies, and how their reason(s) for taking PrEP may affect medication adherence.

Adherence to prophylactic regimens is strongly associated with patient understanding of drug information. Patients beginning a PrEP regimen need a very clear understanding of how to take their medications (i.e., when it is to be administered, how many pills to take at each dose) and what to do if they experience problems (e.g., how long outside the dosing window is a dose considered "missed", what to do if they miss a dose). Side effects are often a cause of non-adherence, so a plan for addressing them should be made. It is recommended that you and the patient develop a plan for addressing side effects that the patient would consider intolerable. The plan may include over-the-counter medications that can mitigate symptoms and should stress the need to use condoms consistently if the patient stops taking PrEP medication.

You should also discuss the need for the patient to be tested for HIV every 3 months. Although patients may feel anxious about such frequent testing, it is important that patients understand that frequent testing is needed to prevent drug resistance if they become infected while taking PrEP medication. Be prepared to answer other questions, such as,: "What if people see the medications and think I am HIV-positive?" "Do I need to tell my partner?" "Do I need to take the medication regularly when I am not having sex?"; "Will it help to take extra doses?" "How long can I take the medication?". When you begin a discussion around adherence, emphasize the normalcy of missing occasional doses and the importance of a plan to try to minimize missed doses (see Box 6.1 for an example of how to introduce this issue).

Box 6.1: Adherence Discussion

You are going to have to take the pill once a day, every day. Although this seems easy, we know that people forget to take their medicines, especially when they are not sick. It will be easier to take your medicine if you think through now some plans about how you'll do it. First, let's briefly discuss your experiences other times you might have taken medicine.

- *When you've taken medicines before, how did you remember to take them?
- Please tell me about any problems you had taking your pill.
- *What was most helpful for remembering to take them?

An adherence plan should include the following: (1) tailoring the dosing time to correspond with the patient's regularly scheduled activities so that medication taking becomes integrated into the patient's daily routine, (2) using reminders or technical devices (e.g., beepers, alarms) to minimize forgetfulness, (3) considering organizational needs and tools (e.g., calendars, strategies for weekends away from home) to address changes in routine and schedule, and (4) reviewing disclosure issues to identify those who can support the patient's intentions to adhere or barriers to adherence due to lack of disclosure/privacy at home. (See Box 6.2 for sample questions.)

Box 6.2: Developing an adherence plan

OK, now let's come up with a plan for taking your medicine.

1. Scheduling

What is your schedule like during a typical week day?
At what point in the day do you think it would be easiest to take the pill? That is, is there a time when you are almost always at home, and not in too much of a rush?
How does your schedule differ on weekends?

2. Reminder devices

How will you remember to take the pill each day?
One way to remember is to take the pill at the same time that you are doing another daily task, such as brushing your teeth or eating breakfast. Which of your daily tasks might be used for this purpose? Try to pick something that happens every day. Sometimes we might pick something that is not always done on the weekends or during other days, and then we are more likely to forget. (For example, … **One potential example follows**: sometimes I don't shave on Saturdays, but I always brush my teeth, so linking taking the medicine to brushing my teeth might be better than linking it to shaving.) It also helps to store the pills near the place where you perform this daily task.
Some people use a reminder device to help them remember. Do you have any reminder devices that you have used in the past? For example, watches, beepers, or cell phones.

3. Organizational skills

Where will you store the bottle of pills?
When you travel or spend the night outside of your home, what will you do about taking the pill?

4. Social support & disclosure

Who in your household will know the reason that you are taking the pills? Are they supportive of you taking them? Are there individuals who might make assumptions about your serostatus because you have these medicines?

You may wish to explore other potential barriers that emerged in initial conversations (e.g., beliefs and attitudes), including factors (e.g., as substance use, depression or unstable housing) known to negatively affect medication adherence, such. To adhere to PrEP medication well, some patients may need access to mental health or social services.

MONITORING PREP PATIENTS: ASSESSING SIDE EFFECTS AND ADHERENCE

Assess medication adherence as well as adherence to HIV testing at every visit. Self-reported adherence is typically an overestimate of true adherence, but patients may over report their adherence when they fear that a more accurate report would results in a negative judgment from their clinician. When asking patients about their adherence, do your best to adopt a non-judgmental attitude, giving the patient permission to share adherence difficulties without worrying that you will reproach them. Asking patients to help you understand how they are doing with their medications will provide more information and thus allow for a better diagnostic picture of a patient's needs than will a more prescriptive approach.

Begin follow-up visits by asking the patient how well they have been doing with taking all of their medicines as scheduled. Accept more general responses (e.g., "so so", "pretty good", "excellent", "perfect") before asking for specific information about the frequency and the context of missed doses. Provide reinforcement for patients who report that they are doing well: ask questions such as "What are you doing to keep this going so well?" or "That's great. Can you see anything getting in the way of this?" These exchanges can help solidify the factors that are supporting your patients' adherence while helping them prepare for any barriers that may arise in the future.

When talking with patients who are not reporting perfect adherence, ask as to how many doses they have missed during a specific period. Assessing a longer period (e.g., 30 days, 7 days) is preferred to shorter periods (e.g., 3 days), not only because adherence can vary with changes in schedule (e.g., weekends, holidays) that may not have occurred during the shorter assessment period, but because many patients increase medication-taking just before medical appointments, a phenomenon supported by blood level assessments in the iPrEx trial.[2] When asking about many doses were missed (e.g., "In the last 30 days, how many times have you missed your PrEP medication?"), also (1) ask whether this was typical since their last clinic visit in order to gain a sense of adherence patterns, (2) ask for specific information about when they most recently missed dose(s), and (4) determine the circumstances during which those missed doses occurred (e.g., "Where were you?" "Who were you with?" "What happened just before you were supposed to take your medicine?"). Asking what happened on the day the dose was missed, and getting the patient's perspective on what generally gets in the way of taking medications regularly, will facilitate a conversation that will help to identify the patient's specific adherence barriers as well as the type of adherence support the patient needs.

On the basis of this conversation, develop a plan to address adherence barriers. Questions such as "What do you think you can do differently?" "What things make it easier to take your medications?" "What things need to happen for you to take your medications regularly?" or "What might you try [to not forget your weekend doses]?" bring the patient into the planning process and thus facilitate identification of the strategies most likely to be implemented. It's important for you to be familiar with a range of adherence strategies that can be shared with patients who require help with this task.

Finally, assess whether the patient is experiencing any side effects of medication, the severity of the side effects, and their role as an adherence barrier determined. Currently, most of what is

known about antiretroviral therapy (ART) side effects is derived from patients with HIV. Healthy people may be more concerned about side effects than HIV patients. Try to determine whether clinical symptoms attributed to PrEP medication could possibly be due to other disorders (e.g., depression) or natural processes (e.g., aging). If necessary, include medications to treat side effects in the adherence plan.

Section 11 Supplemental Counseling Information – HIV Risk Reduction

Determining whether the patient is a good candidate for PrEP is not strictly objective, and should be based on an ongoing discussion between you and your patient. Risk screening can be conducted using various approaches: face-to-face interviews, written forms, or computer-based tools. Written forms and computer-based tools are effective and can be conducted with fewer staff resources[33]. However, self-administered written forms are not recommended for persons with low literacy.

Using risk screening information and the HIV test results, provide your patients with services that are appropriate for their level of risk and are tailored to their prevention needs. Patients who report no or few risk factors, may have minimal prevention needs. In the absence of other information, these patients do not need PrEP. For patients for whom PrEP is appropriate, provide risk-reduction counseling and support services before, during, and after PrEP you prescribe PrEP.

Sexual Risk Reduction Counseling

Address the sexual health of your patients, including risk behaviors that increase the likelihood of acquiring HIV or other sexually transmitted infections. Several discussion areas are recommended even in brief discussions of sexual risk behavior. For patients who demonstrate an elevated risk of sexual HIV acquisition, provide a brief risk reduction intervention onsite or link them to a program that provides those services (see http://www.effectiveinterventions.org). For patients who are continuing to engage in high-risk sexual behaviors or who need additional prevention services (beyond a brief risk-reduction intervention), link them to a program that provides more intense interventions, such as those in the Compendium of Evidence-based HIV Prevention Interventions (see http://www.cdc.gov/hiv/topics/research/prs/evidence-based-interventions.htm) which are often provided by local health departments or community-based organizations. These patients may also be good candidates for continued use of PrEP until they are consistently practicing effective behavioral risk reduction.

- Counseling patients who test HIV-negative. Guidelines have emphasized the importance of risk-reduction counseling for persons determined to be at substantial risk of sexual HIV acquisition[34]. It is recommended that you select the most appropriate brief sexual risk-reduction intervention that can address the immediate prevention needs of HIV-negative patients at substantial risk for acquiring HIV infection. One counseling approach designed for STD clinic providers, the RESPECT model[35], can be used. The model consists of two brief, 20-minute, interactive, patient-focused counseling sessions that are conducted during HIV testing, and have been found to significantly reduce sexual risk behaviors and prevent new STDs among HIV-negative patients (although not HIV incidence). Besides RESPECT, there are now several other effective brief sexual risk-reduction intervention models that should be considered when providing HIV-negative

patients appropriate prevention counseling. Although no brief counseling models have yet proven effective for patients taking PrEP, some of the models developed for persons with HIV infection, (Partnership for Health[36], and motivational interviewing[37,38)] may be appropriate for adaptation to counseling patients who are taking PrEP.

Intensive sexual risk reduction interventions may be appropriate for some patients, who should be referred to appropriate providers. In general, HIV risk-reduction interventions have been shown through numerous systematic reviews, to be efficacious in reducing HIV sexual risk behaviors, promoting protective behaviors, and reducing the incidence of new sexually transmitted infections among high-risk populations from various demographic, racial/ethnic, or behavioral risk groups[39,40].

- Counseling patients who test HIV-positive. Provide emotional support and counseling to patients who receive preliminary or confirmed positive HIV test results to help them understand the test result, the benefits of initiating and remaining in HIV medical care, and the importance of reducing their HIV-related sexual and/or injection risk behaviors to help protect their health and the health of their partners. Link all HIV-positive patients to HIV medical care, prevention services that routinely offer risk screening and ongoing risk-reduction interventions, and other health services as needed.

PrEP Follow-up Visits

Provide brief behavioral HIV risk assessment and supportive counseling at each follow-up visit while the patient is taking PrEP medication. For important components of these sessions, see Box 7.1. At least annually discuss with the patient whether discontinuation of PrEP is warranted. If the decision is made to discontinue PrEP, a plan for periodic reassessment should be made and any indicated referrals to community programs or other support services should be arranged.

Box 7.1: Elements of brief HIV risk-reduction counseling in clinical settings

- Create and maintain a trusting and confidential environment for discussion of sexual or substance abuse behaviors.
- Build an ongoing dialogue with the patient regarding their risk behavior (and document presence or absence of risk behaviors in the confidential medical record).
- Reinforce the fact that PrEP is not always effective in preventing HIV infection particularly if used inconsistently, but that consistent use of PrEP together with other prevention methods (consistent condom use, discontinuing drug injection or never sharing injection equipment) confers very high levels of protection.

Section 12 PrEP-Related ICD, CPT and LOINC codes

ICD-10 codes	Description
Z20	Contact with and (suspected) exposure to communicable diseases
Z20.2	Contact with and (suspected) exposure to infections with a predominantly sexual mode of transmission
Z20.5	Contact with and (suspected) exposure to viral hepatitis
Z20.6	Contact with and (suspected) exposure to human immunodeficiency virus (HIV)
Z20.828	Contact with and (suspected) exposure to other viral communicable diseases
Z77.21	Contact with and (suspected) exposure to potentially hazardous body fluids
W46	Contact with hypodermic needle: "the appropriate 7th character is to be added to each code from category W46" A- initial encounter, D- subsequent encounter, S-sequela
W46.0	Contact with hypodermic needle (hypodermic needle stick NOS)
W46.1	Contact with contaminated hypodermic needle
Z20.8	Contact with and (suspected) exposure to other communicable diseases
Z20.81	Contact with and (suspected) exposure to other bacterial communicable diseases
Z79	Long term (current) drug therapy. Includes long term (current) drug use for prophylactic purposes
Z51.81	Therapeutic drug level monitoring
Z51.89	Encounter for other specified aftercare
Z79.899	Other long term (current) drug therapy
B20	Human immunodeficiency virus (HIV) disease. Includes: AIDS; AIDS-related complex (ARC); HIV infection, symptomatic
Z21	Asymptomatic human immunodeficiency virus (HIV) infection status
B16.9	Acute hepatitis B without delta-agent and without hepatic coma
B16.1	Acute hepatitis B with delta-agent without hepatic coma
B17.0	Acute delta-(super) infection of hepatitis B carrier
Z22.51	Carrier of viral hepatitis B
B18.0	Chronic viral hepatitis B with delta-agent
B18.1	Chronic viral hepatitis B without delta-agent
B16.0	Acute hepatitis B with delta-agent with hepatic coma
B16.2	Acute hepatitis B without delta-agent with hepatic coma
Z00.0	Encounter for general adult medical examination
Z01.812	Encounter for preprocedural laboratory examination (blood and urine tests prior to treatment or procedure)
Z11.3	Encounter for screening for infections with a predominantly sexual mode of transmission
Z11.4	Encounter for screening for human immunodeficiency virus (HIV)
Z11.59	Encounter for screening for other viral diseases
Z11.8	Encounter for screening for other infectious and parasitic diseases
Z13.89	Encounter for screening for other disorder (encounter for screening for genitourinary disorders)
Z13.9	Encounter for screening unspecified

ICD-10 codes	Description
Z32.0	Encounter for pregnancy test
Z70.0	Counseling related to sexual attitude
Z70.1	Counseling related to patient's sexual behavior and orientation
Z70.3	Counseling related to sexual behavior and orientation of third party (child, partner, spouse)
Z72.5	High risk sexual behavior
Z72.51	High risk heterosexual behavior
Z72.52	High risk homosexual behavior
Z72.53	High risk bisexual behavior

Sources: http://www.cdc.gov/nchs/icd/icd9cm.htm and http://www.cdc.gov/nchs/icd/icd10cm.htm

CPT Codes	Description
4276F	Potent antiretroviral therapy prescribed (HIV)
4270F	Patient receiving potent antiretroviral therapy for ≥6 months (HIV)
4290F	Patient screened for injection drug use (HIV)
4293F	Patient screened for high-risk sexual behavior (HIV)
86701	HIV antibody test performed (HIV-1 only)
86703	HIV antibody test performed (HIV-1 and HIV-2)
87389	HIV-1 EIA antibody with HIV1&2 antigens
87390	HIV-1 detection by immunoassay (IAAD EIA HIV-1)
87534	HIV-1 detection by nucleic acid, direct probe
87535	HIV-1 detection by nucleic acid, amplified probe
87536	HIV-1 quantitation
87900	Infectious agent drug susceptibility phenotype prediction using regularly updated genotypic bioinformatics
87901	HIV-1 genotype by nucleic acid (RNA or DNA)
80074	Hepatitis panel
86704	HBcAb
86705	HBcAb, IgM antibody
87340	HBsAg
87517	Hepatitis B quantitation

Source: http://online.statref.com/titleinfo/fxid-24.html

LOINC Codes				
Order Test Number	Order Test Name	Result Test Number	Result Test Name	Result LOINC Code
0020025	Creatinine, Serum or Plasma	0020025	Creatinine, Serum or Plasma	2160-0
0020144	Renal Function Panel	0020025	Creatinine, Serum or Plasma	2160-0
0020399	Basic Metabolic Panel	0020025	Creatinine, Serum or Plasma	2160-0
0020408	Comprehensive Metabolic Panel	0020025	Creatinine, Serum or Plasma	2160-0
0085024	CTT Chemistry 20 Profile	0020025	Creatinine, Serum or Plasma	2160-0
0085025	CTT Chemistry 27 Profile	0020025	Creatinine, Serum or Plasma	2160-0
0020089	Hepatitis B Surface Ag w/ Reflex to Conf	0020089	Hepatitis B Surface Antigen	5196-1
0020090	Hepatitis B Virus Surface Antibody	0020090	Hepatitis B Surface Antibody	5193-8
0020091	Hepatitis B Virus Core Antibodies, Total	0020091	Hepatitis B Core Antibodies, Total	13952-7
0020092	Hepatitis B Virus Core Antibody, IgM	0020092	Hepatitis B Core Antibody, IgM	24113-3
0020128	Hepatitis B Virus Surface Ag, Confirm	0020128	Hepatitis B Surface Antigen Confirmation	7905-3
0020454	Hepatitis Panel, Chronic HBV	0020089	Hepatitis B Surface Antigen	5196-1
0020454	Hepatitis Panel, Chronic HBV	0020522	Chronic Hepatitis B Panel Interpretation	45159-1
0020454	Hepatitis Panel, Chronic HBV	0020090	Hepatitis B Surface Antibody	5193-8
0020457	Hepatitis Panel, Acute	0020092	Hepatitis B Core Antibody, IgM	24113-3
0020457	Hepatitis Panel, Acute	0020179	Acute Hepatitis Panel Interpretation	13169-8
0020457	Hepatitis Panel, Acute	0020089	Hepatitis B Surface Antigen	5196-1
0056025	Hepatitis B Virus DNA Quant RT- PCR	0051820	HBV DNA Interpretation	29610-3
0056025	Hepatitis B Virus DNA Quant RT- PCR	0056026	HBV DNA (log IU/mL)	48398-2
0056025	Hepatitis B Virus DNA Quant RT- PCR	2002322	HBV DNA (IU/mL)	42595-9
2001567	Hepatitis B Virus Genotype	2001569	Hepatitis B Genotype	32366-7
2001567	Hepatitis B Virus Genotype	2001569	Hepatitis B Genotype	32366-7
2006526	HIV-1,2 Combo Ag/Ab EIA w/Reflex	2006611	HIV-1,2 Combo Antigen/Antibody	56888-1
2007980	HIV-1,2 Combo Ag/Ab EIA w/Reflx	2007986	HIV Interpretation	69668-2
2007980	HIV-1,2 Combo Ag/Ab EIA w/Reflx	2007982	HIV-1/HIV-2 Antibody Differentiation	42768-2
2007980	HIV-1,2 Combo Ag/Ab EIA w/Reflx	2007985	_HIV-2 Antibody by Multispot	30361-0

LOINC Codes				
Order Test Number	Order Test Name	Result Test Number	Result Test Name	Result LOINC Code
2007980	HIV-1,2 Combo Ag/Ab EIA w/Reflx	2007984	_HIV-1 Antibody by Multispot	29893-5
2007980	HIV-1,2 Combo Ag/Ab EIA w/Reflx	2007981	HIV 1,2 Combo Antigen/Antibody	56888-1
0020284	HIV 1 Antibody Confirm, Western blot	0020284	HIV-1 Antibody Confirm, Western blot	5221-7
0020698	HIV-1 Ab Confirm, Western blot w/Reflex	0020284	HIV-1 Antibody Confirm, Western blot	5221-7
2005375	HIV-1 w/Reflex to HIV-1 Western blot	2005376	HIV-1 Antibody	29893-5
0051250	HIV-2 Antibody w/Reflex to Supplemental	2008282	HIV-2 Antibody, Supplemental	30361-0
0051250	HIV-2 Antibody w/Reflex to Supplemental	0051251	HIV-2 Antibody by ELISA	30361-0
0093061	HIV-1 PCR, Qualitative	0093062	HIV-1 PCR, Qualitative	44871-2
0093061	HIV-1 PCR, Qualitative	0093062	HIV-1 PCR, Qualitative	44871-2
0020466	HIV 1 RNA Quantitative by bDNA	0020464	HIV-1 RNA Quant bDNA, Log	29539-4
0020466	HIV 1 RNA Quantitative by bDNA	2002687	HIV-1 RNA Quant bDNA, Copy	23876-6
0055598	HIV-1 RNA Qnt By Real-Time PCR	0051817	HIV-1 RNA Qnt Real-Time PCR Interp	24013-5
0055598	HIV-1 RNA Qnt By Real-Time PCR	2002646	HIV-1 RNA Qnt Real-Time PCR, Copy	20447-9
0055598	HIV-1 RNA Qnt By Real-Time PCR	0020297	HIV-1 RNA Qnt Real-Time PCR, Log	29541-0
2002688	HIV-1 RNA Quant bDNA reflex to Genotype	0020464	HIV-1 RNA Quant bDNA, Log	29539-4
2002688	HIV-1 RNA Quant bDNA reflex to Genotype	2002687	HIV-1 RNA Quant bDNA, Copy	23876-6
2002689	HIV-1 RNA Quant reflex to Genotype	0051817	HIV-1 RNA Qnt Real-Time PCR Interp	24013-5
2002689	HIV-1 RNA Quant reflex to Genotype	2002646	HIV-1 RNA Qnt Real-Time PCR, Copy	20447-9
0051186	HIV 1, vircoTYPE	0055648	Vircotype Information	45182-3
0051186	HIV 1, vircoTYPE	0055648	Vircotype Information	45182-3
0055670	HIV-1 Genotyping	0051722	HIV-1 Genotyping	49659-6
0055670	HIV-1 Genotyping	2002141	EER HIV-1 Genotyping	11526-1
0055670	HIV-1 Genotyping	0051722	HIV-1 Genotyping	49659-6
0055670	HIV-1 Genotyping	2002141	EER HIV-1 Genotyping	11526-1
2004331	HIV GenoSure MG	0092073	Viral Load - RT	8251-1
2004331	HIV GenoSure MG	0092074	Viral Load Date - RT	19151-0

Source: http://loinc.org/

Section 13 Potential Practice Quality Measures[37,38]

Primary (Outcome) Measures

Quality Indicator	Eligible Population	Numerator	Denominator
HIV testing, baseline	All persons prescribed PrEP medication	Number of patients with negative HIV test result documented within 1 week prior to initial prescription of PrEP medication	Number of persons prescribed PrEP
HIV testing, interval	All persons prescribed PrEP medications	Number of PrEP patients with an HIV test result documented at least every 3 months while PrEP medication prescribed	Number of persons prescribed PrEP for >3 months continuously
PrEP medication adherence	All persons prescribed PrEP medications	Number of PrEP patients with adherence assessment noted in the medical record for any visits when prescribed PrEP medication	Number of persons prescribed PrEP medication
Seroconversion	All persons prescribed PrEP medications	Number of patients with a confirmed HIV positive test result while PrEP medications prescribed	Number of persons prescribed PrEP medication for >1 month
Seroconversion, resistant virus	All persons prescribed PrEP medication who received a genotypic resistance test within 4 weeks after an HIV positive test result	Number of persons seroconverting while taking PrEP who have resistant virus detected by genotypic test	Number of persons prescribed PrEP medication who received a genotypic resistance test within 4 weeks after a confirmed HIV positive test result

Section 14 Methods for Developing the PrEP Clinical Practice Guideline

In 2009, in recognition of the lead time needed to develop clinical guidance for the safe and effective use of PrEP should clinical trials results support it, CDC initiated a formal guidelines development process to allow for early review of the relevant literature, discussion of potential guidelines content given scenarios of potential trial results, and fostering the development of expert and stakeholder consensus. This process was designed to provide a basis for the rapid issuance of interim guidance, to be followed by Public Health Service guidelines as soon as the earliest trial findings indicated sufficient PrEP efficacy and safety to merit its implementation for HIV prevention through one or more routes of transmission.

This guidelines development process was based on a review of experience with the development of other clinical and nonclinical guidelines at CDC, including those for STD treatment and antiretroviral prevention of mother-to-child transmission following the ACTG 076 trial results.

There were five basic components to the process for developing the 2014 PrEP guidelines:

1. An **HHS Public Health Service (PHS) Working Group** to develop interagency consensus on major points of implementation policy and provide agency review of guidelines. This working group included representatives from agencies that would formally clear PHS guidelines (FDA, HRSA, NIH, HHS/OHAP) as well as agencies that may implement such guidance (IHS, VA).
2. A **CDC writing team** responsible for preparing draft guidance documents based on the recommendations of the other groups involved in the guidelines process
3. A number of **external work groups** responsible for considering specific sets of issues for the planned guidance. Each work group was composed of 5-8 members representative of the following:
    - Members of the academic community and scientists with expertise in the content area to ensure that the guideline elements are science-based
    - Health department and clinical users of the guidelines to ensure the feasibility of implementing guideline elements in local and state HIV prevention programs
    - At least one advocate or community-based organization member with personal or professional experience in the content area to serve as an ongoing bridge to community discussions and to supplement the advocate input received by other activities.
    - Geographic diversity (multiple US regions and small/medium/large jurisdictions)
    - Experience with PrEP issues when possible

    External work groups were convened to consider the following areas:
    - Clinical care guidance
    - Clinic-based counseling guidance
    - Integrating PrEP with other prevention services
    - Persons potentially exposed by injection drug use
    - MSM
    - Women
    - African American, Hispanic/Latino, and other heterosexual men
    - Adolescents

In addition to these standing work groups, technical expert panels were convened to inform guidelines for PrEP use in the following areas:

- Public health and clinical ethics
- Monitoring and evaluation framework
- Financing and reimbursement issues
- Preconception and intrapartum use of PrEP
- Public health legal and regulatory issues
- Issues relevant to benefits managers and insurers

4. A series of **stakeholder web/phone conferences** were held to receive input on questions, concerns, and preferences from a variety of perspectives including those of community-based organizations, state and local AIDS offices, professional associations, and others.
5. After the publication of the first efficacy trial results, a **face-to-face consultation** of external experts, partners, agencies, and other stakeholders was held to consider the recommendations for guidance made by the above groups and to discuss any additional ideas for inclusion in PrEP guidelines.

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The working groups and expert panels listed here were convened by teleconference before trial results were available (2009-2010) and some were reconvened after each trial results for each population group were published. As technical experts, prevention partners, and key stakeholders, they were asked to assist us to identify relevant scientific/medical literature and share thoughts on topics that would inform the

development of possible future guidelines for PrEP use in the US. They did not participate in the writing of these guidelines. No financial disclosures were sought. See Clinical Providers' Supplement section 14 for a description of the criteria use for constitution of the working groups and expert panels. Institutional associations listed for participants are those at the time of the group discussions and may have changed since.

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CDC and individual employees involved in the guideline development process are named in US government patents and patent applications related to methods for HIV prophylaxis.

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This process allowed wide input, transparency in discussing the many issues involved, time for the evolution of awareness of PrEP and ideas for its possible implementation, in addition to facilitating the development of a consensus base for the eventual guidance. At the same time, it allowed for guidelines based on expert opinion, and recommendations deemed feasible by clinical providers and policymakers.

On the basis of results from the first 4 activities listed above and the publication in late November 2010 of results from the first clinical trial to show substantial efficacy and safety[2], CDC issued interim guidance for PrEP use among men who have sex with men in January 2011.

This interim guidance was followed by a face-to-face meeting of external in May 2011. As efficacy and safety results were published, additional interim guidance documents were issued for heterosexually active adults (August 2012) and injection drug users (July 2013).

SYSTEMATIC LITERATURE REVIEW METHODS

For the 2014 guidelines, a systematic review was conducted of PrEP studies published from January 2010 through December 2013. For the 2017 guidelines, the same search strategy was run to update studies published through June 2017. Searches were conducted of MEDLINE, Embase, CINAHL, and Cochrane Library databases. The search strategy used the following criteria:

- Pre-Exposure Prophylaxis/ OR Chemoprevention/ OR (((Preexposure OR Pre-exposure) adjacent to prophylaxis) OR PrEP OR (topical adjacent to (prevention OR prophylaxis OR microbicide* OR gel OR pericoital OR precoital OR vaginal OR rectal OR anal)) OR chemoprophylaxis OR chemoprevention OR chemo-prophylaxis OR chemo-prevention OR iPrEX).mp.
- AND
- (exploded terms) Anti-HIV Agents/ OR Anti-Retroviral Agents/ OR HIV Infections/pc OR ((HIV OR human immunodeficiency virus) AND (antiretroviral* OR anti-retroviral* OR antiretrovirus* OR anti-retrovirus* OR Truvada OR tenofovir OR emtricitabine OR (TDF ADJ5 FTC)))
- AND NOT animals
- in the title, abstract, keyword heading word, subject heading fields

Retrieved citations were provided in an Endnote reference file for deduplication. Then 2 scientists independently reviewed the citations and removed those that were not published in English, did not contain data (e.g., editorials, reviews, news reports), or did not contain data about oral TDF/FTC for PrEP. The next step was to screen citations to remove those that did not contain new data about oral PrEP (data/analyses not previously published). For the 2017 update, year of publication, author, and titles were compared with the 2014 Endnote library as necessary to identify already exiting entries. During this step, abstracts or full articles were read and publications were categorized into the following groups.

- New clinical trial results
- New human observational study results
- New survey, focus group, or other behavioral study results
- New cost analysis results (e.g., program cost, cost benefit analysis)
- New modeling results (e.g., impact models)
- New laboratory human study results (e.g., drug levels, resistance)
- None of the above

The coding by the two reviewers was then compared and discrepancies were reconciled. Citations with no new data about daily oral PrEP with TDF/FTC were deleted from the updated Endnote 2017 library.

Data from the clinical trial, human observational study, and laboratory human study results were added to the evidence tables. Study findings presented in the evidence tables were each assessed for quality of the study using GRADE criteria[39] (see guidelines Appendix 1, Table 13). Then all data supporting a specific recommendation were given a summary strength of evidence rating (across all studies relevant to that recommendation) using the same system as used for the DHHS antiretroviral treatment guidelines[32] (see PrEP clinical practice guidelines Appendix 1, Table 12).

Draft Guideline Writing and Review Prior to Publication

The draft was written to address guidelines standards for review of the strength of evidence (GRADE approach[41]) as well as a format designed to promote guideline implementation (GLIA [42]), dissemination (GEM[43]), and adoption (AGREE[44,45]).

The 2014 draft clinical practice guideline and clinical providers supplement were reviewed by CDC, FDA, NIH, HRSA, and HHS, and a series of webinars were held in 2012 and 2013 to obtain additional expert opinion and public engagement on draft recommendations for PrEP use. The draft guideline and supplement were then reviewed by a panel of 6 external peer reviewers who had not been involved in their development. At each step, revisions were made in response to reviewer and public comments received.

For the 2017 update, the 2014 systematic review of published literature was updated through June 2017. Although no changes to the graded recommendations were indicated, additions to the evidence review tables were made; minor clarifying edits to the supporting text were made to enhance consistency with recently updated STD, nPEP, and perinatal guidelines sections relevant to PrEP; and updated references were added. These changes were shared with a group of 4 external peer reviewers for comment.

Plans for Updates to the Guideline

PrEP is a rapidly changing field of HIV prevention with several additional clinical trials and studies are now underway or planned. Updates to these guidelines are anticipated as studies provide new information on PrEP efficacy, HIV testing, drug levels, adherence, longer term clinical safety, and changes in HIV risk behaviors associated with PrEP medication use for HIV uninfected MSM, heterosexuals, injection drug users, pregnant women and their newborns; as well as information on the efficacy and safety of other antiretroviral medications, and other routes and schedules of medication delivery for PrEP.

When significant new data become available that may affect patient safety or graded recommendations for PrEP use, an announcement with suggested revisions to the existing guidelines will be posted on the CDC web site and the public will be given a 2-week period to submit comments. These comments will be reviewed and a determination made as to whether additional revisions are indicated. Final updated guidelines will then be posted on the CDC web site.

References

4. Grohskopf LA, Chillag KL, Gvetadze R, et al. Randomized trial of clinical safety of daily oral tenofovir disoproxil fumarate among HIV-uninfected men who have sex with men in the United States. *J Acquir Immune Defic Syndr*. 2013;64(1):79-86.

5. 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.

6. 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.

4. 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.

5. Food and Drug Administration. Truvada approved to reduce the risk of sexually transmitted HIV in people who are not infected with the virus. 2012; http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm311821.htm . Accessed February 6, 2017.

6. Gilead Sciences. Truvada Package Insert. 2017. http://gilead.com/~/media/files/pdfs/medicines/hiv/truvada/truvada_pi.pdf. Accessed July 26, 2017

7. 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.

8. Centers for Disease C, Prevention. Interim guidance for clinicians considering the use of preexposure prophylaxis for the prevention of HIV infection in heterosexually active adults. *MMWR. Morbidity and Mortality Weekly Report.* 2012;61(31):586-589.

9. Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission. Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States. 2017. http://aidsinfo.nih.gov/contentfiles/lvguidelines/PerinatalGL.pdf. Accessed November 1, 2017.

10. Brooks JT, Kawwass JF, Smith DK, et al. Effects of antiretroviral therapy to prevent HIV transmission to women in couples attempting conception when the man has HIV infection — United States, 2017. *MMWR Morb Mort Wkly Rep.* 2017;66:859-860.

11. Lampe MA, Smith DK, Anderson GJE, et al. Achieving safe conception in HIV-discordant couples: the potential role of oral preexposure prophylaxis (PrEP) in the United States. *Am J Obstet Gynecol.* 2011;204(6).

12. Matthews LT, Smit JA, Cu-Uvin S, Cohan D. Antiretrovirals and safer conception for HIV-serodiscordant couples. *Curr Op HIV/AIDS.* 2012;7(6):569-578.

13. Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med.* 2011;365(6):493-505.

14. Crepaz N, Tang T, Marks G, Hall H. VIral suppression patterns among persons in the United States with diagnosed HIV infection in 2014. *Ann Intern Med*. 2017;167(6):446-447.

15. Vernazza PL, Graf I, Sonnenberg-Schwan U, et al. Preexposure prophylaxis and timed intercourse for HIV-discordant couples willing to conceive a child. *AIDS.* 2011;25(16):2005-2008.

16. Mmeje O, Cohen CR, Cohan D. Evaluating safer conception options for HIV-serodiscordant couples (HIV-infected female/HIV-uninfected male): a closer look at vaginal insemination. *Infect Dis Obstet Gynecol.* 2012;2012.

17. Kawwass JF, Smith DK, Kissin DM, et al. Strategies for preventing HIV infection among HIV-uninfected women attempting conception with HIV-infected men—United States. MMWR. Morbidity and Mortality Weekly Report. 2017;66: 554–557.

18. Semprini AE, Macaluso M, Hollander L, et al. Safe conception for HIV-discordant couples: insemination with processed semen from the HIV-infected partner. *Am J Obstet Gynecol.* 2013;208(5):402.e401-402.e409.

19. Mugo NR, Heffron R, Donnell D, et al. Increased risk of HIV-1 transmission in pregnancy: a prospective study among African HIV-1-serodiscordant couples. *AIDS.* 2011;25(15):1887-1895.

20. Johnson LF, Stinson K, Newell M-L, et al. The contribution of maternal HIV seroconversion during late pregnancy and breastfeeding to mother-to-child transmission of HIV. *Journal of Acquired Immune Deficiency Syndromes (1999).* 2012;59(4):417.

21. Foster C, Lyall H, Olmscheid B, et al. Tenofovir disoproxil fumarate in pregnancy and prevention of mother-to-child transmission of HIV-1: is it time to move on from zidovudine? *HIV Med.* 2009;10(7):397-406.

22. Gibb DM, Kizito H, Russell EC, et al. Pregnancy and infant outcomes among HIV-infected women taking long-term ART with and without tenofovir in the DART trial. *PloS Med.* 2012;9(5):e1001217.

23. Nachega JB, Uthman OA, Mofenson LM, et al. Safety of tenofovir disoproxil fumarate-based antiretroviral therapy regimens in pregnancy for HIV-infected women and their infants: a systematic review and meta-analysis. *J Acquir Immune Defic Syndr*. 2017;76(1):1-12.

24. The Antiretroviral Pregnancy Registry. Interim Report: 1 January 1989 through 31 January 2017. 2017; http://www.apregistry.com/forms/interim_report.pdf. Accessed July 26, 2017.

25. Benaboud S, Pruvost A, Coffie PA, et al. Concentrations of tenofovir and emtricitabine in breast milk of HIV-1-infected women in Abidjan, Cote d'Ivoire, in the ANRS 12109 TEmAA Study, Step 2. *Antimicrobial Agents and Chemotherapy.* 2011;55(3):1315-1317.

26. Mirochnick M, Best BM, Clarke DF. Antiretroviral pharmacology: special issues regarding pregnant women and neonates. *Clinics in Perinatology.* 2010;37(4):907-927.

27. Mugwanya KK, Hendrix CW, Mugo NR, Marzinke M, Katabira ET, Ngure K, Semiyaga NB, John-Stewart G, Muwonge TR, Muthuri G, Stergachis A. Pre-exposure prophylaxis use by breastfeeding HIV-uninfected women: a prospective short-term study of antiretroviral excretion in breast milk and infant absorption. *PLoS Med*. 2016;13(9):e1002132.

28. Smith DK, Pals SL, Herbst JH, Shinde S, Carey JW. Development of a clinical screening index predictive of incident HIV infection among men who have sex with men in the United States. *J Acquir Immune Defic Syndr.* 2012;60(4):421-427.

29. Smith DK, Pan Y, Rose CE, et al. A brief screening tool to assess the risk of contracting HIV infection among active injection drug users. *Journal of Addiction Medicine.* 2014;9(3):226-232.

30. Knox DC, Anderson PL, Harrigan PR, Tan DHS. Multidrug-resistant HIV-1 infection despite preexposure prophylaxis. *N Engl J Med* 2017; 376 (5):501-502.

31. Hoornenborg E, Prins M, Achterbergh RC, et al. Acquisition of wild-type HIV-1 infection in a patient on pre-exposure prophylaxis with high intracellular concentrations of tenofovir diphosphate: a case report. Lancet HIV. 2017. Available at https://doi.org/10.1016/S2352-3018(17)30132-7.

32. Department of Health and Human Services. Panel on Antiretroviral Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. 2017. Available at http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf. Accessed July 26, 2017.

33. Reichmann WM, Losina E, Seage GR, et al. Does modality of survey administration impact data quality: audio computer assisted self interview (ACASI) versus self-administered pen and paper? *PLoS one.* 2010;5(1):e8728.

34. Centers for Disease Control and Prevention, Branson BM, Handsfield HH, et al. Revised Recommendations for HIV Testing of Adults, Adolescents, and Pregnant Women in Health-Care Settings. *Morbidity and Mortality Reports and Recommendations.* 2006;September 22, 2006 / 55(RR14);1-17.

35. Kamb ML, Fishbein M, Douglas JM, Jr., et al. Efficacy of risk-reduction counseling to prevent human immunodeficiency virus and sexually transmitted diseases: a randomized controlled trial. Project RESPECT Study Group. *JAMA.* 1998;280(13):1161-1167.

36. Centers for Disease Control and Prevention. Partnership for Health. 2015. http://www.cdc.gov/hiv/pdf/research/interventionresearch/compendium/cdc-hiv-partnership_for_health_lf_good_rr.pdf. Accessed August 8, 2016.

37. Grodensky C, Golin C, Boland M, et al. Translating concern into action: HIV care providers' views on counseling patients about HIV prevention in the clinical setting. *AIDS Behav.* 2008;12(3):404-411.

38. Golin CE, Patel S, Tiller K, et al. Start talking about risks: development of a motivational interviewing-based safer sex program for people living with HIV. *AIDS Behav.* 2007;11(5 Suppl):S72-83.

39. Herbst JH, Sherba RT, Crepaz N, et al. A meta-analytic review of HIV behavioral interventions for reducing sexual risk behavior of men who have sex with men. *J Acquir Immune Defic Syndr.* 2005;39(2):228-241.

40. Lyles CM, Kay LS, Crepaz N, et al. Best-evidence interventions: Findings from a systematic review of HIV behavioral interventions for US populations at high risk, 2000-2004. *Am J Public Health.* 2007;97(1):133-143.

41. Guyatt G, Oxman AD, Akl EA, et al. GRADE guidelines: 1. Introduction--GRADE evidence profiles and summary of findings tables. *J Clin Epidemiology.* 2011;64(4):383-394.

42. Shiffman RN, Dixon J, Brandt C, et al. The GuideLine Implementability Appraisal (GLIA): development of an instrument to identify obstacles to guideline implementation. *BMC Med Inform Decis Mak.* 2005;5:23.

43. Shiffman RN, Michel G, Essaihi A, Thornquist E. Bridging the guideline implementation gap: A systematic, document-centered approach to guideline implementation. *J Am Med Informatics Assoc.* 2004;11(5):418-426.

44. Cluzeau F, Burgers J, Brouwers M, et al. Development and validation of an international appraisal instrument for assessing the quality of clinical practice guidelines: the AGREE project. *Qual Saf Health Care.* 2003;12(1):18-23.

45. Brouwers MC, Kho ME, Browman GP, et al. Development of the AGREE II, part 1: performance, usefulness and areas for improvement. *Canadian Med Assoc J.* 2010;182(10):1045-1052.

	MSM Risk Index [28]		
1	How old are you today?	If <18 years, score 0 If 18-28 years, score 8 If 29-40 years, score 5 If 41-48 years, score 2 If 49 years or more, score 0	_____
2	In the last 6 months, how many men have you had sex with?	If >10 male partners, score 7 If 6-10 male partners, score 4 If 0-5 male partners, score 0	_____
3	In the last 6 months, how many times did you have receptive anal sex (you were the bottom) with a man when he did not use a condom?	If 1 or more times, score 10 If 0 times, score 0	_____
4	In the last 6 months, how many of your male sex partners were HIV-positive?	If >1 positive partner, score 8 If 1 positive partner, score 4 If <1 positive partner, score 0	_____
5	In the last 6 months, how many times did you have insertive anal sex (you were the top) with a man who was HIV- positive when you did not use a condom?	If 5 or more times, score 6 If 0-4 times, score 0	_____
6	In the last 6 months, have you used methamphetamines such as crystal or speed?	If yes, score 6 If no, score 0	_____
		Add down entries in right column to calculate total score	_____ TOTAL SCORE*

* If score is 10 or greater, evaluate for intensive HIV prevention services including PrEP.
If score is below 10, provide indicated standard HIV prevention services.

PWID (IDU) Risk Index [29]				
1	How old are you today (in years)?	If <30 years, score 38 If 30- 39 years, score 24 If 40-49 years, score 7 If ≥50 years, score 0		_____
2	In the last 6 months, were you in a methadone maintenance program?	If yes, score 0 If no, score 31		_____
3	In the last 6 months, how often did you inject heroin?	If 1 or more times, If 0 times,	Injection sub-score 1 Injection sub-score 0	_____
	In the last 6 months, how often did you inject cocaine?	If 1 or more times, If 0 times,	Injection sub-score 1 Injection sub-score 0	_____
	In the last 6 months, how often did you share a cooker?	If 1 or more times, If 0 times,	Injection sub-score 1 Injection sub-score 0	_____
	In the last 6 months, how often did you share needles?	If 1 or more times, If 0 times,	Injection sub-score 1 Injection sub-score 0	_____
	In the last 6 months, how often did you visit a shooting gallery?	If 1 or more times, If 0 times,	Injection sub-score 1 Injection sub-score 0	_____
Add the five injection subscores to obtain a Composite Injection Subscore		If sum of five injection subscores is; then Composite Injection Score is: 0 0 1 7 2 21 3 24 4 24 5 31		_____
Add the scores for age and methadone use to the Composite Injection Subscore to yield a Total Score				_____ Total Score*

* If the total score is 46 or greater, evaluate for PrEP or other intensive HIV prevention services for PWID. If score is 45 or less, provide indicated standard HIV prevention services for PWID. To identify active PWID in a clinician's practice, we recommend asking all their patients a routine question: "Have you ever injected drugs that were not prescribed for you by a physician?" If yes, ask, "When was the last time you injected any drugs?" Only complete PWID risk index if they have injected any nonprescription drug during the past 6 months.

Billing for services

BILLING CODING GUIDE FOR HIV PREVENTION

PrEP, SCREENING, AND LINKAGE SERVICES

NASTAD

NASTAD is a member of the **CBA Provider Network** and has a long history of providing technical assistance and Capacity Building Assistance (CBA) to health departments to support HIV testing. This document is part of NASTAD's Sustainability and Innovation CBA resources. This and other resources are available for download at **www.NASTAD.org**.

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Health departments and other medical providers are billing Medicaid, Medicare and private insurers for services related to HIV prevention. The counseling services needed for the treatment and discussion of lab tests are intensive. While some of the services are provided in traditional healthcare settings and can be billed to public and private insurance, some of these services are provided in non-traditional settings by non-licensed professionals making it a challenge to bill insurance for these services. This guide describes the procedure and diagnosis codes that are accepted by public and private insurance, along with specific requirements for some Current Procedural Terminology (CPT®) billing codes. It also describes some of the challenges in obtaining reimbursement for testing, counseling, linkage to care and adherence services.

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Table of Contents

Introduction 1

- Coding overview and obstacles to payment 1
- The goal of this guide 2

PrEP initiation and follow up in medical offices and clinics 3

- Medical office visits for PrEP initiation 4
- Shared medical visits 5
- Preventive medicine CPT codes 6
- Labs for PrEP initiation 7

Adherence, linkage and other counseling services 10

- PrEP adherence counseling by a physician, advance practice registered nurse (APRN), physician assistant (PA) 10
- High intensity behavioral counseling to prevent STIs 11
- Chronic care management (CCM) services 12
- Screening and behavioral counseling in a primary care setting to reduce alcohol misuse 14
- Care coordination, linkage and adherence services by community health workers (CHWs) and other non-licensed/peer providers in non-traditional healthcare settings 16
- Targeted case management 17
- Mental health assessment by non-physician 18

Lab tests for HIV and other STIs 19

- HIV screening 19
- HIV screening in a non-primary care setting 22
- Screening for other STIs 23

Appendix 25

- Common diagnosis codes 25
- Pregnancy related diagnosis codes 26
- CPT® codes 27
- United States Preventive Services Task Force (USPSTF) recommendations 29

Glossary 31

Acknowledgements 32

Introduction

Health department HIV prevention programs and the medical providers they support offer a range of vital prevention services—including HIV Pre-exposure prophylaxis (PrEP) access services, linkage to care services, adherence counseling and HIV testing. Some of these services are performed by physicians, APRNs or PAs or the staff working under the supervision of these medical professionals. As an alternative, some of these same services are provided by community health workers (CHWs) or other non-licensed health professionals and peers.[1] Payment by insurance companies for these services can be problematic, depending upon whether the payer (e.g., Medicare, Medicaid or private insurance plans) recognizes the service, the credentials of the person proving the service, and the setting in which the service is provided. As a result of the Affordable Care Act (ACA), the percentage of uninsured patients has decreased (especially in states with Medicaid expansion). Medical practices and health departments are being encouraged to bill patients' insurance for reimbursement for these important services. This coding guide will describe procedure (CPT®) and diagnosis code (International Classification of Diseases, 10th revision, Clinical Modification, ICD-10) that health care professionals can use when submitting claims for reimbursement for these important services.

As a result of the ACA, the **percentage of uninsured patients has decreased**. Medical practices and health departments are being encouraged to bill patients' insurance for reimbursement for these important services.

CODING OVERVIEW AND OBSTACLES TO PAYMENT

Insurance companies pay for services that are described by a CPT® code and performed by a licensed practitioner or for work performed under the supervision of a licensed practitioner. Services are paid based on a fee associated with each CPT® code. In some instances, a set of services will be reimbursed at a "bundled" rate instead of based on fee-for-service. (A bundled payment covers multiple services, and may include services provided by two or more providers for a single episode of care.) The American Medical Association develops these CPT® codes to describe services performed by healthcare providers. Individual insurance companies and state Medicaid programs are free to develop a set of reimbursement and payment guidelines, and are not required to cover all services described by a CPT® code.

[1] In 2013, the Centers for Medicare and Medicaid Services (CMS) amended federal preventive services Medicaid regulations to allow CHWs and other non-licensed providers to provide preventive services and have those services paid by state Medicaid programs when the services are *recommended* by a physician or other licensed provider. However, the state Medicaid program department must apply to CMS to be able to do this. CMS Center for Medicaid and CHIP Services Bulletin, Update on Preventive Services Initiatives, available at https://www.medicaid.gov/Federal-Policy-Guidance/Downloads/CIB-11-27-2013-Prevention.pdf; CMS Presentation "Medicaid Preventive Services Regulatory Change" Division of Benefits and Coverage, Disabled and Elderly Health Programs Group, Center for Medicaid and CHIP Services, April 2014, available at https://www.medicaid.gov/Medicaid-CHIP-Program-Information/By-Topics/Benefits/Downloads/Preventive-Webinar-Presentation-4-9-14.pdf.

Return to Table of Contents

All services require a medically necessary International Statistical Classification of Diseases and Related Health Problems (ICD-10) diagnosis code in order to be reimbursed. A medical practice or health department could provide a service that is covered and described by a CPT® code, but not have the allowable (proper) diagnosis code that justifies reimbursement by the payer. In which case, the claim is rejected and the service will not be reimbursed.

In summary . . .

In summary, a group may only be paid by an insurance company or government payer for services, which are:

- Described by CPT® code,
- Performed by a licensed provider (credentialed for the provision of services by the payor) or under the supervision of the credentialed licensed provider, and
- Supported by an allowable ICD-10 diagnosis code.

THE GOAL OF THIS GUIDE

The goal of this coding guide is to describe scenarios for PrEP initiation and follow-up, adherence, linkage and other counseling services, and for lab tests for HIV and other STIs. It will discuss CPT® codes and ICD-10 diagnosis codes that could be reported as part of filing a claim with the patient's insurance company or government payer. It will also include a discussion of who may provide this service either directly or under the supervision of a licensed medical professional. Unfortunately, there are many services provided by HIV and other public health program staff members that are either not described by a CPT® code, or not performed by a healthcare professional who is credentialed by an insurance company or for which there is not a covered ICD-10 diagnosis code. This limits the ability to seek reimbursement from the insurer for the service.

Return to Table of Contents

PrEP initiation and follow up in medical offices and clinics

Prior to receiving a prescription for PrEP, an individual needs counseling and lab testing. The Centers for Disease Control and Prevention (CDC) has published Clinical Guidelines for PrEP.[2] Lab tests must be ordered by a physician, advanced practice nurse or physician assistant. If the counseling is done by one of these professionals, this counseling can be billed in one of three ways:

1. Office/outpatient facility submits a claim for a new or established encounter with a billable provider (physician, APRN or PA) and all other services using appropriate CPT codes linked to the allowable ICD-10 diagnostic codes;

2. Office/outpatient facility submits a claim for a shared medical appointment provided by a billable provider and all services provided; or

3. Office/outpatient facility submits a claim for "Preventive health counseling" proved by a billable provider for patients who don't have an established diagnosed illness.

[2] CDC PrEP Clinical Guidelines, available at http://www.cdc.gov/hiv/pdf/prepguidelines.pdf

Return to Table of Contents

MEDICAL OFFICE VISITS FOR PrEP INITIATION

Codes: Evaluation and Management (E/M) services

99201–99205 for "new" patients
99211–99215 for "established" patients.

Who can perform: Credentialed physicians, APRN, and PAs

Location: Office, clinic or outpatient department

Can a staff member perform the service under the supervision of a licensed provider?

Note: Insurance companies and state Medicaid programs develop their own rules about services performed by a staff member "incident" to a licensed clinician and supervised by the clinician. This guide addresses the Medicare rules and many state Medicaid programs and private insurance companies follow these rules.

A staff member who is not a physician, APRN, or PA may only report the lowest level established patient visit, 99211. This code, 99211, is commonly known as a "nurse" visit. For Medicare, or payers that follow Medicare rules, this must meet "incident to" guidelines.

How to use the E/M codes:

- Select the level of service based on the history, exam and medical decision making.
- If counseling dominates the visit, use time in minutes to select the code. Document the total face-to-face time of the service, the statement that more than 50% of the time was spent in discussion and the nature of the discussion (e.g., I spent 15 minutes in face-to-face with Mr. XXX discussing the risks, benefits, limitations, possible complications, dosing, importance of adherence, and required conditions for continued prescribing of PrEP. He voiced an understanding and wishes to proceed).

Return to Table of Contents

SHARED MEDICAL VISITS

Codes: Use CPT® codes 99201–99205 for "new" patients, 99211–99215 for "established" patients

Who can perform: These codes (99201–99215) may only be reported by physicians, APRNs, and PAs.

Location: Office, clinic or outpatient department

Can a staff member perform the services under the supervision of a licensed provider?

No. These E/M codes cannot be used for that purpose. A staff member could participate in the shared medical appointment with the licensed clinician, but the physician, APRN, or PA would need to document the services in the patient's record.

How to use these codes for shared medical appointments:

Some medical groups use the office/outpatient codes to report a shared medical visit.

- Neither CMS nor CPT® has commented in their manuals on the use of office visit codes for this purpose.
- The American Association of Family Physicians (AAFP) has published a notification of a communication with CMS, allowing this.[3]
- The billing physician, APRN, or PA may see the patient in the presence of other group members, but must document in each patient's chart.
- Select the level of service based on the key components (history, exam and medical decision making) documented for each patient, not based on the time of the group.

NOTE: There is a code for group services, 99078. Physician or other qualified health care professional qualified by education, training, licensure/regulation (when applicable) educational services rendered to patients in a group setting (e.g., prenatal, obesity, or diabetic instructions). It has a status indicator of bundled, so it would not usually be paid. CMS assigns status indicators to CPT® codes. The most common are "active," "non-covered" and "bundled." An "active" code is paid by Medicare and most payers. A "non-covered" status indicator means that the service is not covered by the payer but may be billed to the patient. If a CPT® code has a status indicator of "bundled," it is not paid by the payer and typically cannot be billed to the patient.

[3] American Association of Family Physicians (AAFP), CMS Coding Notification, available at http://www.aafp.org/practice-management/payment/coding/group-visits.html

Return to Table of Contents

PREVENTIVE MEDICINE CPT CODES

Prior to receiving a prescription for PrEP, a medical professional has a discussion with the patient and orders lab testing. As mentioned above, these discussions may be reported by billable health care professionals using individual office visit codes or with a shared medical appointment. However, an alternative is to bill for the counseling with "preventive medicine" codes. CPT® has a series of preventive medicine codes for risk factor reduction. The preventive medicine codes are intended to be used in the absence of an established diagnosis.

Codes:

Preventive medicine counseling and/or risk factor reduction intervention(s) provided to an individual (separate procedure);

99401 approximately 15 minutes
99402 approximately 30 minutes
99403 approximately 45 minutes
99404 approximately 60 minutes

Preventive medicine counseling and/or risk factor reduction intervention(s) provided to individuals in a group setting (separate procedure);

99411 approximately 30 minutes
99412 approximately 60 minutes

Who can perform: physicians, APRNs, or PAs

Location: Office, clinic or outpatient department

Can a staff member perform the service under the supervision of a licensed provider?

It would be prudent to ask payers if these counseling services could be performed by a staff member under the supervision of a physician, APRN, or PA.

How to use these codes:

- These time-based codes are used to document preventive counseling in patients without a diagnosis. Counseling for PrEP adherence in patients without HIV fits into this description.
- According to the CPT® book, "Risk factor reduction services are used for persons without a specific illness for which the counseling might otherwise be used as part of treatment."[4]
- The codes in the 99401–99404 series are for individual counseling and codes 99411 and 99412 are for group counseling.
- Document the time of the face-to-face counseling in the medical record, and describe the counseling.
- These codes have a status indicator of "non-covered" for Medicare, but some private payers recognize and will reimburse for them.

[4] 2016 Current Procedural Terminology, American Medical Association.

Return to Table of Contents

Diagnosis coding

A list of relevant diagnosis codes is at the end of this guide. For the purposes of PrEP counseling, many groups use **ICD-10 Z20.2** "Contact with and (suspected) exposure to infections with a predominantly sexual mode of transmission." Two other commonly used codes are:

- **Z11.4** "Encounter for screening for human immunodeficiency virus [HIV])" and
- **Z11.3** "Encounter for screening for infections with a predominantly sexual mode of transmission."

LABS FOR PrEP INITIATION

The lab tests described below are ordered by a billable healthcare professional prior to PrEP initiation. They may also be ordered in other situations for HIV and STI screening.

Prior to starting PrEP, the billable healthcare professional orders screening laboratory tests. These include HIV serology, and screening for sexually transmitted infections. The medical provider may also order a metabolic panel and/or pregnancy test.

After starting PrEP medication, the medical provider will order surveillance lab tests every three-months. Although screening for HIV has an "A" rating from the USPSTF and is covered without a "patient due balance," insurers may not treat the tests provided every three months in the same way. The more frequently obtained HIV tests may be considered diagnostic, rather than screening, once treatment is initiated. As a result, patients may have a co-pay and/or deductible for these lab tests.

Return to Table of Contents

Code	Description
86689	HTLV or HIV antibody, confirmatory test (eg, Western Blot)
	Antibody
86701	HIV-1
86702	HIV-2
86703	HIV-1 and HIV-2, single result
	(For HIV-1 antigen(s) with HIV-1 and HIV-2 antibodies, single result, use 87389)
	(When HIV immunoassay [HIV testing 86701-86703 or 87389] is performed using a kit or transportable instrument that wholly or in part consists of a single use, disposable analytical chamber, the service may be identified by adding modifier 92 to the usual code)
	Infectious agent detection by nucleic acid (DNA or RNA)
87534	HIV-1, direct probe technique
87535	HIV-1, amplified probe technique, includes reverse transcription when performed
87536	HIV-1, quantification, includes reverse transcription when performed
87357	HIV-2, direct probe technique
87538	HIV-2, amplified probe technique, includes reverse transcription when performed
87539	HIV-2, quantification, includes reverse transcription when performed
	Infectious agent antigen detection by immunoassay technique, (eg, enzyme immunoassay [EIA], enzyme- linked immunosorbent assay [ELISA], immunochemiluminometric assay [IMCA]) qualitative or semiquantitative, multiple-step method
87389	HIV-1 antigen(s), with HIV-1 and HIV-2 antibodies, single result
87390	HIV-1
87391	HIV-2
	For Medicare patients
G0432	Infectious agent antibody detection by enzyme immunoassay (EIA) technique, HIV-1 and/or HIV-2, screening
G0433	Infectious agent antibody detection by enzyme-linked immunosorbent asssay (ELISA) technique, HIV-1 and/or HIV-2, screening
G0435	Infectious agent antibody detection by rapid antibody test, HIV-1 and/or HIV-2, screening

Please see the discussion of modifiers after the HIV testing section of this guide.

Return to Table of Contents

ICD-10 Code	Description	Use for
Z01.812	Encounter for preprocedural laboratory examination	Use for blood or urine tests prior to treatment.
Z11.3	Encounter for screening for infections with a predominantly sexual mode of transmission	STI screening
Z11.4	Encounter for screening for human immunodeficiency virus [HIV]	HIV screening
Z20.2	Contact with and (suspected) exposure to infections with a predominantly sexual mode of transmission	HIV, STI screening
Z20.6	Contact with and (suspected) exposure to human immunodeficiency virus [HIV]	HIV screening
Z51.81	Encounter for therapeutic drug level monitoring	PrEP monitoring
Z72.51	High risk heterosexual behavior	HIV, STI screening
Z72.52	High risk homosexual behavior	HIV, STI screening
Z72.53	High risk bisexual behavior	HIV, STI screening
Z72.89	Other problems related to lifestyle	Use for drug seeking behavior or unhealthy drinking behavior
Z79.899	Other long term (current) drug therapy	PrEP monitoring
Z86.59	Personal history of other mental and behavioral disorders	History of drug use. For opioid dependence in remission, use code from F11.
Z87.898	Personal history of other specified conditions	Use for a history of drug use, non-dependent, in remission.
	Opioid abuse—no specific code for IV use	
F11.20	Opioid dependence, uncomplicated	
F11.21	Opioid dependence in remission	
F11.10	Opioid abuse, uncomplicated	
F11.90	Opioid use, uncomplicated	

Return to Table of Contents

Adherence, linkage and other counseling services

PrEP ADHERENCE COUNSELING BY A PHYSICIAN, ADVANCE PRACTICE REGISTERED NURSE (APRN), PHYSICIAN ASSISTANT (PA)

Adherence counseling performed in a physician office may be billed with the same codes as listed in PrEP initiation, at the start of this guide, new and established patient E/M services (99201–99215) and preventive medicine counseling (99401–99412). With appropriate documentation, a physician, APRN, or PA could provide time-based counseling for a patient using office visit codes or preventive medicine counseling codes. See the section on PrEP initiation for a discussion of these services.

In addition, there is a code for high intensity behavioral counseling to prevent STIs, which can be billed in primary care settings, G0445. There are restrictions on G0445, described below.

Return to Table of Contents

HIGH INTENSITY BEHAVIORAL COUNSELING TO PREVENT STIs

Code: G0445: Semiannual high intensity behavioral counseling to prevent STIs, individual, face-to- face, includes education skills training & guidance on how to change sexual behavior, 20–30 minutes

Who can perform: The patient must be referred by a primary care provider to be eligible to receive this service, according to Medicare. Physicians, APRNs, and PAs may provide the service.

Location: A primary care setting.

Can a staff member perform the service under the supervision of a licensed provider?

It would be prudent to ask payers if these counseling services could be performed by a staff member under the supervision of a physician, APRN, or PA.

How to use this code:

- Use this code for individual face-to-face counseling, which includes education skills training and guidance on how to change sexual behavior.
- The service can be provided to individuals with multiple sex partners, those who are using barrier protection inconsistently, those were having sex under the influence of alcohol or drugs, those were having sex in exchange for money or drugs, age (24 years or younger and sexually active for women with chlamydia and gonorrhea), those who have had an STI within the past year, IV drug use (hepatitis B only), and for men those are having sex with men and engaged in high-risk sexual behavior.
- The patient must be referred for this service by a primary care provider and the service must be provided by a Medicare-eligible primary care provider in a primary care setting. For the purpose of this service, Medicare defines a primary care physician as someone who is a general practitioner, family practitioner, general internist, or an obstetrician or gynecologist, or a geriatric medicine physician or pediatric medicine physician or a clinical nurse specialist, a nurse practitioner, or physician assistant.
- A primary care setting is describe as one in which the provision of integrated accessible health care services by clinicians who are accountable for addressing a large majority of personal healthcare needs, developing a sustained partnership with patients, and practicing in the context of family and community.[5]
- This would seem to require that the patient was referred by one of the primary care specialty physicians listed above, it could be provided in a health department or infectious disease practice the provided majority of the patient's care.
- These codes could be used for HIV negative or positive individuals.

[5] Department of Health and Human Services, CMS, MLN Matters MM7610

Return to Table of Contents

CHRONIC CARE MANAGEMENT (CCM) SERVICES

As of this writing, one year after CMS allowed payment for chronic care management codes, provider billing for these services remains very limited. CMS allows for a physician, APRN, or PA to bill for services provided by staff members in coordinating care and providing non-face-to-face services to patients. However, the restrictions and difficulties of providing chronic care management are such that very few practices are attempting to do it. It is described below for the sake of completeness in this guide, but will probably be used infrequently.

Code: 99490: chronic care management services, at least 20 minutes of clinical staff time directed by a physician or other qualified healthcare professional, per calendar month, with the following elements:

- Multiple (two or more) chronic conditions expected to last at least 12 months, or until the death of the patient,
- Chronic conditions placed the patient at significant risk of death, acute exacerbation/ decompensation, or functional decline,
- Comprehensive care plan established, implemented, revised, or monitored.

The problems must be of the type of conditions that pose a risk to the patient's health and well-being.

Who can perform:

Clinical staff under the supervision of a physician, APRN, or PA

Location: Office, clinic or outpatient department

How to use these codes:

- The practice must implement a care plan that addresses the patient's conditions and a clinical staff member must spend 20 minutes during a calendar month coordinating care and communicating with the patient.
- The practice must use a certified electronic health record.
- The physician, APRN, or PA develops a care plan, which is stored electronically. Everyone whose minutes "count" towards the 20 clinical staff minutes/month must have access to the care plan.
- Other key healthcare professionals must have electronic access to care plan: fax is insufficient as a means of communicating.
- A copy of the care plan is provided to the patient, electronically or on paper.
- The electronic record must include a full list of problems and medications and should facilitate caring for the patient during care transitions.
- Medication reconciliation is required as part of the service.
- The patient must have access to the practice 24 hours a day, seven days a week.
- One provider must be designated for continuity of care.

Return to Table of Contents

Care management includes assessment of the patient's medical, functional and psychosocial needs manage care transitions, and coordinate with home and community services.

How to get started:

- The service must be implemented at a "comprehensive" E/M service (wellness visit or problem oriented service)
- Informed consent is required before starting the service. The practice must inform the patient that they will provide this service and get written consent from the patient to do so and to share information with other providers.
- The practice must also inform that patient that they can revoke this consent and stop receiving care management services at any time.
- Document these communications in the record, and give the patient a written or electronic copy of the care plan.

Supervision of clinical staff is general, not direct, supervision. That means the billing provider does not need to be in the suite of offices when the clinical staff provides the non-face-to-face care.

The practice may only report this service during the month in which the clinical staff has 20 minutes of non-face-to-face time with the patient.

Key points

- Work is done by clinical staff.
- May not count any clinical staff time on a day when the physician or qualified healthcare professional (APRN/PA) has an evaluation and management service with the patient.
- E/M services may be reported during the same calendar month the chronic care management is provided.

Return to Table of Contents

SCREENING AND BEHAVIORAL COUNSELING IN A PRIMARY CARE SETTING TO REDUCE ALCOHOL MISUSE

The USPSTF recommends screening for alcohol misuse and behavioral interventions for individuals whose screening results are positive. CMS covers this service, but with limitations on which specialties can perform and be paid for the service. State Medicaid programs can individually decide whether or not to restrict coverage based on specialty designation of the provider.

Codes:

G0442 annual alcohol misuse screening, 15 minutes
G0443 Brief face-to-face behavioral counseling for alcohol misuse, 15 minutes

Who can perform: Physicians, APRNs, or PAs

Location: Office, clinic, outpatient department or local or state health department

Screening can be performed in any location. Counseling is furnished by qualified physicians, advanced practice nurses and physician assistants in a primary care setting. These services may be provided to patients with or without HIV.

Can a staff member perform the service under the supervision of a licensed provider?

Medicare indicates that the counseling is performed furnished by "qualified primary care physicians or other primary care practitioners in a primary care setting."

How to use these codes:

Medicare states: For the purposes of this covered service, the following provider specialty types may submit claims for G0442 and G0443. Infectious Disease is not a specialty on CMS' list.

- 01-General Practice
- 08-Family Practice
- 11-Internal Medicine
- 16-Obstetrics/Gynecology
- 37-Pediatric Medicine
- 38-Geriatric Medicine
- 42-Certified Nurse Midwife
- 50-Nurse Practitioner
- 89-Certified Clinical Nurse Specialist
- 97-Physician Assistant

Return to Table of Contents

For purposes of this covered service, the following Place of Service (POS) codes are applicable:

- 11 Physician's office
- 22 Outpatient hospital
- 49 Independent clinic
- 71 State or local public health clinic

The screening is covered annually by Medicare and up to four brief interventions are covered annually. State Medicaid programs and private payers may have their own rules and frequency limitations.

Each of the four behavioral counseling interventions must be consistent with the 5As approach that has been adopted by the USPSTF to describe such services:

1. **Assess:** Ask about/assess behavioral health risk(s) and factors affecting choice of behavior change goals/methods.

2. **Advise:** Give clear, specific, and personalized behavior change advice, including information about personal health harms and benefits.

3. **Agree:** Collaboratively select appropriate treatment goals and methods based on the patient's interest in and willingness to change the behavior.

4. **Assist:** Using behavior change techniques (self-help and/or counseling), aid the patient in achieving agreed-upon goals by acquiring the skills, confidence, and social/environmental supports for behavior change, supplemented with adjunctive medical treatments when appropriate.

5. **Arrange:** Schedule follow-up contacts (in person or by telephone) to provide ongoing assistance/support and to adjust the treatment plan as needed, including referral to more intensive or specialized treatment.

Return to Table of Contents

CARE COORDINATION, LINKAGE AND ADHERENCE SERVICES BY COMMUNITY HEALTH WORKERS (CHWs) AND OTHER NON-LICENSED/ PEER PROVIDERS IN NON-TRADITIONAL HEALTHCARE SETTINGS

As mentioned in the introduction of this guide, government healthcare payers and private insurance companies pay for services performed by licensed professionals in medical settings. This is an obstacle for payment for health departments and public health clinics that employ CWHs, peers, and other non-licensed staff for outreach and linkage services. On July 15, 2013, CMS changed a rule related to Medicaid coverage of preventive services in a non-traditional setting, provided by non-licensed staff members. This rule allows for state Medicaid programs to pay for preventive services provided by a non-licensed professional when the services are recommended by a physician, APRN, or PA. The definition of preventive services did not change. A CMS document describes these services as those that involve direct patient care and for the express purpose of diagnosing, treating or preventing illness or injury or other impairments to an individual's physical or mental health[6]

This allows CHWs or other non-licensed professionals to perform and bill Medicaid for services that would typically only be billed by physicians, advanced practice nurses or physician assistants. However, it requires that each individual state Medicaid program apply to CMS in order to be eligible to cover the services in this way. State health departments and public health clinics must query their own state Medicaid agency to determine if their state Medicaid has made this application to CMS.

If so, there are self-management education and training codes that can be billed by CHWs. Although coverage will vary by state Medicaid programs these will likely include self-management education and training. The CHWs must be supervised by a physician, APRN, or PA depending on the state.

Codes:

98960 Self management education and training face-to-face, 1 patient
98961 Self management education and training face-to-face, 2–4 patients
98962 Self management education and training, face-to-face, 5–8 patients

Location: Office, clinic or outpatient department

Can a staff member perform the service under the supervision of a licensed professional?

Check with your state Medicaid program and private insurers.

- In the Medicare fee schedule, these three codes have a status indicator of "bundled." That means that Medicare will not cover them, and many private insurers may not pay for these either. However, if a state Medicaid program has opted to expand their coverage of preventive services and received permission from CMS these codes could be used by CHWs or other non-licensed professionals.
- CPT® describes these services as performed by a physician, APRN, or PA, so check with your private insurers about CHWs or other non-licensed professionals performing them under the supervision of those licensed professionals.

[6] CMS Presentation "Medicaid Preventive Services Regulatory Change" Division of Benefits and Coverage, Disabled and Elderly Health Programs Group, Center for Medicaid and CHIP Services, April 2014, available at https://www.medicaid.gov/Medicaid-CHIP-Program-Information/By-Topics/Benefits/Downloads/Preventive-Webinar-Presentation-4-9-14.pdf.

Return to Table of Contents

TARGETED CASE MANAGEMENT

In many cases, it is a CHW who is reaching out to individuals to encourage screening, to support the initiation of PrEP and to support the continued PrEP treatment. The work of CHWs is critical but too often, their work isn't recognized and paid by insurance companies. There are codes for this work described by the Healthcare Common Procedure Coding System (HCPCS). HCPCS codes are developed by CMS for its own use, but the codes are often also recognized by state Medicaid programs and commercial payers.

Codes:

T1017 Targeted case management, each 15 minutes

Although CMS developed this code, Medicare does not recognize it or set a fee for it. However, some state Medicaid programs do recognize and pay for the service performed by a CHW. For example, the state of Mississippi allows the service to be billed in the patient's home, in a school, in a community mental health center and in "other place of service not identified."[7] Texas allows targeted case management to be performed over the phone or face-to-face using these codes. The provider should append modifier IU when the service is performed face-to-face.[8] Florida Medicaid pays for targeted case management using these codes for group services.[9] Each state Medicaid program sets its own policies and payment amounts. Groups and organizations that are providing these services will need to check with their own state Medicaid program about coverage of this targeted case management.

Who can perform: This is a case management service, and may be performed by CHWs.

Location: Check with the state Medicaid program.

How to use these codes: Use these codes for case management services performed by CHWs. Document time in the medical record.

[7] Community/Private Mental Health Center Billing Guidelines, available at https://www.medicaid.ms.gov/wp-content/uploads/2014/03/CommunityMentalHealthCenter.pdf.

[8] 2012 Texas Medicaid Provider Procedures Manual, Targeted Case Management, available at http://www.tmhp.com/HTMLmanuals/TMPPM/2012/Vol2_Children's_Services_Handbook.17.081.html.

[9] Florida Medicaid, Mental Health Targeted Case Management Handbook, available at http://www.flatherapy.com/therapy/wp-content/uploads/2010/05/CTCM-Handbook.pdf.

Return to Table of Contents

MENTAL HEALTH ASSESSMENT BY NON-PHYSICIAN

When a mental health assessment is performed by a physician, APRN, or PA, the clinician use E/M codes. Psychiatrists, social workers and psychologists use psychiatric diagnostic interview codes, in the Psychiatry section of the CPT® book when performing an initial evaluation. Some state Medicaid programs allow payment for a mental health assessment by non-licensed professionals, who are not listed above and not able to use the CPT® codes to report the evaluation.

Code: H0031: Mental health assessment, by non-physician

This code is not covered by Medicare, but may be covered by state Medicaid programs. Groups and organizations need to check with their individual state Medicaid programs. The service will typically be covered once per year. There may be diagnosis related restrictions related to the evaluation. It would be prudent to review if there are restrictions based on age, that is, if the service is only covered for children. One managed Medicaid program limits this to one assessment per year and does not require a prior authorization. This may require modifier "MO" indicating a master level provider has done the assessment.[10] Medicaid in the state of Georgia covers the service and has variable payment depending on the credentials of professional performing it.[11]

Who can perform:

Although this will vary by state, the code is applicable to trained para-professionals.

Location:

The service may be covered when done in a school, the patient's home or in some cases, in "other place of service."

How to use this code:

The provider must document a mental health assessment that includes the patient's past history, social, and family history. The assessment should include documentation of the patient's current functioning and an assessment of mental status. The history includes education, employment and any legal involvement as well as relationships and living environment. Document use of alcohol, tobacco and other drugs and behaviors that put the individual at risk.

[10] Magellan of Florida, Behavioral Health Therapy Services, available at https://www.magellancompletecareoffl.com/media/916790/appendix_k_combined.pdf.

[11] Georgia, Medicaid State Plan, Policy and Methods for Establishing Payment Rates for Other Types of Care for Services, available at https://www.medicaid.gov/State-resource-center/Medicaid-State-Plan-Amendments/Downloads/GA/GA-11-007-Att.pdf.

Return to Table of Contents

Lab tests for HIV and other STIs

HIV SCREENING

Testing in the setting or PrEP initiation and adherence was discussed earlier in this guide, but the same CPT® codes are used for screening for HIV and other STI in other settings and situations.

Codes: HIV screening has an "A" rating from the USPSTF. It is a covered service by Medicare, Medicaid and commercial insurance companies. The USPSTF has not recommended specific screening intervals, but does describe recommendations for those intervals. That discussion is below.

PROCEDURE CODES

Code	Description
86689	HTLV or HIV antibody, confirmatory test (eg, Western Blot)
	Antibody
86701	HIV-1
86702	HIV-2
86703	HIV-1 and HIV-2, single result
	(For HIV-1 antigen(s) with HIV-1 and HIV-2 antibodies, single result, use 87389)
	(When HIV immunoassay [HIV testing 86701-86703 or 87389] is performed using a kit or transportable instrument that wholly or in part consists of a single use, disposable analytical chamber, the service may be identified by adding modifier 92 to the usual code)
	Infectious agent detection by nucleic acid (DNA or RNA)
87534	HIV-1, direct probe technique
87535	HIV-1, amplified probe technique, includes reverse transcription when performed
87536	HIV-1, quantification, includes reverse transcription when performed
87357	HIV-2, direct probe technique
87538	HIV-2, amplified probe technique, includes reverse transcription when performed
87539	HIV-2, quantification, includes reverse transcription when performed
	Infectious agent antigen detection by immunoassay technique, (eg, enzyme immunoassay [EIA], enzyme- linked immunosorbent assay [ELISA], immunochemiluminometric assay [IMCA]) qualitative or semiquantitative, multiple-step method
87389	HIV-1 antigen(s), with HIV-1 and HIV-2 antibodies, single result
87390	HIV-1
87391	HIV-2

Return to Table of Contents

HCPCS code	Description
	Screening for Medicare patients
G0432	Infectious agent antibody detection by enzyme immunoassay (EIA) technique, HIV-1 and/or HIV-2, screening
G0433	Infectious agent antibody detection by enzyme-linked immunosorbent asssay (ELISA) technique, HIV-1 and/or HIV-2, screening
G0435	Infectious agent antibody detection by rapid antibody test, HIV-1 and/or HIV-2, screening

Modifiers are two-digit codes that are added to a procedure code when submitting a claim to an insurance company. These two digit modifiers do not change the definition of the code, but inform the payer of special circumstances related to the provision of the service.

There are three modifiers that could be used when screening for HIV.

- Use of modifier 33: In response to the ACA, CPT® developed a modifier to be used when a service is provided that is a service that carries an "A" or "B" rating from the USPSTF (and is thus required to be provided without patient cost sharing). Modifier 33 **Services:** When the primary purpose of the service is the delivery of an evidence based service in accordance with a USPSTF "A" or "B" rating in effect and other preventive services identified in preventive services mandates (legislative or regulatory), the service may be identified by adding 33 to the procedure. For separately reported services specifically identified as preventive, the modifier should not be used.[12] It is correct coding to append modifier 33 to any service that meets this description.

Use modifier 33 on the CPT code for HIV screening. This informs the payer that the service is a service recommended by the USPSTF. For patients with commercial policies, it insures that the insurance company will pay the claim without a patient due amount. No co-pay or deductible should be applied to a service with a USPSTF "A" or "B" rating.

- Modifier 92 **Alternative Laboratory Platform Testing:** When laboratory testing is being performed using a kit or transportable instrument that wholly or in part consists of a single use, disposable analytical chamber, the service may be identified by adding modifier 92 to the usual laboratory procedure code (HIV testing 86701–86703, and 87389). The test does not require permanent dedicated space, hence by its design may be hand carried or transported to the vicinity of the patient for immediate testing at that site, although location of the testing is not in itself determinative of the use of this modifier.

Use this modifier on the HCPCS codes for Medicare patients, G0432, G0433, G0435.

Modifier QW CLIA waived test

- CLIA waived tests on this list are 86701, G0433, G0434 87389

[12] Current Procedural Terminology 2016, American Medical Association

Return to Table of Contents

DIAGNOSIS CODES

ICD-10 Code	Description	Use For
Z11.4	Encounter for screening for human immunodeficiency virus [HIV]	HIV screening
Z20.2	Contact with and (suspected) exposure to infections with a predominantly sexual mode of transmission	HIV, STI screening
Z20.6	Contact with and (suspected) exposure to human immunodeficiency virus [HIV]	HIV screening
Z51.81	Encounter for therapeutic drug level monitoring	PrEP monitoring
Z72.51	High risk heterosexual behavior	HIV, STI screening
Z72.52	High risk homosexual behavior	HIV, STI screening
Z72.53	High risk bisexual behavior	HIV, STI screening

- The USPSTF recommends that all pregnant women be screened, and any woman who presents while in labor whose HIV status is unknown. It also recommends screening in individuals who are age 15–65, and states that younger and older individuals who are increased risk should be screened.
- Medicare has aligned its HIV testing coverage determination with CDC and USPSTF recommendations, allowing for one, annual voluntary screening for all adolescents and adults between the age of 15 and 65, without regard to perceived risk and testing three times per pregnancy for pregnant women. While all commercial carriers will cover the test, because the USPSTF does not give a frequency recommendation, commercial carriers and state Medicaid programs are free to develop their own guidelines. For example, Aetna simply quotes the USPSTF and does not specifically state what their frequency limitations are.[13]

UnitedHealthcare, in its National Coverage Determination N210.7 gives these frequency limits states that except for pregnant beneficiaries, it covers one annual screening. UnitedHealthcare's preventive medicine policy for screening for non-Medicare replacement plans lists the lab service as covered, but does not describe frequency. It can be assumed that it will have similar frequency limitations.

Complications

A screening test may be denied because:

- The patient is already diagnosed with the condition, and no longer needs to be screened for the illness.
- An incorrect diagnosis is reported.
- The payer has established frequency limits for the service.

[13] Aetna, HIV Testing Policy, available at http://www.aetna.com/cpb/medical/data/500_599/0542.html

Return to Table of Contents

HIV SCREENING IN A NON-PRIMARY CARE SETTING

An insurance company is required to cover any service given an "A" or "B" grade from the USPTSF. This includes HIV screening. (See the appendix for a table that lists related services with an A or B rating.) Emergency departments, conducting routine HIV screening of patients, have reported payment challenges. Details on the USPSTF HIV screening recommendations are available online.[14]

A screening test may be denied because:

- The test was done in a setting in which a bundled payment was negotiated for the service, and the screening is not included in the negotiated rate.
- The patient is already diagnosed with the condition, and no longer needs to be screened for the illness.
- An incorrect diagnosis is reported.
- The payer has established frequency limits for the service.[15]
- Modifier 33 was not appended to the CPT® or HCPCS code.

[14] See U.S. Preventive Services Task Force. H. *Human Immunodeficiency Virus (HIV) Infection: Screening.* Release Date: April 2013, available at: http://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/human-immunodeficiency-virus-hiv-infection-screening.

[15] From the USPSTF regarding screening intervals: "The evidence is insufficient to determine optimum time intervals for HIV screening. One reasonable approach would be one-time screening of adolescent and adult patients to identify persons who are already HIV-positive, with repeated screening of those who are known to be at risk for HIV infection, those who are actively engaged in risky behaviors, and those who live or receive medical care in a high-prevalence setting. According to the CDC, a high-prevalence setting is a geographic location or community with an HIV seroprevalence of at least 1%. These settings include sexually transmitted disease (STD) clinics, correctional facilities, homeless shelters, tuberculosis clinics, clinics serving men who have sex with men, and adolescent health clinics with a high prevalence of STDs. Patient populations that would more likely benefit from more frequent testing include those who are known to be at higher risk for HIV infection, those who are actively engaged in risky behaviors, and those who live in a high-prevalence setting. Given the paucity of available evidence for specific screening intervals, a reasonable approach may be to rescreen groups at very high risk (see Assessment of Risk) for new HIV infection at least annually and individuals at increased risk at somewhat longer intervals (for example, 3 to 5 years). Routine rescreening may not be necessary for individuals who have not been at increased risk since they were found to be HIV-negative. Women screened during a previous pregnancy should be rescreened in subsequent pregnancies."

Return to Table of Contents

Screening for syphilis

One annual screening for syphilis in men or women at increased risk. For pregnant women, one screening per pregnancy; two additional screenings in the third trimester and at delivery if at increased risk for STIs.

CPT® Code	Description
86592	Syphilis test, non-treponemal antibody; qualitative (eg, VDRL, RPR, ART)
86593	Syphilis test, non-troponemal antibody; quantitative
86780	Treponema pallidum

Screening for gonorrhea

One annual screening for gonorrhea in women who are not at increased risk. For pregnant women, up to two screenings per pregnancy who are at increased risk and who continue at risk for the second screening. The USPSTF does not have sufficient information to recommend screening for gonorrhea in men, and this will affect payer policies. The ACA mandated that health insurers cover screening services that the USPSTF gives an A or B rating.

CPT® Code	Description
87590	Infectious agent detection by nucleic acid (DNA or RNA) Neisseria gonorrhoeae, direct probe technique
87591	Infectious agent detection by nucleic acid (DNA or RNA) Neisseria gonorrhoeae, amplified probe technique
87592	Infectious agent detection by nucleic acid (DNA or RNA) Neisseria gonorrhoeae, quantification

Screening for hepatitis B

The USPSTF recommends screening for individuals at risk. Frequency is not described. For pregnant women, screening is recommended at the first visit. Medicare recommends and covers an additional screening at delivery if the individual is still at increased risk for STIs.

CPT® Code	Description
Infectious agent antigen detection by immunoassay technique, (eg, enzyme immunoassay [EIA], enzyme-linked immunosorbent assay [ELISA], immunochemiluminometric assay [IMCA]) qualitative or semiquantitative, multiple-step method;	
87340	hepatitis B surface antigen (HBsAg)
87341	hepatitis B surface antigen (HBsAg) neutralization

Return to Table of Contents

Screening for chlamydia

One annual screening for chlamydia in women who are not at increased risk. For pregnant women, up to two screenings per pregnancy who are at increased risk and who continue to be at risk for the second screening. The USPSTF does not have sufficient information to recommend screening for chlamydia in men.

CPT® Code	Description
86631	Antibody Chlamydia
86632	Antibody Chlamydia, IgM
87110	Culture, chlamydia, any source
87270	Infectious agent antigen detection by immunofluorescent technique chlamydia trachomatis
87320	Infectious agent antigen detection by immunoassay technique (eg, enzyme immunoassay {EIA}, enzyme–linked immunosorbent assay [ELISA], immunochemiluminometric assay [IMCA]) qualitative or semiquantitative, multiple-step method, chlamydia trachomatis
87490	Infectious disease agent detection by nucleic acid (DNA or RNA) Chlamydia trachomatis, direct probe technique
87491	Infectious diseases agent detection by nucleic acid (DNA or RNA) Chlamydia trachomatis, amplified probe technique
87810	Infectious agent antigen detection by immunoassay with direct optical observation chlamydia trachomatis

Other codes

CPT® Code	Description
87800	Infectious agent detection by nucleic acid (DNA or RNA), multiple organisms; direct probe(s) technique

Return to Table of Contents

Appendix

COMMON DIAGNOSIS CODES

ICD-10 code	Description	Use for
Z01.812	Encounter for pre-procedural laboratory examination	Use for blood or urine tests prior to treatment.
Z11.3	Encounter for screening for infections with a predominantly sexual mode of transmission	STI screening
Z11.4	Encounter for screening for human immunodeficiency virus [HIV]	HIV screening
Z20.2	Contact with and (suspected) exposure to infections with a predominantly sexual mode of transmission	HIV, STI screening
Z20.6	Contact with and (suspected) exposure to human immunodeficiency virus [HIV]	HIV screening
Z51.81	Encounter for therapeutic drug level monitoring	PrEP monitoring
Z72.51	High risk heterosexual behavior	HIV, STI screening
Z72.52	High risk homosexual behavior	HIV, STI screening
Z72.53	High risk bisexual behavior	HIV, STI screening
	Opioid abuse—no specific code for IV use	
F11.20	Opioid dependence, uncomplicated	
F11.21	Opioid dependence in remission	
F11.10	Opioid abuse, uncomplicated	
F11.90	Opioid use, uncomplicated	
Z86.59	Personal history of other mental and behavioral disorders	History of drug use. For opioid dependence in remission, use code from F11.
Z87.898	Personal history of other specified conditions	Use for a history of drug use, non-dependent, in remission.
Z72.89	Other problems related to lifestyle	Use for drug seeking behavior or unhealthy drinking behavior
Z79.899	Other long term (current) drug therapy	PrEP monitoring
Z86.59	Personal history of other mental and behavioral disorders	History of drug use. For opioid dependence in remission, use code from F11.
Z87.898	Personal history of other specified conditions	Use for a history of drug use, non-dependent, in remission.

Return to Table of Contents

PREGNANCY RELATED DIAGNOSIS CODES

ICD-10 code	Description
O09.90	Supervision of high risk pregnancy, unspecified, unspecified trimester
O09.91	Supervision of high risk pregnancy, unspecified, first trimester
O09.92	Supervision of high risk pregnancy, unspecified, second trimester
O09.93	Supervision of high risk pregnancy, unspecified, third trimester
Z34.00	Encounter for supervision of normal first pregnancy, unspecified trimester
Z34.01	Encounter for supervision of normal first pregnancy, first trimester
Z34.02	Encounter for supervision of normal first pregnancy, second trimester
Z34.03	Encounter for supervision of normal first pregnancy, third trimester
Z34.80	Encounter for supervision of other normal pregnancy, unspecified trimester
Z34.81	Encounter for supervision of other normal pregnancy, first trimester
Z34.82	Encounter for supervision of other normal pregnancy, second trimester
Z34.83	Encounter for supervision of other normal pregnancy, third trimester
Z34.90	Encounter for supervision of normal pregnancy, unspecified, unspecified trimester
Z34.91	Encounter for supervision of normal pregnancy, unspecified, first trimester
Z34.92	Encounter for supervision of normal pregnancy, unspecified, second trimester
Z34.93	Encounter for supervision of normal pregnancy, unspecified, third trimester
Z32.00	Encounter for pregnancy test result unknown
Z32.01	Encounter for pregnancy test result positive
Z32.02	Encounter for pregnancy test result negative

Return to Table of Contents

CPT® CODES

CPT® Code	Description
99201	Office or other outpatient visit for the evaluation and management of a new patient, which requires these 3 key components: A problem focused history; A problem focused examination; Straightforward medical decision making. Counseling and/or coordination of care with other physicians, other qualified health care professionals, or agencies are provided consistent with the nature of the problem(s) and the patient's and/or family's needs. Usually, the presenting problem(s) are self limited or minor. Typically, 10 minutes are spent face-to-face with the patient and/or family.
99202	Office or other outpatient visit for the evaluation and management of a new patient, which requires these 3 key components: An expanded problem focused history; An expanded problem focused examination; Straightforward medical decision making. Counseling and/or coordination of care with other physicians, other qualified health care professionals, or agencies are provided consistent with the nature of the problem(s) and the patient's and/or family's needs. Usually, the presenting problem(s) are of low to moderate severity. Typically, 20 minutes are spent face-to-face with the patient and/or family.
99203	Office or other outpatient visit for the evaluation and management of a new patient, which requires these 3 key components: A detailed history; A detailed examination; Medical decision making of low complexity. Counseling and/or coordination of care with other physicians, other qualified health care professionals, or agencies are provided consistent with the nature of the problem(s) and the patient's and/or family's needs. Usually, the presenting problem(s) are of moderate severity. Typically, 30 minutes are spent face-to-face with the patient and/or family.
99204	Office or other outpatient visit for the evaluation and management of a new patient, which requires these 3 key components: A comprehensive history; A comprehensive examination; Medical decision making of moderate complexity. Counseling and/or coordination of care with other physicians, other qualified health care professionals, or agencies are provided consistent with the nature of the problem(s) and the patient's and/or family's needs. Usually, the presenting problem(s) are of moderate to high severity. Typically, 45 minutes are spent face-to-face with the patient and/or family.
99205	Office or other outpatient visit for the evaluation and management of a new patient, which requires these 3 key components: A comprehensive history; A comprehensive examination; Medical decision making of high complexity. Counseling and/or coordination of care with other physicians, other qualified health care professionals, or agencies are provided consistent with the nature of the problem(s) and the patient's and/or family's needs. Usually, the presenting problem(s) are of moderate to high severity. Typically, 60 minutes are spent face-to-face with the patient and/or family.
99211	Office or other outpatient visit for the evaluation and management of an established patient, that may not require the presence of a physician or other qualified health care professional. Usually, the presenting problem(s) are minimal. Typically, 5 minutes are spent performing or supervising these services.
99212	Office or other outpatient visit for the evaluation and management of an established patient, which requires at least 2 of these 3 key components: A problem focused history; A problem focused examination; Straightforward medical decision making. Counseling and/or coordination of care with other physicians, other qualified health care professionals, or agencies are provided consistent with the nature of the problem(s) and the patient's and/or family's needs. Usually, the presenting problem(s) are self limited or minor. Typically, 10 minutes are spent face-to-face with the patient and/or family.
99213	Office or other outpatient visit for the evaluation and management of an established patient, which requires at least 2 of these 3 key components: An expanded problem focused history; An expanded problem focused examination; Medical decision making of low complexity. Counseling and coordination of care with other physicians, other qualified health care professionals, or agencies are provided consistent with the nature of the problem(s) and the patient's and/or family's needs. Usually, the presenting problem(s) are of low to moderate severity. Typically, 15 minutes are spent face-to-face with the patient and/or family.

Return to Table of Contents

CPT® CODES (continued)

CPT® Code	Description
99214	Office or other outpatient visit for the evaluation and management of an established patient, which requires at least 2 of these 3 key components: A detailed history; A detailed examination; Medical decision making of moderate complexity. Counseling and/or coordination of care with other physicians, other qualified health care professionals, or agencies are provided consistent with the nature of the problem(s) and the patient's and/or family's needs. Usually, the presenting problem(s) are of moderate to high severity. Typically, 25 minutes are spent face-to-face with the patient and/or family.
99215	Office or other outpatient visit for the evaluation and management of an established patient, which requires at least 2 of these 3 key components: A comprehensive history; A comprehensive examination; Medical decision making of high complexity. Counseling and/or coordination of care with other physicians, other qualified health care professionals, or agencies are provided consistent with the nature of the problem(s) and the patient's and/or family's needs. Usually, the presenting problem(s) are of moderate to high severity. Typically, 40 minutes are spent face-to-face with the patient and/or family.
99401	Preventive medicine counseling and/or risk factor reduction intervention(s) provided to an individual (separate procedure); approximately 15 minutes
99402	approximately 35 minutes
99403	approximately 45 minutes
99404	approximately 60 minutes
99411	Preventive medicine counseling and/or risk factor reduction intervention(s) provided to individuals in a group setting (separate procedure); approximately 30 minutes
99412	approximately 60 minutes
98960	Self management education and training face-to-face, 1 patient
98961	Self management education and training face-to-face, 2-4 patients
98962	Self management education and training face-to-face, 5-8 patients
G0442	Annual alcohol misuse screening, 15 minutes
G0443	Brief face-to-face behavioral counseling for alcohol misuse, 15 minutes
G0445	Semiannual high intensity behavioral counseling to prevent STIs, individual, face-to- face, includes education skills training & guidance on how to change sexual behavior, 20-30 minutes
HCPCS code	**Description**
T1017	Targeted case management, each 15 minutes
H0031	Mental health assessment, by non-physician
CPT® Code	**Description**
81025	Urine pregnancy test, by visual color comparison methods
84702	Gonadotropin, chorionic (hCG); quantitative
84703	Gonadotropin, chorionic (hCG); qualitative
80053	Comprehensive metabolic panel
82565	Creatinine; blood
82570	Creatinine other source (urine)
82575	Creatinine clearance

Return to Table of Contents

UNITED STATES PREVENTIVE SERVICES TASK FORCE (USPSTF) RECOMMENDATIONS

Population	Recommendation	Grade
	HIV SCREENING	
Adolescents and Adults 15–65 Years Old	The USPSTF recommends that clinicians screen for HIV infection in adolescents and adults aged 15 to 65 years. Younger adolescents and older adults who are at increased risk should also be screened. Go to the Clinical Considerations for more information about screening intervals.	A
Pregnant Women	The USPSTF recommends that clinicians screen all pregnant women for HIV, including those who present in labor who are untested and whose HIV status is unknown.	A
	ALCOHOL MISUSE SCREENING	
Adults aged 18 and older	The USPSTF recommends that clinicians screen adults aged 18 years or older for alcohol misuse and provide persons engaged in risky or hazardous drinking with brief behavioral counseling interventions to reduce alcohol misuse	B
Adolescents (under 18 years of age)	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening and behavioral counseling interventions in primary care settings to reduce alcohol misuse in adolescents.	I
	CHLAYMIDIA AND GONORRHEA	
Sexually Active Women	The USPSTF recommends screening for chlamydia in sexually active women age 24 years and younger and in older women who are at increased risk for infection.	B
Sexually Active Women	The USPSTF recommends screening for gonorrhea in sexually active women age 24 years and younger and in older women who are at increased risk for infection.	B
Sexually Active Men	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for chlamydia and gonorrhea in men.	I
	HEP B IN PREGNANT WOMEN	
Pregnant Women	The USPSTF recommends screening for hepatitis B virus (HBV) infection in pregnant women at their first prenatal visit	A
	HEP B AT HIGH RISK FOR INFECTION	
Persons at High Risk for Infection	The USPSTF recommends screening for hepatitis B virus (HBV) infection in persons at high risk for infection.	B
	HEP C	
Adults at High Risk	The USPSTF recommends screening for hepatitis C virus (HCV) infection in persons at high risk for infection. The USPSTF also recommends offering 1-time screening for HCV infection to adults born between 1945 and 1965.	B
	HIV	
Adolescents and Adults 15–65 Years Old	The USPSTF recommends that clinicians screen for HIV infection in adolescents and adults aged 15 to 65 years. Younger adolescents and older adults who are at increased risk should also be screened. Go to the Clinical Considerations for more information about screening intervals.	A

Return to Table of Contents

UNITED STATES PREVENTIVE SERVICES TASK FORCE (USPSTF) RECOMMENDATIONS (continued)

Population	Recommendation	Grade
	HIV	
Pregnant Women	The USPSTF recommends that clinicians screen all pregnant women for HIV, including those who present in labor who are untested and whose HIV status is unknown.	A
	SYPHILIS IN PREGNANCY	
Pregnant Women	The USPSTF recommends that clinicians screen all pregnant women for syphilis infection.	A
	SYPHILIS SCREENING	
Persons at Increased Risk	The USPSTF strongly recommends that clinicians screen persons at increased risk for syphilis infection.	A
Pregnant Women	The USPSTF strongly recommends that clinicians screen all pregnant women for syphilis infection.	A
Asymptomatic Persons, Not at Increased Risk	The USPSTF recommends against routine screening of asymptomatic persons who are not at increased risk for syphilis infection	D
	COUNSELING-ALCOHOL	
Adults aged 18 and older	The USPSTF recommends that clinicians screen adults aged 18 years or older for alcohol misuse and provide persons engaged in risky or hazardous drinking with brief behavioral counseling interventions to reduce alcohol misuse.	B
Adolescents (under 18 years of age)	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening and behavioral counseling interventions in primary care settings to reduce alcohol misuse in adolescents.	I
	COUNSELING-BEHAVIORAL	
Sexually Active Adolescents and Adults	The USPSTF recommends intensive behavioral counseling for all sexually active adolescents and for adults who are at increased risk for sexually transmitted infections (STIs).	B

Return to Table of Contents

Glossary

AMA	American Medical Association
APRN	Advance Practice Registered Nurse
CCM	Chronic Care Management
CDC	Centers for Disease Control and Prevention
CMS	Centers for Medicare and Medicaid Services
CHW	Community Health Workers
E/M	Evaluation and Management
HCPCS	Healthcare Common Procedure Coding System
HIV	human immunodeficiency virus
ICD-10-CM	International Classification of Diseases, 10th revision, Clinical Modifications
NASTAD	National Alliance of State & Territorial AIDS Directors
PA	Physician Assistant
PrEP	Pre-exposure prophylaxis
STI	Sexually transmitted infection
USPSTF	United States Preventive Services Task Force

Return to Table of Contents

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Murray C. Penner, Executive Director

Andrew Gans, New Mexico, Chair

April 2016

Return to Table of Contents


NASTAD

HARFORD COUNTY HEALTH DEPARTMENT POLICY

Title of Policy: Overview of HCHD Clinical Services Billing Policy & Procedures	
Program Area: Clinical Service Programs	
Approved By: Russell Moy, M.D.	Original Effective Date: 11/1/2013
	Revised Dates: 4/18/18, 11/17/17, 10/16/17, 7/1/17

1.0 POLICY

As a unit of the Maryland Department of Health, the Harford County Health Department (HCHD) follows regulations for determining CPT/HCPCS-based charges for local health department clinical services (COMAR 10.02.01). For low income patients needing financial assistance, local health departments may discount service charges, using the MDH approved sliding fee scale.

2.0 PURPOSE

HCHD is a major safety net provider of clinical services for Harford County residents. Patients are not turned away for inability to pay. HCHD's Clinical Services Billing Policy and Procedures, which includes the Sliding Fee Scale Program, provides a mechanism for discounting service charges in accordance with a patient's ability to pay. In order to sustain these safety net clinical services to those in need in the community, HCHD must maximize third party insurance reimbursements for services rendered.

3.0 PROCEDURES

3.1 Practice Administrator is responsible, on behalf of HCHD Executive Direction, for assuring an effective and efficient patient flow and revenue cycle management for all Departmental clinical services **(Attachment 1).**

3.1.1 The Practice Administrator reports to HCHD Executive Direction.

3.1.2 The Practice Administrator works with the Program Manager to assure that a senior programmatic staff person has responsibility for administrative and clinical coverage for each individual HCHD clinic session.

3.1.3 The Practice Administrator assures that all front-end revenue cycle management processes are in place.

3.1.3.1 Patient demographics, photo identification, insurance and income information are collected.

3.1.3.2 Insurance coverage is verified.

3.1.3.3 Financial obligations and responsibilities are clarified.

3.1.3.4 Eligibility and benefits verification tools are utilized (e.g., EVS Medicaid, MCO and other payer web sites/provider portals/telephone calls, insurance identification cards, practice management systems electronic eligibility, clearinghouse electronic eligibility).

3.1.4 The Practice Administrator also has oversight responsibility for HCHD's Central Billing Office back-end revenue cycle management processes in Bel Air.

3.1.4.1 Assures that encounter form/superbill information needed for charge entries is in place.

3.1.4.2 Monitors changes in HCHD services, determines a charge for such services, and obtains approval from the Maryland Department of Health to add such services to their list of charges.

3.1.4.3 Monitors and updates CPT/HCPCS codes and fees in the practice management system as needed.

3.1.4.4 Verifies that claims information is complete and accurate, prior to submission.

3.1.4.5 Verifies that electronic claim files are received by the clearinghouse.

3.1.4.6 Prints and sends paper claims when required by insurance.

3.1.4.7 Assures that patient statements are sent on a monthly cycle.

3.1.4.8 Manages account receivables and insurance payment postings.

3.1.4.9 Manages insurance claim denials.

3.1.4.10 Manages aging accounts and central collections unit submissions.

3.1.4.11 Produces and reviews with HCHD Executive Direction key performance indicators and management control reports.

3.1.4.12 Assures that clinic billing practices are consistent with federal and state requirements, including those for Title X Federal Family Planning and the Vaccines for Children (VFC) Program.

3.2 Program Manager is responsible, on behalf of HCHD's programmatic service (such as Behavioral Health or Women's Health), for clinical activities, as well as for the safety of patients and staff, for the assigned clinic session.

3.2.1 The Program Manager reports to HCHD Executive Direction.

3.2.2 The Program Manager works with the Practice Administrator to assure that a senior programmatic staff person is identified and has overall responsibility for each HCHD clinic session.

3.2.3 The Program Manager has responsibility for the quality and efficiency of the HCHD programmatic service.

3.3 Scheduler:

3.3.1 Clinic scheduling is a joint responsibility of the Practice Administrator and Program Manager.

3.3.1.1 The Practice Administrator is primarily responsible for efficient scheduling of patients in order to maximize the number of patients served and the amount of revenue collected.

3.3.1.2 The Program Manager is primarily responsible for assuring quality of care and safety in the clinic.

3.3.2 Scheduler determines what type of visit is being requested (e.g., problem visit; new patient visit; established patient visit; emergencies should be referred to the Emergency Department).

3.3.3 Scheduler obtains pertinent information (including name, address, telephone, date of birth, insurance information, employment and/or other information) and enters this information into the practice management system.

3.3.4 Scheduler informs the patient of other documents to bring (including legal identification, insurance card, co-payments, and proof of income if uninsured).

3.3.5 Scheduler gives an estimated charge for the visit and informs the patient that co-pays or other fees due are expected at the time of visit.

3.3.6 Scheduler asks that the patient arrive at least 15 minutes before appointment time in order to complete the necessary paperwork.

3.3.7 On the day of the appointment, the Medicaid EVS system is checked to see if the patient has Medicaid coverage (and documentation is scanned into the practice management system).

3.4 Front Desk Associate

3.4.1 The patient is greeted and offered Limited English Proficiency (LEP) services and/or other accommodation services, as appropriate.

3.4.2 The patient signs in and the reason for the visit is verified.

3.4.3 The Front Desk Associate determines the patient's method of payment and obtains insurance information, as needed. Pertinent information, including insurance card and driver's license, is scanned, entered and updated into the practice management system.

3.4.4 **"HCHD Consent, Financial Agreement, Notice of Privacy Practices and Other Information for Patients Form" (Attachment 2),** as well as other pertinent forms, are reviewed with the patient. Important items include:

3.4.4.1 **Consent to Treatment**: Patients sign the Form to consent to treatment.

3.4.4.2 **Authorization to Release Information and Pay Insurance Benefits**: Patients sign the Form to authorize release of information to other health care providers as necessary and to insurance companies for payment.

3.4.4.3 **Notice of HCHD's HIPAA Privacy Practices**: Patients sign the Form acknowledging their understanding of how medical information may be used and disclosed, including the sharing of their information with CRISP, Maryland's statewide health information exchange and the patient's right to opt-out of CRISP.

3.4.5 A full financial intake interview is conducted for those patients who ask to apply for the Sliding Fee Scale Program.

3.4.6 A full financial intake interview is not required for patients with Medicaid (including Medicaid MCO) insurance coverage.

3.5 Financial Associate reviews and verifies that the patient has signed, electronically or by hard copy, the HCHD Consent, Financial Agreement, Notice of Privacy Practices Form. Pertinent points include the following:

3.5.1 **For patients with Medicaid/Medicaid MCO insurance**, full financial intake interview is not required at the initial visit.

3.5.2 **For patients with commercial insurance or Medicare** that may require co-payments, deductibles, coinsurance or other cost-sharing reductions, full financial intake interview should be done at the initial visit.

3.5.3 **For patients who ask to apply for HCHD's Sliding Fee Scale Program**, a full financial intake interview will be required.

3.5.4 **The Client must apply for Medicaid or Qualified Health Plan, if eligible**: Patients who are eligible for Medicaid or Qualified Health Plans are expected to apply for this coverage. Assistance with the application process will be offered to those who request it.

3.5.5 **No co-payments, deductibles, coinsurance or other cost-sharing reductions are required, if Medicaid/MCO is the patient's only insurance**: HCHD is a participating provider with Medicaid; consequently, patients who have Medicaid (including all MCOs) coverage will have no

cost sharing responsibilities, i.e., the patient will not have to pay anything for the visit.

3.5.6 **No co-payments, deductibles, coinsurance or other cost-sharing reductions are required, if Medicaid/MCO is the patient's secondary payer**: Patients with primary commercial insurance and secondary Medicaid insurance will also have no cost sharing responsibilities, i.e., the patient will not have to pay anything for the visit.

3.5.7 **Co-payments, deductibles, coinsurance or other cost-sharing reductions are required, if on commercial insurance or Medicare**: For commercial insurance, co-payments are expected at time of service, regardless of HCHD being a participating or non-participating provider. However, under federal health care reform, many preventive services (including annual well-woman visit and contraceptive services visit) will not require co-payments.

3.5.8 **HCHD is currently not a participating provider with all commercial insurance companies**: Patients should be informed that HCHD is currently not a participating provider with some commercial insurers; consequently, the patient will be responsible for the balance unpaid by insurance. For this reason, the patient may elect to be seen by a participating provider, instead of the HCHD Clinic.

3.5.9 **After HCHD receives the commercial insurance or Medicare "paid amount" portion of the charge, it will then bill the patient for the remaining "patient liability" portion of the charge:** HCHD will submit billing for medical services to the patient's commercial insurance company on file; however, the patient/guarantor remains responsible for the balance due.

3.5.10 **Pre-authorization** for services will be obtained, if needed.

3.5.11 **Sliding Fee Scale Program**: Patients who are not eligible for Medicaid or Qualified Health Plans, who are uninsured or underinsured, and who need financial assistance may apply for HCHD's Sliding Fee Scale Program. The Sliding Fee Scale is available to all patients who qualify even if they have insurance, but will have difficulty paying their co-payments, deductibles, coinsurance or other fees.

3.5.11.1 **Based on Ability to Pay:** The Sliding Fee Scale Program, based on household income and family size, reduces the amount the patient must pay for clinical services. This Program is based on the Maryland Department of Health's "Ability to Pay" schedule **(Attachment 3).**

3.5.11.2 **Income documentation is required** for the Sliding Fee Scale Program and includes: (1) identification with address (e.g., driver's license, gas and electric bill, telephone bill); and (2) one of the following: pay stubs, 1040 tax form, government benefits letter, statement of wages on company letterhead, unemployment stubs, letter of reference from a charitable organization, verification of no income support letter or a self-report of income.

Although not required to do so, we have lawful access to other valid means of income verification because of the client's participation in another program and may use those data rather than re-verify income or rely solely on client's self-report.

3.5.11.3 **Financial Agreement**: Acceptance into the Sliding Fee Scale Program will require a financial intake interview in which the patient will be informed of the discounted amount owed and a financial agreement will be signed by the patient.

3.5.11.4 **Annual redetermination**: Eligibility for the Sliding Fee Scale Program will be re-determined at least once every 12 months.

3.5.11.5 **Choosing not to disclose family income**: Those patients who choose not to disclose family income, or who do not provide proof of income within 30 days of their initial visit, will not be eligible for the Sliding Fee Scale Program and will be responsible for full fee, non-discounted, charges according to HCHD's established fee policy.

3.5.11.6 **Payment due on day of service**: Full fee and sliding fee scale patients are expected to pay all or part of their charges, including any administrative fees, on the day of service.

3.5.11.7 **No other discounted services**: Except for the Sliding Fee Scale Program, HCHD offers no other discounted services, including reduced fee or payment plans. Requests to waive charges must have the written approval of the Program Director and Health Officer/designee.

3.5.12 **Waiving Charges:** Consistent with Maryland Health-General §3-306, "Health Officers and Baltimore City Commissioner of Health – Authority to Retain Collections and Waive Charges," a charge may be waived if a Health Officer considers it to be in the best interest of public health.

3.5.12.1 **HCHD will bill all applicable out-of-pocket amounts and make reasonable efforts to collect such amounts** in accordance with our collection practices and procedures. However, if HCHD determines that the patient's financial situation meets the criteria in this policy and that a patient is financially unable to pay out-of-pocket amounts, the HCHD Health Officer/designee may waive or lower such amounts.

3.5.12.2 **Waiver of Clinic Charge Request:** On a case-by-case basis, if the HCHD Program Manager has reviewed a patient's financial and health situation and determined that it is appropriate to waive or reduce the patient's clinic charge, then a written waiver request to the Health Officer and/or designee should be submitted **(Attachment 5).**

3.5.12.3 **Required Written Documentation** for waiving charges includes:

3.5.12.3.1 **Identifying information for the patient**, including name, date of birth, date of service.

3.5.12.3.2 **Name of the HCHD Program Manager** requesting the charge waiver.

3.5.12.3.3 **Amount of the charge** for which the waiver is being requested.

3.5.12.3.4 **Justification for the waiver request**, including a review of the patient's financial intake and health information and the rationale for waiving the clinic charges, should be submitted to the Health Officer/designee.

3.5.12.4 **Health Officer/designee will ultimately approve or deny the waiver charge request,** on a case by case basis. The Health Officer/designee's written decision will be included/scanned into the patient's medical record.

3.6 Central Collections Unit: HCHD follows State law and utilizes/follows CCU collection procedure protocols. Unpaid patient balances are due within 90 days of the date that the first Patient Statement was mailed.

3.6.1 **By State law**, patient accounts that are unpaid within this timeframe must then be forwarded to the State Central Collection Unit (CCU) which charges the patient a 17% penalty, in addition to the amount owed.

3.6.2 **Per CCU protocol, patient balances less than $30 will not be forwarded to CCU.** A complete copy of the CCU protocol can be found in the DHMH Billing Manual at: http://forms.dhmh.maryland.gov/lhdbilling/index.html

3.6.3 **Health Officer/designee will review the patient account and ultimately make the decision** to forward a patient's account to CCU. The Health Officer/designee's written decision will be included/scanned into the patient's medical record.

3.7 Clinical Encounter

3.7.1 Trained health care professional conducts a clinical assessment of the patient.

3.7.2 The provider (physician/nurse practitioner/counselor/other clinician) conducts the clinical examination or encounter.

3.7.2.1 The provider is responsible for the documentation of the clinical visit.

3.7.2.2 The provider is responsible for indicating the most appropriate and specific ICD 10 diagnosis code and designate the appropriate service/treatment (CPT/HCPCS) code(s) on the patient's superbill.

3.7.2.3 The provider is responsible for linking the appropriate ICD 10 code to the appropriate CPT/HCPCS code.

3.7.2.4 The provider is responsible for designating the appropriate number of units and NDC code to the service/treatment CPT/HCPCS code.

3.7.3 Trained health care professional carries out post-examination/encounter orders, including medication, laboratory, referral orders, and provides educational training and documents, as needed.

3.8 Check-Out Process. Front Desk Associate or Financial Associate is responsible for the check-out process which includes the following:

3.8.1 Determines and posts into the practice management system the appropriate fees based on the fee schedule and procedures performed, as stated in the Superbill completed by the provider.

3.8.2 Collects the fees and generates a Patient Receipt from the billing system.

3.8.3 Reviews encounter forms for sufficiency and completeness.

3.8.4 Makes the follow up appointment, as needed.

3.8.5 At the end of each business day, the Practice Administrator and Program Manager are jointly responsible for close out procedures, including the reconciliation of cash, checks, credit card transactions, charges, and other clinic service documents that will be forwarded to the HCHD Central Billing Office in Bel Air.

3.8.6 The Practice Administrator oversees the back-end revenue cycle management duties in the HCHD Central Billing Office.

BOTTOM	TOP	1	2	3	4	5	6	7	8	9	10
$0	$5,700	Patients that fall into this bracket need to apply for Medical Assistance									
$5,701	$6,200	$5									
$6,201	$6,700	$5	$5								
$6,701	$7,200	$5	$5	$5							
$7,201	$7,752	$5	$5	$5	$5						
$7,753	$8,376	$5	$5	$5	$5	$5					
$8,377	$9,240	$5	$5	$5	$5	$5	$5				
$9,241	$10,008	$5	$5	$5	$5	$5	$5	$5			
$10,009	$10,692	$5	$5	$5	$5	$5	$5	$5	$5		
$10,693	$11,412	$5	$5	$5	$5	$5	$5	$5	$5	$5	
$11,413	$11,770	$5	$5	$5	$5	$5	$5	$5	$5	$5	$5
$11,771	$13,328	5%	$5	$5	$5	$5	$5	$5	$5	$5	$5
$13,329	$15,930	10%	$5	$5	$5	$5	$5	$5	$5	$5	$5
$15,931	$16,500	15%	5%	$5	$5	$5	$5	$5	$5	$5	$5
$16,501	$17,992	20%	10%	$5	$5	$5	$5	$5	$5	$5	$5
$17,993	$20,090	25%	15%	$5	$5	$5	$5	$5	$5	$5	$5
$20,091	$22,350	30%	20%	10%	$5	$5	$5	$5	$5	$5	$5
$22,351	$24,250	35%	25%	15%	$5	$5	$5	$5	$5	$5	$5
$24,251	$27,010	40%	30%	20%	10%	$5	$5	$5	$5	$5	$5
$27,011	$28,410	50%	35%	25%	15%	$5	$5	$5	$5	$5	$5
$28,411	$30,970	60%	40%	30%	20%	10%	$5	$5	$5	$5	$5
$30,971	$32,570	70%	45%	35%	25%	15%	$5	$5	$5	$5	$5
$32,571	$34,930	80%	50%	40%	30%	20%	10%	$5	$5	$5	$5
$34,931	$36,730	90%	55%	45%	35%	25%	15%	$5	$5	$5	$5
$36,731	$38,890	100%	60%	50%	40%	30%	20%	10%	$5	$5	$5
$38,891	$40,890	100%	70%	55%	45%	35%	25%	15%	$5	$5	$5
$40,891	$41,500	100%	80%	60%	50%	40%	30%	20%	10%	$5	$5
$41,501	$45,050	100%	90%	65%	55%	45%	35%	25%	15%	$5	$5
$45,051	$46,000	100%	100%	70%	60%	50%	40%	30%	20%	10%	$5
$46,001	$49,210	100%	100%	75%	65%	55%	45%	35%	25%	15%	$5
$49,211	$51,000	100%	100%	80%	70%	60%	50%	40%	30%	20%	10%
$51,001	$55,710	100%	100%	90%	75%	65%	55%	45%	35%	25%	15%
$55,711	$58,875	100%	100%	100%	80%	70%	60%	50%	40%	30%	20%
$58,876	$61,600	100%	100%	100%	85%	75%	65%	55%	45%	35%	25%
$61,601	$63,470	100%	100%	100%	90%	80%	70%	60%	50%	40%	30%
$63,471	$65,890	100%	100%	100%	100%	90%	80%	65%	55%	45%	35%
$65,891	$67,760	100%	100%	100%	100%	100%	90%	70%	60%	50%	40%
$67,761	$69,925	100%	100%	100%	100%	100%	100%	80%	65%	55%	45%
$69,926	$71,795	100%	100%	100%	100%	100%	100%	90%	70%	60%	50%
$71,796	$73,665	100%	100%	100%	100%	100%	100%	95%	75%	65%	55%
$73,666	$75,535	100%	100%	100%	100%	100%	100%	100%	80%	70%	60%
$75,536	$77,405	100%	100%	100%	100%	100%	100%	100%	85%	75%	65%
$77,406	$80,753	100%	100%	100%	100%	100%	100%	100%	90%	80%	70%
$80,754	$82,623	100%	100%	100%	100%	100%	100%	100%	95%	85%	75%
$82,624	$84,493	100%	100%	100%	100%	100%	100%	100%	100%	90%	80%
$84,494	$86,363	100%	100%	100%	100%	100%	100%	100%	100%	95%	85%
$86,364	$88,233	100%	100%	100%	100%	100%	100%	100%	100%	100%	90%
$88,234	$89,025	100%	100%	100%	100%	100%	100%	100%	100%	100%	95%
$89,026	$90,895	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
$90,896	$92,765	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
$92,766	$94,635	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
$94,636	and up	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%

Sliding Fee Scale Notes

FOR INTERNAL USE ONLY

Legend:

Purple - These patients need to apply for Medical Assistance

Red - These patients fall below the povery line and pay:
Non family planning services - $5.00 per visit
Family planning services - $0.00 - no charge for the visit

Blue - Patient is responsible for the percentage shown of each CPT code
There is a minimum visit charge of $8.00

Green - Patient does not qualify for a reduction of charges

*Always round income to the closest whole dollar, never use cents

Dependents	100% of Poverty
1	11,770
2	15,930
3	20,090
4	24,250
5	28,410
6	32,570
7	36,730
8	40,890
9	45,050
10	49,210

Public Health
Prevent. Promote. Protect.

Harford County Health Department

PatagoniaHealth

Health Department HCHD Woodbridge

Welcome, Jean M Toth, RN

Page Settings | Sign Out

Harford County

Patient search

FeeSchedule | Sliding Fee Scale Administration | Service Billing Mapping

Fee scales defined in this department are listed below. Click on a row to edit a fee scale.

Loading...

Sliding Fee Scale List

	Name	Start Date	End Date
☐	Maryland 2019 Ability to Pay No Minimum	07/01/2018	06/30/2019
☐	Maryland 2019 Ability to Pay with 5 8 minimum	07/01/2018	06/30/2019
☐	Maryland SFS-Only0	07/01/2018	06/30/2019
☐	Maryland SFS-Only0	07/01/2017	06/30/2018

Page 1 of 1 10

Add New Fee Scale **Import Fee Scale** **Export Fee Scale**

FPL - Editing Maryland 2019 Ability to Pay with 5 8 minim

1. **Programs Included**
Following programs apply to this Fee Scale. Select programs to add from down below

Select programs to include in the SFS

CH-PREP

2.

Name : Marylar

Status : Activ

Start Date : 07/01

Sliding Fee Scale :

Family Size	Partial Pay Bracket (0.01%) From	To	Partial Pay Bracket (0.05%) From	To	Partial Pay Bracket (5%) From	To	Partial Pay Bracket (10%) From	To	Partial Pay Bracket (15%) From	To	Partial Pay Bracket (20%) From	To	Partial Pay Bracket (25%) From	To	Partial Pay Bracket (30%) From	To	Partial Pay Bracket (35%) From	To	Partial Pay Bracket (40%) From	To	Partial Pay Bracket (45%) From	To	Partial Pay Bracket (50%) From	To	Partial Pay Bracket (55%) From	To	F
1	$0	$6,2	$6,211	$12,	$12,14	$14,	$14,08	$16,	$16,46	$17,	$17,99	$19,	$19,09	$20,	$20,78	$22,	$22,46	$25,	$25,10	$27,	$27,01	$27,	$27,01	$29,	$29,42	$29,	$
2	$0.1	$6,6	$6,601	$16,	$16,46	$17,	$17,99	$19,	$19,09	$20,	$20,78	$22,	$22,46	$25,	$25,10	$27,	$27,01	$29,	$29,42	$30,	$30,45	$33,	$33,74	$34,	$34,93	$38,	$
3	$0.2	$7,5	$7,501	$20,	$20,78	$20,	$20,78	$22,	$22,46	$25,	$25,10	$27,	$27,01	$29,	$29,42	$30,	$30,45	$33,	$33,74	$34,	$34,93	$38,	$38,06	$41,	$41,15	$42,	$
4	$0.3	$8,1	$8,181	$25,	$25,10	$25,	$25,10	$27,	$27,01	$29,	$29,42	$30,	$30,45	$33,	$33,74	$34,	$34,93	$38,	$38,06	$41,	$41,15	$42,	$42,38	$44,	$44,19	$46,	$
5	$0.4	$8,7	$8,733	$29,	$29,42	$29,	$29,42	$30,	$30,45	$33,	$33,74	$34,	$34,93	$38,	$38,06	$41,	$41,15	$42,	$42,38	$44,	$44,19	$46,	$46,70	$49,	$49,74	$51,	$
6	$0.5	$9,3	$9,357	$33,	$33,74	$33,	$33,74	$34,	$34,93	$38,	$38,06	$41,	$41,15	$42,	$42,38	$44,	$44,19	$46,	$46,70	$49,	$49,74	$51,	$51,02	$53,	$53,00	$55,	$
7	$0.6	$10,	$10,22	$38,	$38,06	$38,	$38,06	$41,	$41,15	$42,	$42,38	$44,	$44,19	$46,	$46,70	$49,	$49,74	$51,	$51,02	$53,	$53,00	$55,	$55,71	$58,	$58,87	$61,	$
8	$0.7	$10,	$10,98	$42,	$42,38	$42,	$42,38	$44,	$44,19	$46,	$46,70	$49,	$49,74	$51,	$51,02	$53,	$53,00	$55,	$55,71	$58,	$58,87	$61,	$61,60	$63,	$63,74	$65,	$

Family Size	Partial Pay Bracket (0.01%)		Partial Pay Bracket (0.05%)		Partial Pay Bracket (5%)		Partial Pay Bracket (10%)		Partial Pay Bracket (15%)		Partial Pay Bracket (20%)		Partial Pay Bracket (25%)		Partial Pay Bracket (30%)		Partial Pay Bracket (35%)		Partial Pay Bracket (40%)		Partial Pay Bracket (45%)		Partial Pay Bracket (50%)		Partial Pay Bracket (55%)		
	From	To	From	To	From	To	From	To	From	To	From	To	From	To	From	To	From	To	From	To	From	To	From	To	From	To	F
9	$0.8	$11,	$11,66	$46,	$46,70	$46,	$46,70	$49,	$49,74	$51,	$51,02	$53,	$53,00	$55,	$55,71	$58,	$58,87	$61,	$61,60	$63,	$63,74	$65,	$65,89	$67,	$67,76	$69,	$
10	$0.9	$11,	$11,84	$51,	$51,02	$51,	$51,02	$53,	$53,00	$55,	$55,71	$58,	$58,87	$61,	$61,60	$63,	$63,74	$65,	$65,89	$67,	$67,76	$69,	$69,92	$71,	$71,79	$73,	$

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PATIENT RESOURCES

What is PrEP?

PrEP 101

Are you HIV-negative but at very high risk for HIV? Taken every day, PrEP can help keep you free from HIV.

What Is PrEP?

- PrEP, or pre-exposure prophylaxis, is daily medicine that can reduce your chance of getting HIV.
- PrEP can stop HIV from taking hold and spreading throughout your body.
- Daily PrEP reduces the risk of getting HIV from sex by more than 90%. Among people who inject drugs, it reduces the risk by more than 70%.
- Your risk of getting HIV from sex can be even lower if you combine PrEP with condoms and other prevention methods.



Is PrEP Right For You?

PrEP may benefit you if you are HIV-negative and **ANY** of the following apply to you.

You are a gay/bisexual man and

- have an HIV-positive partner.
- have multiple partners, a partner with multiple partners, or a partner whose HIV status is unknown–and you also
  - have anal sex without a condom, or
  - recently had a sexually transmitted disease (STD).

You are a heterosexual and

- have an HIV-positive partner.
- have multiple partners, a partner with multiple partners, or a partner whose HIV status is unknown–and you also
  - don't always use a condom for sex with people who inject drugs, or
  - don't always use a condom for sex with bisexual men.

You inject drugs and

- share needles or equipment to inject drugs.
- recently went to a drug treatment program.
- are at risk for getting HIV from sex.



Visit Your Healthcare Provider

- To find out if PrEP is right for you.
- Every 3 months, if you take PrEP, for repeat HIV tests, prescription refills, and follow-up.
- If you have any symptoms while taking PrEP that become severe or don't go away.
- If you don't have a provider, visit https://preplocator.org to locate one.



How Can You Get Help To Pay For PrEP?

- Most private and state Medicaid plans cover PrEP. If you are on Medicaid, check with your benefits counselor.
- If you have health insurance, you may receive co-pay assistance from drug manufacturers or patient advocacy foundations.
- If you are without medical insurance, consider enrolling in an insurance marketplace, manufacturer patient assistance program, or your state's Medicaid plan, if you are eligible for it.
- Learn more about paying for PrEP at www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-paying-for-prep.pdf.

For more information please visit www.cdc.gov/hiv

National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention
Division of HIV/AIDS Prevention

Marzo de 2018

Información básica sobre la PrEP

¿Es usted VIH negativo, pero tiene un alto riesgo de contraer el VIH? Si toma los medicamentos de la PrEP todos los días, estos pueden mantenerlo libre de la infección por el VIH.

¿Qué es la PrEP?

- La PrEP, o profilaxis prexposición, son medicamentos diarios que pueden reducir las probabilidades de contraer el VIH.
- La PrEP puede impedir que el VIH se establezca y se propague en el cuerpo.
- La PrEP diaria puede reducir en más del 90 % el riesgo de que usted contraiga el VIH a través de las relaciones sexuales. En las personas que se inyectan drogas, reduce el riesgo en más del 70 %.
- El riesgo de contraer el VIH a través de las relaciones sexuales puede reducirse aún más si la PrEP se combina con el uso de condones y otros métodos de prevención.



¿Es la PrEP lo adecuado para usted?

La PrEP puede ser de beneficio si usted es VIH negativo y si **CUALQUIERA** de las siguientes condiciones aplican a usted:

Usted es un hombre gay o bisexual y

- tiene una pareja VIH positiva;
- tiene múltiples parejas sexuales, su pareja tiene múltiples parejas o si usted no sabe si su pareja tiene el VIH; y también
  - tiene relaciones sexuales anales sin condón, o
  - tuvo hace poco una enfermedad de transmisión sexual (ETS).

Usted es heterosexual y

- tiene una pareja VIH positiva;
- tiene múltiples parejas sexuales, su pareja tiene múltiples parejas o si usted no sabe si su pareja tiene el VIH; y
  - no siempre usa condones cuando tiene relaciones sexuales con personas que se inyectan drogas, o
  - no siempre usa condones cuando tiene relaciones sexuales con hombres bisexuales.

Usted se inyecta drogas y

- comparte las agujas o los implementos para inyectarse las drogas;
- fue hace poco a un programa de tratamiento para la drogadicción; o
- está en riesgo de contraer el VIH a través de las relaciones sexuales.



Visite a su proveedor de atención médica

- Para averiguar si la PrEP es lo adecuado para usted.
- Cada 3 meses si está tomando los medicamentos de la PrEP, para repetir las pruebas de detección del VIH, surtir sus medicamentos y hacer seguimiento.
- Si mientras está tomando los medicamentos de la PrEP tiene algún síntoma que se ha vuelto intenso o no desaparece.
- Si no tiene un proveedor, visite https://preplocator.org para localizar uno.



¿Cómo puede obtener ayuda para pagar la PrEP?

- La mayoría de los planes privados y los planes estatales de Medicaid cubren la PrEP. Si tiene la cobertura de Medicaid, hable con su asesor de beneficios.
- Si tiene seguro médico, puede recibir asistencia del fabricante del medicamento o de una fundación de defensa del paciente para cubrir el copago.
- Si no tiene seguro médico, piense en inscribirse en uno de los planes del mercado de seguros, en el programa de asistencia del fabricante o en el plan de Medicaid de su estado si cumple los requisitos.
- Obtenga más información sobre cómo pagar la PrEP en www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-paying-for-prep.pdf.

Para obtener más información visite la página www.cdc.gov/hiv/spanish

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MLS-280328_r

PrEP Information Sheet

Pre-exposure Prophylaxis (PrEP) for HIV Prevention

Frequently Asked Questions

What is PrEP?

"PrEP" stands for preexposure prophylaxis. The word "prophylaxis" (pronounced pro fil ak sis) means to prevent or control the spread of an infection or disease. The goal of PrEP is to prevent HIV infection from taking hold if you are exposed to the virus. This is done by taking a pill that contains 2 HIV medications every day. These are the same medicines used to stop the virus from growing in people who are already infected.

Why take PrEP?

The HIV epidemic in the United States is growing. About 50,000 people get infected with HIV each year. More of these infections are happening in some groups of people and some areas of the country than in others.

Is PrEP a vaccine?

No. PrEP medication does not work the same way as a vaccine. When you take a vaccine, it trains the body's immune system to fight off infection for years. You will need to take a pill every day by mouth for PrEP medications to protect you from infection. PrEP does not work after you stop taking it. The medication that was shown to be safe and to help block HIV infection is called "Truvada" (pronounced tru va duh). Truvada is a combination of 2 drugs (tenofovir and emtricitabine). These medicines work by blocking important pathways that the HIV virus uses to set up an infection. If you take Truvada as PrEP daily, the presence of the medication in your bloodstream can often stop the HIV virus from establishing itself and spreading in your body. If you do not take the Truvada pills every day, there may not be enough medicine in your blood stream to block the virus.

Should I consider taking PrEP?

PrEP is not for everyone. Doctors prescribe PrEP for some patients who have a very high risk of coming in contact with HIV by not using a condom when they have sex with a person who has HIV infection. You should consider PrEP if you are a man or woman who sometimes has sex without using a condom, especially if you have a sex partner who you know has HIV infection. You should also consider PrEP if you don't know whether your partner has HIV infection but you know that your partner is at risk (for example, your partner inject drugs or is having sex with other people in addition to you) or if you have recently been told by a health care provider that you had a sexually transmitted infection. If your partner has HIV infection, PrEP may be an option to help protect you from getting HIV infection while you try to get pregnant, during pregnancy, or while breastfeeding.

How well does PrEP work?

PrEP was tested in several large studies with men who have sex with men, men who have sex with women, and women who have sex with men. All people in these studies (1) were tested at the beginning of the trial to be sure that they did not have HIV infection, (2) agreed to take an oral PrEP tablet daily, (3) received intensive counseling on safer-sex behavior, (4) were tested regularly for sexually transmitted infections, and (5) were given a regular supply of condoms.

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Several studies showed that PrEP reduced the risk of getting HIV infection.

- Men who have sex with men who were given PrEP medication to take, were 44% less likely to get HIV infection than were those men who took a pill without any PrEP medicine in it (a placebo). Forty-four percent was an average that included men who didn't take the medicine every day and those who did. Among the men who said they took most of their daily doses, PrEP reduced the risk of HIV infection by 73% or more, up to 92% for some.
- Among men and women in couples in which one partner had HIV infection and the other partner initially did not ("HIV-discordant" couples), those who received PrEP medication were 75% less likely to become infected than those who took a pill without any medicine in it (a placebo). Among those who said they took most of their daily doses, PrEP reduced the risk of HIV infection by up to 90%.
- In one study of men and women who entered the study as individuals (not as a couple), PrEP worked for both men and women in one study: those who received the medication were 62% less likely to get HIV infection; those who said they took most of their daily doses, were 85% less likely to get HIV infection. But in another study, only about 1 in 4 women (<26%) had PrEP medication found in their blood when it was checked. This indicated that few women were actually taking their medication and that study found no protection against HIV infection.

More information on the details of these studies can be found at www.cdc.gov/hiv/prep.

Is PrEP safe?

The clinical trials also provided safety information on PrEP. Some people in the trials had early side effects such as an upset stomach or loss of appetite but these were mild and usually went away within the first month. Some people also had a mild headache. No serious side effects were observed. You should tell your doctor if these or other symptoms become severe or do not go away.

How can I start PrEP?

If you think you may be at high risk for HIV, talk to your doctor about PrEP. If you and your doctor agree that PrEP might reduce your risk of getting HIV infection, you will need to come in for a general health physical, blood tests for HIV, and tests for other infections that you can get from sex partners. Your blood will also be tested to see if your kidneys and liver are functioning well. If these tests show that PrEP medicines are likely to be safe for you to take and that you might benefit from PrEP, your doctor may give you a prescription after discussing it with you.

Taking PrEP medicines will require you to follow-up regularly with your doctor. You will receive counseling on sexual behaviors and blood tests for HIV infection and to see if your body is reacting well to Truvada. You should take your medicine every day as prescribed, and your doctor will advise you about ways to help you take it regularly so that it stands the best chance to help you avoid HIV infection. Tell your doctor if you are having trouble remembering to take your medicine or if you want to stop PrEP.

If I take PrEP can I stop using condoms when I have sex?

You should not stop using condoms because you are taking PrEP. If PrEP is taken daily, it offers a lot of protection against HIV infection, but not 100%. Condoms also offer a lot of protection against HIV infection if they are used correctly every time you have sex, but not 100%. PrEP medications don't give you any protection from other infections you can get during sex, but condoms do. So you will get the most protection from HIV and other sexual infections if you consistently take PrEP medication and consistently use condoms during sex.

How long do I need to take PrEP?

You should discuss this with your doctor. There are several reasons that people stop taking PrEP. If your risk of getting HIV infections becomes low because of changes that occur in your life, you may want to stop taking PrEP. If you find you don't want to take a pill every day or often forget to take your pills, other ways of protecting yourself from HIV infection may work better for you. If you have side effects from the medication that are interfering with your life or if blood tests show that your body is reacting to PrEP in unsafe ways, your doctor may stop prescribing PrEP for you.

Hoja informativa sobre la PrEP

Profilaxis prexposición (PrEP) para prevenir el VIH

Preguntas frecuentes

¿Qué es la PrEP?

"PrEP" es la sigla en inglés de "profilaxis prexposición". La palabra "profilaxis" significa prevención o control de la propagación de una infección o enfermedad. El objetivo de la PrEP es evitar que usted adquiera la infección por el VIH si está expuesto al virus. Esto se puede lograr tomando todos los días una pastilla que contiene 2 medicamentos contra el VIH. Estos son los mismos medicamentos que se utilizan para detener la multiplicación del virus en las personas que ya están infectadas.

¿Por qué debo recibir la PrEP?

La epidemia por el VIH está creciendo en los Estados Unidos. Cerca de 50 000 personas se infectan con el VIH cada año. Estas infecciones están ocurriendo con más frecuencia en algunos grupos de personas y en algunas áreas del país que en otras.

¿La PrEP es una vacuna?

No. Los medicamentos de la PrEP no funcionan de la misma manera que una vacuna. Cuando usted recibe una vacuna, esta entrena al sistema inmunitario para que combata una infección determinada por años. En cambio usted tendrá que tomar una pastilla todos los días para que los medicamentos de la PrEP eviten que contraiga una infección. La PrEP no funciona después de que usted deja de recibirla. La pastilla que ha demostrado ser segura y que ayuda a bloquear la infección por el VIH se llama "Truvada" y es una combinación de dos medicamentos (tenofovir y emtricitabina). Estos medicamentos funcionan bloqueando algunas vías importantes que el VIH utiliza para iniciar la infección. Si usted toma Truvada como PrEP diariamente, la presencia de los medicamentos en su torrente sanguíneo puede a menudo impedir que el virus del VIH se establezca y se propague por su organismo. Si usted no toma la pastilla de Truvada todos los días, puede que no haya suficiente medicamento en su torrente sanguíneo para bloquear el virus.

¿Debo considerar la posibilidad de recibir la PrEP?

La PrEP no es para todo el mundo. Los médicos recetan la PrEP a algunos pacientes que tienen un riesgo muy alto de entrar en contacto con el VIH por tener relaciones sexuales sin protección con una persona infectada por ese virus. Usted debería considerar la PrEP si es un hombre o una mujer que a veces tiene relaciones sexuales sin usar condón, especialmente si tiene una pareja sexual que sabe que está infectada por el VIH. Usted también debería considerar la PrEP si desconoce si su pareja está infectada por el VIH, pero sabe que corre riesgo (por ejemplo, si su pareja se inyecta drogas o tiene relaciones sexuales con otras personas además de usted), o si un proveedor de atención médica le dijo recientemente que usted tiene una infección de transmisión sexual. Si su pareja está infectada con el VIH, la PrEP puede ser una opción para protegerse de contraer esta infección mientras intenta quedar embarazada, durante el embarazo o al amamantar.

¿Qué tan eficaz es la PrEP?

La PrEP se ha probado en varios estudios a gran escala en hombres que tienen relaciones sexuales con hombres, en hombres que tienen relaciones sexuales con mujeres y en mujeres que tienen relaciones sexuales con hombres. Todas las personas en estos estudios (1) se hicieron exámenes al comienzo del ensayo para asegurarse de que no estuvieran infectadas con el VIH, (2) aceptaron tomar una pastilla de PrEP diariamente, (3) recibieron consejería intensiva sobre comportamientos sexuales seguros, (4) se hicieron exámenes regularmente para detectar infecciones de transmisión sexual y (5) se les dio un suministro periódico de condones.

Varios estudios mostraron que la PrEP redujo el riesgo de contraer la infección por el VIH.

- Los hombres que tenían relaciones sexuales con hombres y que recibieron los medicamentos de la PrEP tuvieron un 44 % menos de probabilidad de contraer la infección por el VIH que los que tomaron una pastilla sin medicamento alguno (un placebo). Ese 44 % fue un promedio que incluyó a hombres que no tomaron los medicamentos diariamente y a aquellos que sí los tomaron. Entre los hombres que dijeron que tomaron la mayoría de sus dosis diarias, la PrEP redujo el riesgo de infección por el VIH un 73 % o más, hasta un 92 % en algunos casos.

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- Entre los hombres y mujeres en parejas en las que uno de los dos tenía la infección por el VIH y el otro no (parejas "VIH discordantes"), aquellos que recibieron los medicamentos de la PrEP tuvieron un 75 % menos de probabilidad de infectarse que los que tomaron una pastilla que no contenía ningún medicamento (un placebo). Entre los que dijeron que tomaron la mayoría de sus dosis diarias, la PrEP redujo el riesgo de infección por el VIH en hasta un 90 %.
- En un estudio hecho a hombres y mujeres que comenzaron el ensayo de manera individual (no en pareja), la PrEP fue eficaz tanto en los hombres como en las mujeres: aquellos que recibieron los medicamentos tuvieron un 62 % menos de probabilidad de contraer la infección por el VIH; los que dijeron que tomaron la mayoría de sus dosis diarias tuvieron un 85 % menos de probabilidad de infectarse con el virus. Sin embargo, en otro estudio, solamente cerca de 1 de cada 4 mujeres (<26 %) tenía los medicamentos de la PrEP en su torrente sanguíneo cuando se le hicieron los análisis. Esto indicó que en realidad pocas mujeres estaban tomando los medicamentos y que el estudio no halló protección contra la infección por el VIH.

Puede obtener más información sobre los detalles de estos estudios en www.cdc.gov/hiv/prep.

¿Es segura la PrEP?

Los ensayos clínicos también permitieron obtener información sobre la seguridad de la PrEP. Algunos de los participantes en los ensayos presentaron efectos secundarios en un comienzo —como malestar estomacal o pérdida del apetito—, pero estos fueron leves y por lo general desaparecieron durante el primer mes. Algunas personas también tuvieron dolores de cabeza leves. No se observaron efectos secundarios graves. Usted debe decirle a su médico si estos u otros síntomas se agravan o no desaparecen.

¿Cómo puedo comenzar a recibir la PrEP?

Si cree que puede tener un alto riesgo de contraer el VIH, hable con su médico acerca de la PrEP. Si usted y su médico están de acuerdo en que la PrEP puede reducir su riesgo de contraer la infección por el VIH, tendrá que hacerse un examen físico general, análisis de sangre para detectar el VIH y pruebas para detectar otras infecciones que pueda contraer de sus parejas sexuales. También se analizará su sangre para saber si los riñones y el hígado funcionan correctamente. Si estas pruebas muestran que probablemente puede tomar los medicamentos de la PrEP de forma segura y que puede beneficiarse con el uso de la PrEP, su médico podría darle una receta después de hablar de esto con usted.

Tomar los medicamentos de la PrEP requiere ir a citas de seguimiento periódicas con su médico. Recibirá consejería sobre conductas sexuales y se le harán análisis de sangre para saber si tiene o no la infección por el VIH y comprobar si su organismo está reaccionando bien a Truvada. Usted debe tomar la pastilla todos los días según las indicaciones que le den; el médico le dará consejos sobre métodos para ayudarlo a que la tome regularmente de tal forma que tenga la mejor probabilidad de evitar la infección por el VIH. Dígale a su médico si tiene problemas para acordarse de tomar los medicamentos o si desea interrumpir la PrEP.

Si recibo la PrEP, ¿puedo dejar de usar condones cuando tenga relaciones sexuales?

Usted no debería dejar de usar condones si está recibiendo la PrEP. Si los medicamentos de la PrEP se toman todos los días, estos ofrecen una gran protección contra la infección por el VIH, pero esa protección no es del 100 %. Los condones también proporcionan gran protección contra esa infección si se usan correctamente cada vez que tenga relaciones sexuales, pero tampoco protegen 100 %. Los medicamentos de la PrEP no lo protegen para nada contra otras infecciones que pueda contraer al tener relaciones sexuales, en cambio los condones sí. Así que recibirá la mayor protección contra el VIH y otras infecciones de transmisión sexual si habitualmente toma los medicamentos de la PrEP y usa condones durante las relaciones sexuales.

¿Por cuánto tiempo tengo que tomar los medicamentos de la PrEP?

Tiene que hablar sobre esto con su médico. Hay varias razones por las cuales las personas dejan de tomar los medicamentos de la PrEP. Si su riesgo de contraer la infección por el VIH disminuye debido a cambios en su vida, es posible que quiera dejar de tomarlos. Si ya no desea tomar una pastilla todos los días, o a menudo se le olvida tomársela, hay otras formas de protegerse contra la infección por el VIH que podrían ser mejores para usted. Si el medicamento le causa efectos secundarios que interfieren con su vida o si los análisis de sangre muestran que su cuerpo está reaccionando de manera insegura a la PrEP, es posible que su médico deje de recetarle la PrEP.

MYTHS and FACTS about Pre-Exposure Prophylaxis (PrEP)

MYTH: PrEP encourages, and increases unprotected sex and promiscuity
FACT: In numerous studies looking at the efficacy of PrEP, condom use and number of sexual partners among people using PrEP were similar to those reported in other reports of sexual behavior in these groups (men who have sex with men, transgender women). Those on PrEP may be having unprotected sex at high rates, and may have numerous partners – but this means that PrEP is getting to the right people (at risk).

MYTH: PrEP use will increase rates of other Sexually Transmitted Infections
FACT: PrEP doesn't really affect condom use (see above), and the medication itself does not increase the risk of getting an STI. Recent research shows that rates of STIs may appear higher in those using PrEP, but researchers have concluded that this is likely the result of two factors: increased screening (once every 3 months) that is required to stay on PrEP leads people to get diagnosed and treated more often, and providers prescribing PrEP under the CDC guidelines have increased their knowledge of and use of multi-site STI testing (throat swab, rectal swab in addition to urine test) – leading to providers identifying more STIs that were otherwise being missed. Current research suggests that even with decreased condom use, this routine, multi-site testing will actually REDUCE rates of STIs over time.

MYTH: HIV medications have nasty side effects, so PrEP has bad side effects and isn't safe to use for a long time
FACT: HIV medications, at the beginning of the HIV epidemic, were known for having very bad side effects and toxicity (having a negative, toxic effect on the body or its organs). The medications used today, including Truvada that is used for PrEP, have very few side effects that tend to go away within a few weeks. In fact, most people taking PrEP report no side effects at all. There are some potential risks to using PrEP; these are extremely rare, and doctors monitor patients closely in the first few months of PrEP use to make sure that the medication is stopped if needed.

MYTH: If I take PrEP and get infected with HIV, medications won't work for me
FACT: If someone takes PrEP every day, as prescribed, the risk of getting HIV is very low. Because providers test their patients for HIV regularly, even if someone got HIV, their risk of becoming resistant to the medications in Truvada would be very low because HIV would quickly be detected and PrEP would be stopped. Even in the rare case of someone becoming resistant to the medications in Truvada because of PrEP use, there are more than twenty other medications that could be used to treat HIV.

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701
Maryland Department of Health and Mental Hygiene
Prevention and Health Promotion Administration
Center for HIV/STI Integration and Capacity
(800) 358-9001 • phpa.dhmh.maryland.gov

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MYTH: If I start PrEP, I have to take it for the rest of my life
FACT: Most people who take PrEP have what we call "seasons of risk," meaning that at a certain point in their life, they have a higher risk of HIV. PrEP is one great option for someone during that season. But a lot can change over someone's life – marriage, a monogamous relationship, decreased sex drive, increased condom use, or a number of other possible changes – that could make someone realize they no longer need PrEP.

MYTH: Because PrEP is so effective against HIV, I can stop using condoms
FACT: PrEP is highly effective against HIV, *when taken every day as prescribed,* however PrEP does not protect against other sexually transmitted infections or pregnancy. Some STIs can be treated, and others are lifelong infections. Most people believe that PrEP is not a permission slip to change their sexual or drug behaviors, but another "tool" in their HIV prevention "toolbelt."

MYTH: Taking PrEP may make me test positive for HIV
FACT: HIV tests look for one of two things: the immune system's response to HIV, or the presence of HIV in a blood sample. Some people confuse PrEP and HIV vaccines; some people who have received an HIV vaccine in a research trial do in fact test positive for HIV, and must receive a special test where they originally got the vaccine. PrEP does not effect HIV test results and testing can be done anywhere while on PrEP.

MYTH: Taking PrEP is expensive
FACT: The medication for PrEP, Truvada, is quite expensive if paid for without insurance. But most people taking PrEP in Maryland report paying very little (or nothing) for their prescription after insurance and generous assistance programs from the pharmaceutical company that makes the medication. Maryland Medicaid covers PrEP medication and the provider visits and bloodwork that are needed 2-4 times a year to be on it. Someone on a private insurance plan may find their yearly healthcare costs go up from these extra visits, if they don't currently go to their provider or only go for an annual visit.

MYTH: PrEP is another way for pharmaceutical companies to profit from the HIV epidemic
FACT: The development and research of PrEP was driven by activists, scientists and community leaders. Gilead, the pharmaceutical company that makes Truvada, was not allowed to actively participate in the research used to prove that PrEP works other than to provide the drug. Though the company makes profit from the sale of most of their PrEP medication, the company makes generous financial assistance available; those without insurance who cannot afford the medication receive their medication for free, and those with high co-pays, deductibles and co-insurance under a private health plan can receive thousands of dollars in support each year.

Is PrEP right for me?

What Questions Should I Ask My Doctor?

- ❑ Am I a good candidate for PrEP?
- ❑ What other options can I use to lower my risk of getting HIV infection?
- ❑ How effective would PrEP be at reducing my risk of HIV infection?
- ❑ Are there any side effects?
- ❑ Can you prescribe PrEP for me here?
- ❑ Are there ways to help me to pay for PrEP if I need assistance?
- ❑ Are you willing to prescribe and manage PrEP for me?
- ❑ How often will I have to be tested for HIV and other STDs?

Additional questions for women:

- ❑ Can PrEP help me to get pregnant safely if my partner has HIV?
- ❑ Can I take PrEP if I am pregnant or breastfeeding?

Resources for your Provider

Preexposure Prophylaxis for the Prevention of HIV Infection - 2014: A PHS Clinical Practice Guideline
http://www.cdc.gov/hiv/pdf/guidelines/PrEPguidelines2014.pdf

Preexposure Prophylaxis for the Prevention of HIV Infection - 2014: Clinical Providers' Supplement
http://www.cdc.gov/hivpdf//guidelines/PrEPProviderSupplement2014.pdf

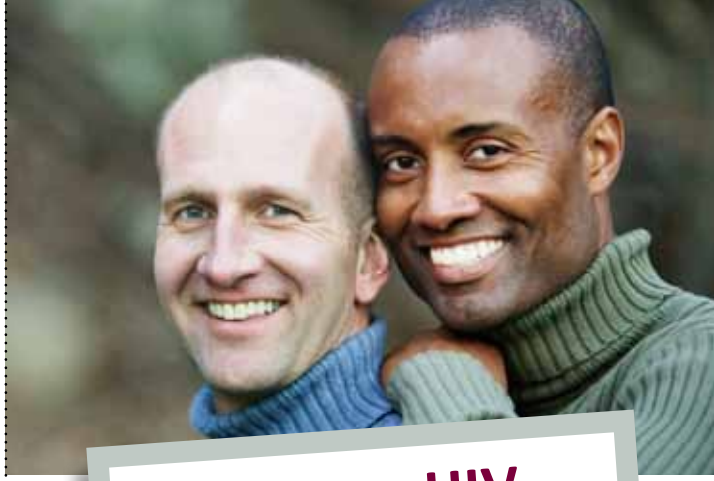
Gilead Sciences PrEP Website: contains information about the drug, its use for PrEP, and information about the Medication Assistance Program. https://start.truvada.com

Resources for You

My PrEP Experience Blog
http://myprepexperience.blogspot.com

Project Inform: PrEP
http://www.projectinform.org/prep

CS247902-A



Are you **HIV negative** but worry you might become **positive?**

Take Charge

TALK TO YOUR DOCTOR ABOUT PrEP

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

What is PrEP?

PrEP stands for "pre-exposure prophylaxis".

Taking a daily dose of Truvada®* was approved in July 2012 for reducing the chance of getting HIV infection in people who don't have HIV.

When used with other safer sex practices (like condoms), PrEP can help protect you from getting HIV from an infected partner.

Truvada®* can be used for HIV prevention by men who have sex with men, men who have sex with women, women who have sex with men, and injection drug users.

*The use of trade names and commercial sources is for identification only and does not imply endorsement by the U.S. Department of Health and Human Services.





HOW TO TALK TO YOUR DOCTOR ABOUT PrEP



Before Your Visit

Make an appointment with your health care provider. Your doctor can help you to decide if PrEP would be a good choice for you.

Do research. Make a list of reasons that you think that PrEP would be a good choice for you.

Think about your routine, especially things that might make it easy or hard to take a daily medication.

Make a health history list for your doctor. That includes any past illnesses or concerns you have, as well as a list of your current medications (including supplements, herbs, etc.).

Make sure a translator is available or bring someone who can translate if you would prefer to speak a language other than English during your appointment.

During Your Visit

Be clear. Take out your notes and tell your doctor that you are interested in PrEP right away.

Do not be shy. Give your doctor all the details about your life that could be important to your health. Don't worry about being judged.

If your sex life is a hard topic to talk about, say that to your doctor. It will help to start the conversation.

Ask questions. You want to be sure that you understand what your doctor is telling you.

Take notes during your visit so that you can remember what your doctor said.

After Your Visit

Review your notes or any information provided by your doctor.

Consider your options. Your doctor gave you a lot of information. Now it is up to you to make the right decision for you.
http://www.cdc.gov/hiv/risk/behavior/index.html

Call your doctor if you have more questions. Ask to speak to a nurse if your doctor is unavailable.

Schedule tests or follow-up appointments your doctor requested.

Get your results if you had tests done at your appointment.

If you feel comfortable, you may want to discuss this choice with your partners, family, or friends.

¿Qué preguntas debo hacerle a mi médico?

- ❑ ¿Soy un buen candidato para recibir la PrEP?
- ❑ ¿Qué otras opciones tengo para reducir mi riesgo de infectarme por el VIH?
- ❑ ¿Qué tan eficaz es la PrEP para reducir mi riesgo de infección por el VIH?
- ❑ ¿Hay efectos secundarios?
- ❑ ¿Me puede recetar la PrEP aquí?
- ❑ ¿Hay formas de ayudarme a pagar por la PrEP en caso de que necesite asistencia?
- ❑ ¿Estaría dispuesto a recetarme la PrEP y hacerme los controles?
- ❑ ¿Con qué frecuencia me tendré que hacer la prueba del VIH y otras ETS?

Preguntas adicionales para las mujeres:

- ❑ ¿Puedo tratar de quedar embarazada de manera segura con la PrEP, si mi pareja tiene el VIH?
- ❑ ¿Puedo recibir la PrEP si estoy embarazada o amamantando?

Recursos para usted

Preexposure Prophylaxis for the Prevention of HIV Infection - 2014: A PHS Clinical Practice Guideline
http://www.cdc.gov/hiv/pdf/guidelines/PrEPguidelines2014.pdf

Preexposure Prophylaxis for the Prevention of HIV Infection - 2014: Clinical Providers' Supplement
http://www.cdc.gov/hivpdf//guidelines/PrEPProviderSupplement2014.pdf

Recursos para su proveedor médico

Sitio web de Gilead Sciences sobre la PrEP: Contiene información sobre el medicamento, su uso para la PrEP e información sobre el programa de asistencia para la obtención de medicamentos. https://start.truvada.com

Recursos para usted

My PrEP Experience Blog
http://myprepexperience.blogspot.com

Project Inform: PrEP
http://www.projectinform.org/prep

CS247902-B



Usted no tiene el VIH (VIH negativo), pero le preocupa infectarse por el virus (VIH positivo)

¡Tome el control!

Hable con su médico acerca de la PrEP

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

¿Qué es la PrEP?

PrEP son las siglas en inglés de profilaxis prexposición.

En julio del 2012, se aprobó el uso de una dosis diaria de Truvada®* para reducir la posibilidad de infección por el VIH en las personas que no tienen el virus.

Si se usa en combinación con otras prácticas sexuales más seguras (como usar condones), la PrEP puede ayudar a proteger contra el virus a la pareja de una persona infectada.

Truvada®* se puede usar para la prevención del VIH en hombres que tienen relaciones sexuales con hombres, hombres que tienen relaciones sexuales con mujeres, mujeres que tienen relaciones sexuales con hombres y usuarios de drogas inyectables.

* El uso de marcas y de sus fuentes comerciales se hace solamente con fines de identificación y no implica respaldo alguno por parte del Departamento de Salud y Servicios Humanos de los EE. UU..





Cómo hablar con su médico acerca de la PrEP



Antes de su visita

Haga una cita con su proveedor de atención médica. Su médico le puede ayudar a decidir si la PrEP es una buena opción para usted.

Infórmese. Haga una lista de las razones por las que cree que la PrEP puede ser algo bueno para usted.

Analice su rutina, especialmente las cosas que le puedan facilitar o dificultar tomarse los medicamentos diariamente.

Dele a su médico una lista con sus antecedentes médicos. En ella incluya las enfermedades que ha tenido o cualquier preocupación que tenga, así como la lista de los medicamentos que está tomando (como los suplementos, las hierbas, etc.).

Asegúrese de tener un intérprete o traer a alguien para que le ayude a comunicarse, en caso de que prefiera hablar en un idioma diferente al inglés durante su cita médica.

Durante su visita

Sea bien claro. Saque sus notas y dígale al médico enseguida que está interesado en la PrEP.

No sea tímido. Dele a su médico todos los detalles personales que puedan ser importantes para su salud. No se preocupe de que lo vaya a juzgar.

Si su vida sexual es un tema que se le hace difícil de tratar, dígaselo a su médico. Lo ayudará a empezar la conversación.

Haga preguntas. Asegúrese de que entiende lo que su médico le dice.

Tome notas durante la cita para que pueda recordar lo que le dijo su médico.

Después de su visita

Revise sus notas o cualquier información que le dio el médico.

Considere sus opciones. Su médico le dio bastante información. Ahora, depende de usted tomar la decisión que más le convenga. http://www.cdc.gov/hiv/risk/behavior/index.html

Llame a su médico si tiene más preguntas. Si el médico no está disponible, pida hablar con la enfermera.

Programe citas para las pruebas o citas de seguimiento que su médico le ordenó.

Pida que le den los resultados, si le hicieron pruebas durante su cita.

Si se siente cómodo, hable sobre su decisión con sus parejas, familiares o amigos.

Truvada Medication Information Sheet

Truvada Medication Information Sheet for Patients

Brand name: Truvada (tru va duh)

Generic name: tenofovir disoproxil fumarate and emtricitabine

Why is this medication prescribed?

- Truvada is one of several medications that are currently used to treat human immunodeficiency virus (HIV) and hepatitis B virus infection.
- Truvada is now being used to *prevent* HIV infection.
- Truvada is sometimes prescribed to some people who do not have HIV infection (for example, those who do not always use condoms or who have a sex partner that has HIV infection) to help reduce their chances of getting HIV infection
- When you take Truvada to prevent HIV infection, doctors refer to this use as "pre-exposure prophylaxis" or "PrEP".

How does Truvada (PrEP) help prevent HIV infection?

- HIV is a virus that attacks your body's immune cells (the cells that work to fight infections).
- The 2 medications that make up Truvada (tenofovir and emtricitabine) block important pathways that viruses use to set up infection.
- If you take Truvada as PrEP daily, the presence of the medication in your bloodstream can sometimes stop the virus from establishing itself and slow the spread of HIV in your body.
- By itself, PrEP with Truvada does not work all the time so youshould also use condoms during sex for the most protection from HIV infection.

How should this medicine be used?

- You must take one tablet of Truvada by mouth every day .
- Follow the directions on your prescription label carefully, and ask your doctor or pharmacist to explain any part you do not understand.
- Do not stop taking Truvada without talking to your doctor. When your supply of Truvada starts to run low, contact your doctor or pharmacist to get more.
- You may be at higher risk of becoming infected with HIV if you miss doses or stop taking Truvada than if you take it every day.

What special precautions should I follow?

Before taking Truvada (tenofovir and emtricitabine) you must do the following:

- Tell your doctor and pharmacist if you are allergic to tenofovir, emtricitabine, or any other medications.
- Tell your doctor and pharmacist about all prescription and nonprescription medications, (vitamins, nutritional supplements, and herbal products) you are taking. Your doctor may need to change the doses of your medications or monitor you carefully for side effects.
- Tell your doctor if you have or have ever had kidney or liver disease.
- Tell your doctor if you become pregnant or if you are breastfeeding

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What special dietary instructions should I follow?

- Continue your normal diet unless your doctor tells you otherwise.

What should I do if I forget a dose?

- Take the missed dose as soon as you remember it. However, if it is almost time for the next dose, skip the missed dose and continue your regular dosing schedule.
- Do not take a double dose to make up for a missed one.

What side effects can this medication cause?

You may experience the following side effects while taking Truvada:

- upset stomach
- headache
- vomiting
- loss of appetite

These side effects usually fade during the first month of taking Truvada for PrEP. Tell your doctor if any of these symptoms are severe or do not go away.

Truvada may cause other side effects. Some side effects can be serious. Call your doctor immediately if you have any unusual problems while taking this medication or if you have any of the following:

- fever or chills especially with
- sore throat, cough, rash or other signs of infection

If you experience a serious side effect, you or your doctor may send a report to the Food and Drug Administration's (FDA) MedWatch Adverse Event Reporting program online (at http://www.fda.gov/Safety/MedWatch) or by phone (1-800-332-1088).

How should I store Truvada in my home?

- You should keep Truvada in the container it came in, tightly closed, and out of reach of children.
- You must store it at room temperature and away from excessive heat and moisture.
- Throw away any medication that is outdated or no longer needed. Talk to your pharmacist about the proper disposal of your medication.

What should I do in case of emergency/overdose?

- In case of overdose, call your local poison control center at 1-800-222-1222. If the person has collapsed or is not breathing, call local emergency services at 911.

What other information should I know?

- Do not let anyone else take your medication.
- Ask your pharmacist if you have any questions about refilling your prescription.
- Write a list of all of your prescription and over-the-counter medicines, as well as any vitamins, minerals, or other dietary supplements that you take.
- Bring your medication list with you each time you visit a doctor or if you are admitted to a hospital. Keep it with you always in case of emergencies.

Hoja informativa sobre el medicamento Truvada

Hoja informativa para pacientes sobre el medicamento Truvada

Marca comercial: Truvada

Nombre genérico: fumarato de disoproxilo de tenofovir y emtricitabina

¿Por qué se receta este medicamento?

- Truvada es uno de varios medicamentos que se utilizan actualmente para tratar la infección por el virus de la inmunodeficiencia humana (VIH) y la infección viral de hepatitis B.
- Truvada también se está utilizando ahora para prevenir la infección por el VIH.
- A veces se les receta a algunas personas que no tienen la infección por el VIH (por ejemplo, a quienes no siempre usan condones o que tienen una pareja sexual infectada con ese virus) para ayudar a reducir sus probabilidades de contraerla.
- Cuando usted toma Truvada para prevenir la infección por el VIH, los médicos se refieren a este tratamiento como "profilaxis prexposición" o "PrEP", por sus siglas en inglés.

¿De qué manera Truvada (PrEP) ayuda a prevenir la infección por el VIH?

- El VIH es un virus que ataca las células inmunitarias de su cuerpo (las células que luchan contra las infecciones).
- Los dos medicamentos que componen Truvada (tenofovir y emtricitabina) bloquean vías importantes que usan los virus para comenzar la infección.
- Si usted toma Truvada diariamente como PrEP, la presencia de los medicamentos en su torrente sanguíneo a veces puede impedir que el virus se establezca y hacer más lenta la propagación del VIH en su organismo.
- Por sí sola, la PrEP con Truvada no funciona todo el tiempo; por lo tanto, usted también debe utilizar condones cuando tenga relaciones sexuales para lograr una mayor protección contra la infección por el VIH.

¿Cómo se debe usar este medicamento?

- Usted debe tomar una pastilla de Truvada todos los días.
- Siga cuidadosamente las instrucciones de la etiqueta del medicamento y pídale a su médico o farmacéutico que le explique cualquier parte que no entienda.
- No deje de tomar Truvada sin consultar a su médico. Cuando su provisión de Truvada comience a acabarse, comuníquese con su médico o farmacéutico para obtener más.
- Si se salta dosis o deja de tomar Truvada, usted puede tener un riesgo más alto de infectarse con el VIH que si la toma todos los días.

¿Qué precauciones especiales debo tomar?

Antes de tomar Truvada (tenofovir y emtricitabina), usted debe hacer lo siguiente:

- Decirle a su médico y al farmacéutico si usted es alérgico al tenofovir, la emtricitabina o cualquier otro medicamento.
- Informar al médico y al farmacéutico acerca de todos los medicamentos recetados y no recetados, vitaminas, suplementos nutricionales y productos herbarios que esté tomando. Puede ser que su médico tenga que cambiar las dosis de sus medicamentos o hacerle un seguimiento cuidadoso sobre los efectos secundarios.
- Decirle a su médico si tiene o ha tenido alguna vez enfermedad de los riñones o del hígado.
- Avisarle al médico si queda embarazada o si está amamantando.

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¿Qué directrices alimentarias especiales debo seguir?

- Continúe con su alimentación normal a menos que su médico le indique lo contrario.

¿Qué debo hacer si se me olvida tomar una dosis?

- Tómela tan pronto como se acuerde. Sin embargo, si ya casi es la hora de la dosis siguiente, no tome la dosis que olvidó y siga con el horario normal.
- No tome dos dosis para reponer la que olvidó tomar.

¿Qué efectos secundarios puede causar este medicamento?

Usted puede presentar los siguientes efectos secundarios mientras tome Truvada:

- Malestar estomacal
- Dolor de cabeza
- Vómitos
- Pérdida del apetito

Por lo general, estos efectos secundarios desaparecen durante el primer mes en que se toma Truvada para la PrEP. Dígale a su médico si alguno de estos síntomas es intenso o no se va.

Truvada puede causar otros efectos secundarios y algunos pueden ser graves. Llame a su médico inmediatamente si tiene cualquier problema inusual mientras toma este medicamento o si presenta lo siguiente:

- fiebre o escalofríos especialmente con
- dolor de garganta, tos, sarpullido u otros signos de infección.

Si presenta un efecto secundario grave, usted o su médico puede enviar un informe al programa de Notificación de Reacciones Adversas MedWatch de la Administración de Alimentos y Medicamentos (FDA) a través de la Internet (en http://www.fda.gov/Safety/MedWatch) o por teléfono (1-800-332-1088).

¿Cómo debo guardar Truvada en mi casa?

- Usted debe mantener Truvada en el envase original, cerrado herméticamente y lejos del alcance de los niños.
- Debe guardarlo a temperatura ambiente y donde no haya calor ni humedad excesivos.
- Deseche todo medicamento que esté vencido o que ya no sea necesario. Hable con su farmacéutico sobre la manera adecuada de desechar sus medicamentos.

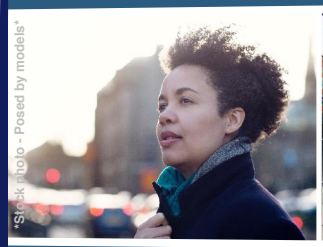
¿Qué debo hacer en caso de una emergencia o sobredosis?

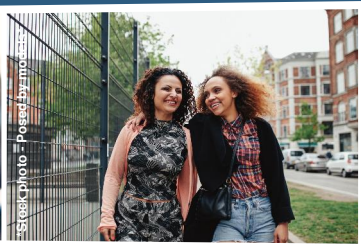
- En caso de una sobredosis, llame a su centro de control de intoxicaciones local al 1-800-222-1222. Si la persona se ha desmayado o no está respirando, llame al servicio de emergencias local al 911.

¿Qué otra información debo saber?

- No deje que nadie más tome su medicamento.
- Hágale a su farmacéutico cualquier pregunta que tenga acerca del surtido de su receta.
- Escriba una lista de todos los medicamentos —los recetados y los que se venden sin receta—, así como de todas las vitaminas, minerales u otros suplementos nutricionales que esté tomando.
- Lleve su lista de medicamentos cada vez que vaya al médico o si es hospitalizado. Manténgala con usted siempre en caso de emergencia.

PrEP for women











Benefits of PrEP

- PrEP is a **once daily pill** that gives **YOU** the power to control **YOUR** health and avoid getting HIV
- PrEP is a way to **protect yourself against changing life situations**, including your partners' sexual practices, HIV status, and condom use
- PrEP **does not interact with any form of birth control** including the oral pill, DEPO, or IUDs
- PrEP may be an option to **protect you and your baby** against HIV while trying to get pregnant with an HIV positive partner

What you need to know

- PrEP only works if taken **EVERY DAY**, and you will need to take it for at least **10 days** before you are fully protected
- You may have some minor stomach discomfort when you start PrEP. This usually goes away after the first month
- Research has shown that women who took PrEP before or shortly after they got pregnant had **no serious health risks** during their pregnancy. Babies exposed to PrEP during pregnancy or breastfeeding had no serious side effects

How do you access PrEP?

- **The decision to go on PrEP is yours**. PrEP is not just a medication. PrEP is part of a program that connects you with a health care provider to develop a full approach to reducing your HIV risk
- Talk with a PrEP navigator about finding a clinic or provider to get started
- If you do not have a trusted health care provider, we can help you find one. Visit **www.prepmaryland.org** or call/text **888-788-PREP** to connect with a PrEP provider anywhere in Maryland
- PrEP is covered by most insurance plans as well as Medicaid. Payment assistance programs are available, even if you are uninsured

What else can I do to protect myself?

Use Condoms · Use Lube · Get HIV Tested · Test & Treat STIs · Partner Testing · Partner Support · Avoid Substances · Use Clean Needles · Use PEP

PrEP 101

What if there was a pill that could prevent HIV?

There is.



What is Pre-Exposure Prophylaxis (PrEP)?

Let's break it down:

Pre = Before | **Exposure** = Coming into contact with HIV | **Prophylaxis** = preventing an infection from occurring

PrEP is a way to prevent HIV infection by taking **one pill once a day.** Research has shown that PrEP can be up to **99% effective** at preventing HIV infection when taken every day.

PrEP can be used by heterosexual, bisexual, gay and transgender individuals, and also by persons who inject drugs and pregnant women

PrEP is not a cure for HIV and it cannot protect you from pregnancy or other sexually transmitted infections (STIs), like gonorrhea or chlamydia



Is taking PrEP difficult?

No! You will have some things to remember while using PrEP, including:

- Taking one pill once a day, around the same time every day. The pill is called Truvada®
- Getting regular testing for HIV and STIs (every 3 months); and
- Having regular visits with your healthcare provider to get your labs checked and refill your medication

You may have some minor stomach discomfort or headaches when you start PrEP, but this usually goes away after the first month

You should consider PrEP if:

- You don't always use condoms when you have anal or vaginal sex
- You don't always ask your partner(s) to wear a condom
- You've been diagnosed with a sexually transmitted infection in the last 6 months
- You're unsure of the HIV status of your sexual partner(s)
- You're in a relationship with a partner who has HIV (who may or may not be on HIV treatment)
- You are a person who injects drugs, or you're in a sexual relationship with a person who injects drugs
- You don't have HIV and are interested in PrEP

PrEP is covered by most insurance plans as well as Medicaid. There are also payment assistance programs available for people who are insured or uninsured. Your health care provider and PrEP navigator can help you figure out insurance coverage and assistance programs

Visit
www.prepmaryland.org
www.cdc.gov/hiv/risk/prep

Call
888-788-PREP

Search the App Store for
PrEPme

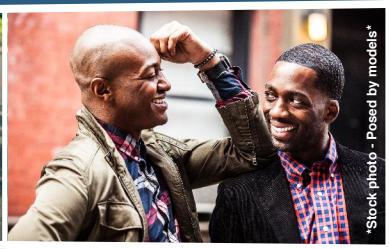
#Bmore4PrEP

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#PrEPme

PrEP for men who have sex with men









>> 2 out of every 3 people who get infected with HIV each year are MSM <<

Benefits of PrEP

PrEP is a **once daily pill** that gives **YOU** the power to control **YOUR** health and avoid getting HIV

PrEP **reduces HIV infection by up to 99%** when taken daily

PrEP is a way to **protect yourself against changing life situations**, including condom use or your partners' sexual practices and HIV status. This is important because 1 in 5 MSM living with HIV don't know they are infected

What you need to know

PrEP only works if taken **EVERY DAY**, and you will need to take it for at least **10 days** before you are fully protected

You may have some minor stomach discomfort when you start PrEP. This usually goes away after the 1st month

PrEP will not protect you from getting STIs (sexually transmitted infections), like gonorrhea, chlamydia or syphilis. You should continue to use condoms and get tested for STIs every 3 months

How do you access PrEP?

The decision to go on PrEP is yours. PrEP is not just a medication. PrEP is part of a program that connects you with a health care provider to develop a full approach to reducing your HIV risk

Talk with a PrEP navigator about finding a clinic or provider to get started

If you do not have a trusted health care provider, we can help you find one. Visit **www.prepmaryland.org** or call/text **888-788-PREP** to connect with a PrEP provider anywhere in Maryland

Search the App Store for **PrEPme** to connect with a PrEP provider

PrEP is covered by most insurance plans as well as Medicaid. Payment assistance programs are available, even if you are uninsured

What else can I do to protect myself?

Use Condoms | Use Lube | Get HIV Tested | Test & Treat STIs | Partner Testing | Partner Support | Avoid Substances | Use Clean Needles | Use PEP

PrEP 101

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PrEP can be used by heterosexual, bisexual, gay and transgender individuals, and also by persons who inject drugs and pregnant women

PrEP is not a cure for HIV and it cannot protect you from pregnancy or other sexually transmitted infections (STIs), like gonorrhea or chlamydia



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No! You will have some things to remember while using PrEP, including:

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You should consider PrEP if:

- You don't always use condoms when you have anal or vaginal sex
- You don't always ask your partner(s) to wear a condom
- You've been diagnosed with a sexually transmitted infection in the last 6 months
- You're unsure of the HIV status of your sexual partner(s)
- You're in a relationship with a partner who has HIV (who may or may not be on HIV treatment)
- You are a person who injects drugs, or you're in a sexual relationship with a person who injects drugs
- You don't have HIV and are interested in PrEP

PrEP is covered by most insurance plans as well as Medicaid. There are also payment assistance programs available for people who are insured or uninsured. Your health care provider and PrEP navigator can help you figure out insurance coverage and assistance programs

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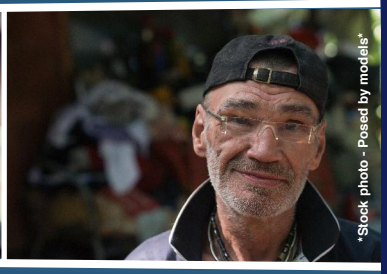
#PrEPme

PrEP for people who inject drugs









>> 1 out of every 10 new HIV infections is caused by sharing needles <<

Benefits of PrEP

PrEP is a **once daily pill** that gives **YOU** the power to control **YOUR** health and avoid getting HIV

PrEP is a way to **protect yourself against changing life situations**, including sharing needles, condom use, and your partners' sexual practices and HIV status

PrEP reduces HIV infection by 48-70% in people who inject drugs. If you combine PrEP with other ways of protecting yourself, like using **clean needles, avoiding needle sharing, and using condoms,** you can can greatly reduce your risk of getting HIV

What you need to know

PrEP only works if taken **EVERY DAY**. For optimal protection against HIV, you will need to take it for at least **7 days** for receptive anal sex and **20 days** for vaginal sex, insertive anal sex, or if you inject drugs

PrEP will not protect you from getting STIs (sexually transmitted infections), Hepatitis or other infections associated with injecting drugs

You may have some minor stomach discomfort when you start PrEP. This usually goes away after the 1st month

How do you access PrEP?

The decision to go on PrEP is yours. PrEP is not just a medication. PrEP is part of a program that connects you with a health care provider to develop a full approach to reducing your HIV risk

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PrEP is covered by most insurance plans as well as Medicaid. Payment assistance programs are available, even if you are uninsured

Baltimore has several needle exchange vans, which provide **free clean needles** for extra protection against HIV and Hepatitis C. Call 410-396-3731 to connect with the needle exchange program

What else can I do to protect myself?

Use Condoms | Use Lube | Get HIV Tested | Test & Treat STIs | Partner Testing | Partner Support | Avoid Substances | Use Clean Needles | Use PEP

PrEP 101

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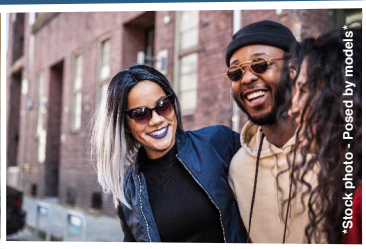
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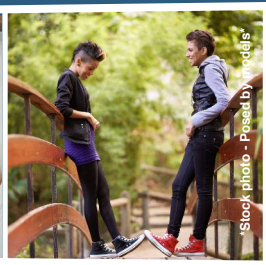
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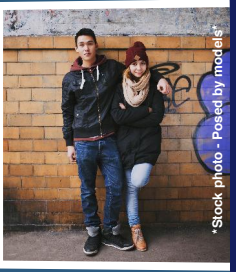
PrEP for serodifferent











>> **Serodifferent means that one partner is HIV positive and the other partner is HIV negative** <<

Benefits of PrEP

PrEP is a **once daily pill** that gives **YOU** the power to control **YOUR** health and avoid getting HIV

PrEP can give you **extra protection**, especially if your HIV positive partner is not on medication, was recently diagnosed, or if you are unsure of their status. It is important to talk to your HIV positive partner about his or her HIV

If you are HIV negative and want to get pregnant with an HIV positive partner, PrEP can **protect you while you try to get pregnant**. PrEP does not change your ability to get pregnant

What you need to know

PrEP only works if taken **EVERY DAY**, and you will need to take it for at least **10 days** before you are fully protected

You may have some minor stomach discomfort when you start PrEP. This usually goes away after the first month

PrEP will not protect you from getting STIs (sexually transmitted infections), like gonorrhea, chlamydia, or syphilis. You should continue to use condoms and get tested for STIs every 3 months

How do you access PrEP?

The decision to go on PrEP is yours. PrEP is not just a medication. PrEP is part of a program that connects you with a health care provider to develop a full approach to reducing your HIV risk

Talk with a PrEP navigator about finding a clinic or provider to get started

If you do not have a trusted health care provider, we can help you find one. Visit **www.prepmaryland.org** or call/text **888-788-PREP** to connect with a PrEP provider anywhere in Maryland

Search the App Store for **PrEPme** to connect with a PrEP provider

PrEP is covered by most insurance plans as well as Medicaid. Payment assistance programs are available, even if you are uninsured

What else can I do to protect myself?

Use Condoms | Use Lube | Get HIV Tested | Test & Treat STIs | Partner Testing | Partner Support | Avoid Substances | Use Clean Needles | Use PEP

PrEP 101

What if there was a pill that could prevent HIV?

There is.



What is Pre-Exposure Prophylaxis (PrEP)?

Let's break it down:

Pre = Before | **Exposure** = Coming into contact with HIV | **Prophylaxis** = preventing an infection from occurring

PrEP is a way to prevent HIV infection by taking **one pill once a day.** Research has shown that PrEP can be up to **99% effective** at preventing HIV infection when taken every day.

PrEP can be used by heterosexual, bisexual, gay and transgender individuals, and also by persons who inject drugs and pregnant women

PrEP is not a cure for HIV and it cannot protect you from pregnancy or other sexually transmitted infections (STIs), like gonorrhea or chlamydia



Is taking PrEP difficult?

No! You will have some things to remember while using PrEP, including:

- Taking one pill once a day, around the same time every day. The pill is called Truvada®
- Getting regular testing for HIV and STIs (every 3 months); and
- Having regular visits with your healthcare provider to get your labs checked and refill your medication

You may have some minor stomach discomfort or headaches when you start PrEP, but this usually goes away after the first month

You should consider PrEP if:

- You don't always use condoms when you have anal or vaginal sex
- You don't always ask your partner(s) to wear a condom
- You've been diagnosed with a sexually transmitted infection in the last 6 months
- You're unsure of the HIV status of your sexual partner(s)
- You're in a relationship with a partner who has HIV (who may or may not be on HIV treatment)
- You are a person who injects drugs, or you're in a sexual relationship with a person who injects drugs
- You don't have HIV and are interested in PrEP

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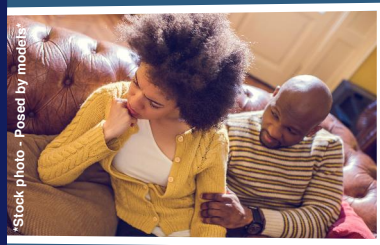
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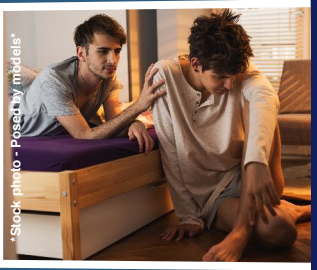
PrEP for intimate partner violence











Intimate Partner Violence (IPV) includes physical violence, sexual violence, coercion or threats

>> IPV can affect anyone - all races, ethnicities, genders and sexual orientations <<

Benefits of PrEP

PrEP is a **once daily pill** that gives **YOU** the power to control **YOUR** health and avoid getting HIV

PrEP is a way to **protect yourself against changing life situations**, including IPV, sharing needles, condom use, or your partners' sexual practices and HIV status. This is important because people who experience IPV are at increased risk for HIV

What you need to know

PrEP only works if taken **EVERY DAY**. For optimal protection against HIV, you will need to take it for at least **7 days** for receptive anal sex and **20 days** for vaginal sex, insertive anal sex, or if you inject drugs

You may have some minor stomach discomfort when you start PrEP. This usually goes away after the first month

People who experience violence may be worried about choosing PrEP. Make sure you speak with your provider about any concerns for your safety

How do you access PrEP?

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Search the App **Store** for
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PrEP for sex workers











>> Sex workers are 12 times more likely to be infected with HIV <<

Benefits of PrEP

PrEP is a **once daily pill** that gives **YOU** the power to control **YOUR** health and avoid getting HIV

PrEP is a way to **protect yourself against changing life situations**, including condom use or your partners' sexual practices and HIV status.

PrEP is important because **sex work makes you more vulnerable to HIV** because of the large numbers of sex partners, unsafe working conditions, and not always being able to use a condom

What you need to know

PrEP only works if taken **EVERY DAY**. For optimal protection against HIV, you will need to take it for at least **7 days** for receptive anal sex and **20 days** for vaginal sex, insertive anal sex, or if you inject drugs

You may have some minor stomach discomfort when you start PrEP. This usually goes away after the 1st month

PrEP will not protect you from getting STIs (sexually transmitted infections), like gonorrhea, chlamydia or syphilis. You should continue to use condoms and get tested for STIs every 3 months

How do you access PrEP?

The decision to go on PrEP is yours. PrEP is not just a medication. PrEP is part of a program that connects you with a health care provider to develop a full approach to reducing your HIV risk

Talk with a PrEP navigator about finding a clinic or provider to get started

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PrEP is not a cure for HIV and it cannot protect you from pregnancy or other sexually transmitted infections (STIs), like gonorrhea or chlamydia



Is taking PrEP difficult?

No! You will have some things to remember while using PrEP, including:

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You should consider PrEP if:

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- You're unsure of the HIV status of your sexual partner(s)
- You're in a relationship with a partner who has HIV (who may or may not be on HIV treatment)
- You are a person who injects drugs, or you're in a sexual relationship with a person who injects drugs
- You don't have HIV and are interested in PrEP

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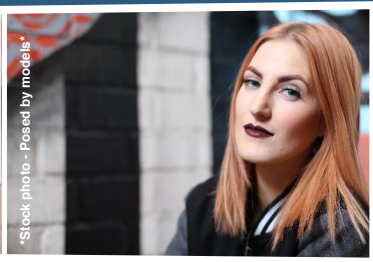
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PrEP for trans women











>> Transgender women are 49 times more likely to be infected with HIV <<

Benefits of PrEP

PrEP is a **once daily pill** that gives **YOU** the power to control **YOUR** health and avoid getting HIV

PrEP is a way to **protect yourself against changing life situations**, including condom use or your partners' sexual practices and HIV status.

What you need to know

PrEP only works if taken **EVERY DAY**, and you will need to take it for at least **10 days** before you are fully protected

You may have some minor stomach discomfort when you start PrEP. This usually goes away after the first month

At this time, no studies have shown drug interactions between PrEP and hormone therapy used for transitioning. The medicine used for PrEP has been around for over 10 years and successfully used by individuals taking it and hormone therapy without decreasing the effects of the pill or hormone therapy

How do you access PrEP?

The decision to go on PrEP is yours. PrEP is not just a medication. PrEP is part of a program that connects you with a health care provider to develop a full approach to reducing your HIV risk

Talk with a PrEP navigator about finding a clinic or provider to get started

If you do not have a trusted health care provider, we can help you find one. Visit **www.prepmaryland.org** or call/text **888-788-PREP** to connect with a PrEP provider anywhere in Maryland

If you're concerned about the interactions between PrEP and your hormone therapy, we can help link you to a provider who is trained to understand your therapy and manage your PrEP accordingly

PrEP is covered by most insurance plans as well as Medicaid. There are also payment assistance programs available for people who are insured or uninsured

What else can I do to protect myself?

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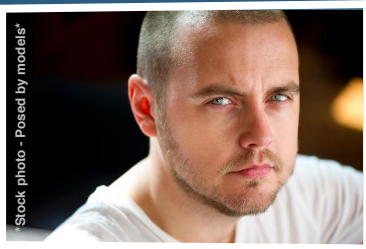
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PrEP for trans men


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Stock photo - Posed by models


Stock photo - Posed by models


Stock photos - Posed by models

Benefits of PrEP

PrEP is a **once daily pill** that gives **YOU** the power to control **YOUR** health and avoid getting HIV

PrEP is a way to **protect yourself against changing life situations**, including condom use or your partners' sexual practices and HIV status

What you need to know

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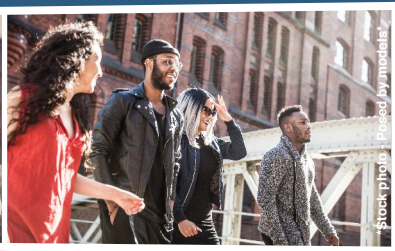
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PrEP for youth









>> 1 out of every 4 new HIV infections is amongst youth aged 13 to 24 <<

Benefits of PrEP

PrEP is a **once daily pill** that gives **YOU** the power to control **YOUR** health and avoid getting HIV

PrEP **reduces HIV infection by up to 99%** when taken daily

PrEP is a way to **protect yourself against changing life situations**, including condom use or your partners' sexual practices and HIV status. This is important because more than 50% of youth with HIV in the US do not know they are infected

What you need to know

PrEP only works if taken **EVERY DAY**, and you will need to take it for at least **10 days** before you are fully protected

You may have some minor stomach discomfort when you start PrEP. This usually goes away after the first month

Like many drugs out there, most (but not all!) of the research on PrEP has been on people over the age of 18. This means current PrEP research does not show us how PrEP affects youth who are still growing. Talk to your provider about the benefits and risks

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Paying for PrEP

Resources

To apply for health insurance on the federal exchange: www.healthcare.gov

Community Health Center Locator:
http://findahealthcenter.hrsa.gov/

Washington state (residents):

PrEP drug assistance program (PrEP-DAP)
http://www.doh.wa.gov/YouandYourFamily/IllnessandDisease/HIVAIDS/HIVCareClientServices/PrEPDAP

New York state (residents):

PrEP assistance program (PrEP-AP)
Call 1-800-542-2437

Gilead Sciences:

Medication Assistance Program and Co-Pay Assistance
https://start.truvada.com/individual/truvadaprep-copay

Patient Advocate (PAF) Foundation:

Co-Pay Relief Program
https://www.copays.org/diseases/hiv-aids-and-prevention

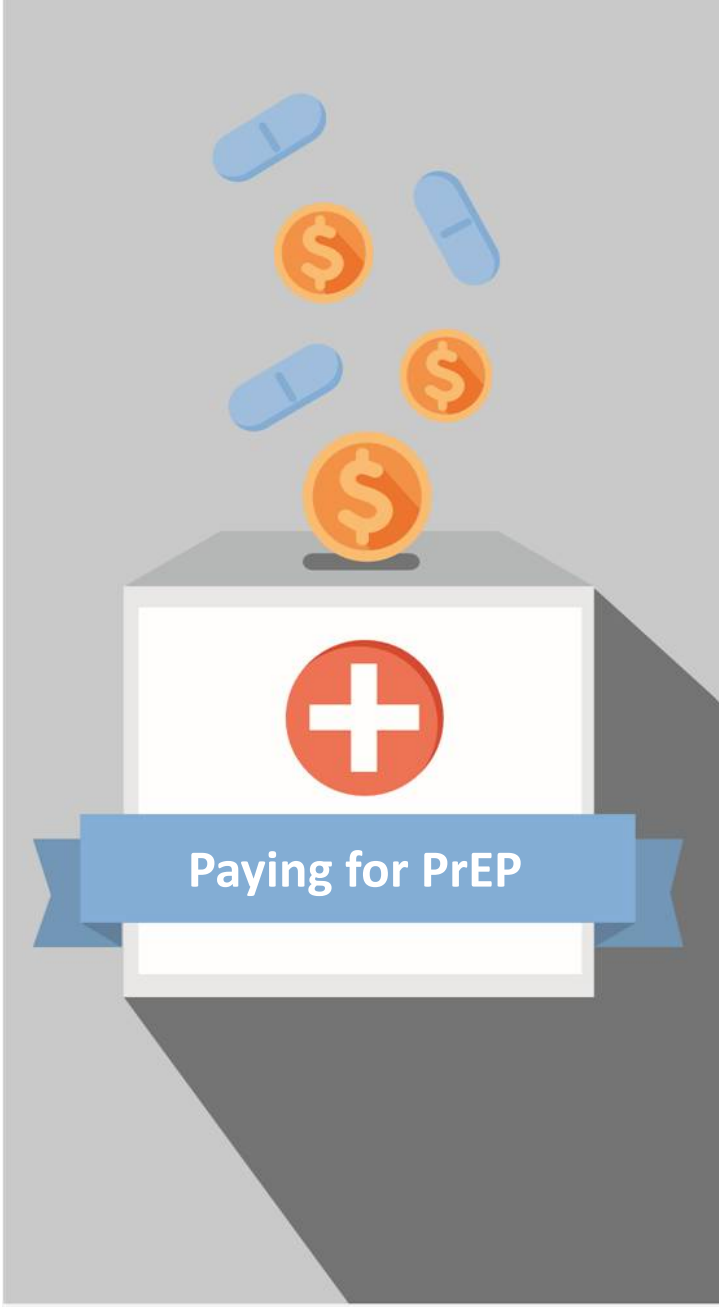
Division of HIV/AIDS Prevention,

National Center for HIV/AIDS,

Viral Hepatitis, STD, and TB Prevention

Centers for Disease Control and Prevention
1600 Clifton Road
Atlanta, GA 30329-4027 USA
Phone: 800-232-4636

December 2015



Centers for Disease Control and Prevention
National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention

Covering the Cost of PrEP Care

Insured

Medication	Lab Test	Clinic Visits
• Bill insurance • Apply for copay assistance from Gilead or PAF	• Bill insurance	• Bill insurance

Not insured
But may be eligible for Medicaid or ACA Plans

Apply

Household Income 500% FPL or less

Medication	Lab Test	Clinic Visits
• Gilead Medication Assistance Plan • WA State Medication Assistance	• Care at CHC with sliding fee scale • NY State PrEP Assistance Plan	• Care at CHC with sliding fee scale • NY State PrEP Assistance Plan

Not eligible for Medicaid or ACA plans OR Insurance denies claim

Household Income more than 500% FPL

Medication	Lab Test	Clinic Visits
• Bill insurance • Apply for copay assistance from Gilead or PAF	• Bill insurance	• Bill insurance

Abbreviations

ACA - Affordable Care Act
FPL - Federal Poverty Level
CHC - Community Health Center
PAF - Patient Advocate Foundation

Definitions:

PrEP	Daily pill to prevent HIV infection (pre-exposure prophylaxis)
Co-pay	Fixed amount to be paid by insured person per prescription
Co-insurance	Fixed percentage of prescription cost to be paid by insured person
Deductible	Amount of health care cost (including prescriptions) that must be paid by the insured person before insurance begins to cover costs

PrEP Medication Assistance Program

(Gilead Sciences)

People eligible for this program must:

- Be 18 years of age or older
- Be without insurance or have payment declined by their insurance carrier
- Be resident in the US (social security number not required)
- Have family income ≤ 500% of the federal poverty level

Once enrolled in this program:

- Medication will be sent to the provider, a pharmacy, or the patient's home
- Patients can get their medication at no charge from their provider or pharmacy for as long as they are eligible
- Eligibility must be confirmed every 6 months by the provider

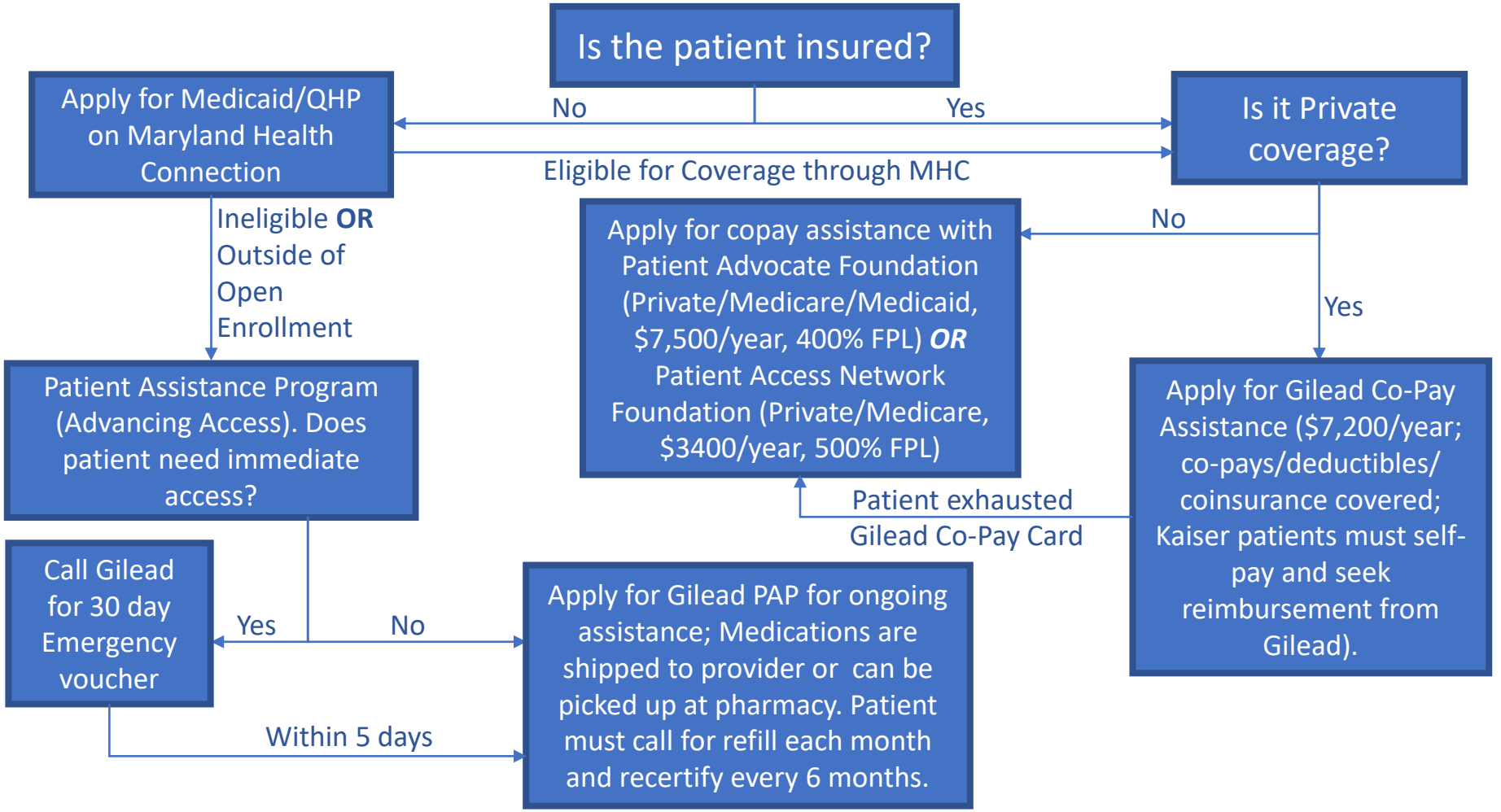
PrEP Medication Assistance Program

Family Size	500% Federal Poverty Level Household Annual Income must be less than:
1	$58, 850
2	$79, 650
3	$100, 450
4	$121,250
5	$142,050
6	$162,850

*Source: https://www.healthcare.gov/glossary/federal-poverty-level-FPL/

PrEP Medication & Co-Pay Assistance Program Flowchart

MARYLAND Department of Health
HIV Pre-Exposure Prophylaxis Program
Center for HIV/STI Integration and Capacity
Infectious Disease Prevention and Health Services Bureau
Prevention and Health Promotion Administration



HARFORD COUNTY HEALTH DEPARTMENT

HOW CAN I PAY FOR PrEP?

I have private insurance. Will my health insurance cover PrEP?

To date, we have not heard any reports of health insurance companies denying requests to fill prescriptions for PrEP in the United States. Some health insurance companies have pre-authorization requirements to determine if you are eligible to have it covered under insurance. This doesn't necessarily mean that your particular plan will cover it—we can't guarantee that! However, reports indicate that most people have no trouble getting their private healthcare insurance to cover PrEP.

My PrEP Experience has a wonderful resource monitoring insurance and Medicaid coverage of Truvada for PrEP. If you have trouble getting a prescription for Truvada as PrEP, or getting a PrEP prescription covered by insurance or Medicaid, please send an email to myprepexperience@gmail.com.

I have private insurance. How much does PrEP cost?

If you have private healthcare insurance, you can expect to pay your normal co-pay associated with brand-name drugs. This varies from plan to plan. PrEP is not cheap. Without insurance, out-of-pocket costs can be as high as $13,000 per year.

I have private insurance. My insurance coverage charges me a high copay for Truvada. Is there any way I can get assistance to cover my co-pay?

Yes! Gilead's co-pay assistance program is specifically set-up for this purpose and can help those eligible cover the cost of co-pays. Contact Gilead for more information and to find out if you are eligible, http://www.gileadcopay.com.

My PrEP Experience has a wonderful resource monitoring insurance and Medicaid coverage of Truvada for PrEP. If you have trouble getting a prescription for Truvada as PrEP, or getting a PrEP prescription covered by insurance or Medicaid or Gilead, please send an email to myprepexperience@gmail.com.

I do not have private insurance and PrEP is too expensive. Can I get Truvada for low cost or for free?

Yes! If you don't have insurance, there are ways to get Truvada for PrEP at no or low cost: Gilead's prescription assistance programs, clinical trials, and Medicaid (differs state to state).

My PrEP Experience has a wonderful resource monitoring insurance and Medicaid coverage of Truvada for PrEP. If you have trouble getting a prescription for Truvada as PrEP, or getting a PrEP prescription covered by insurance or Medicaid or Gilead, please send an email to myprepexperience@gmail.com.

I have Medicaid. Does Medicaid cover PrEP?

Medicaid is covering PrEP in most states, but actual Medicaid coverage varies from state to state, so check with your benefits counselor. Public policy advocates will have to tackle this issue in the coming months and years to make sure PrEP is accessible to everyone who needs it.

The Patient Advocate Foundation can offer assistance if income is less than $47,080. Individuals must be insured with drug coverage of at least $1.00. You must also live in the US, have a utility bill, and either a social security number or an alien number in order to apply. Apply at https://www.copays.org/diseases/hiv-aids-and-prevention.

My PrEP Experience has a wonderful resource monitoring insurance and Medicaid coverage of Truvada for PrEP. If you have trouble getting a prescription for Truvada as PrEP, or getting a PrEP prescription covered by insurance or Medicaid or Gilead, please send an email to myprepexperience@gmail.com.

I don't have private health insurance. How much does PrEP cost?

PrEP is not cheap. Without insurance, out-of-pocket costs can be as high as $13,000 per year.

I don't have private health insurance. How do I find a doctor to prescribe Truvada for PrEP? How do I bring it up?

Since you will need a prescription for Truvada for PrEP, you will need to get connected with a healthcare provider to access it. If you do not have insurance and do not regularly see a doctor, please locate a community health center near you. Most of these centers will have insurance navigators to help you obtain health insurance and PrEP providers. Prepmaryland.org can also direct you to PrEP providers in your area.

ADDITIONAL RESOURCES FOR PROVIDERS

MARYLAND PrEP NEWSLETTER

WELCOME!

MARYLAND
Department of Health

IN THIS ISSUE

- WELCOME—PG. 1
- DORCHESTER & HOWARD COUNTIES PrEParing TO LAUNCH PrEP SERVICES—PG. 1
- HARFORD COUNTY "SWIPES RIGHT" TO PROMOTE PrEP ON DATING APPS—PG. 2
- MDH & *IMPACT* PARTNERS "PrEP" FOR A STATEWIDE SUMMIT—PG. 2
- PrEPCOST.ORG ASSISTS WITH HEALTH PLAN SELECTION—PG. 2
- PrEP ACCESS EXPANDING WORLDWIDE—PG. 3
- STI PROPHYLAXIS—SHORT TERM BENEFIT VS. LONG TERM RISK—PG. 4
- GILEAD PROMISES $100 MILLION TO ADDRESS HIV IN SOUTHERN US—PG. 4

WELCOME TO THE SECOND MARYLAND DEPARTMENT OF HEALTH PrEP NEWSLETTER!

PrEP access continues to expand statewide, as does PrEP uptake and awareness, which has led to the need for this newsletter.

Delivered at least twice each fiscal year, MDH's PrEP newsletter provides vital info to funded PrEP programs, providers, health professionals, navigators, as well as Maryland residents interested in PrEP.

The newsletter highlights the growth of the PrEP program through MDH, new research findings related to PrEP, best practices from State Health Departments and PrEP clinics across the US, training opportunities, new developments related to PrEP, and more!

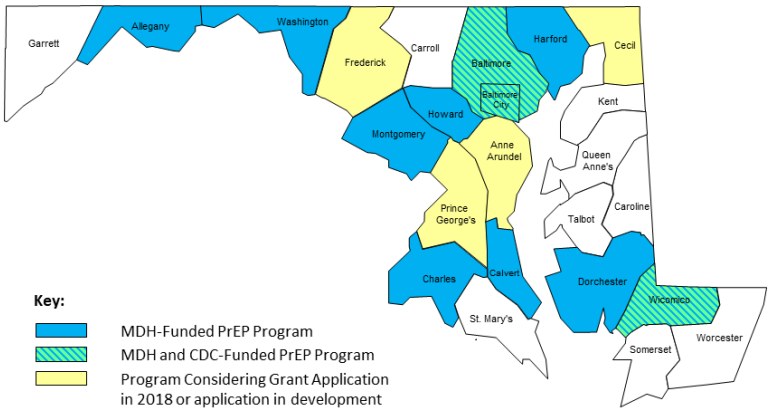
If you have ideas for a future article, please reach out to Paul Foster, PrEP Program Coordinator, at paul.foster@maryland.gov!

DORCHESTER AND HOWARD COUNTIES PrEParing TO LAUNCH PrEP SERVICES

The MDH PrEP team was excited to begin funding Dorchester and Howard County Health Departments for PrEP services in October 2017! Existing programs may be contacted by staff at the newest funded programs; we (and they!) are thankful that program staff share ideas and allow for site observations.

MDH is also funding Baltimore City Health Department, helping to continue the work of the IMPACT Campaign that launched with 1506/1509 CDC Funds. This brings us to 11 Health Department-based programs funded by MDH, with three programs also receiving CDC Funding (Baltimore City, Baltimore County & Wicomico County). See our map below.

Welcome to our newest programs!

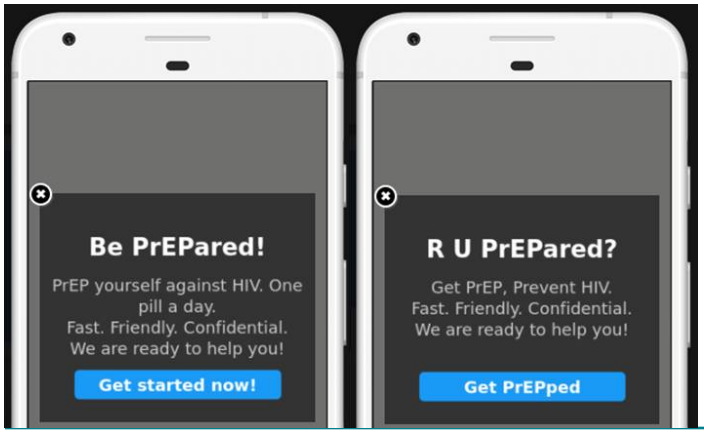


HARFORD COUNTY "SWIPES RIGHT" AS IT PROMOTES PrEP ON DATING APPS

By Lynda Boegner, Harford County Health Department

To raise PrEP awareness and promote its PrEP Program, Harford County Health Department is turning to dating apps - specifically Jack'd and Manhunt. Harford County's team contacted Online Buddies to discuss advertising across their Jack'd and Manhunt platforms. (For those unaware, Jack'd is an app for gay, bisexual and same-gender loving men, and launched after Grindr but quickly became the most popular in parts of the country, largely due to its racial diversity and high customer satisfaction ratings). The teams collaborated to design an ad campaign to engage sexually active people with sex-positive health messages, and to determine the appropriate language and format, target populations, and budget costs. The campaign includes banner ads that will appear on user screens for several months, plus direct message ads that target users in Harford County and surrounding areas. Users can click the "call to action" and be directed to the Harford County Health Department's site for comprehensive PrEP information. Online Buddies can track how many received the message and how many engaged with it. Harford County is also monitoring website traffic to see how the ads affect visits to the PrEP page.

Truvada as PrEP has shown great clinical promise in HIV prevention, but the message has not yet been widely heard. Dating apps have up to 7 million active users at one time; potentially this is a significant consumer platform to engage. Harford County Health Department hopes to capitalize on this phenomenon and promote PrEP across our county! We have started receiving contact with potential clients as a result of the ads, and will know more as the team provides us with analytics. Below are some screenshots of the ads!



MDH AND *IMPACT* PARTNERS "PrEP" FOR A STATEWIDE SUMMIT

Last month, the PrEP leaders at MDH joined with colleagues at Baltimore City Health Department, Johns Hopkins REACH Initiative and Johns Hopkins John G. Bartlett Specialty Practice, all members of IMPACT (Initiative to Maximize Prevention, Access, Care, and Treatment) to lay the groundwork for a Statewide PrEP/Biomedical HIV Prevention Summit. REACH and the Bartlett Specialty Practice are the clinical technical assistance and capacity building providers funded through the Initiative. The Summit, tentatively occurring in September 2018, will likely feature session tracks geared toward providers, PrEP Navigators, and program managers, and potentially tracks related to working with specific populations who could most benefit from PrEP. Stay tuned for more information on what should be an exciting and informative day-long Summit! We hope you attend!

PrEPCOST.ORG ASSISTS WITH HEALTH PLAN SELECTION

At the end of 2017, NASTAD released an online tool called PrEPCost.org, which allows people who need a health plan on a State exchange or Healthcare.gov to quickly see the total cost to get on PrEP. The tool factors estimated monthly premium (after potential premium assistance based on income, age and zip code), recommended visits and lab services, and co-medication costs (after the $4,800 co-pay assistance from Gilead). The tool is a great launching point for a client to quickly see which plan would save them the most money in overall PrEP costs. Clients should consider other health needs when choosing a plan.

Many times, the cheapest plan by monthly premium has a large deductible or cost-sharing (coinsurance, copays) that make a plan quickly lose its appeal. For many, those deductibles result in prohibitive costs early in the year. A more expensive plan may instead spread healthcare costs over the year. PrEPCost.org is a helpful tool during Open Enrollment and year-round for clients eligible for a special enrollment period (those who have a qualifying life event)!

PrEP ACCESS EXPANDING WORLDWIDE

By Paul Foster

As evidence of the real-world efficacy and cost-effectiveness of PrEP is released, state governments across the US and national governments worldwide are making PrEP awareness, access, and availability a high priority.

In December 2017, South Africa reported that in the first year of their PrEP initiatives, thousands have gained access to free PrEP. South Africa was the first country in Africa to approve emtricitabine/tenofovir for PrEP, and by September 2017 was providing free PrEP to sex workers, men who have sex with men and other vulnerable groups at 17 health centers, 9 youth-serving clinics, and 7 student health clinics at public universities.

That same month, Brazilian officials announced that PrEP would be free for eligible Brazilians, in response to a sharp rise in new HIV infections among youth. Beginning with 35 public health clinics across 22 cities, the program aims to provide PrEP to those who are most vulnerable to HIV, particularly youth. From 2006 to 2015, new HIV infections nearly tripled among men 15-19 years old, and nearly doubled among men 20-24 years old in Brazil. Nearly 1 in 10 gay, bisexual and other men who have sex with men in Brazil are living with HIV. This new program was made possible by past advocacy in Brazil that negotiated low prices for HIV medications; while the cost of PrEP in the US can be more than $1,600 a month at retail cost Brazil pays just 75 cents per Truvada® pill. Because of this, the 3.6 million pills they expect to give out in the first year of the program cost just $2.7 million, versus $192 million at retail cost. Two manufacturers applied in Brazil for licensure of their generic emtricitabine/tenofovir, which would lower the cost of this program further and enable the continued expansion of access.

Also in December, the Canadian province of British Columbia announced that it would be providing PrEP for free to eligible residents. They followed shortly in the footsteps of Ontario and Quebec, which both began providing free PrEP earlier in the year. PrEP access in Canada is expected to continue to increase; Teva, Pharmascience and Mylan all received approval in July for generic versions of Truvada. The cost of PrEP medication is expected to be cut by three-quarters as a result, putting pressure on the provinces to expand access to generic PrEP.

Meanwhile, state health departments across the US are funding PrEP Clinics and Navigation / Outreach services to promote PrEP awareness among providers and clients, and to increase uptake and adherence. Some states, including Colorado, Illinois, Massachusetts, Washington, and New York, launched PrEP Drug Assistance Programs, also known as PrEP-DAPs. Modeled after ADAP—the AIDS Drug Assistance Program—PrEP-DAPs assist with PrEP medication costs for those vulnerable to HIV. Most programs utilize existing infrastructure of the ADAP program; staff are cross-trained and partially funded by each program, eligibility requirements are mirrored, and computer systems are shared. PrEP DAPs, like Ryan White funding, are usually designed as a “payor of last resort,” requiring clients to seek out other available assistance for PrEP before getting state funds. Additionally, New York State allows providers to enroll in the NY PrEP-AP, enabling their patients to receive free visits and labs in addition to medications. Other states are learning from PrEP-DAP staff and hope to launch similar programs in the future.

PrEP access may continue to increase in the US, as the FDA approved generic Truvada® in June of 2017. Gilead continues to hold a patent for one of the medications in Truvada® until 2021, so the move has been deemed surprising, but has intensified negotiations between Gilead Sciences and Teva Pharmaceuticals to potentially allow for generic Truvada® to become available sooner. The fate of generic PrEP remains uncertain to date, but would greatly enhance the ability of state and local programs to afford to continue expanding access.

Sources:

www.nytimes.com/2017/12/12/world/americas/prep-brazil-hiv-aids.html

www.cbc.ca/news/canada/british-columbia/province-announces-hiv-drug-coverage-1.4467003

www.theconversation.com/one-year-in-lessons-on-rolling-out-an-hiv-prevention-pill-in-south-africa-88255

timeslive.co.za/news/south-africa/2017-09-26-hiv-prevention-pills-now-available-to-university-students

www.cbc.ca/news/health/hiv-prep-coverage-1.4302184

www.huffingtonpost.co.za/2017/12/01/prep-miracle-hiv-prevention-pill-could-save-sa-lives_a_23293823/

www.poz.com/article/fda-approves-generic-truvada

www.nastad.org/prepcost

STI PROPHYLAXIS: SHORT-TERM BENEFIT VERSUS LONG-TERM RISK

In the field, we are all too aware that PrEP has a few key limitations, one being lack of protection against other STIs. Rates of reportable STIs have increased or largely remained steady in nearly every county of Maryland for the last several years. PrEP clinic staff and others in public health (rightfully) want to ensure that PrEP is promoted and provided to those who really need it, but that we increase to quarterly STI testing, conduct multi-site testing (urine, pharyngeal, rectal), and continue to promote STI prevention and safer sex behaviors for clients. One question that researchers have wondered is: can we prevent STIs in our PrEP patients using a similar strategy of post-exposure prophylaxis?

To answer this question, researchers utilized the open-label extension of the ANRS IPERGAY study—which looked at on-demand PrEP use—to conduct an open-label randomized sub-study. Patients in the treatment arm were given 100mg doxycycline pills and told to take two within 72 hours of condomless sex for STI post-exposure prophylaxis, not to exceed six pills per week.

Overall, STI incidence was reduced by 53% in the PEP/treatment arm, with Chlamydia incidence reduced by 70%, Syphilis by 73% and Gonorrhea by only 17%.

Given the already present threat of antibiotic resistance in Gonorrhea, the researchers and others have noted that additional studies will need to be conducted to look at the long-term efficacy of STI post-exposure prophylaxis, and the long-term impact on antibiotic resistance needs to be thoroughly evaluated. For now, the CDC and USPSTF are not making any statement or recommendations regarding STI PEP.

As savvy patients learn about this strategy and these studies, they may have questions for their PrEP provider and may wonder if STI PEP can become part of their standard PrEP care. Currently, providers are evaluating the available evidence and using their clinical judgment to decide if this is something they are comfortable providing, given the possible benefits and long-term risks.

Sources: Molina, J.M., Charreau, I., Chidiac, C., et al. *Post-exposure prophylaxis with doxycycline to prevent sexually transmitted infections in men who have sex with men: an open-label randomised substudy of the ANRS IPERGAY trial.* Lancet Infect Dis. 2017; (published online Dec 8.)http://dx.doi.org/10.1016/S1473-3099(17)30725-9

Fairley, C.K., Chow, E.P.F., *Doxycycline post-exposure prophylaxis: let the debate begin.* Lancet Infect Dis. 2017; (published online Dec 8.) http://dx.doi.org/10.1016/S1473-3099(17)30726-0

GILEAD PROMISES $100 MILLION TO ADDRESS HIV IN SOUTHERN US

For many areas of the US, new HIV infections dropped dramatically in recent years. Some States including Maryland saw new infections drop to rates near those seen at the start of the HIV epidemic, likely due to enhanced efforts to support retention in care and increase viral load suppression for people living with HIV, earlier initiation of HIV treatment, and increased use of PrEP and non-occupational Post-Exposure Prophylaxis (nPEP) to prevent HIV. Progress has not been equal, however, according to CDC data; in areas of the South, new infection rates increased across all groups. While the South represents roughly one-third of the US population, the South represents nearly half of people living with HIV and nearly half of HIV-related deaths, and 8 of the 10 States with the highest HIV incidence (rate of new HIV infections) are in the South.

Given this harrowing information, Gilead Sciences, the largest manufacturer of antiretrovirals, promised $100 million in funding to curb these trends. The initiative, COMPASS, was announced at the NMAC Biomedical HIV Prevention Summit in New Orleans on December 4, to considerable excitement and applause. (COMPASS stands for **COM**ittment to **P**artnership in **A**ddressing HIV/AIDS in **S**outhern **S**tates). Gilead announced plans to partner with leaders like the Emory University Rollins School of Public Health, Southern AIDS Coalition and University of Houston Graduate College of Social Work to locate and fund local organizations that are making an impact on HIV care and prevention.



Gregg Alton, EVP of Corporate & Medical Affairs at Gilead announces the COMPASS Initiative at the Biomedical HIV Prevention Summit, December 4, 2017, New Orleans, LA. *Image: @GileadSciences Twitter*

Sources: www.cdc.gov/hiv/pdf/policies/cdc-hiv-in-the-south-issue-brief.pdf
www.hivequal.org/what-s-new/gilead-unveils-100m-commitment-to-ending-hiv-in-the-u-s-south

MARYLAND Department of Health

That's all for this newsletter! Thanks for reading!

MSM Sexual Health Standards of Care

Addressing the Sexual Health Crisis among Gay, Bisexual, and Other Men who have Sex with Men (MSM)





The National Coalition of STD Directors (NCSD) is a partnership of public health professionals dedicated to advancing effective STD prevention programs and services in every community across the country. NCSD does this as the voice of their membership. NCSD provides leadership, build capacity, convene partners, and advocate. For more information, visit www.NCSDDC.org.

NASTAD is a leading non-partisan non-profit association that represents public health officials who administer HIV and hepatitis programs in the U.S. and around the world. Its mission is to end the intersecting epidemics of HIV, viral hepatitis, and related conditions. NASTAD does this work by strengthening domestic and global governmental public health through advocacy, capacity building, and social justice. For more information, visit www.NASTAD.org.

The National Network of STD Clinical Prevention Training Centers (NNPTC) is a CDC-funded group of training centers created in partnership with health departments and universities. The PTCs are dedicated to increasing the knowledge and skills of health professionals in the areas of sexual health. The NNPTC provides health professionals with a spectrum of state-of-the-art educational opportunities including experiential learning with an emphasis on STD treatment and prevention.



Table of Contents

Blue Ribbon Panel Members	4
Foreward	5
Executive Summary	6
Goals and Objectives of the Blue Ribbon Panel	7
Social Determinants of Health and Stigma	7
Primary Findings from the Blue Ribbon Panel	9
Culturally Competent Sexual History-Taking	9
Education and Counseling	9
Clinical Assessment and Testing	10
How to implement the MSM Standards of Sexual Health Care	12
Conclusions	12
APPENDIX A: Resources	13
APPENDIX B: Case Studies	15
APPENDIX C: References	17

Blue Ribbon Panel Members

Meeting Co-Chairs

Leandro A. Mena, MD, MPH – Crossroads Clinic, Mississippi Department of Health; Open Arms Healthcare Center, University of Mississippi Medical Center
Leo Moore, MD – University of California, Los Angeles
Mark Thrun, MD – Denver Department of Public Health

Blue Ribbon Panelists

Michelle Allen – Georgia Department of Public Health
Gail Bolan, MD – Division of STD Prevention, Centers for Disease Control & Prevention (CDC)
Demetre C. Daskalakis, MD – New York City Department of Health & Mental Hygiene
John A. Davis, PhD, MD – Gay and Lesbian Medical Association, The Ohio State University
Bruce W. Furness, MD – District of Columbia Department of Health, Whitman-Walker Health, CDC
Stephen Goldstone, MD – Mount Sinai Hospital
Tam Ho, MPA – MAC AIDS Fund
Edward "Ned" Hook III, MD – University of Birmingham, Alabama; Jefferson County Department of Public Health
Peter Leone, MD – Gillings School of Public Health
David Malebranche, MD, MPH – University of Pennsylvania
Eugene McCray, MD – Division of HIV/AIDS Program, CDC
Jonathan Mermin, MD, MPH – National Center for HIV/AIDS, Viral Hepatitis, STD, and Tuberculosis Prevention, CDC
Greg Millett, MPH – amfAR
Susan Philip, MD – San Francisco Department of Public Health
Raul Romaguera, DMD, MPH – Division of STD Prevention, CDC
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Kevin Shi, MMSc, PA-C – The Fenway Institute
Juliet Stoltey, MD, MPH – California Department of Public Health
Melanie Thompson, MD – AIDS Research Consortium of Atlanta
Tim Vincent, MS – California Prevention Training Center
Gene Voskuhl, MD – AIDS Arms - Peabody Health Center

Blue Ribbon Staff

Devin Barrington-Ward -- NCSD
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Jessica Frasure-Williams, MPH – NCSD
Stephen Hicks, MPH – NCSD
Rebekah Horowitz, JD, MPH – NCSD
Justin Rush, JD – NASTAD
William "Bill" Smith – NCSD
Isaiah Webster III – NASTAD

* NOTE: Listed organizations reflect the Blue Ribbon members' affiliations during the March 2015 meeting.

Foreward

We are faced with a sexual health crisis for gay, bisexual, and other men who have sex with men (MSM). In 2015, 82 percent of male primary and secondary syphilis cases and 70 percent of new HIV cases[2] were among MSM. Disparities in race/ethnicity and age are also staggering, with young Black and Latino MSM bearing the greatest burden of STD and HIV infections. Medical providers and health departments have long needed a standard of care for the sexual health of gay, bisexual, and other MSM. We must reinvigorate the health care field with the tools to better engage MSM in the care continuum, as individual health care providers and as a larger community, or health disparities will continue to flourish.

Health care providers remain vital to our progress, and we congratulate the exemplary providers and encourage them to share their strategies with those not as well-versed in MSM sexual health. We strive to equip providers and health departments with tools for high-quality, culturally competent, LGBT-affirming care that is derived from a menu of options based on the whole person.

This MSM Sexual Health Standards of Care is a natural progression from materials developed by the National Coalition of STD Directors (NCSD) and the National Alliance of State and Territorial AIDS Directors (NASTAD): *Providing Optimal Care for Your MSM Patients, For Men Only: Your Sexual Health,* and the toolkit *Addressing Stigma: A Blueprint for Improving HIV/STD Prevention and Care Outcomes for Black and Latino Gay Men*. This document builds on the foundation laid by those materials and the triumphant efforts of so many dedicated advocates.

The recommendations in this document come from a wealth of clinical and programmatic experience including pleasure in the sexual health discourse. They also tackle the disease burden disproportionately faced by MSM. While we primarily educate providers, we must also educate communities to empower MSM to demand the care they need and equip them with the knowledge of the quality sexual health care they deserve.

We thank the many members of our Blue Ribbon Panel who tirelessly dedicated themselves to bringing this document to fruition. We remain committed to equipping providers with the best tools possible. NCSD and NASTAD also utilize the Gay Men's Health Equity Workgroup for additional expertise in MSM sexual health.

Executive Summary

The National Coalition of STD Directors (NCSD) and the National Alliance of State and Territorial AIDS Directors (NASTAD) convened a Blue Ribbon Panel of experts from academia, city and state health departments, the Centers for Disease Control and Prevention (CDC), and the National Network of STD/HIV Prevention Training Centers (NNPTC) to develop optimal standards of client-focused clinical care for gay, bisexual, and other men who have sex with men (MSM). These standards illustrate the highest quality of sexual health care for MSM, expanding beyond federal guidelines to incorporate the collective experience of experts in the field of sexual health.

Implementation of quality sexual health care must be set in the context of social determinants of health. Clinical environments and systems should be thoughtfully designed to be inclusive of lesbian, gay, bisexual, and transgender (LGBT) patients and patients of all races and ethnicities. Clinic staff, from receptionists to clinicians, should be trained and assessed for LGBT inclusivity in their interactions with patients.

Screening should occur at least annually, and every three to six months for sexually active MSM with multiple partners. The recommendations of the Blue Ribbon Panel suggest that providers offer the following to all of their gay, bisexual, and other MSM patients. Please note that this document is focused on cisgender men who have sex with cisgender men. Some of the material may also apply to transgender women, depending on their sexual practices they engage in. Whitman-Walker Health has an excellent document to guide sexual health conversations with transgender patients *(see Appendix A).*

Sexual Health Protocol At-A-Glance

Culturally Competent Staff & LGBT-friendly Environment

	Comprehensive sexual history	Mental health assessment and referrals	Counseling about condoms, lubrication, enemas, and douches	Discussion about sexual satisfaction and pleasure
	Visual exam to check for signs of HPV, syphilis, or other STDs			
	Urethral swab or urine-based chlamydia and gonorrhea screening		Rectal and pharyngeal chlamydia and gonorrhea screening	
	Syphilis screening	HIV screening	Hepatitis C screening	
	Hepatitis A vaccine	Hepatitis B vaccine	HPV vaccine	
	Post-exposure prophylaxis, as indicated	Pre-exposure prophylaxis, as indicated	Expedited Partner Therapy for chlamydia or gonorrhea infection	

Goals and Objectives of the Blue Ribbon Panel

NCSD, in partnership with NASTAD and the NNPTC, hosted a meeting on March 19-20, 2015, titled *Improving the Sexual Health of MSM through Establishing a Sexual Health Standard of Care.* This convening, supported by MAC AIDS Fund, included participants from academia, city and state health departments, the CDC, NCSD, and NASTAD to form a Blue Ribbon Panel of sexual health experts. The core goal of the meeting was to develop optimal standards of client-focused clinical care and communication for gay, bisexual, and other MSM. The three objectives of the meeting were to:

- Convene a strategic consultation of experts to work toward developing a consensus of MSM sexual health needs
- Foster shared understanding among interested partners in STD/HIV prevention about a MSM sexual health standard of care
- Develop, publish, and disseminate a shared standard of care or package of services for MSM

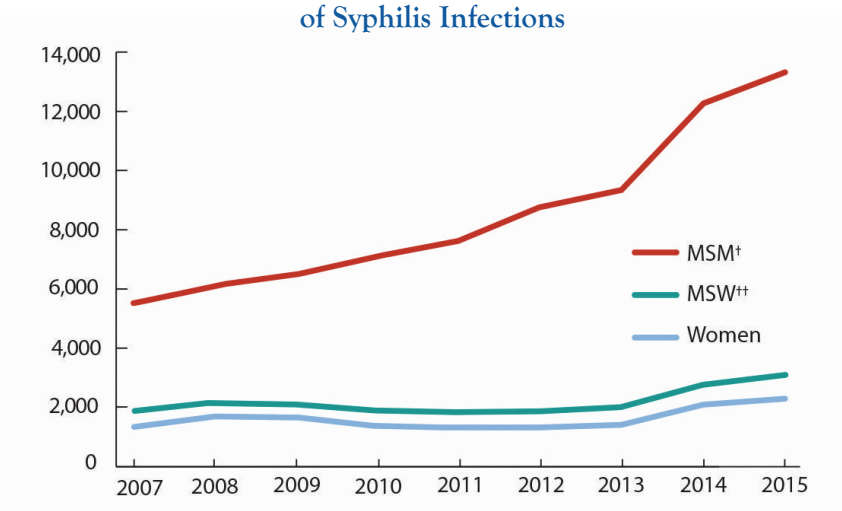
Social Determinants of Health and Stigma

Before delving into clinical approaches to sexual health, it is vital to set the social landscape in which MSM are operating before they walk through a clinic door. There is significant evidence that social factors, such as racism, homophobia, immigration status, unemployment, mass incarceration, and homelessness are associated with poor health outcomes, even when controlling for other factors. These social determinants of health often intersect among gay, bisexual and other MSM, diminishing quality of life and creating barriers to sexual health along the spectrum of health care, including knowledge of the need for access.

For example, the unemployment rate for Black men is 10.4 percent, and for Latino men 6.6 percent.[3] Unemployment reduces access to quality health insurance for those individuals and their families. Additionally, the mass incarceration of Black and Latino men, who comprise 58 percent of all prisoners despite making up only 25 percent of the population,[4,5] disrupts social and sexual networks in communities.

The effects of these social factors compound and can manifest in higher rates of disease in specific communities. Throughout the last decade, there have been outbreaks of syphilis, gonorrhea, and HIV in Black and Latino MSM. In 2015, MSM accounted for more of these cases than heterosexual men or women in all racial and ethnic groups, comprising 82 percent of all male primary and secondary syphilis cases[6] (Figure 1). Rates of new HIV infection by race and age among MSM point to the urgent need for interventions that address race and age disparities among MSM populations, in particular among young Black and Latino MSM[7] (Figure 2).

Gay and Bisexual Men Face Highest – and Rising – Number of Syphilis Infections

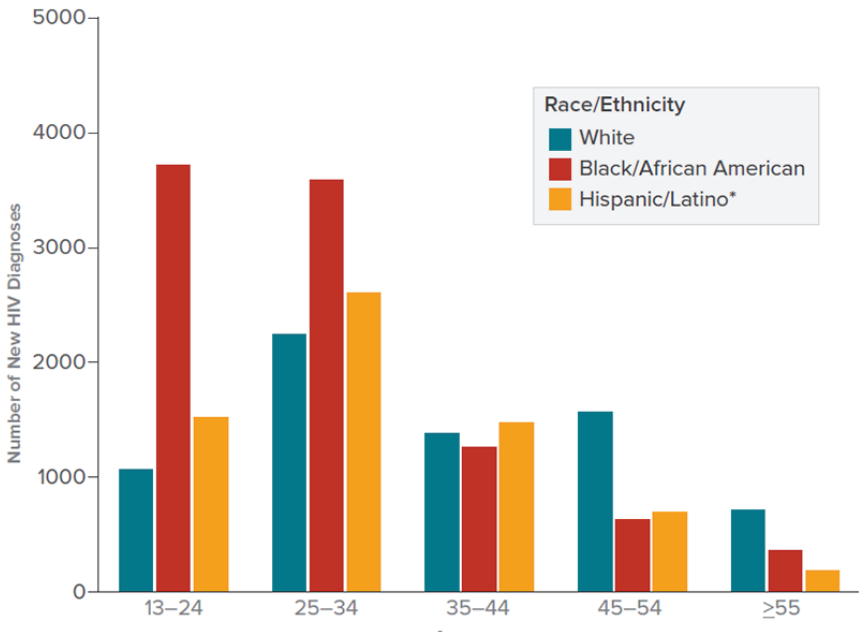


†Men who have sex with men ††Men who have sex with women

Note: Based on available data from states reporting sex of sex partners

Source: CDC

Figure 2. Estimated HIV Diagnoses Among Men Who Have Sex With Men, by Race/Ethnicity and Age at Diagnosis, 2014—United States

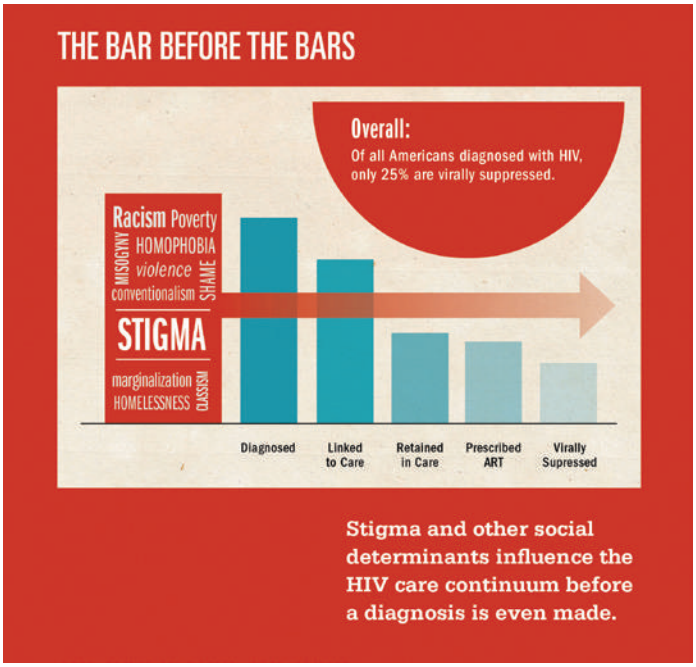


* Hispanics/Latinos can be of any race
Source: CDC. Diagnoses of HIV infection in the United States and dependent areas, 2014. *HIV Surveillance Report 2015;26.*

Stigma, an indicator that negatively marks a person or group for a specific characteristic or behavior, is another barrier to optimal care for MSM. Stigma influences both patient and provider comfort with discussing sexual practices and risk behaviors, and exposure to stigma in communities or in the medical system can create discomfort or fear about disclosing sexual orientation or sexual practices to health care professionals. Nearly 40 percent of MSM do not share their sexual orientation with medical providers[8] and many expect health care providers to initiate sexual health discussions.[9] For example, only 25 percent of patients receiving care in Ryan White clinics report that they discuss HIV transmission prevention with their providers,[10] and only six percent of patients diagnosed with HIV report discussing sexual practices with their primary providers.[11]

Some physicians identify stigma-related barriers as the reason for not recommending HIV testing, as they are concerned that a recommendation to test would be perceived as accusatory or judgmental.[12] It is critical that health care providers recognize the role that stigma may play in their own perceptions of their patients when taking sexual histories, and ensure that assumptions about individual patient risk are not being made.

To that end, NCSD and NASTAD created a document, *Addressing Stigma: A Blueprint for Improving HIV/STD Prevention and Care Outcomes for Black and Latino Gay Men* and other MSM.[13] Stigma, along with other social determinants of health, is an unmeasured factor that impacts the acquisition of HIV and STDs and has repercussions all along the HIV care continuum (See Figure 3).



This image is taken from the NASTAD/ NCSD toolkit, *Addressing Stigma: A Blueprint for Improving HIV/STD Prevention and Care Outcomes for Black and Latino Gay Men*. It illustrates how stigma prevents Black and Latino MSM from achieving viral suppression.

Interventions to reduce STD and HIV infection should focus on the populations most affected, accounting for social determinants and the experience of stigma, and use a community-based approach to ensure cultural competency and acceptance.

Primary Findings from the Blue Ribbon Panel

The MSM Sexual Health Standards of Care described below combine current CDC recommendations for quality sexual health care for MSM with recommendations from the collective expertise of the Blue Ribbon Panel. See Appendix A for additional resources.

Culturally Competent Sexual History-Taking

To bring MSM sexual health standards to scale, providers must talk to all of their patients about sex, including questions about sexual orientation, gender identity, and sexual practices, to guide appropriate STD screening. Providers should build relationships with their patients to put them at ease and reduce barriers to open lines of communication.

Quality sexual history-taking is client-centered, enforces strategies that patients are already using to maintain sexual health, and provides insight or information about other strategies that may work for patients. If providers are unaware that their male patients are having sex with men, they will not be equipped to address their sexual health care. Yet even well-intentioned physicians may not have these conversations with their patients.

The CDC recommends using the Five Ps (Partners, Practices, Past history of STDs, Protection, and Pregnancy) as the foundation for sexual history-taking.[14] The Blue Ribbon Panel extends this approach to include a sixth P: Pleasure. Sexual health should not be limited to risk management but tailored to each individual's needs, including talking to patients about pleasure and sexual satisfaction.

Education and Counseling

The following information should be included in discussions with gay, bisexual, and other MSM patients.

Condoms, Lubricant, and Douching

- Discuss current condom use practices. Recommend latex, polyurethane, or polyisoprene condoms to prevent HIV and STD transmission. "Natural" condoms (made of animal skin) are not effective for preventing STD and HIV transmission.[15]
- Educate patients about use of the "female" or insertive condom for receptive anal intercourse. This condom can be safely inserted into the rectum and is an alternative to the traditional male condom that may be preferred by some patients.[16,17]

- Discuss use of water- or silicone-based lubricants that do not include nonoxynol-9. Lubricant can increase comfort and pleasure, and reduce micro-tears in the anus.
- Have free condoms available in the office, waiting area, and restrooms. Condom distribution programs are effective for reducing STDs, including HIV.[18]
- Educate patients about increased risk of HIV acquisition with rectal douching and discuss safe rectal douching practices for patients who like to use douches or enemas. Less frequency of enemas is recommended. When performed, warm water is strongly suggested. Polyethylene glycol suppositories or enemas may be least irritating.

Mental Health, Substance Use, and Safety

- Screen for mental health and substance use concerns, as these impact all other aspects of health care and prevention. Refer patients to MSM-affirming and harm-reduction resources within their communities.
- Screen for common conditions like depression, anxiety, and post-traumatic stress disorder.
- Consider discussing/screening for sexual addiction if patient reports what they would consider high activity. Be mindful of the stigma of queer sexuality being considered oversexualized and how a sexual addiction diagnosis can be perceived by a patient.
- Screen for history of sexual abuse/violence and intimate partner violence. Refer patients to MSM-affirming resources within their communities.

Clinical Assessment and Testing

According to CDC, one in three primary care providers and nurses have not heard about pre-exposure prophylaxis (PrEP),[19] and the lack of extragenital screening for gonorrhea and chlamydia are missed opportunities for diagnosis and subsequent treatment. Incorporating the following clinical recommendations will ensure that MSM patients receive comprehensive sexual health care.

Chlamydia and Gonorrhea Screening

- Test for chlamydia and gonorrhea at least annually, and every three-six months for men who have factors that may increase their potential exposure to STDs.[20] Nucleic Acid Amplification Tests (NAATs) should be used wherever available for chlamydia and gonorrhea testing.[21]
- Screen patients for urethral, rectal, and pharyngeal chlamydia and gonorrhea at least annually. For patients with increased potential exposure to STDs, recommend more frequent screening (three to six months).[22]
- Screen for urethral gonorrhea and chlamydia through urine-based testing, or with a clinician-collected or self-collected urethral swab.[23]
- Screen for rectal and pharyngeal gonorrhea and chlamydia using clinician or self-collected swabs. Most extragenital infections have no symptoms, and many occur without a simultaneous urethral infection, making urine-only testing insufficient for MSM.[24] Extragenital tests for gonorrhea and chlamydia are not approved by the Food and Drug Administration, but many commercial and public health laboratories have verified the test for use.
- Encourage any patient treated for pharyngeal gonorrhea using an alternative regimen to return 14 days after treatment for a test of cure.[25]
- Review clinical recommendations for suspected antibiotic treatment failure.[26] Antibiotic resistance to gonorrhea has been reported in Asia and Europe, and is expected to occur in the United States. Consider contacting your local health department or the National Network of STD Clinical Prevention Training Centers for consultation.
- Offer expedited partner therapy (EPT) to patients being treated for gonorrhea or chlamydia by dispensing oral medication or prescriptions for the treatment of their sexual partners. Check state laws to ensure that EPT is allowable in your state. NCSD maintains updated information about state EPT laws.[27]
- Retest patients for chlamydia or gonorrhea three months after treatment, regardless of potential partner treatment.[28]

Syphilis Screening

- Screen patients for syphilis at least annually. For patients with multiple partners, recommend more frequent screening (every three to six months).[29]
- Consider using a treponemal Rapid Syphilis Test for persons without history of syphilis infection.[30]
- Collaborate with health department staff to aid in the timely interview and partner services for patients with early syphilis infection.[31]

Human Papillomavirus (HPV) Assessment and Vaccination

- Discuss and offer HPV vaccine to all MSM patients, regardless of age and current HPV status, but remain cognizant of financial barriers to immunization and inform patients of potential out-of-pocket costs.[32]

- Conduct an annual visual rectal exam and/or digital rectal exam for all MSM patients. MSM who do not report receptive anal intercourse may still acquire anal HPV. Consider anal pap smear if there is infrastructure locally to follow up abnormal results. Many experts and some guidelines recommend anal pap smears for MSM living with HIV.[33]
- Consider condyloma (genital warts) a marker of potentially oncogenic types of HPV. Condyloma should be removed and trigger patient referral for high-resolution anoscopy. HPV types 16, 18, 31, 33, 45, 52 and 58 can cause cancer and HPV types 6 or 11 can cause warts.[33]
- Inform patients that HPV infection may clear, and is not necessarily a chronic infection like HIV.

Viral Hepatitis Vaccination and Screening

- Vaccinate for Hepatitis A if patients have not been previously vaccinated. Some experts recommend pre-vaccination screening on the same visit as vaccination.[34]
- Screen for chronic Hepatitis B and offer vaccine if patients have not yet been vaccinated or completed the full three doses. Screening should occur on the same date as vaccination.[35]
- Recognize that adult men over 30 years old are less likely to have been vaccinated for Hepatitis B as infants.[36]
- Screen annually for Hepatitis C.[37]

Meningitis Risk and Vaccination

- Discuss sexual networks and history of Meningitis vaccination. Offer vaccine if traveling to areas with reported outbreaks.

Herpes Simplex Virus (HSV) Screening

- Routine blood screening for HSV1 and HSV2 antibodies is NOT recommended. Serum testing and cultures of skin lesions should be guided by the patient's clinical presentation and/or history of known exposure to a partner with HSV infection.[14,15]

HIV Screening, PEP, and PrEP

- Use sex-affirming messaging, such as gain- and loss-framed messaging, when discussing prevention options.[38]
- Screen patients for HIV at least annually. For patients with multiple partners, recommend more frequent screening (every three to six months).[39] Use fourth-generation HIV tests for screening and prior to initiating (PrEP). If fourth-generation tests are not available, use lab or point-of-care antibody tests with whole or fingerstick blood specimens. Supplement antibody tests with HIV viral load testing (NAATs) if there is concern about acute HIV infection.[40]
- Consider Post-Exposure Prophylaxis (PEP) for persons who report consensual or non-consensual exposure to HIV within the past 72 hours. Emphasize the need for rapid initiation of PEP and completion of the full 28-day regimen for maximal effectiveness.[41] Patients with ongoing HIV risk should also be educated about PrEP at the time of PEP initiation.
- Providers do not have to be HIV specialists to prescribe PrEP. Consider PrEP for persons who are eligible per the CDC *PrEP Clinical Guidelines*.[42] Patients on PrEP should be screened for all STDs including HIV every three months.[42] Because most STDs are asymptomatic, STD symptom assessment without screening is not sufficient for management.
- Discuss PrEP with patients living with HIV as a way to inform them of strategies their seronegative partners may use to prevent HIV infection.
- Encourage condom use among PrEP users to prevent other bacterial and viral STDs.

Appendix B provides case studies to illustrate best practices in applying these recommendations in a clinical setting.



How to Implement the MSM Standards of Sexual Health Care

State and Local STD Programs can implement these standards by doing the following:

- Incorporate this document and listed resources to educate providers about quality standards for the health care of gay, bisexual, and other MSM.
- Link to the standards and listed resources on STD program websites.
- Encourage health plans or provider groups to adopt quality improvement activities based on the standards. Effective strategies for improving rates of testing include standing orders for tests, and self-collected rectal and pharyngeal specimens when a full exam is not feasible.
- Partner with national and community-based organizations to promote and educate consumers about optimal sexual health care for gay, bisexual, and other MSM.
- Identify and link providers to laboratories that have validated rectal and pharyngeal specimens for gonorrhea and chlamydia testing. The Association of Public Health Laboratories (APHL) can support this process.

Medical Providers and Plans can incorporate these standards into medical practice by doing the following:

- Ensure that clinical settings are LGBT-friendly and affirming, including providing cultural competency training and monitoring performance of all clinic staff.
- Ensure providers receive cultural competency training specific to sexual history taking and MSM sexual health care. Training resources are listed in Appendix A.
- Document sexual orientation and gender identity in health records to inform health care decision-making and enable quality measurement of health care.
- Incorporate quality standards and adopt quality improvement activities related to MSM sexual health care.
- Consider standing orders for patients with multiple partners to reduce barriers to testing.
- Consider self-collected specimens to reduce barriers to testing if there are concerns about the time required to conduct a full exam.

Academic institutions can incorporate these standards into medical training for medical health professionals, including nurses, nurse practitioners, physicians, and physician assistants, by doing the following:

- Build learners' knowledge, skills, and abilities in conducting quality, LGBT-affirming sexual history taking as a core activity.
- Educate, model, and incorporate practice of all aspects of the physical exam in a sensitive way.
- Educate medical professionals on how to craft gain-frame, sex-positive messaging for all patients, including gay, bisexual, and other MSM.
- Provide opportunities for continuing education accreditation for experienced providers

Gay, bisexual, and other MSM consumers can be empowered to request the health care they need and deserve by being encouraged to do the following:

- Seek providers to whom they feel comfortable disclosing their sexual behaviors. Some large provider groups have lists of LGBT-friendly providers. The Gay and Lesbian Medical Association has a searchable list of LGBT-friendly providers.
- Ask for the tests that they think they need—not all providers will know to test for rectal and pharyngeal infections. NCSD and NASTAD have an optimal care checklist that can be used as a reference.

Conclusions

Quality sexual health care is a right that should be afforded to all people. Working together as a community of providers, health departments, advocates, and consumers, we can shift the paradigm of sexual health to be inclusive of pleasure, and to meet the clinical needs of gay, bisexual, and other MSM of all races, ethnicities, and ages.



APPENDIX A: Resources

Stigma, Inclusivity, and Sexual History Taking

Addressing Stigma: A Blueprint for Improving HIV/STD Prevention and Care Outcomes for Black and Latino Gay Men (NCSD and NASTAD). This report provides recommendations to help health centers reduce stigma around sexuality, race, and gender identity in order to enhance HIV/STD prevention services for Black and Latino MSM. http://www.ncsddc.org/sites/default/files/nastad_ncsd_report_addressing_stigma_may_2014.pdf.pdf

Provider Perspectives on the Needs of Gay and Bisexual Male and Transgender Youth of Color (The Williams Institute). This guide includes recommendations for improving support for GBTQ youth of color in clinical settings. http://williamsinstitute.law.ucla.edu/wp-content/uploads/ACCESS-final-rev-aug-2013.pdf

Sexual History Taking Resources (National Network of Prevention Training Centers). This bank of resources provides tools and training for improving skills related to sexual history taking. http://nnptc.org/resourcetags/sexual-history/

Clinician Guide to Sexual History Taking (California Department of Public Health). This document provides specific questions that follow the 5-P's approach to sexual history taking. https://www.cdph.ca.gov/pubsforms/Guidelines/Documents/CA-STD-Clinician-Guide-Sexual-History-Taking.pdf

Healthcare Equality Index 2016 (Human Rights Campaign). This report rates 2,060 healthcare facilities throughout the U.S. on their inclusion and LGBT equality. http://www.hrc.org/campaigns/healthcare-equality-index

Resources for Providers and Researchers (Gay and Lesbian Medical Association). This site includes resources for improving cultural competence for LGBT patients and a provider directory. http://www.glma.org/index.cfm?fuseaction=Page.viewPage&pageId=940&parentID=534

Safer Sex for Trans Bodies (Whitman-Walker Health). This resource relates to transgender sexual health and can serve as a complement to this document with greater body inclusivity. https://www.whitman-walker.org/wp-content/uploads/2014/11/Trans-Safer-Sex-Guide-FINAL-1.pdf

Understanding and Eliminating Health Disparities (National LGBT Health Education Center). This report outlines basic LGBT terminology, demographics, and health disparities, and describes key issues to address within the healthcare setting in order to provide LGBT-friendly medical care. http://www.lgbthealtheducation.org/wp-content/uploads/12-054_LGBTHealtharticle_v3_07-09-12.pdf

Legislative trends for STD Prevention in 2014, Part II: EPT (NCSD). This article outlines the changes in EPT laws from 2006 to 2014, with information about the status of EPT laws in each state. http://www.ncsddc.org/blog/legislative-trends-std-prevention-2014-part-ii-ept

National Clinical Guidelines and Recommendations

2015 STD Treatment Guidelines (CDC). These guidelines provide clinical guidelines for prevention, screening, treatment, and partner management. http://www.cdc.gov/std/tg2015/

HIV Guidelines and Recommendations (CDC). This site includes links to clinical guidelines for HIV prevention, testing, and treatment. http://www.cdc.gov/hiv/guidelines/

HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C (American Association for the Study of Liver Disease). http://www.hcvguidelines.org/

Clinical Resources and Training

Providing Optimal Care for Your MSM Patients (NCSD and NASTAD). This brochure is intended as a guide for providers and can be used as a supplement to these standards. http://www.ncsddc.org/sites/default/files/provider_brochure2.pdf

The National Network of STD Clinical Prevention Training Centers. These training centers offer resources, training, and clinical consultation for STD providers across the United States. http://nnptc.org/

His Health (NASTAD). This resource supports building capacity to deliver high-quality, affirming care for Black LGBT patients with an accredited CME/CNE course series. https://www.hishealth.org/

A Clinician's Resource for STDs in Gay Men and Other MSM (California Department of Public Health). This comprehensive guide includes information about clinical manifestations, screening protocols, treatment recommendations, and model language for intake forms for MSM patients. http://www.cdph.ca.gov/programs/std/Documents/MSMToolkit.pdf

A Provider's Introduction to Substance Abuse Treatment for Lesbian, Gay, Bisexual, and Transgender Individuals (SAMHSA). This guide provides background information on cultural and clinical considerations for counselors, therapists, administrators, and other substance abuse treatment providers working with LGBT clients. https://store.samhsa.gov/shin/content/SMA12-4104/SMA12-4104.pdf

Preventive Male Sexual and Reproductive Health Care: Recommendations for Clinical Practice (Male Training Center for Family Planning and Reproductive Health). These recommendations include discussion of reproductive health options for men who are interested in family planning. http://www.maletrainingcenter.org/wp-content/uploads/2014/09/MTC_White_Paper_2014_V2.pdf

Resources for Advocates and Consumers

For Men Only: Your Sexual Health (NCSD and NASTAD). This brochure is intended as a guide for gay, bisexual, and other MSM of color. http://www.ncsddc.org/sites/default/files/patient_brochure2.pdf

Well Versed (NASTAD). A consumer-facing tool for Black Gay, Bisexual, and MSM in having conversations with their health care provider. https://www.wellversed.org/

CDC Fact Sheet: What Gay, Bisexual and Other Men Who Have Sex with Men Need to Know About Sexually Transmitted Diseases (CDC). This fact sheet is intended for MSM consumers. http://www.cdc.gov/std/life-stages-populations/stdfact-msm.htm

Building Healthy Online Communities (NCSD). A partnership of public health and mobile dating app owners in to support gay men's sexual health. https://www.bhocpartners.org *PrEPLocator.org* (Emory University). This website lists pre-exposure prophylaxis (PrEP) prescribers in the United States using zip codes. There are additional settings for uninsured persons and persons in need of patience assistance. https://preplocator.org/

Straight for Equality in Healthcare Chapter Field Guide (PFLAG). This resource describes actions that advocates and consumers can do to improve healthcare for LGBT patients. https://www.pflag.org/publication/straightforequalityhealthcarechapterguide

Gay and Lesbian Medical Association Provider Directory. This directory is a searchable list of primary care and other providers that have affirmed their commitment to LGBT-inclusive health care. http://www.glma.org/index.cfm?fuseaction=Page.



APPENDIX B: Case Studies

Below are two examples and follow-up questions were provided by physicians on the Blue Ribbon Panel. These case studies illustrate some of the considerations when discussing an approach to sexual health care that if affirming and strengths-based.

Case Study #1

A 23-year-old white male presents to your practice to be treated for syphilis. The patient states that he is "straight," but that he sometimes has sex with other straight men. He does not use condoms for anal sex because he states that his older partners prefer "raw" sex. The patient denies being a receptive anal sex partner. When asked permission to do an exam of his rectum, he declines exam. A review of his medical record demonstrates a previous diagnosis of rectal chlamydia. The doctor approaches him about PrEP, but the patient states that he does not think he needs it. He says that it is good for "gay guys," but not for him. He has heard that all guys who use PrEP are bottoms and that taking PrEP means that they are "whores."

How do you deal with stigma related to same-sex behaviors in this patient?

It is important to meet the patient where he is. Not every MSM fits neatly into a category of gay, bisexual, etc. Being open-minded and open in language to match how the patient expresses his sexuality is critical. Misnaming him, or forcing him into a category based on provider experience, is both detrimental to the relationship and potentially stigmatizing. It is important to allow the patient to have the self-efficacy to make decisions while still providing him with care that matches his sexual life.

What is the strategy for providing him good clinical care given the limits he has set?

Do what you can and what he allows you to do. If he will not let you examine his genitals, then offer STD testing alone. If he will not let you swab his anus, offer him the option of self-collection of swabs. After all, it is his body, and he calls the shots. Meeting him where he is at will allow for frank discussions and alliance building that a more dictatorial strategy would potentially compromise.

Case Study #2

Paul is a 19-year-old black man who is living with HIV who presents with dysuria (painful urination). He is a member of the house ball community and refers to them as his family. His biological family kicked him out of their house when they discovered his HIV medications under his mattress. Paul has not engaged with any medical care for nearly two years. Paul's last T cells were 378 and his VL was undetectable. He hasn't taken meds for over 18 months. He currently does not have housing. He uses hook-up apps to find people whose apartments he can sleep in, often in exchange for sex. When you examine Paul, you find that he has some rectal bleeding. He confirms that he was recently sexually assaulted by someone he met on an app.

How does the issue of equity for LGBTQ youth enter the story of movements for race equity?

It is important for providers taking care of LGBTQ youth. It is equally important to address the intersectionality that exists between age, race/ethnicity, and sexual orientation that often is neglected by LGBTQ health initiatives.

While there are overlapping disparities among racial/ethnic and sexual and gender minorities, there are unique differences that impact Black and Latino LGBTQ youth that need to be considered when caring for these populations. Paul's experiences as a Black man in our society need to be taken into account and considered when providing health services.

This understanding needs to be reflected in the way that we communicate with Paul and how we formulate our health plans or strategies with, and for, him. For example, as providers we should consider that many African Americans may have a general distrust of the healthcare system. This and other issues may impact Paul's adherence to medications. It is important for clinicians to see Paul as he exists outside of his marginalization. Though he might be at a sensitive social location--his culture, resilience, and individuality should still be centered. Often times, well-meaning individuals get into the habit of equating certain identities as lived oppression and nothing more. Consider his marginalization and keep it in mind, but don't have that substitute over his agency and uniqueness as an individual. He is not just a black MSM and treating him holistically can affirm this.

How can HIV or sexual health concerns be made more important when basics in Paul's hierarchy of needs are not being addressed?

It's very challenging for patients to focus on sexual (or HIV and STD) health concerns when some basic needs are not being addressed. We know that the most fundamental causes of health disparities are socioeconomic disparities. Providers will find this information helpful in establishing a relationship with their patients and in developing a more effective therapeutic plan to inquire and identify potential socioeconomic stressors (lack of money, homelessness, etc.) that may compete with the patient's ability to participate in the management of his sexual health. This is true for almost any kind of patient–provider relationship, but it is particularly important when working with LGBTQ youth, especially youth from disadvantaged communities.

It is equally important for providers to be aware of support services and other resources available in their communities, and to have a referral system in place to assist those patients with identified needs. Paul's history merits an assessment of his social and possible mental health needs. He can benefit from emergency housing or some assistance that may provide temporary shelter until things are more stable and he can find more permanent housing, employment assistance, access to food services (food pantry or food stamps), and social and emotional support that may help him to recover from what seems to be a low point in his life. The expectation that Paul will be attending clinical appointments regularly or taking medications every day unless some of these major life issues are addressed is unrealistic.



APPENDIX C: References

[1]CDC. *Sexually Transmitted Disease Surveillance 2015*. Atlanta: U.S. Department of Health and Human Services, 2016. https://www.cdc.gov/std/stats15/

[2]CDC. *HIV Surveillance Report*, 2015; vol. 27. http://www.cdc.gov/hiv/library/reports/hiv-surveillance.html. Published November 2016. Accessed May 5, 2017.

[3]Morrison, A. (2015). *Black Unemployment Rate 2015: In Better Economy, African-Americans See Minimal Gains.* International Business Times. http://www.ibtimes.com/black-unemployment-rate-2015-better-economy-african-americans-see-minimal-gains-1837870

[4]NAACP. *Criminal Justice Fact Sheet* (2015). http://www.naacp.org/pages/criminal-justice-fact-sheet

[5]Kerby, S. *The Top 10 Most Startling Facts About People of Color and Criminal Justice in the United States: A Look at the Racial Disparities Inherent in Our Nation's Criminal-Justice System.* Center for American Progress. 2012. https://www.americanprogress.org/issues/race/news/2012/03/13/11351/the-top-10-most-startling-facts-about-people-of-color-and-criminal-justice-in-the-united-states/

[6]CDC. *Sexually Transmitted Disease Surveillance 2015*. Atlanta: U.S. Department of Health and Human Services; 2016. https://www.cdc.gov/std/stats15/

[7]CDC. *HIV Surveillance Report, 2014*; vol. 26. http://www.cdc.gov/hiv/library/reports/surveillance/. Published November 2015.

[8]Petrolli, et al. *Physician awareness of sexual orientation and preventive health recommendations to men who have sex with men.* Sex Transm Dis, 2011. (38;1:63–67).

[9]Bernstein, K., et al. *Same-sex Attraction Disclosure to Health Care Providers Among New York City Men Who Have Sex With Men.* Annals of Internal Medicine. 168 (2008):1448–1464.

[10]Morin, et al. APHA Annual Meeting, 2003. Abstract #60724.

[11]CDC. *STD Treatment Guidelines, 2015*. MMWR. 2015; 64(RR3). www.cdc.gov/std/tg2015/clinical.htm

[12]Epstein, R., et al. *Awkward Moments in Patient–Physicians Communication about HIV Risk.* Annals of Internal Medicine. 128 (1998):435–442.

[13]NCSD and NASTAD. *Addressing Stigma: A Blueprint for Improving HIV/STD Prevention and Care Outcomes for Black and Latino Gay Men.*Washington, DC: 2014.

[14] CDC. *STD Treatment Guidelines, 2015.* MMWR. 2015; 64(RR3). http://www.cdc.gov/std/tg2015/clinical.htm

[15]CDC. *STD Treatment Guidelines, 2015.* MMWR. 2015;64(RR3). www.cdc.gov/std/tg2015/clinical.htm

[16]Mantell, J., Kelvin, E., Exner, T., Hoffman, S., Needham, S., & Stein, Z. *Anal Use of the Female Condom: Does Uncertainty Justify Provider Inaction?* AIDS Care. 2009 Sep; 21(9):1185–1194.

[17]Gibson, S., McFarland, W., Wohlfeiler, D., Scheer, K., & Katz, M. *Experiences of 100 men who have sex with men using the Reality condom for anal sex.* AIDS Education and Prevention. 1999 Feb; 11(1):65–71.

[18]Charania, M.R, et al. *Efficacy of Structural-Level Condom Distribution Interventions: A Meta-Analysis of U.S. and International Studies, 1998–2007*. AIDS Behav (2011) 15:1283–1297.

[19]CDC. *CDC Vital Signs.* Available at: http://www.cdc.gov/vitalsigns/hivprep/

[20]CDC. *STD Treatment Guidelines, 2015* MMWR. 2015; 64(RR3). https://www.cdc.gov/std/tg2015/specialpops.htm

[21]CDC. *Recommendations for the Laboratory-Based Detection of Chlamydia trachomatis and Neisseria gonorrhoeae—2014.* MMWR 2014; 63 (No. RR-2). http://www.cdc.gov/std/laboratory/2014labrec/default.htm

[22]CDC. *STD Treatment Guidelines, 2015.*MMWR. 2015; 64(RR3). https://www.cdc.gov/std/tg2015/specialpops.htm

[23]CDC. *STD Treatment Guidelines, 2015.* MMWR. 2015; 64(RR3). https://www.cdc.gov/std/tg2015/specialpops.htm

[24]Patton, E. et al. *Extragenital Gonorrhea and Chlamydia Testing and Infection Among Men Who Have Sex With Men—STD Surveillance Network, United States, 2010-2012.* Clinical Infectious Diseases, 2014; 58(11):1564–70.

[25]CDC. *STD Treatment Guidelines, 2015.* MMWR. 2015; 64(RR3). https://www.cdc.gov/std/tg2015/specialpops.htm

[26]CDC. *STD Treatment Guidelines, 2015.* MMWR. 2015; 64(RR3). http://www.cdc.gov/std/tg2015/gonorrhea.htm

[27]NCSD. Legislative trends for STD Prevention in 2014, Part II: EPT. http://www.ncsddc.org/blog/legislative-trends-std-prevention-2014-part-ii-ept

[28]CDC. *STD Treatment Guidelines, 2015.* MMWR. 2015; 64(RR3). https://www.cdc.gov/std/tg2015/gonorrhea.htm

[29]CDC. *STD Treatment Guidelines, 2015*. MMWR. 2015;64(RR3). https://www.cdc.gov/std/tg2015/specialpops.htm

[30]Hess, K., Fisher, D., & Reynolds, G. *Sensitivity and specificity of point-of-care rapid combination syphilis-HIV–HCV tests. PLoS One*. 2014 Nov 6; 9(11):e112190.

[31]CDC. *Recommendations for Partner Services Programs for HIV Infection, Syphilis, Gonorrhea, and Chlamydial Infection.* MMWR. November 07, 2008/57(RR09); 1–63. http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5709a1.htm

[32]CDC. *STD Treatment Guidelines, 2015.*MMWR. 2015; 64(RR3). http://www.cdc.gov/std/tg2015/hpv.htm

[33]California Department of Public Health. *A Clinician's Resource for Sexually Transmitted Diseases (STDs) in Gay Men and Other Men Who Have Sex with Men (MSM)—The MSM Toolkit.* Published July 2015. Available at: http://std.ca.gov/msmtoolkit

[34]CDC. *STD Treatment Guidelines, 2015.* MMWR. 2015; 64(RR3). http://www.cdc.gov/std/tg2015/hepatitis.htm

[35]CDC. *STD Treatment Guidelines, 2015*. MMWR. 2015; 64(RR3). http://www.cdc.gov/std/tg2015/hepatitis.htm

[36]Reiter, P. & Brewer, N. *Hepatitis B Vaccination among a National Sample of Gay and Bisexual Men.* Sex Transm Dis. 2011 Mar; 38(3):235–238.

[37]American Association for the Study of Liver Diseases—Infectious Diseases Society of America. *Recommendations for testing, managing, and treating hepatitis C.* http://www.hcvguidelines.org.

[38]Rothman, A. J., Bartels, R. D., Wlaschin, J.,&Salovey, P. *The Strategic Use of Gain- and Loss-Framed Messages to Promote Healthy Behavior: How Theory Can Inform Practice*. Journal of Communication, 2006; 56:S202–S220.

[39]CDC. *Revised Recommendations for HIV Testing of Adults, Adolescents, and Pregnant Women in Health-Care Settings.* September 22, 2006/55(RR14); 1–17. http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5514a1.htm

[40]CDC and Association of Public Health Laboratories. *Laboratory Testing for the Diagnosis of HIV Infection: Updated Recommendations.* Available at http://dx.doi.org/10.15620/cdc.23447. Published June 27, 2014.

[41]CDC. *Updated guidelines for antiretroviral postexposure prophylaxis after sexual, injection drug use, or other nonoccupational exposure to HIV—United States, 2016.* Published April 18, 2016. https://stacks.cdc.gov/view/cdc/38856

[42]NCSD. *NCSD Sends Third Letter to CDC Regarding STD Screening Intervals and PrEP.* March 11, 2016. http://www.ncsddc.org/policy-updates/ncsd-sends-third-letter-cdc-regarding-std-screening-intervals-and-preponsidviewPage&pageId=939&grandparentID=534&parentID=938&nodeID=1

NCSD
National Coalition of STD Directors
Promoting Sexual Health Through STD Prevention

NASTAD

National Network of STD Clinical Prevention Training Centers






TAKING ROUTINE HISTORIES OF SEXUAL HEALTH:
A System-Wide Approach for Health Centers

New Edition: November 2015

NATIONAL LGBT HEALTH EDUCATION CENTER
A PROGRAM OF THE FENWAY INSTITUTE

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TAKING ROUTINE HISTORIES OF SEXUAL HEALTH:
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November 2015

Introduction

Learning about the sexual health and behavior of patients is an important part of providing high-quality, patient-centered, accessible, and efficient health care to the people in your health center. This toolkit has been created to help develop and implement systems for collecting routine histories of sexual health with all adult patients. Sexual histories should also be taken with adolescent patients. However, because the history-taking approach differs somewhat for adolescents, we recommend supplementing the information provided here with additional resources focused on adolescents. Understanding that all health centers are different, the tools have been designed to be adaptable to different practices and patient populations. Additionally, an extensive list of resources has been included to further your learning about sexual health and behavior and taking routine sexual histories.

This toolkit is divided into three sections:

- The Routine Sexual History Tool 2
- Special Populations and Considerations 16
- Getting it Done: Recommendations and Tools for Implementing Routine Sexual Histories in your Health Center 22

Section I. The Routine Sexual History Tool

We can learn about our patients' sexual health and behavior by taking a routine sexual history. Sexual history information should be taken from all adolescent and adult patients, regardless of gender, race, ethnicity, socioeconomic status, sexual orientation, and gender identity.

IN THIS SECTION:

- The Routine Sexual History: What, Why, and How? 3
- Asking Sexual History Questions: How to Begin 5
- Sexual Risk Assessment 8
- Counseling and Education 12
- Sexual Health, Function, and Identity Questions 14
- Resources for Further Learning 15

The Routine Sexual History: What, Why, and How?

WHAT IS A ROUTINE SEXUAL HISTORY?

The routine sexual history is an essential part of a patient's comprehensive history during an annual prevention visit. In busy health care practices, it is not uncommon for providers to skip the sexual history unless a patient has signs or symptoms of sexually transmitted diseases (STDs). Providers may also avoid taking sexual histories because they do not feel comfortable asking sensitive and potentially embarrassing questions. However, the sexual history can be done in a timely and straightforward manner when health centers take a few initial steps to set up systems that support providers, and other members of the clinical care team, in taking histories.

WHY IS THE ROUTINE SEXUAL HISTORY IMPORTANT FOR PATIENT HEALTH?

When we ask about our patient's sexual partners and practices, we are practicing patient-centered care. Studies show that our patients want us to ask about sexual issues. In a survey of 500 men and women over age 25, 85% of respondents expressed an interest in talking to their providers about sexual concerns, even though 71% thought their provider would likely dismiss their concerns.[1] Moreover, a sexual history followed by appropriate, targeted discussion about ways to stay healthy can enhance the patient-provider relationship.

The sexual history not only gives opportunities to educate and counsel patients about HIV, STDs, and viral hepatitis, but also allows providers, or other members of the clinical care team, to connect patients to treatment and care. Without taking a sexual history, it is difficult to know what tests or vaccinations are needed. These mostly "silent" diseases can go unnoticed for long periods of time until they lead to more serious illness. Without treatment, they can also spread to other partners and increase disease in the community.

There are new federal government programs and initiatives that have the goal of greatly reducing HIV, STDs, and viral hepatitis in the U.S. health care system. Community health centers and other health care practices that care for underserved and vulnerable populations are essential to reaching these goals because their patients are often most at risk.

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1 Marwick C. Survey says patients expect little physician help on sex. *JAMA*. 1999;281:2173-4.

HOW IS THE SEXUAL HISTORY TAKEN?

Ideally, a patient's sexual history should be taken at their initial visit to the health center, and at annual prevention visits. There are two methods for taking the sexual history:

1. By the provider, or other member of the clinical care team, during the visit
2. Filled out by the patient in a paper or electronic form in advance of the visit, and then reviewed with the provider, or other member of the clinical care team, during the visit

Your team can decide what works best for your practice. Paper and electronic forms can provide more information in a shorter amount of time, and can save a lot of time during the visit. Because the questions are standard across all patients, this makes it easier for entering information into electronic health records, ensures that these questions are asked, and helps your team measure and track population health. Templates for sexual histories can often be built into electronic medical records (see the sample at the end of this tool kit).

If using paper or electronic forms, you should consider the following:

- Will paper forms be sent to patients' homes and/or filled out in the waiting rooms?
- Do the waiting rooms offer enough privacy when filling out forms?
- Might patients feel uncomfortable handing forms to receptionists or medical assistants, some of whom they might know from the community? How can you train staff to handle the forms?
- How will you ensure protection of data in electronic forms?
- Is the health literacy level of the questions and instructions appropriate for your population?

Asking Sexual History Questions: How to Begin

For a customizable Word version of this section, visit
http://www.lgbthealtheducation.org/?attachment_id=3122 or
http://www.nachc.org/client//AskingSexualHistoryQuestions%200513.docx

1. SET THE STAGE:

- The sexual history can come up naturally when talking with a patient as part of the social history. It can also be asked in relation to their past medical history or history of reproductive health.
- Before starting, you can let the patient know that you ask sexual history questions of all patients every year as part of their routine care. You can use a statement such as:
    - I am going to ask you a few questions about your sexual history. I ask these questions at least once a year of all my patients because they are very important for your overall health. Everything you tell me is confidential. Do you have any questions before we start?
- If patients want to know why you need to ask these questions, and why they are important to their health, you can use statements such as:
    - Your sexual health is important for your overall emotional and physical health.
    - We ask these questions every year because it is common for people's sexual behaviors and partners to change over time.
    - As you may know, sexual activity without protection can lead to sexually transmitted diseases. These kinds of diseases are very common and often there is no way for you to tell you have them. If we don't catch and treat these diseases, you can become very sick.
    - These questions can also help guide a conversation about ways to protect yourself from sexually transmitted diseases, unwanted pregnancy, or other things that may concern you. It will also give you an opportunity to talk about problems with, or changes in, sexual desire and functioning.
- If the patient declines to complete a sexual history with you, ask if there is another member of the clinical care team with whom they might be more comfortable. If they have already provided this information to someone else (e.g., social worker), see if they will sign a release to allow primary care to obtain that information.
- Be straightforward, but sensitive and open to different behaviors (See Effective Communication Strategies When Taking a Sexual History in Section III for more recommendations on ways to do this).

2. ASK THREE SCREENING QUESTIONS:

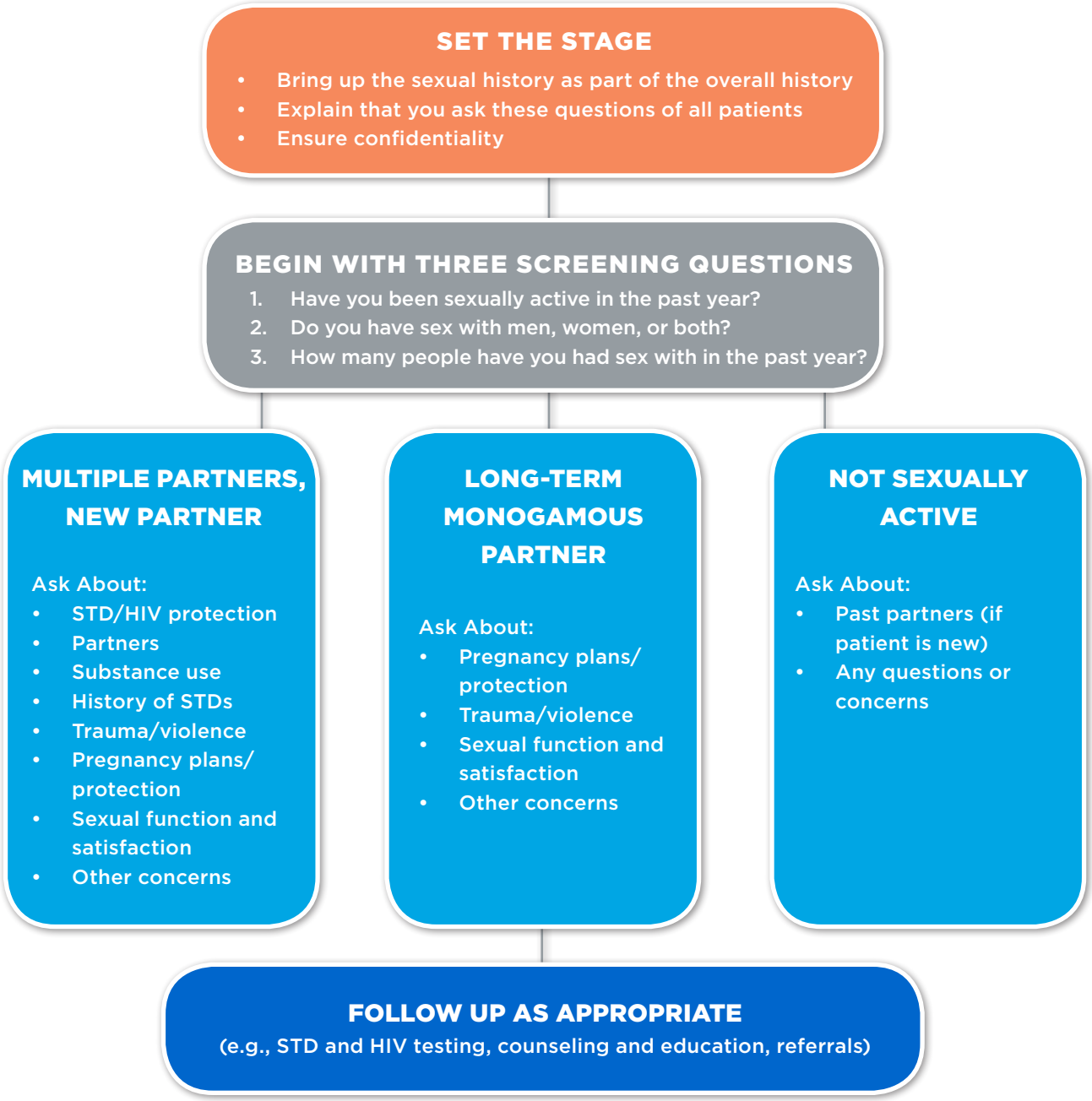
- Have you been sexually active in the past year?
- Do you have sex with men, women, or both? (If both, ask the next question twice—once for male partners, and once for female partners.)
- How many people have you had sex with in the past year?

3. DETERMINE IF THE PATIENT NEEDS A MORE DETAILED RISK ASSESSMENT:

- In general, patients with multiple sex partners, and male patients who have sex with men, should be asked additional questions to assess their risk for HIV and STDs.
- If a patient reports only one partner, ask if this is a casual or long-term partner, and if the patient knows if their partner is having sex with other people. Questions about the use of protection, history of STDs, and other risk factors may still be needed for these patients.
- If a patient has not been sexually active in the past year, but this is the first time you have taken their sexual history, ask if they've ever been sexually active, the gender of their past partners, and how many partners they have had. Again, you may wish to do further screening questions about protection, relationship to partners, etc.
- All patients, regardless of sexual history, should also be asked whether or not they have any concerns about keeping themselves sexually safe and healthy.
- Although these questions are brief, it is important for providers, or other members of the clinical care team, to recognize that a sexual history will, in some situations, lead to a longer discussion of important sexual health and related issues.

ALGORITHM FOR CONDUCTING A SEXUAL HISTORY

For a customizable Word version of this section, visit
http://www.lgbthealtheducation.org/?attachment_id=3072
or www.nachc.org/client/SexualHealthAlgorithm%200513.docx



Sexual Risk Assessment[2, 3]

The Centers for Disease Control and Prevention (CDC) has developed a simple categorization of sexual history questions that may help providers, or other members of the clinical care team, remember which topics to cover. These are called the Five P's:



Partners **Practices** **Past History of STDs** **Protection from STDs** **Pregnancy Plans**

The following risk assessment questions are organized according to these categories.

PARTNERS

These questions may already have been covered during the first three screening questions (see page 6) of the sexual history. They are listed again here but do not need to be repeated.

- Do you have sex with men, women, or both? (if both, ask the next question twice - once for male partners, and once for female partners)
- How many people have you had sex with in the past year?

Additional questions about partners:

- Is it possible that any of your sex partners in the past year had sex with someone else while they were still in a sexual relationships with you?
- Have you experienced physical, sexual, or emotional violence from a partner?

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2 This risk assessment has been adapted from: Centers for Disease Control and Prevention. A guide to taking a sexual history. Available at: http://www.cdc.gov/lgbthealth/

3 STD/HIV Risk Assessment & Risk Reduction: A Quick Reference Guide. March 2008. Mountain Plains AIDS and Education Training Center. Seattle STD/HIV Prevention Training Center.

PRACTICES AND PROTECTION FROM STDS

Some patients respond better to open-ended questions about their sexual practices, and some prefer yes or no questions. For transgender patients, younger patients, and women who have sex with women, for example, you may find that open-ended questions are preferred and may bring you more accurate information. These questions can be asked in a conversational manner, and may make your patient feel more comfortable. Here are some examples:

- What kinds of sex are you having? (for example, oral sex, vaginal sex, anal sex, sharing sex toys)
- What do you do to protect yourself from HIV and STDs?
- Tell me about when you use condoms.
- When was the last time you had unprotected sex?
- What do you know about your partner(s)' past or other sexual activities?
- Do you have any concerns about your sex life?

Below are simple, direct questions about sexual practices and condom use. Some patients may feel more comfortable with these rather than more open-ended questions. Choose questions based on the sex of partners.

- I am going to ask you some questions about the kinds of sex you have and whether you use protection.
- In the past year, have you had:
    - Anal sex? (penis in the anus/rear end)
      Do you use condoms never, sometimes, or always when you have anal sex?
      For men who have sex with men, you will need to ask if they received and/or gave anal sex
    - Vaginal sex? (penis in the vagina)
      Do you use condoms never, sometimes, or always when you have vaginal sex?
    - Oral sex? (mouth on penis, vagina, or anus)
      Do you use condoms/dental dams never, sometimes, or always when you have oral sex?
- If condom use is sometimes:
    - Can you tell me when you use condoms? With which partners?
- If never:
    - There are a lot of reasons why people don't use condoms. Can you tell me why you are not using them for sex?

PRACTICES: ADDITIONAL QUESTIONS TO IDENTIFY HIV AND VIRAL HEPATITIS RISK

These questions are very sensitive, so you can remind patients that their answers are confidential.

- Have you or any of any of your partners ever injected drugs / shot drugs into their bodies?
- Have you or any of your partners ever received or given money, shelter, or drugs for sex?
- Have you or any of your partners ever been in jail?

PRACTICES: SUBSTANCE USE DURING SEX

Drugs and alcohol can increase risk for HIV and STDs and can affect decisions about the types of counseling and referrals patients need. Additional resources on this topic can be found in the resources section.

- Do you use alcohol or drugs when you have sex?
- Do/does your partner(s)?

PAST HISTORY OF STDS

- Have you ever had a sexually transmitted disease?
    - These are often called STDs. They are diseases you can get from a sexual partner.
        - Some examples are gonorrhea, chlamydia, herpes, genital warts, and syphilis.
    - Sometimes, but not always, when you have an STD, there will be itching, burning, dripping, or warts or sores on or near your (vagina / penis / genitals) or buttocks (rear end, bottom).
    - If yes:
        - What kind have you had?
        - When did you have it?
        - How were you treated/what medications did you take?
        - Have you noticed any symptoms, like burning, itching, sores or dripping, since you were treated?
- Have you ever been tested for any (other) STDs?
    - If yes, when and what were the test results?

- To your knowledge, have you ever had sex with someone who has been diagnosed with an STD?
    - If yes, did you see a health professional for the same STD?
    - Were you treated? What medications did you take?
    - If you don't know, do you want to talk to someone about how to talk to your partner(s) about STDs?
- Have you ever been tested for HIV?
    - If yes, when were you tested? Can you tell me the test result?
        - ☐ If patient did not return for test result, ask why.
    - If no, would you consider being tested today? It is recommended that everyone in the country get tested for HIV at least once, just to be safe and sure.
        - ☐ There are recommended tracking tools for routine HIV testing. A good resource for this is: NACHC's Integrating HIV Screening into Routine Primary Medical and Dental Care: A Health Center Model (www.nachc.com/hiv andmodel.cfm).

PREGNANCY PLANS

When asking questions about contraception, it is important to avoid assumptions about pregnancy risk or need for prevention. For example, people who exclusively have same-sex partners may feel misunderstood or invisible if they are asked about contraceptives and pregnancy prevention without acknowledgement that this may not apply to them.

At the same time, do not assume that LGBT patients are not interested in having children. For all patients, be sure to have adoption, insemination, and surrogacy referrals on hand.

Sample questions (choice of questions will depend on how the patient answered questions on partners and practices):

- Do you have any plans or desires to have (more) children?
- Do you or your partner(s) ever have a need for a contraceptive to avoid pregnancy?
- Do you want information on birth control?
- Do you have any questions or concerns about pregnancy prevention?
- What are you doing to prevent yourself or your partner from getting pregnant?

Counseling and Education

COUNSELING AND REFERRALS

During the visit, you can talk to all patients about their interest in learning risk reduction behaviors. Let them know there are a number of steps they can take to protect themselves, such as:

- Reduce number of partners
- Avoid or reduce having anonymous partners or "one night stands"
- Only engage in lower-risk activities, like oral sex or mutual masturbation
- Carry condoms at all times
- Use condoms consistently (at every encounter) for anal and vaginal sex
- Write down ideas about how you might protect yourself and your partners. Think about situations where you find yourself taking risks. What could you do differently?
- Do not have sex while drunk or high, or develop a plan for how you can make sure you are protecting yourself
- Talk to your partners about HIV and STD status
- Talk to your partners about using condoms before you have sex
- Make sure you are following directions on how to use condoms correctly

It will be very helpful if you have resources on hand to support the above points. Offer brochures, websites, referrals, etc.

For very high-risk patients, especially those with complicating behavioral, drug and alcohol use issues and/or history of trauma, you can manage their care in conjunction with appropriate counseling resources and colleagues. As part of your practice's transformation to a patient-centered medical home, create a team-based care plan with behavioral health staff and patient input. Make sure you have network systems in place to ease the referral process.

You may also need to look into referrals to outside service agencies and community-based organizations. Some organizations offer evidence-based behavioral interventions appropriate for different populations, such as youth, racial/ethnic minorities, and gay and bisexual men.

EDUCATION

Some patients want to understand the difference between HIV prevention and STD prevention. Here are a few points you can share:

- It is not likely you will get HIV from oral sex. However, giving and receiving oral sex can give you STDs
- Sharing sex toys without condoms or other latex barriers can give you STDs
- Condoms greatly reduce the risk of STDs, but it is still possible to get them through areas not covered by the condom
- Even when both partners are HIV-infected they should still use condoms to avoid STD transmission and the (small) possibility of infection with a second strain of HIV
- Having an STD can make it more likely you will get HIV

Sexual Health, Function, and Identity Questions

In addition to sexual risk questions, there are a few questions to assess your patients' sexual health, function, and comfort with their sexuality. These issues are very important to a person's emotional and physical health. We recommend you ask these periodically.

- Do you have any concerns about your sexual function? For example, do you have trouble with (maintaining an erection, ejaculation, achieving orgasm?)
- Have you had any changes in sexual desire or satisfaction?
- Do you have any concerns or questions about your sexual orientation, sexual identity, or sexual desires?
    - Do you feel you are getting enough support and acceptance of your sexual / gender identity from friends and/or family?
    - Do you want to speak with anyone further (or join a support group) about any concerns you have about your sexual / gender identity? (Have appropriate behavioral health referrals on hand.)

Resources for Further Learning

NATIONAL HIV/STD INITIATIVES

National HIV/AIDS Strategy www.whitehouse.gov/administration/eop/onap/nhas

CDC's HIV/AIDS Testing Recommendations www.cdc.gov/hiv/topics/testing/guideline.htm

Combating the Silent Epidemic of Viral Hepatitis: Action Plan for the Prevention, Care and Treatment of Viral Hepatitis www.aids.gov/news-and-events/hepatitis/

NACHC video series on HIV and Related Issues www.nachc.com/clinical-issues.cfm

TAKING A SEXUAL HISTORY

Patient sexual health history: What you need to know to help. (free training video) American Medical Association: www.bigshouldersdubs.com/clients/AMA/23-AMA-HealthHistory.htm

CDC's A Guide to Taking a Sexual History. (Brochure) www.cdc.gov/std/treatment/SexualHistory.pdf

The Proactive Sexual Health History. (Journal article) Margaret R.H. Nusbaum, Carol D. Hamilton, *Am Fam Physician*. 2002 Nov 1;66(9):1705-1713. www.aafp.org/afp/2002/1101/p1705.html

Section II. Special Populations and Considerations

Gay and bisexual men, or other men who have sex with men (MSM), and transgender women are at high risk for HIV, STDs and viral hepatitis. In order to better serve these populations, it is important for sexual histories to be sensitive to and inclusive of these patients.

IN THIS SECTION:

- Some Helpful Definitions to Start 17
- Special Considerations for Men who Have Sex with Men 18
- Special Considerations for Transgender People 20
- Resources for Further Learning 21

Some Helpful Definitions to Start

LGBT stands for lesbian, gay, bisexual, and transgender people. LGBT Americans are diverse in terms of race, ethnicity, age, income levels, education, personality, and all other factors that make individuals unique. What unites them is the fact that they are sexual and gender minorities. In other words, their sexual orientation or gender identity is different than the majority of the population, and they experience discrimination and stigma based on this status.

Sexual orientation tells you about a person's sexual and romantic attractions. Common words used to describe sexual orientations:

- Lesbian describes women who are emotionally and sexually attracted mostly to women.
- Gay describes men who are emotionally and sexually attracted mostly to men. Gay is sometimes used to describe all people who have same-sex attractions.
- Bisexual describes people who are emotionally and sexually attracted to both men and women.
- Heterosexual (straight) describes people who are emotionally and sexually attracted mostly to people of the opposite gender.

Gender Identity is one's internal sense of being a man, woman, or other gender (such as transgender). Everyone has a gender identity. Most people feel their gender identity is the same as the sex they were assigned at birth (for example, a person born male who feels male). But some people feel their gender identity is different than their birth sex (for example, a person who is born female but feels male). Some people have a gender identity that is both male and female, or that is neither male nor female.

Transgender does not have one single accepted definition. Most commonly, transgender refers to people whose gender identity is not the same as the sex they were assigned at birth. There are many terms to describe people within this group, including male-to-female (MTF), female-to-male (FTM), trans woman, trans man, gender-affirmed female, gender-affirmed male, and gender affirmed person. Some patients may choose to refer to themselves as the gender they identify with (man or woman).

Transgender individuals choose to present themselves to the world in a variety of ways.

- Some, but not all, choose to take hormones or surgically change their body to align with their gender identity
- Some, but not all, change hairstyle, dress, mannerisms, etc.
- Most, but not all, will change their given name
- Most, but not all, will use the pronouns that match their gender identity

Transgender is also sometimes used to include all people who feel their gender does not conform with what culture and society traditionally thinks is appropriate for that gender. This includes individuals who prefer not to define themselves by any gender; those who feel their gender contains both male and female parts; and those who feel their gender changes from day to day or week to week, etc. Some people, especially younger people, use identity terms other than transgender, such as genderqueer, queer, or gender fluid. They also may use "he" pronouns one day, and change to "she" pronouns another day.

Special Considerations for Men who Have Sex with Men

The Centers for Disease Control and Prevention (CDC) reports that in 2010, 63% of new HIV infections in the U.S. were transmitted through male-to-male sexual contact.[4] Gay and bisexual men, and other men who have sex with men (MSM), may also be at increased risk for certain STDs, including syphilis, hepatitis A and B, gonorrhea, anal HPV, and chlamydia. Young (13-24 years) black MSM are at the highest risk of HIV in the U.S., accounting for more than half of new HIV infections among young MSM.[4]

Because of increased risk, it is recommended that health care providers perform more frequent and detailed screenings for MSM. The following recommendations are based on the CDC's 2010 STD Treatment Guidelines.[5]

HOW OFTEN SHOULD MSM BE TESTED FOR HIV AND STDS?

- Sexually active MSM should be tested *at least annually*
  - Exceptions are MSM who are in a long-term mutually monogamous relationship (neither they nor their primary partner have had sex outside the relationship in the last year)
- MSM who have multiple or anonymous partners, use illicit drugs in conjunction with sex, use methamphetamines, or inject any illicit drugs, should be tested every 3-6 months

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4 CDC. HIV incidence. Available at: www.cdc.gov/hiv/topics/surveillance/incidence.htm

5 CDC. Sexually Transmitted Disease Treatment Guidelines, 2010. Available at: www.cdc.gov/std/treatment/2010/toc.htm

WHAT VACCINATIONS SHOULD BE OFFERED TO MSM?

- Hepatitis A and B, unless previous infection or vaccination is documented
- HPV vaccine through age 26, if did not get fully vaccinated when younger
    - It is now recommended that all boys get vaccinated prior to sexual activity. The recommended ages for vaccination are 11–12 years

WHY ARE SOME MSM AT HIGHER RISK FOR HIV AND STDS?

Despite widespread knowledge about how to prevent HIV, some MSM do not consistently protect themselves from risk. The reasons for this are complex and not fully understood, although several theories exist. Certainly, social and cultural biases against homosexuality have played a large role in influencing risk. Feeling shame and hiding one's identity can lead to stress and depression, which are associated with substance use and sexual risk behaviors. Historically, gay and bisexual men have had to hide their sexuality, making it more difficult to find partners in places other than bars and clubs. This can lead to taking drugs and alcohol before sex, making it harder to negotiate safer sex. Stigma against homosexuality has also discouraged the building of long-term relationships that can be celebrated and affirmed by family and friends. Although trends are changing, MSM still often experience familial, religious, and cultural rejection.

Some researchers also believe that the invention of effective HIV medications has led some men to take more risks because they feel they can manage HIV with medication if they become infected. In addition, some young men may believe that no matter what they do, they will eventually become HIV infected. These young men feel they might as well get HIV now rather than continue to worry about when it will happen.

Researchers also have suggested that some MSM decide not to use condoms because they wish to feel more intimate with partners, and/or because they believe that a partner has the same HIV status as themselves (e.g., "they look healthy so they must be negative," "they didn't ask about my status so that means they must be positive too," etc.).

In addition, some men are more at risk simply because of where they live and who they partner with. For example, those who live in an area with a higher prevalence of HIV are simply more likely to find a partner who is positive.

Keep in mind that although some MSM are at high risk of STDs and HIV, this is not the case for all gay, bisexual, or other MSM. Most men take protection very seriously and are very resilient in the face of many health and social barriers.

Special Considerations for Transgender People

Not all primary care providers and clinical care team members can expect to become experts in transgender identity and health. As long as you feel comfortable talking to people of different gender identities, feel you can do so with empathy and respect, and have appropriate and safe referrals on hand, you will be able to provide good preventive care.

When initiating and taking a sexual history with transgender patients, here are some points to keep in mind:

- Make sure you have established a good rapport with the patient before asking about sexual practices or doing a physical exam.
- Be sure you use the patient's preferred name when talking to them (this will not necessarily be the same name that is on insurance and medical records).
- Ask what pronouns your patients prefer to use for themselves. This is best done on an intake form, but may also need to be done in the clinic visit. Some people change their pronoun preference:
    - Many transgender people want you to use the pronoun that matches their gender identity. So, for example, a transgender woman would like you to use "she/her."
    - Some transgender or gender non-conforming people may ask you to use "ze" or "they" or to try to avoid using any pronouns.
- Like anyone else, a transgender person may have partners who are male, female, or transgender.
- When asking about sexual practices, use open-ended questions instead of specific questions about anal, oral, and vaginal sex.
- A transgender person might consider themselves straight, gay, lesbian, bisexual, or other. This can evolve over time. For example, a person could live the first part of their life as a heterosexual man, and then transition into a transgender woman who identifies as a lesbian.
- Transgender women (male-to-female) statistically have a higher risk for HIV and STDs. This maybe because some transgender women become involved in sex work as a means of survival, and/or use drugs as a way to cope in a world that rejects them. Sexual Risk Assessment, located in Section I, includes questions about substance use and exchanging sex for money or drugs.

Resources for Further Learning

WEBSITES WITH LGBT RESOURCES

The National LGBT Health Education Center
www.lgbthealtheducation.org

Human Rights Campaign Healthcare Equality Index www.hrc.org/hei

Center of Excellence for Transgender Health www.transhealth.ucsf.edu

CDC-Lesbian Gay Bisexual and Transgender Health www.cdc.gov/lgbthealth

GLMA: Resources for Providers and Patients www.glma.org

Fenway Health's Transgender Health Program and Resource Links www.fenwayhealth.org/transgender

World Professional Association for Transgender Health www.wpath.org

TEXTBOOKS AND REPORTS

The Fenway Guide to Lesbian, Gay, Bisexual, and Transgender Health. American College of Physicians, 2008. (new edition forthcoming in 2015)

The Health of Sexual Minorities: Public Health Perspectives on Lesbian, Gay, Bisexual and Transgender Populations. Springer, 2006.

The Health of Lesbian, Gay, Bisexual, and Transgender People: Building a Foundation for Better Understanding. Institute of Medicine, March 31, 2011. www.iom.edu/Reports/2011/The-Health-of-Lesbian-Gay-Bisexual-and-Transgender-People

Reaching Out to Other Special Populations: Providing Services to Gay, Lesbian, Bisexual and Transgender Patients. NACHC. Special Population Series' Information Bulletin #11. http://www.nachc.com/client/LGBTInformationBulletinAugust20072.pdf

Section III. Getting it Done: Recommendations and Tools for Implementing Routine Sexual Histories in your Health Center

Before launching routine sexual history taking within primary care, there are steps your organization can take to facilitate successful implementation. These steps take an organization-wide approach and involve all staff.

IN THIS SECTION:

- Getting Started 23
- Staff Roles and Responsibilities 23
- Creating a Safe Space for Patients to Talk about Sex, Sexual Orientation, and Gender Identity 24
- Effective Communication Strategies When Taking a Sexual History 28
- Coding Related to Sexual History and Screening 30
- Sample Risk Assessment Forms in an Electronic Medical Record 31
- Resources for Further Learning 34

Getting Started

- Build routine sexual history taking into your organization's strategic planning process and Quality Improvement plans.
- Choose a "champion." A champion is a respected staff member (or two) who can lead the practice in strategic direction, implementation, and operations of sexual health histories. They will be the one(s) who help create "buy in" and make sure tasks are completed.
- Health center leadership should gather all staff together to 1) demonstrate their commitment to routine sexual history taking; 2) present the need and importance of sexual history information; and 3) explain the systems that will be implemented for routine sexual history taking. A PowerPoint presentation has been developed for this kind of all-staff training and is available online at www.lgbthealtheducation.org/?attachment_id=3150 and www.nachc.org/client//SexualHealthAllStaff0513.pptx. This training can also be included in new-employee orientations.
- Create a reminder system to take sexual histories. Some electronic health record software allows you to do this.
- Develop ways to track and measure how often providers are taking histories; track for increases in detection of STDs, HIV, and viral hepatitis.
- Develop a system for providers to do sexual history peer reviews with each other.
- Develop partnerships with organizations that can help you develop and implement sexual histories, as well as provide resources and referrals. Consider inviting partners to your all-staff orientation.

Staff Roles and Responsibilities

- Leadership: Build routine sexual histories into the strategic planning process and staff education program; foster a culture of acceptance and respect for all sexual behaviors and identities.
- Medical staff: Take and document regular histories; peer review of sexual history taking; appropriately communicate medically necessary information with the clinical care team.
- Front Desk and Patient Services: Practice sensitive and confidential collection of forms and communication with patients; master data collection systems .
- Administrative staff: Revise intake and history forms; develop, plan, and assign staff person to develop metrics and track data for measuring progress; ensure that outreach materials, brochures, and other materials include images and information that reflect people who are LGBT.

- IT: Develop confidential systems that include sexual history, sexual orientation, and gender identity data in electronic records; train staff in systems.
- Human Resources: Create and implement health center policies that support non-discrimination and confidentiality around sexual behaviors and identity; integrate sexual history and LGBT cultural competency training into new employee orientations and annual trainings.
- Finance: Work with medical staff to ensure cost-effective coding and reimbursement for sexual history screenings (ICD-9 codes and a list of additional resources appear later in this Section).
- All: Become familiar with confidentiality requirements, policies protecting patient privacy, and policies regarding discrimination; take trainings that teach about LGBT cultural competency.

Creating a Safe Space for Patients to Talk about Sex, Sexual Orientation, and Gender Identity

All patients want to feel safe, included, and welcome during a health care visit. When talking about sexual matters, the need for patients to feel secure and supported is especially important. This section provides suggestions for changes you can make at your health center that will create a welcoming and comfortable space for all patients.

Talking about sexual behavior can be especially difficult for people who have same-sex partners or who identify as gay, lesbian, bisexual or transgender (LGBT). There has been a long history of stigma and discrimination against LGBT people in the health care world and in society in general. Not surprisingly, many LGBT people do not reveal their sexual orientation and behaviors to their health care providers because they fear a negative reaction. But learning about the true identities, behaviors, and sexual orientations of patients is important to their health. Providers, and other members of the clinical care team, are in a position to help LGBT people find the supports they need. Furthermore, LGBT people are at higher risk of HIV and certain STDs and may need enhanced sexual screening and targeted counseling. Therefore, it is extremely important for health care organizations to create spaces that include and welcome people of all sexual orientations and gender identities.

There are a number of steps that organizations can take to let patients know that no matter what their sexual experiences are, all patients will be treated with respect and understanding. All aspects of the patient experience are to be considered, including front desk and waiting area interactions, intake forms, outreach materials, and provider verbal and nonverbal cues. These will set the stage for patients to feel safe discussing their complete sexual history.

INTAKE AND HISTORY FORMS

- Explain the confidentiality of the information on the forms and why certain questions are asked.
  Sample wording for new patient intake form:

  We'd like to welcome you as a new patient. Please take the time to fill out this form as accurately as possible so we can most appropriately address your health needs.

  The confidentiality of your health information is protected in accordance with federal protections for the privacy of health information under the Health Insurance Portability and Accountability Act (HIPAA).

  You will notice that we ask questions about race and ethnic background, sexual orientation, and gender identity. We do this so we can review the treatment that all patients receive and make sure everyone gets the highest quality of care.

- Include questions on sexual orientation and gender identity on new patient intake forms. Adding these fields is an early sign to your patients that you recognize that people have different sexual orientations and gender identities, and that this is important to their health.

  Suggested questions for forms:

  Do you think of yourself as:

  - ☐ Lesbian, gay, or homosexual
  - ☐ Straight or heterosexual
  - ☐ Bisexual
  - ☐ Something else
  - ☐ Don't know

  What is your current gender identity? (Check and/or circle ALL that apply)

  - ☐ Male
  - ☐ Female
  - ☐ Transgender Male/Transman/FTM
  - ☐ Transgender Female/Transwoman/MTF
  - ☐ Genderqueer
  - ☐ Additional category (please specify): _____
  - ☐ Decline to answer

What sex were you assigned at birth? (Check one)

- □ Male
- □ Female
- □ Decline to answer

What pronouns do you prefer? (e.g., he/him, she/her, ze, zie_____)

- Include a range of options for relationship status in new patient intake forms

  Suggested question for forms:

  What is your relationship status?

  - □ Single
  - □ Married
  - □ Partnered
  - □ Living Together
  - □ Divorced

- Review all patient forms and eliminate any alienating or non-inclusive language.
- Normalize sexual history questions by making them part of the overall history (See more about this in Section I).

POLICIES

- Include sexual orientation and gender identity and expression in all of your non-discrimination policies for both patients and employees.
- Have a structure in place to deal with complaints regarding treatment of LGBT people.

REFERRALS AND RESOURCES

- Create a list of support groups, community organizations, specialists, and behavioral health referrals in your area that are welcoming to LGBT people. Distribute this to relevant staff.

PARTNERS AND OUTREACH

- Partner with LGBT organizations in your community to create LGBT programs, materials, or services.
- Include LGBT individuals on advisory or consumer governing boards.
- Create an LGBT task force for your organization.
- Advertise your services in LGBT media.

PHYSICAL SPACE

- In waiting rooms and exam rooms, display print materials that will let people of different sexual orientations and gender identities feel they are welcome and included.

  Suggestions for print materials:

  - Include images of same-sex couples in posters and brochures.
  - Display HIV testing and awareness posters, safe zone stickers, rainbow flags.
  - Display LGBT news magazines, partner agency literature.
- Prominently display office policies that prohibit discrimination based on sexual orientation and gender identity.
- If possible, offer single stall unisex bathrooms (important for transgender patients).

TRAINING

- Arrange recurring LGBT cultural competency trainings for all health center staff.
- Provide a forum for staff to ask questions and report successes and challenges around cultural competency.

Effective Communication Strategies When Taking a Sexual History

For a customizable Word version of this section, visit www.lgbthealtheducation.org/?attachment_id=3098 or www.nachc.org/client/EffectiveCommunicationStrategies%200513.docx

Below are recommendations and information that can help you talk to patients in a sensitive, open, and non-judgmental manner.

- Avoid asking questions in a way that implies there is a right or wrong answer, such as: "You always use condoms, right?" or "You don't have partners outside your marriage, do you?"
  - Instead, be specific about how behaviors can affect health.
- Avoid using judgmental terms like "wrong," "bad," "promiscuous," or "sleep around" to describe behaviors.
- Even if you personally disagree with the behaviors of your patients, it is important to not let your beliefs interfere with providing the best care.
- Check your body language and facial expressions—you may be sending unintended messages. For example, are you shaking your head "no"? Are you wrinkling your nose? Are you maintaining eye contact?
- Be aware that there are a wide range of sexual behaviors, activities, and expressions. You might be surprised by some of your patients' behaviors, but try to remain open and neutral.
- Avoid making assumptions based on appearance, age, relationship status, sexual orientation, gender and gender identity, and any other personal factors—our assumptions are often wrong. For example, contrary to typical assumptions:
  - Many elderly people are sexually active.
  - Some people in long-term relationships or marriages may not be monogamous. Individuals may have secret affairs. In addition, some couples have "open relationships", i.e. agreements about having sex outside the main relationship.
- How a person identifies their sexuality (e.g., "I am gay, bisexual, lesbian, straight, queer") does not always tell you who they have sex with or who they are attracted to. Examples:
  - Some people who have same-sex partners refer to themselves as heterosexual.
  - In some cultures, "gay" means effeminate (acting like women). Therefore, a "masculine" man who has sex with men may not think of himself as gay or homosexual.

- Some people who identify as lesbian/gay have a recent history of sex with opposite sex partners.
- Some people who identify as bisexual may only have relationships with men (or only with women) but feel desire towards the other sex.
- Some people do not like to use labels to describe their sexual orientation or gender identity.

- Remember that sexual orientation and behaviors often change over time.
- Listen to the words your patients use to talk about themselves and their partners, and try to use the same words (if you feel comfortable using them). If you don't understand something they have said, ask them to explain.
- If you do not yet know the gender of your patient's partners, use words that are gender neutral. Examples:
  - Instead of "Do you have a husband or boyfriend?" ask "Do you have a partner or spouse?" or "Are you currently in a relationship? What do you call your partner?"
- If you slip up, apologize and ask the patient what words they prefer.

It may take time to feel completely comfortable communicating with patients about their sexual health, identities, and behaviors. In particular, you may want to take some time to think about how you might respond if you learn a patient has same-sex partners or identifies as LGB or T. Do you carry any stereotypes? Negative feelings? Try to be honest about your feelings and reactions. Remember that you do not need to know everything or have all the answers. Patients will appreciate and trust providers and other clinical care team members who are willing to listen to their patients and who show respect, empathy, and curiosity[6] (curiosity, however, should be limited to questions that are relevant to the patient's health and general well-being).

6 Carrillo, J., Green, A., Betancourt, J. "Cross-Cultural Primary Care: A Patient-Based Approach." *Annals of Internal Medicine*. 130 (1999): 829-834.

Coding Related to Sexual History and Screening

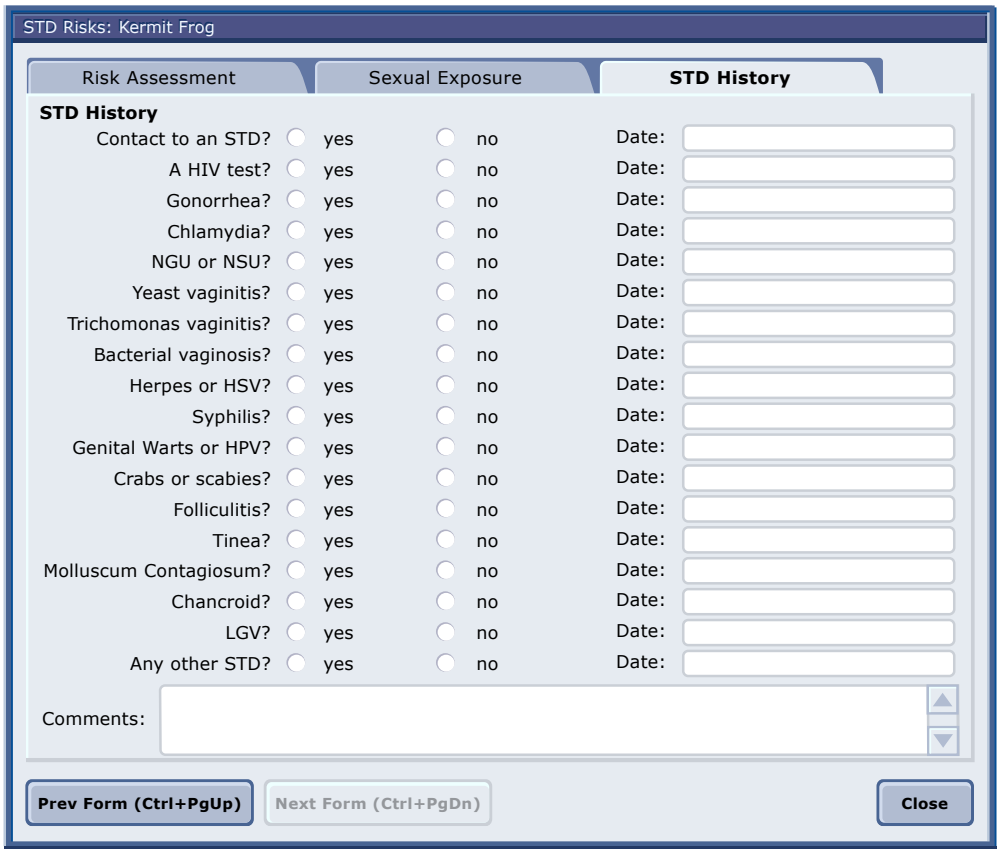
Your organization will want to ensure proper coding for different types of visits related to sexual histories and complaints as part of your overall business strategy. The following ICD-9 Diagnosis Codes are offered as examples. You will find detailed explanations for coding in Resources for Further Learning at the end of this Section.

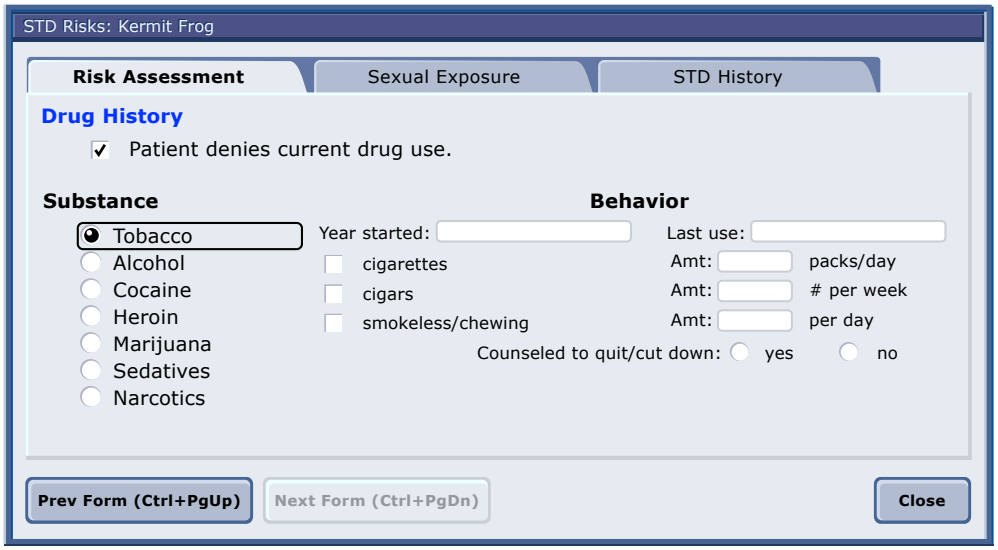
EXAMPLES OF ICD-9 DIAGNOSIS CODES RELEVANT TO SEXUAL HISTORY

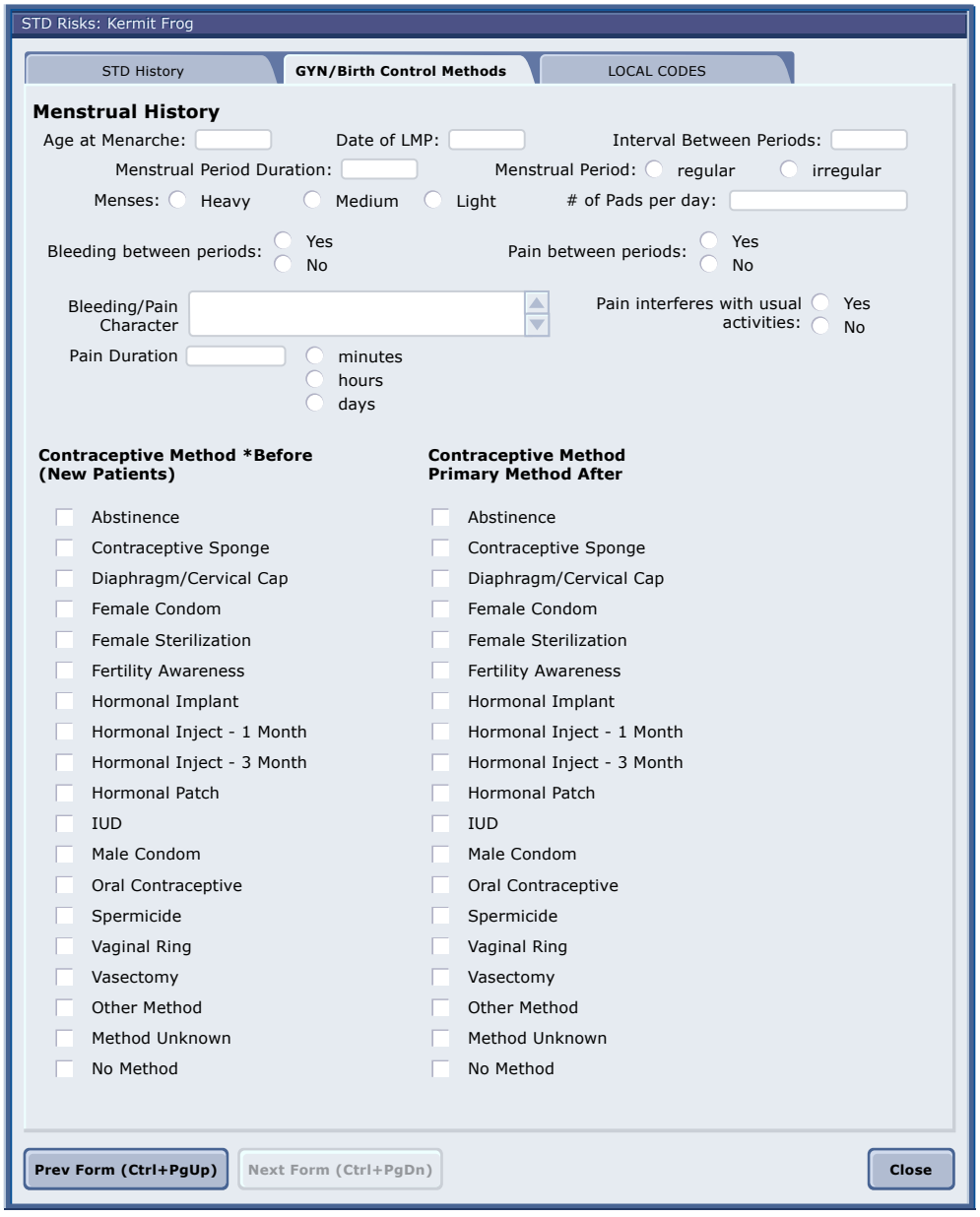
V 70.0	Routine general medical examination at healthcare facility
V73.89	Special screening other specified viral diseases
V74.5	Screening examination for venereal disease
V01.2	Contact with or exposure to venereal diseases
V69.2	High risk sexual behavior
V05.3	Need for prophylactic vaccination and inoculation against single disease: viral hepatitis
V65.44	HIV Counseling
V65.45	Counseling on other sexually transmitted diseases
V65.42	Counseling on substance use and abuse
67.59	STD follow-up exam
V08	Asymptomatic HIV infection status
042	HIV disease

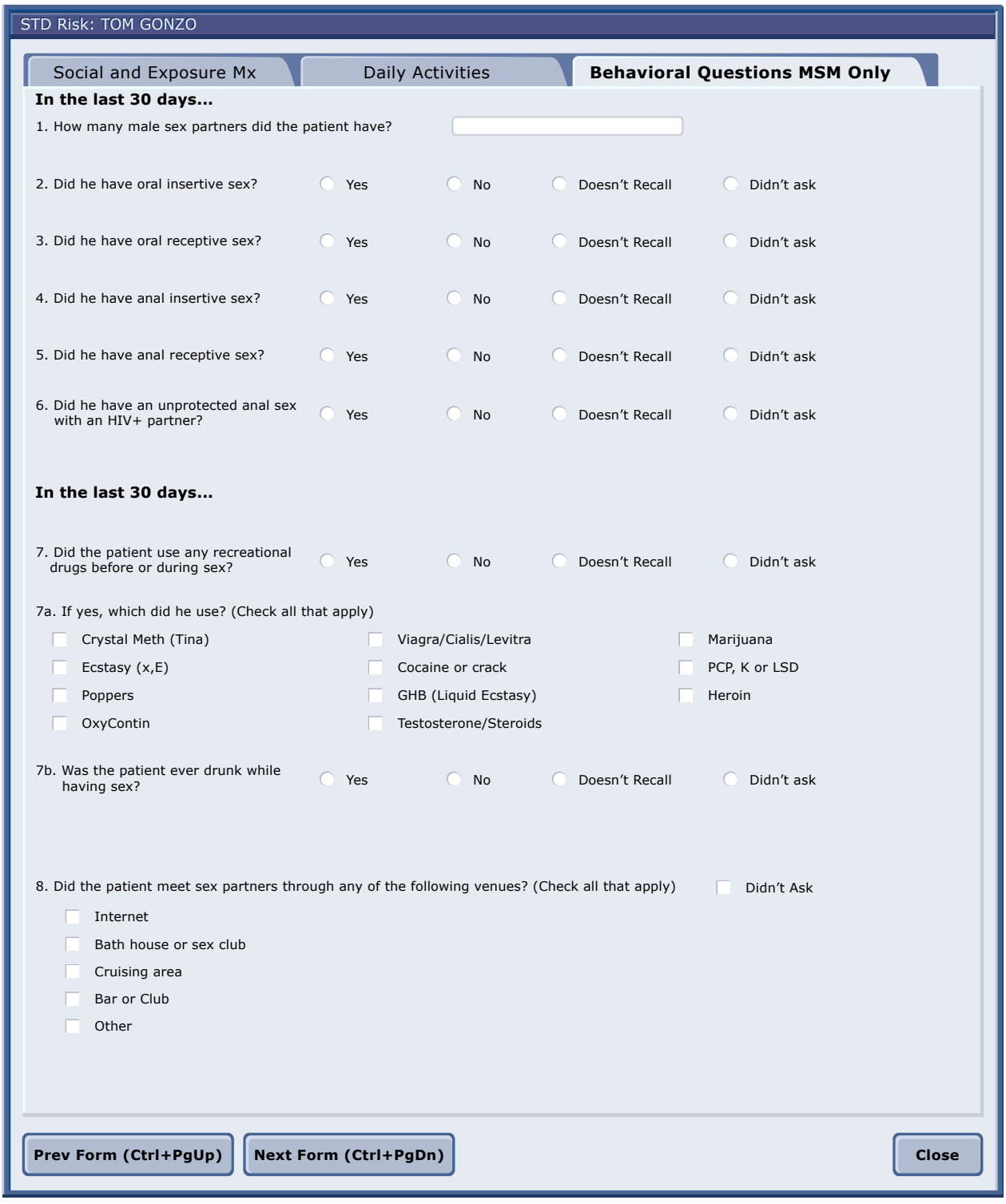
Sample Risk Assessment Forms in an Electronic Medical Record (from Fenway Health)






STD Risks: Kermit Frog
Risk Assessment
Sexual Exposure
STD History
Drug History
Patient denies current drug use.
Substance
Tobacco
Alcohol
Cocaine
Heroin
Marijuana
Sedatives
Narcotics
Year started:
cigarettes
cigars
smokeless/chewing
Behavior
Last use:
Amt: packs/day
Amt: # per week
Amt: per day
Counseled to quit/cut down: yes no
Prev Form (Ctrl+PgUp)
Next Form (Ctrl+PgDn)
Close


STD Risks: Kermit Frog
STD History
GYN/Birth Control Methods
LOCAL CODES
Menstrual History
Age at Menarche:
Date of LMP:
Interval Between Periods:
Menstrual Period Duration:
Menstrual Period: regular irregular
Menses: Heavy Medium Light
# of Pads per day:
Bleeding between periods: Yes No
Pain between periods: Yes No
Bleeding/Pain Character
Pain interferes with usual activities: Yes No
Pain Duration
minutes
hours
days
Contraceptive Method *Before (New Patients)
Contraceptive Method Primary Method After
Abstinence
Contraceptive Sponge
Diaphragm/Cervical Cap
Female Condom
Female Sterilization
Fertility Awareness
Hormonal Implant
Hormonal Inject - 1 Month
Hormonal Inject - 3 Month
Hormonal Patch
IUD
Male Condom
Oral Contraceptive
Spermicide
Vaginal Ring
Vasectomy
Other Method
Method Unknown
No Method
Prev Form (Ctrl+PgUp)
Next Form (Ctrl+PgDn)
Close


STD Risk: TOM GONZO
Social and Exposure Mx
Daily Activities
Behavioral Questions MSM Only
In the last 30 days...
1. How many male sex partners did the patient have?
2. Did he have oral insertive sex?
3. Did he have oral receptive sex?
4. Did he have anal insertive sex?
5. Did he have anal receptive sex?
6. Did he have an unprotected anal sex with an HIV+ partner?
Yes
No
Doesn't Recall
Didn't ask
In the last 30 days...
7. Did the patient use any recreational drugs before or during sex?
7a. If yes, which did he use? (Check all that apply)
Crystal Meth (Tina)
Ecstasy (x,E)
Poppers
OxyContin
Viagra/Cialis/Levitra
Cocaine or crack
GHB (Liquid Ecstasy)
Testosterone/Steroids
Marijuana
PCP, K or LSD
Heroin
7b. Was the patient ever drunk while having sex?
8. Did the patient meet sex partners through any of the following venues? (Check all that apply)
Didn't Ask
Internet
Bath house or sex club
Cruising area
Bar or Club
Other
Prev Form (Ctrl+PgUp)
Next Form (Ctrl+PgDn)
Close

Resources for Further Learning

MATERIALS AND TOOLS FOR CREATING A WELCOMING ENVIRONMENT

The National LGBT Health Education Center www.lgbthealtheducation.org

GLBT Health Access Project www.glbthealth.org/HAPMaterials.htm

The Joint Commission's Advancing Effective Communication, Cultural Competence, and Patient- and Family-Centered Care for the Lesbian, Gay, Bisexual, and Transgender (LGBT) Community. www.jointcommission.org/lgbt

CODING

AMA, CDC, and American Academy of HIV Medicine: Coding Guidelines for Routine HIV Testing in Health Care Settings. www.aahivm.org/codingguide

AMA: Coding Guidelines for Vaccine Preventable Hepatitis: High Risk Populations, Including Men Who Have Sex With Men. www.cdc.gov/hepatitis/Populations/PDFs/04-0103_trifold_sprd1.pdf

AMA, National Network of STD HIV Prevention and Training Centers, HIV Medicine Association: Coding for Nucleic Acid Amplification Testing To Diagnose Nongenital Infections with Gonorrhea and Chlamydia. www.nycptc.org/x/gonococcal-brochure_coding.pdf

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Emtricitabine-tenofovir exposure and pre-exposure prophylaxis efficacy in men who have sex with men

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Abstract

Drug concentrations associated with protection from HIV-1 acquisition have not been determined. This study evaluated drug concentrations among men who have sex with men in a substudy of the iPrEx trial,(1) a randomized placebo controlled trial of daily oral emtricitabine/tenofovir disoproxil fumarate pre-exposure prophylaxis (PrEP). Any detectable drug in blood plasma and viably cryopreserved peripheral blood mononuclear cells (vPBMCs) was less frequent in HIV-infected cases at the visit when HIV was first discovered compared with controls at the matched time point of the study (8% vs 44%, P<0.001) and in the 90 days prior to that visit (11% vs 51%, P<0.001). An intracellular tenofovir-diphosphate (TFV-DP) concentration of 16 fmol per million vPBMCs was associated with a 90% reduction in HIV acquisition relative to the placebo arm. Directly observed dosing in a separate study, STRAND, yielded TFV-DP concentrations that, when analyzed with this iPrEx model, corresponded with HIV-1 risk reduction of 76% for 2 doses per week, 96% for 4 doses per week, 99% for 7 doses per week. Prophylactic benefits were

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Author contributions: PL Anderson helped design the pharmacology studies, oversee the analytical pharmacology work, and analyze the data. DV Glidden helped design the analyses and perform the statistical modeling. A Liu designed and conducted STRAND and assisted with the design and conduct of iPrEx. S. Buchbinder, J Lama, JV Guanira, O Montoya-Herrera, VG Veloso, S Chariyalertsak, K Mayer, LG Bekker, EG Kallás assisted with the design and conduct of iPrEx. LR Bushman oversaw the analytical pharmacology work. V McMahan coordinated the iPrEx study. RM Grant designed and conducted iPrEx, helped design the pharmacology studies, and analyze the data. All authors assisted with writing the manuscript.

Competing interests: Study drugs were donated by Gilead Sciences.

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observed over a range of doses and drug concentrations, suggesting ways to optimize PrEP regimens for this population.

INTRODUCTION

UNAIDS estimates there are 2.6 million new HIV-1 infections per year, despite widespread awareness of the modes of transmission and the protective benefits of condom use.(2) Men who have sex with men carry a disproportionate burden of infection on all continents.(3) The iPrEx trial demonstrated that randomization to daily oral emtricitabine/tenofovir (TFV) disoproxil fumarate (FTC/TDF) PrEP decreased HIV-1 acquisition by 44% compared with placebo among such men, with greater reductions in HIV-1 risk associated with higher reported adherence and detectable drug in the blood. (1)

In a predefined pharmacology substudy of iPrEx, FTC, TFV in plasma and/or FTC-triphosphate (FTC-TP), TFV-DP in vPBMC was detected in 22 of 43 of seronegative subjects (51%) versus 3 of 34 HIV-infected subjects from the active arm (9%) ($P<0.001$). (1) Predicted efficacy in iPrEx increased from 44% to over 90% when detectable drug was accounted for. Thus, adherence to daily FTC-TDF was critical for PrEP efficacy in iPrEx, and the same has been found in other PrEP studies.(4–7) However, the quantitative relationship between drug concentration and/or level of adherence with PrEP efficacy has not been determined. The present study expands on the predefined pharmacology substudy in iPrEx and quantifies the concentrations of drugs associated with protection from HIV-1 acquisition, as well as the frequency of PrEP use required to achieve those concentrations.

RESULTS

Overview

Intracellular tenofovir-diphosphate, the active form of tenofovir, was analyzed in vPBMCs arising from two studies, STRAND and iPrEx. TFV-DP in vPBMC from the STRAND study were used to establish expected concentrations from 2, 4, or 7 doses/week of directly observed TDF therapy, and TFV-DP in vPBMC from iPrEx was used to estimate concentrations associated with decreased HIV acquisition. PrEP efficacy was then quantified for 2, 4, and 7 doses/week by analyzing TFV-DP concentrations from STRAND with the iPrEx HIV risk reduction model. The vPBMC collection, processing and storage for iPrEx and STRAND used identical laboratory protocols, and the drug concentration testing was performed in the same laboratory using identical laboratory methods.

Expected TFV-DP from STRAND

The STRAND study administered oral TDF to 24 HIV-negative adults (FTC was not included), each of whom received 6 weeks of 2, 4, or 7 doses per week. Dosing was directly observed Monday through Friday, including all the 2 and 4 doses per week, and participants provided confirmation of the date and time of doses taken on Saturday and Sunday by text message or telephone contact on the day of use. TFV-DP in vPBMC was measured at the end of the 6 weeks of each dosing regimen. The median (IQR) values were 11 fmol/M (6 to 13) fmol/M for 2 doses per week, 32 fmol/M (25 to 39) for 4 doses per week, and 42 fmol/M (31 to 47) (Figure 1). The median (IQR) times from the last dose to vPBMC collection were 24 hours (20 to 141), 25 hours (22 to 62), and 24 hours (21 to 25) hours, respectively. TFV-DP was quantifiable in all STRAND participants at all visits.

iPrEx analyses

The iPrEx study provided an opportunity to identify vPBMC concentrations associated with different levels of protection from HIV-1 acquisition. Plasma and/or vPBMC were tested for

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FTC-TDF in all 48 seroconverters at the visit when HIV-1 infection was first detected, either by plasma viral RNA, by serum antibodies, or both. The median time between the last HIV-negative test and the first evidence of HIV was 33 days (interquartile range of 28 to 48 days). Each HIV infected case was matched to 3 seronegative controls in the FTC-TDF arm by study site, and duration on study. One of the 3 controls was selected having reported high-risk sexual practices, to assure comparable HIV-1 exposure with cases, and the other two were selected randomly. The cases and controls were comparable with respect to HIV risk factors, level of schooling, and alcohol use (Table 1). Both plasma and PBMC were tested in 42/48 (88%) of cases at the visit when HIV-1 infection was first detected and 144/144 (100%) of controls at the matched time point on study. Plasma and/or PBMC were also tested from other longitudinal study visits in the cases and controls. Drug detection was defined as any quantifiable moiety among plasma TFV, FTC, and intracellular TFV-DP and FTC-TP.

Drug detection in plasma and vPBMC in iPrEx was concordant in >95% of all pairwise comparisons, indicating that plasma and vPBMC analysis yielded similar estimates of the proportion of groups having detectable drug.

Drug detection at the visit with first evidence of HIV-infection

Any drug moiety was detected 5.5-fold less frequently (8% vs 44%; P<0.001) in HIV-positive cases at the visit when HIV infection was first detected compared with the matched time point in HIV-negative controls (Fig. 2). Lower drug detection among cases vs controls (11% vs. 51%; P<0.001) was also observed within the 90 days before the HIV infection visit or matched time point in controls. At time points more than 90 days before HIV was first detected, the proportion of cases and controls with any detectable drug was comparable (36% vs 41%; P=0.77), indicating that HIV infection occurred during periods of low drug exposure in the active arm of iPrEx. These drug detection rates suggest that a substantial fraction of iPrEx participants were dosing with fewer than 2 doses per week, given the 100% TFV-DP detection rate for 2, 4, and 7 doses per week in STRAND (fig 1).

TFV-DP concentrations and risk of HIV-acquisition

Of the iPrEx seronegative controls having quantifiable TFV-DP (36% of the total), the median concentration was 16 fmol/M (IQR 9 to 27) which was between the median concentrations observed for 2 and 4 doses per week in STRAND (Fig. 1). Only 18% of seronegative controls had TFV-DP concentrations in the range associated with daily dosing in STRAND. This suggests that TFV-DP concentrations below those associated with daily dosing were exerting antiviral effects to give the 44% overall efficacy in the group randomized to FTC/TDF versus placebo. Only 3 HIV infected cases had detectable TFV-DP at the time HIV was first detected (the concentrations at the time of infection are not known). These concentrations were in the range of those associated with 2 doses per week in STRAND and none were in the range of daily dosing.

The TFV-DP concentration in vPBMC associated with HIV-1 acquisition was estimated using a Cox proportional hazards model that assessed the risk of HIV infection in the iPrEx trial as a function of TFV-DP (or FTC-TP) concentrations in active arm participants. Exponential regression was also used in a second analysis. Multiple imputation(8, 9) was used to construct a dataset with drug concentrations at each visit when an HIV-1 test was performed. If a drug concentration was not available, imputation was employed using participant and visit level data (age, site, time on study, numbers of partners, creatinine clearance, alcohol use, secondary education, HSV, sexually transmitted disease, pharmacy drug dispensation records and unprotected receptive anal intercourse at baseline and followup) to estimate the missing concentration. This approach allowed HIV-1 risk to be

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estimated for the entire cohort, to estimate how drug exposure as a time dependent variable associated with HIV risk compared with the placebo arm. Drug concentrations below the limit of quantitation (BLQ) were set to 0 fmol/M.

The relationship between drug concentration and HIV infection risk was significant for both TFV-DP (p=0.016) and FTC-TP (p=0.004) among those assigned to receive oral FTC/TDF. Compared with the placebo HIV incidence, the TFV-DP concentrations associated with 50%, 90% and 99% reduced HIV-1 acquisition were 3 (95% CI: <1 to 7), 16 (95% CI: 3 to 28), and 33 (6 to 60) fmol/M vPBMC, respectively. For FTC-TP, the corresponding values were 0.82 (0.1 to 1.6), 3.7 (1.2 to 6.1), and 7.7 (2.6 to 12.9) pmol/M viable cells, respectively. Median (IQR) FTC-TP in cases at the visit when HIV was first detected and at the matching visit in controls were 1.8 (0.9 to 5.1) and 2.9 (1.6 to 5.2) pmol/M, respectively. However, neither TFV-DP nor FTC-TP was independent of the other in a model that included both, therefore further analyses focused upon TFV-DP so that TFV-DP concentrations from STRAND could be utilized.

Dosing and risk of HIV-acquisition

The exponential regression shown in Figure 3 demonstrated that the risk of HIV infection was comparable among participants in the active arm with undetectable TFV-DP compared to the placebo arm (Relative hazard = 0.78; 95% CI: 0.49 to 1.06; p=0.19). Similar to the Cox analysis above, a TFV-DP concentration of 16 fmol/M vPMBCs was associated with 90% HIV risk reduction (EC90) relative to placebo. For perspective, the concentrations from the STRAND study are with colored panels in Figure 3; the EC_{90} (16 fmol/M) was 38% of the median TFV-DP concentration observed in those taking 7 doses per week (42 fmol/M).

Sensitivity analyses were conducted to evaluate the robustness of the estimated vPBMC EC_{90} TFV-DP. An analysis that adjusted for unprotected receptive anal intercourse (the main risk factor for HIV acquisition in this population), and other factors also used for multiple imputation, yielded an estimate of 15 (95% CI: 3 to 27) fmol/M. Allowing drug concentrations below the limit of quantitation to vary uniformly between 0 and 5 yielded an estimate of 20 (95% CI: 7 to 33) fmol/M. Using the averaged drug concentrations from the visit closest to HIV infection with values in the previous 90 days yielded an estimate of 23 (5 to 41) fmol/M. An analysis that brought drug detection at subsequent seroconversion time points to the time of the first detection of HIV-1 RNA yields an estimate of 19 (95% CI: 4 to 33). Adjustment of TFV-DP (from 4.19 to 13.4 fmol/M) in one person whose blood specimen was available 7 days after stopping oral FTC/TDF at seroconversion yielded an estimate of 20 (95% CI: 4 to 36). Estimating a TFV-DP concentration associated with a 90% HIV risk reduction in cases versus controls was also possible using conditional logistic regression without multiple imputation. This analysis yielded a similar estimate for the vPBMC EC_{90} of 16 fmol/M vPBMC (95% CI: 8 to 44). All estimates were comparable with the initial EC_{90} estimate of 16 fmol/M and well within the range of concentrations achieved with 4 to 7 tablets per week in STRAND.

The fraction of case and control time points that exceeded the EC_{90} over time is shown in Figure 4. At the visit when HIV was first detected, no cases (0/42) had TFV-DP ≥ 16 fmol/M compared with 18% (26/144) of seronegative controls at the matched time point (P<0.001; Fig. 4). The proportion of iPrEx participant time points with TFV-DP at or above the EC_{90} decreased among cases (P=0.02) and controls (P<0.001) over time. Reported risk behavior associated with exposure to HIV-1 also decreased overtime in iPrEx.(1)

TFV-DP concentrations arising from 2, 4, and 7 directly observed doses per week in STRAND were analyzed with the exponential regression model from iPrEx described above. The estimated PrEP efficacy was 76% (95% CI: 56 to 96%) for 2 doses per week,

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96% (95% CI: 90 to >99%) for 4 doses per week, 99% (95% CI: 96 to >99%) for 7 doses per week. The proportions of people who attained the TFV-DP EC_{90} were 14% for 2 tablets per week, 90% for 4 tablets per week, and 100% for 7 tablets per week.

DISCUSSION

Drug exposure in HIV-infected cases in iPrEx was critically low at the time of first laboratory evidence of HIV infection, providing a likely explanation for HIV acquisition in these participants. Other evidence indicated negligible drug exposure near the time of HIV infection in cases: plasma HIV-1 RNA levels were comparable in the placebo and active arms, and there was no evidence of TDF or FTC resistance among emergent infections in the active arm.(1) Drug detection in controls was higher than in cases, but was not commensurate with daily dosing in the majority. Only 44% of controls had any detectable drug moiety at the matching time point of the case. Only 18% of seronegative controls had TFV-DP concentrations above 16 fmol/M, a level achieved by 90% of STRAND participants taking 4 or more doses per week, and a level associated with a 90% HIV infection risk reduction.

The minimum protective drug concentrations in the blood, and the required numbers of tablets per week required to achieve those concentrations, may differ depending on the route and frequency of exposure to HIV.(10) For men who have sex with men, the tissue of greatest relevance to the acquisition of HIV-1 infection is the rectal mucosa. Oral dosing has been shown to deliver 20 to 100-fold higher TFV-DP in rectal compared with blood or vaginal/cervical cells/tissue.(11, 12) TFV-DP delivery to penile tissue, relevant for male insertive exposures, has not been determined to our knowledge. The uniquely high delivery of TFV-DP to rectal mucosa suggests that pharmacology findings relevant for MSM, such as in this study, may not directly extrapolate to parenteral, vaginal or penile exposures.

This study demonstrated that the EC_{90} in vPBMC (16 fmol/M) was 38% the median from daily dosing in STRAND (42 fmol/M). With this information, a rectal mononuclear cell EC_{90} can be estimated. The rectal mononuclear cell concentration observed with daily oral dosing was reported to be 1846 fmol/M (95% CI: 931 to 3659).(11) Assuming that the kinetics of TFV-DP in rectal mononuclear cells are similar to PBMC, the EC_{90} in rectal mononuclear cells would be 38% of this value, or approximately 700 fmol/M rectal cells (95% CI: 350 to 1400). This estimate makes several assumptions that require further validation, but nevertheless provides a starting point for a target cell concentration in tissue to translate into animal or ex vivo systems for validation.(13, 14) The threshold identified here is analogous to the TFV concentration threshold of 1000 ng/mL in vaginal fluid identified as protective in the CAPRISA 004 study and in ex vivo assays.(5, 14)

Drug concentrations were measured as close to the HIV infection as possible (at the time HIV infection was first discovered and within 90 days of this time point). Through use of multiple imputation, drug concentrations were assigned to all active arm participants at the time of HIV infection in placebo cases. However, the model could not account for variations in dosing patterns and relationship to timing of HIV exposure and transmission risk.

Confounding is also possible in this analysis, as there may be factors that link higher adherence with lower exposure to HIV. The finding that HIV acquisition among active arm participants with undetectable drug concentrations was not higher than the placebo rate argues against confounding (Fig. 3). In addition, the statistical analysis adjusted for several markers of HIV incidence, including numbers of sexual partners, unprotected anal intercourse, sexually transmitted diseases, age, level of schooling, and substance use.

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vPBMC were available for drug analysis, whereas freshly processed and lysed PBMC are traditionally used for cell pharmacology studies.(15) Measurements of TFV-DP in vPBMC from STRAND were a median of 48% (IQR: 38% to 67%) that of freshly lysed PBMC also collected in that study. Processing vPBMC also introduces additional variability in TFV-DP/FTC-TP measures. Despite this added variation, levels of drug concentrations in blood were found to be strongly associated with reduced HIV risk in the active arm compared with placebo. This finding suggests that drug concentration monitoring could inform HIV acquisition risk in persons taking FTC/TDF for PrEP. Other specimens, such as hair, or dried blood spots, may afford more convenient long term measures of drug exposure which will be particularly useful if they can be correlated with protective drug concentrations in vPBMC.(16, 17)

This study identified a relationship between systemic drug exposure and reduction of HIV acquisition risk in one important population. Protective TFV-DP concentrations were readily achieved with 4 or more doses per week. This study focused on TFV-DP because independent relationships for FTC-TP could not be identified in iPrEx and STRAND did not include FTC-TP so expected concentrations for non-daily dosing are not known. FTC co-administration is not expected to affect intracellular concentrations of TFV-DP in PBMC.(18) Importantly the TFV-DP EC_{90} identified in iPrEx was in the presence of FTC-TP, indicating that reaching these protective TFV-DP concentrations with FTC-TDF dosing is relevant for PrEP efficacy in MSM. Nevertheless, future studies should aspire to evaluate the contribution of FTC-TP to PrEP efficacy.

Alternative dosing regimens, such as pre- and post-intercourse dosing, warrant controlled clinical trials to evaluate the acceptability, behavioral feasibility, and pharmacokinetics of non-daily regimens. The 95% confidence interval for the estimate of the TFV-DP EC_{90} was 3 to 28 fmol/M vPBMC. The lower bound (3 fmol/M vPBMC) would be achievable after a single dose,(19) and 28 fmol/M was just below the median achieved with 4 doses per week. While animal studies indicate that both pre- and post-exposure dosing are important,(20) more information is needed to define the timing and duration of drug exposure that is required to prevent infection. Dose optimization in the absence of a surrogate marker of protection would require prohibitively large trials, so better definition of pharmacological parameters associated with differing dosing strategies (eg: dose and dosing interval) and protection will be essential to move the PrEP field forward. Ultimately, recommendations for daily PrEP use may be more robust, as daily regimens encourage routinization, and afford drug concentrations that are expected to persist in the protective range even if some doses are missed. The low fraction of iPrEx participants with TFV-DP in the range of daily dosing suggests that demonstration projects should optimize ways to promote daily dosing.

In conclusion, a target TFV-DP concentration for MSM was identified. This threshold enables further studies in MSM that evaluate new ways of promoting the consistent use of PrEP, the key determinant of efficacy.

MATERIALS AND METHODS

iPrEx Trial

The design, conduct, and outcomes of the iPrEx trial have been published previously.(1) Briefly, the iPrEx initiative was a randomized, double-blinded, controlled trial of daily FTC-TDF versus placebo in HIV-negative men and transgender women 18 years or older who have sex with men, meeting behavioral criteria that put them at risk for sexual acquisition of HIV. Two thousand four hundred ninety nine participants were randomized and followed monthly through a median of 87 weeks of therapy (IQR 61 to 125). Eighty-three infections

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were observed in the placebo arm versus 48 infections in the FTC-TDF arm (efficacy, 42% (95% CI 18% to 60%).(21)

Plasma specimens were stored every 12 weeks and viably cryopreserved PBMC specimens were stored every 24 weeks and at the time of study discontinuation or seroconversion. Each participant from the active arm who contracted HIV during the study was included in this pharmacology substudy (cases). For each visit week when HIV was detected in cases, samples were selected from 3 HIV negative controls from the active arm at the same site; 2 randomly, and 1 from among those reporting unprotected receptive anal intercourse (URAI) in a recall period prior to the specimen collection. The latter control was chosen to enrich the control sample for people exposed to HIV, to better match the HIV infected cases. Specimens were tested from the time of first evidence of HIV infection in the cases, and the nearest visit week in controls, as well as longitudinally at other available time points during the treatment period.

STRAND Study

The STRAND study was an open label, randomized, 6 sequence, 3-period, single-site, cross-over trial in 24 HIV-negative adults (12 men, 12 women) that tested the effects of three different oral TDF dosing regimens on TFV concentrations in hair, plasma, and PBMC. The 6 sequences were different orders of the 3 dosing strategies: 7 doses/week, 4 doses/week, and 2 doses/week. The 2 doses/week were dosed on Tuesday and Wednesday and 4 doses/week on Monday, Tuesday, Thursday, and Friday. Each dosing period lasted 6 weeks. All doses scheduled Monday through Friday were directly observed by study staff and the doses on the weekend were confirmed by telephone or text message. Stored viably cryopreserved PBMC (using the same method as in iPrEx) were collected at the end of each 6 week dosing period. Freshly processed/lysed PBMC were available from a subset of participants. The study was funded by the US National Institutes of Health and was approved by the UCSF Committee on Human Research.

Analytical pharmacology

An LC/MS/MS assay was validated for the determination of TFV and FTC in human plasma. (22) The method includes protein precipitation and stable isotopic internal standards. The linearity of the concentration curves were in the range 10 ng/mL to 1500 ng/mL for both analytes (250 μL plasma extracted). The lower limit of quantification was 10 ng/mL for both analytes.

The viable PBMC processing procedure involved a quick thaw in a 37°C water bath and mixing by inversion (1 minute). Cells were immediately transferred to a 15 ml centrifuge tube that already contained 10 ml of pre-warmed (37°C) PBS followed by gentle mixing by inversion. Cells were then pelleted and the supernatant discarded. If RBC contamination was visible, the cells were treated with a RBC lysing buffer. Cells were then counted with an automated hemocytometer. Viability and total cell count were recorded; cells were kept on crushed ice through the process. Cells were washed and lysed. Median (IQR) viability at the time HIV was discovered was 66% (56% to 76%) overall, 71% (56% to 79%) in cases and 64% (56% to 73%) in controls.

A validated liquid chromatography tandem mass spectrometry (LC–MS/MS) assay was used for the determination of TFV-DP and FTC-TP from lysed intracellular matrix.(15) The method utilized a strong anion exchange isolation of mono-(MP), di-(DP), and tri-phosphates (TP) from intracellular matrix. The TP fraction was then dephosphorylated to the parent moiety yielding a molar equivalent to the original nucleotide analog intracellular concentration. The analytical portion included desalting/concentration by solid phase

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extraction and detection by LC–MS/MS. The quantifiable linear range for TFV-DP was 2.5–2000 fmol/sample, and that for FTC was 0.1–200 pmol/sample. Stable labeled isotopic internal standards facilitated accuracy and precision in various cell matrices. (15) Two million total cells were typically extracted, constituting the "sample", and results were corrected for cell viability and normalized to fmol or pmol per million (M) viable cells.

Stored viable PBMC samples such as in this study have been used for the measurement of intracellular TFV-DP in previous studies (see appendix in reference 1).(1) These studies demonstrated that values in viably cryopreserved PBMC (median approximately 40 fmol/M viable cells) were lower than those measured in pharmacology studies among HIV-infected subjects where PBMC samples were processed and lysed immediately (median approximately 90 fmol/M cells).(23, 24)

To evaluate viable cells in more detail, an internal study called iOptimum enrolled 10 HIV-infected participants for a single blood draw to assess the TFV-DP and FTC-TP in viable cryopreserved cells. Self-reported adherence in the prior 30 days was 63 to 100% and viral loads were largely suppressed (range, <40 to 240 cp/mL), suggesting good adherence to treatment. Aliquots of viable cells were stored in liquid nitrogen for 4, 12 and 24 weeks. Freshly lysed cells were also collected. Both TFV-DP and FTC-TP were quantifiable in all viable PBMC samples, and above the lower limit of quantitation by several fold. The median (IQR) ratio of viable PBMC/PBMC at weeks 4 and 12 in liquid nitrogen storage were 0.3 (0.22 to 0.38). The median (IQR) value for 24 weeks in liquid nitrogen was 0.56 (0.38 to 0.83), which was similar to STRAND 0.48 (0.38 to 0.67). Median (IQR) time in liquid nitrogen for iPrEx and STRAND samples were 70 (46 to 108) weeks and 57 (52 to 65) weeks, respectively. We have observed no loss in viable cell concentrations for storage times in liquid nitrogen through 119 weeks (2.3 years).(1)

Statistical Methods

All analyses were performed using Stata 12.1.(25)

Model for the Effect of Intracellular Drug Concentration

This analysis fits a (stratified by site) Cox proportional hazards model to the entire cohort with a model

$$h_k(t;Z(t),\mathrm{rx})=h_{ok}(t)\exp(\beta_1\mathrm{rx}+\beta_2 Z(t)) \quad (1)$$

$h_k(t)$ is the hazard of HIV infection at the kth site and rx = 1 if the participant is assigned to FTC/TDF and 0 if the participant is assigned to placebo. The variable Z(t) is a time-dependent covariate for a quantitative drug concentration (e.g., TFV-DP) where Z(t) is set to be a drug concentration of 0 if the participant is on the placebo group. We examined quadratic and logarithmic transformations of the concentration Z(t) but neither improved the fit.

The primary analyses have used models stratified by clinic site to avoid confounding the association between drug concentrations and HIV acquisition. Stratification was incorporated into the design of the nested case control study by matching controls by study site. Stratification can be highly efficient relative to an unstratified model even if confounding by site is weak.(26)

The model (1) uses the placebo group as the baseline hazard function permitting comparison the hazard of HIV acquisition at a given drug concentration to the placebo group. For

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instance, the concentration Z(t) which is associated with a d% reduction is risk relative to placebo is

$$\{\log(1-d/100)-\beta_1\}/\beta_2.$$

The concentration associated with a d% reduction in risk relative to a 0/BLQ concentration on the FTC/TDF arm is

$$\log(1-d/100)/\beta_2$$

Here, β_1, is the log hazard ratio of a 0/BLQ level on the FTC/TDF arm (relative to placebo), β_2 quantifies the change in risk with the concentrations of drug and $h_{0k}(t)$ is the baseline hazard of HIV seroconversion on the placebo arm.

We also fit

$$\alpha(t;Z,\mathrm{rx})=\alpha\exp\{\alpha_1\mathrm{rx}+\alpha_2 Z(t)\} \quad (2)$$

where this exponential model is parameterized to yield the annualized incidence of HIV. The fit of this model to the data yielded similar results to the fit of model (1) and was used as the basis of the annualized HIV incidence graphed in Figure 3.

Note that the models (1) and (2) require a complete set of drug concentrations for participants in the active arm. We must confront two type of missing data. First, only a randomly selected subset of time points had drug concentrations tested. Second, intracellular drug (TFV-DP, FTC-TP) was only tested every 6 months and at the time of HIV seroconversion. Hence, even if a control has drug concentration tested, the information is sparse and may not correspond to an ideal time match to their HIV case.

We used two strategies for fitting model (1) with missing data in the drug concentrations: multiple imputation and conditional logistic regression. Conditional logistic regression functions only as a sensitivity analysis since it is unable to use the placebo group as a reference and does not handle the uncertainty in drug concentrations in the controls due to the long periods of time between measurement of drug concentrations.

Multiple Imputation

The concentration of drug for the HIV-infected cases at the time of HIV infection was taken as the intracellular concentration observed at the first laboratory evidence of HIV infection. Six participants lacked an intracellular specimen at the first laboratory evidence of HIV infection -- all had a plasma specimen at the first evidence of infection and all were BLQ (below the limit of quantitation) for TFV and FTC. In the case control study of 355 plasma specimens which are BLQ for TFV and FTC, 96% were BLQ for TFV-DP and 95% were BLQ for FTC-TP. Hence, the TFV-DP and FTC-TP for these 6 seroconverters were set as BLQ.

For controls, we attempted to infer the drug concentration at the identical day of follow up as seroconverters from the same site. We used the closest intracellular drug concentration within 45 days as the drug concentration if one was available and considered that as a measured drug concentration. If there was no tested drug concentration within 45 days, then

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drug concentrations were imputed. Varying the 45 day window had little effect on the results.

If the visit had plasma but not intracellular concentrations (vPBMC), we used whether the plasma had detectable or not in our imputation model. We performed multiple imputations (9) of TFV-DP, FTC-TP and any detection of drug in plasma or PBMC using medication possession ratio (defined as the number of tablets dispensed at the prior visit divided by days since the last visit at which medication was dispensed), study week, unprotected receptive anal intercourse (URAI) at baseline, URAI at follow-up (most recent report on or after the time point), baseline herpes simplex virus (HSV) status, number of male sexual partners at screening, participant report of a sexual transmitted infection in the six months prior to enrollment, secondary education, age at enrollment (in years) and baseline (estimated) creatinine clearance (by Cockcroft-Gault equation). Plasma and PBMC concentrations have monotone missingness hence chained imputation was used to create joint imputations. The imputation model for detection of drug in plasma was based on logistic regression and imputations for TFV-DP and FTC-TP were based on predictive means matching.(8) Predictive means matching used a regression model to identify observed values in the data which form the most plausible value for the imputations, yielding non-parametric imputations that must follow the observed distribution of the drug concentrations. This method seamlessly imputed concentrations of TFV-DP and FTC-TP that were below the limit of quantitation. This permitted us to form imputations in a first stage of analysis and to vary the strategy for quantifying BLQ values in a second stage. We performed 20 imputations per observation.

Conditional Logistic Regression

Analyses using conditional logistic regression mimics a (stratified) Cox proportional hazards model among participants on the active arm of the form

$$h_k(t;Z)=h_{0k}(t)\exp\beta_3 Z(t) \quad (3)$$

where k is the clinic site and Z(t) is a time-dependent covariate for drug concentration. Prentice and Breslow demonstrated that by measuring covariates in cases and a sample of (time matched) controls, it was possible to fit (3) using a conditional logistic regression model. (27) Hence, the coefficient in the conditional logistic regression is a valid estimator of the log hazard ratio β_3 which is the risk reduction compared to a drug concentration of 0 on the active arm. As a sensitivity analysis, we compared the results of our estimated protective concentrations by calculating the intracellular drug concentrations associated with a d% reduction in risk relative to a 0/BLQ concentration on the FTC/TDF arm as

$$\log(1-d/100)/\beta_3$$

Inferred Protection

Based on estimates for model 1 fit using multiple imputation, we estimated the protective effect of dosing regimens used in STRAND. For this, we combined the parameter estimates from model (1) with the observed TFV-DP from the 2, 4, and 7 tablets per week regimens in STRAND. The estimated relative risk reduction was approximated by

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$$100\left(1-n_D^{-1}\sum_{i=1}^{n_D}\exp\{\widehat{\beta}_1+\widehat{\beta}_2 Z_{iD}\}\right)$$

where (Z_{1D},,....., Z_{nDD}) were the n_D observed TFV-DP concentrations for D tablet per week regimen and the parameter estimates were taken from fitting model 1 using multiple imputation with associated 0.95 level Wald-based confidence intervals.

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References

1. Grant RM, et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. The New England journal of medicine. Dec 30.2010 363:2587. [PubMed: 21091279]
2. UNAIDS. 2010
3. Baral S, Sifakis F, Cleghorn F, Beyrer C. Elevated risk for HIV infection among men who have sex with men in low- and middle-income countries 2000–2006: a systematic review. PLoS Med. Dec. 2007 4:e339. [PubMed: 18052602]
4. Donnell, D., et al. paper presented at the 19th Conference on Retroviruses and Opportunistic Infections; Seattle, WA, USA. March 5–8 2012;
5. Karim SS, Kashuba AD, Werner L, Karim QA. Drug concentrations after topical and oral antiretroviral pre-exposure prophylaxis: implications for HIV prevention in women. Lancet. Jul 16.2011 378:279. [PubMed: 21763939]
6. Thigpen, MC., et al. 6th IAS Conference on HIV Pathogenesis, Treatment and Prevention; Rome, IT. 2011.
7. Van Damme, L., et al. paper presented at the 19th Conference on Retroviruses and Opportunistic Infections; Seattle, WA, USA. March 5–8 2012;
8. Little RJA. Missing-Data Adjustments in Large Surveys. Journal of Business & Economic Statistics. 1988; 6:287.
9. Schafer JL. Multiple imputation: a primer. Statistical Methods in Medical Research. Feb 1.1999 8:3. [PubMed: 10347857]
10. Kashuba AD, Patterson KB, Dumond JB, Cohen MS. Pre-exposure prophylaxis for HIV prevention: how to predict success. Lancet. Dec 6.2011
11. Anderson, PL., et al. 19th Conference on Retroviruses and Opportunistic Infection; Seattle, WA. 2012.
12. Patterson KB, et al. Penetration of tenofovir and emtricitabine in mucosal tissues: implications for prevention of HIV-1 transmission. Sci Transl Med. Dec 7.2011 3:112re4.
13. Anton, P., et al. 18th Conference on Retroviruses and Opportunistic Infections; Boston, MA, USA. 2011.
14. Keller MJ, et al. A randomized trial to assess anti-HIV activity in female genital tract secretions and soluble mucosal immunity following application of 1% tenofovir gel. PLoS ONE. 2011; 6:e16475. [PubMed: 21283552]
15. Bushman LR, et al. Determination of nucleoside analog mono-, di-, and tri-phosphates in cellular matrix by solid phase extraction and ultra-sensitive LC-MS/MS detection. Journal of pharmaceutical and biomedical analysis. Sep 10.2011 56:390. [PubMed: 21715120]
16. Castillo-Mancilla, J., et al. paper presented at the 19th Conference on Retroviruses and Opportunistic Infections; Seattle, WA. March 5–8 2012;

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17. Liu, A., et al. 17th Conference on Reteroviruses and Opportunistic Infections; San Francisco. 2010.
18. Borroto-Esoda K, Vela JE, Myrick F, Ray AS, Miller MD. In vitro evaluation of the anti-HIV activity and metabolic interactions of tenofovir and emtricitabine. Antivir Ther. 2006; 11:377. [PubMed: 16759055]
19. Anderson, PL., et al. paper presented at the 18th Conference on Retroviruses and Opportunistic Infections; Boston, MA. Feb 27–Mar 2 2011;
20. García-Lerma JG, et al. Intermittent prophylaxis with oral truvada protects macaques from rectal SHIV infection. Sci Transl Med. Jan 13.2010 2:14ra4.
21. Grant, R., et al. 6th IAS Conference on HIV Pathogenesis, Treatment and Prevention; Rome, IT. 2011.
22. Delahunty T, Bushman L, Robbins B, Fletcher CV. The simultaneous assay of tenofovir and emtricitabine in plasma using LC/MS/MS and isotopically labeled internal standards. Journal of Chromatography B. 2009; 877:1907.
23. Baheti G, Kiser JJ, Havens PL, Fletcher CV. Plasma and intracellular population pharmacokinetic analysis of tenofovir in HIV-1-infected patients. Antimicrob Agents Chemother. Nov.2011 55:5294. [PubMed: 21896913]
24. Kiser JJ, et al. Pharmacokinetics of antiretroviral regimens containing tenofovir disoproxil fumarate and atazanavir-ritonavir in adolescents and young adults with human immunodeficiency virus infection. Antimicrob Agents Chemother. Feb.2008 52:631. [PubMed: 18025112]
25. StataCorp. StataCorp LP, College Station, TX. 2011.
26. Glidden DV, Vittinghoff E. Modelling clustered survival data from multicentre clinical trials. Statistics in Medicine. 2004; 23:369. [PubMed: 14748034]
27. PRENTICE RL, BRESLOW NE. Retrospective studies and failure time models. Biometrika. Apr 1.1978 65:153.

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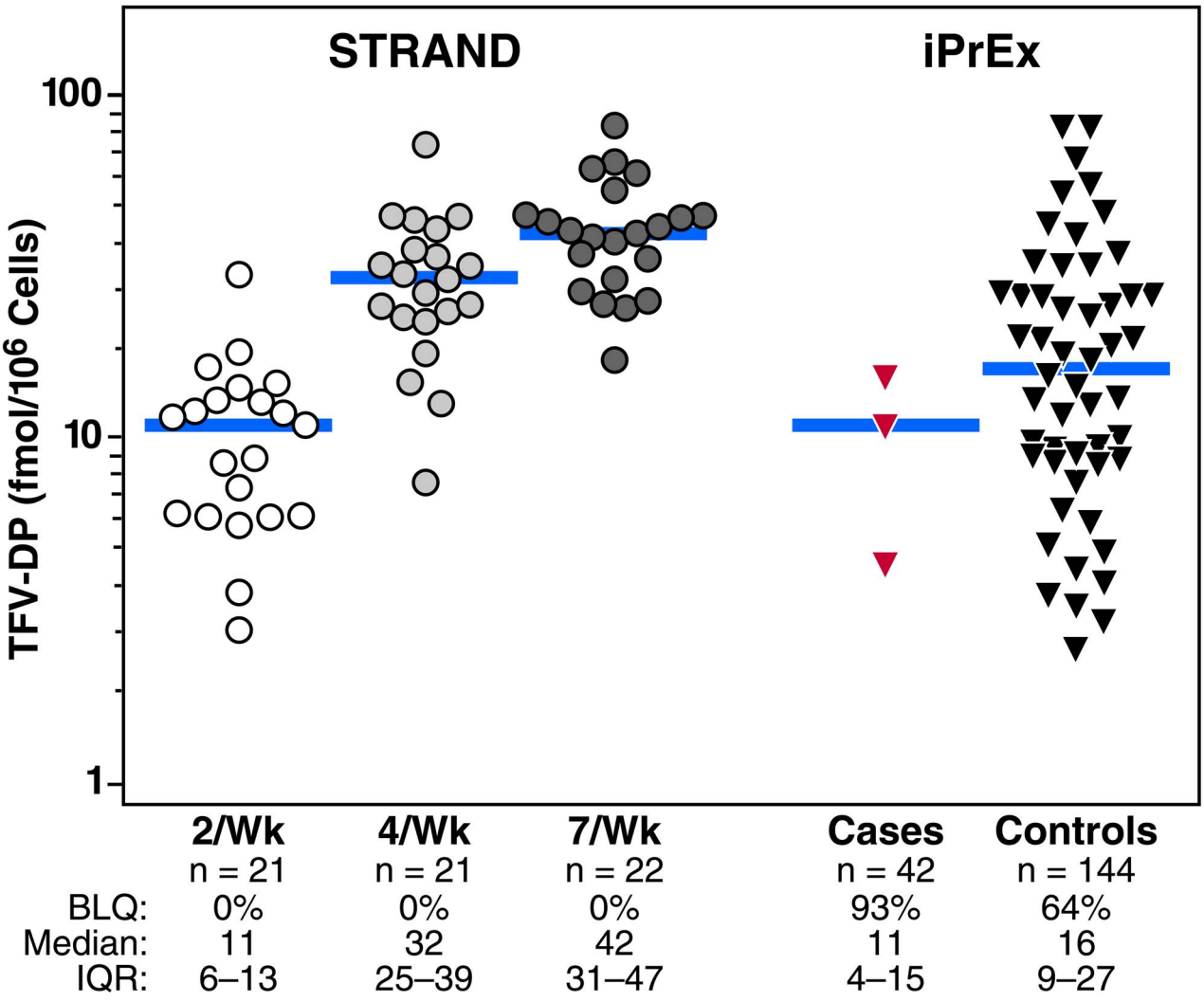


Fig 1.

Observed TFV-DP concentrations from STRAND and iPrEx. The values observed in the STRAND study are shown on the left for 2 doses/week (open circles), 4 doses/week (light-toned circles), and 7 doses/week (dark-toned circles). iPrEx values on the right included those from the visit with first evidence of HIV infection in cases (red triangles) and the matched study visit in HIV-negative controls (dark-toned triangles). The bars represent the medians. The numbers of participants tested, the proportion of vPBMC tested with detectable TFV-DP; the median concentrations among values in the detectable range; and the interquartile ranges are listed below the x-axis.

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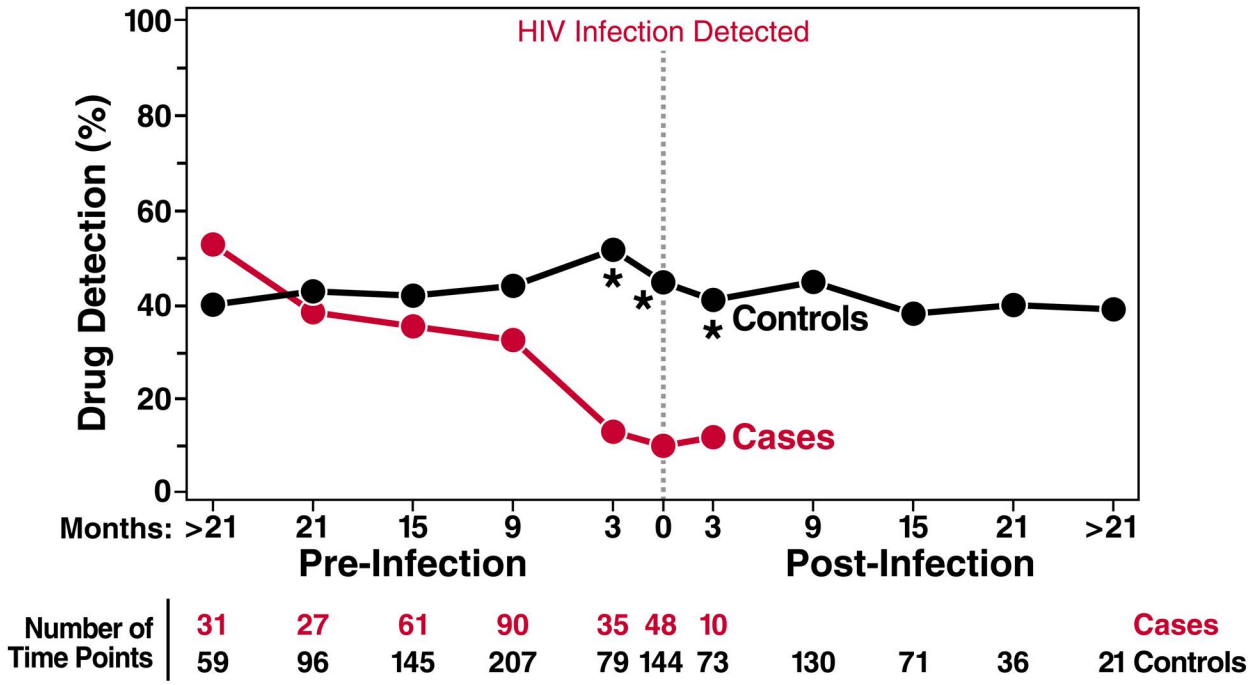


Fig 2.

Longitudinal drug detection relative to the time of first HIV-1 detection. The % of case and control time points with any drug detection in plasma or PBMC including TFV, FTC, TFV-DP, or FTC-TP, at the time of first laboratory evidence of HIV in cases or the matched time point in controls (dashed vertical line), and at pre- and post-HIV infection time points. The pre- and post-HIV infection time points were divided into those within 3 months (90 days) before or after HIV infection, and those within 6 month intervals distal to these time points. The number of time points with either plasma or vPBMC available for testing is listed for each time period.

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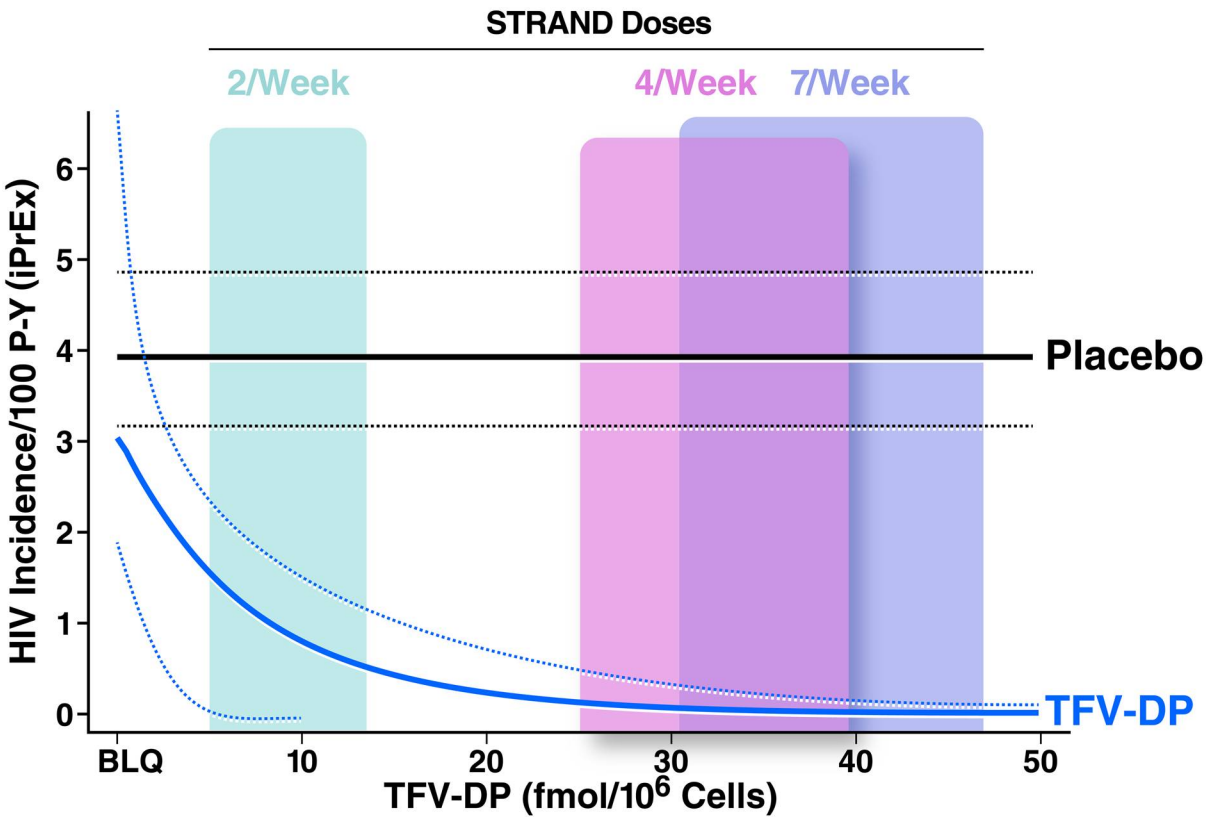


Fig. 3.

Estimated HIV incidence from exponential regression model of TFV-DP concentrations (fmol/M vPBMC) in iPrEx. The placebo HIV infection rate is shown as a horizontal line at 3.9 infections per 100 person years, with the relative rate in the active arm according to TFV-DP concentrations (x-axis). Dashed lines represent the 95% confidence intervals. The IQR of TFV-DP concentrations associated with directly observed dosing in STRAND are provided as colored panels overlying the curves.

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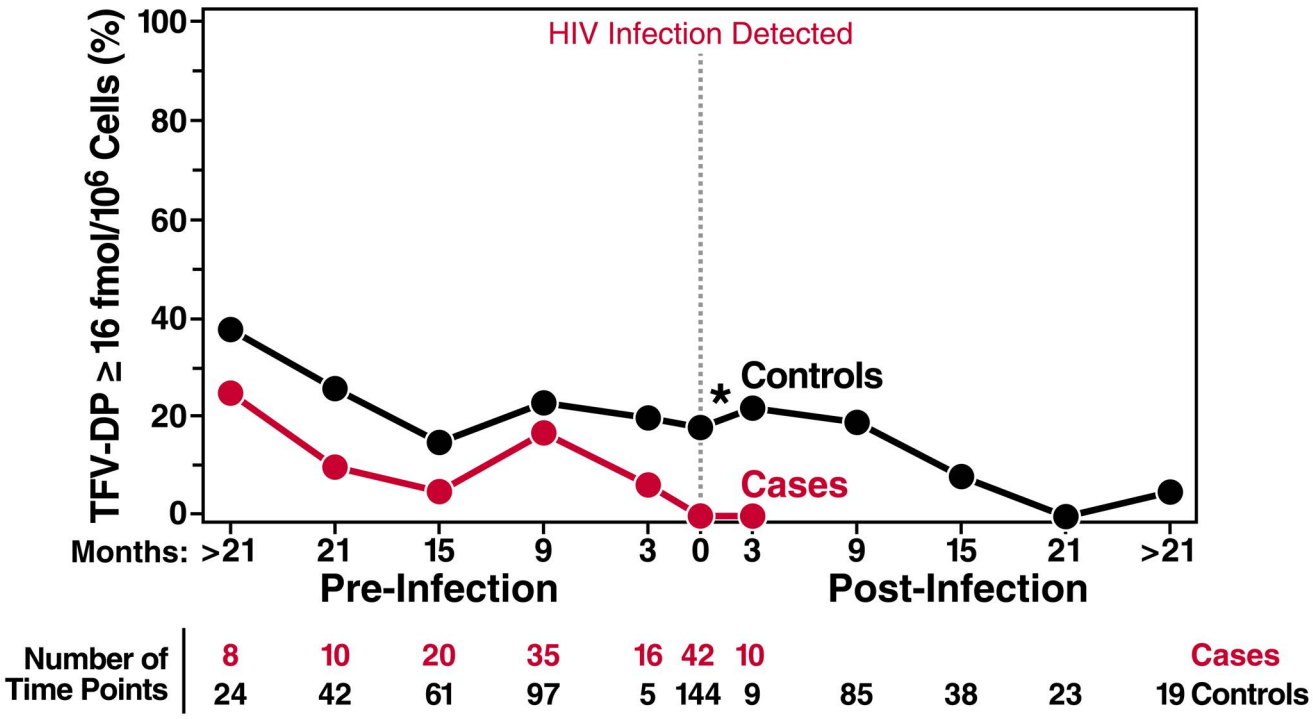


Fig 4.

The % of case and control time points with TFV-DP ≥ 16 fmol/M viable PBMC (estimated EC90). Dark-toned circles represent HIV-negative controls, and red circles represent HIV infected cases. The x-axis represents time relative to the visit with first evidence of HIV infection in the case and the matching time point in controls. Pre- and post-HIV infection time points were divided into those within 3 months (90 days) before or after HIV infection, and those within 6 month intervals distal to these time points. The number of time points with vPBMC tested for TFV-DP is listed for each time period. *indicates significant differences between cases and controls ($P<0.05$).

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Table 1

Demographic and HIV risk characteristics at baseline among analysis groups in the iPrEx study

	Cases N=48	Controls N=144	p-value
Baseline	*mean (sd)*		
Age in years	24 (6)	27 (8)	0.01
Calculated CrCl ml/min	125 (23)	121 (22)	0.30
Male Partners In past 6 months	12 (32)	13 (46)	0.78
	n (%)		
Secondary School	31 (66%)	109 (76%)	0.19
Alcohol Use (≥5 drinks per day on days when drinking)	24 (52%)	74 (54%)	0.87
Unprotected Receptive Anal Intercourse	34 (71%)	109 (76%)	0.57
History of sexually transmitted infection in past 6 months	15 (31%)	52 (36%)	0.60
Herpes seropositive	24 (50%)	69 (48%)	0.87
At Time of HIV Detection in Cases	*mean (sd)*		
Weeks on Study	63 (35)	65 (36)	0.73
	n (%)		
Unprotected Receptive Anal Intercourse	19 (40%)	74 (51%)	0.18

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Sexual risk behavior among HIV-uninfected men who have sex with men (MSM) participating in a tenofovir pre-exposure prophylaxis (PrEP) randomized trial in the United States

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Abstract

Objective—To evaluate for changes in sexual behaviors associated with daily pill-use among MSM participating in a PrEP trial.

Design—Randomized, double-blind, placebo-controlled trial. Participants were randomized 1:1:1:1 to receive tenofovir disoproxil fumarate or placebo at enrollment or after a 9-month delay and followed for 24 months.

Methods—400 HIV-negative MSM reporting anal sex with a man in the past 12 months and meeting other eligibility criteria enrolled in San Francisco, Atlanta, and Boston. Sexual risk was assessed at baseline and quarterly visits using Audio Computer-Assisted Self-Interview. The association of pill-taking with sexual behavior was evaluated using logistic and negative-binomial regression for repeated measures.

Results—Overall indices of behavioral risk declined or remained stable during follow-up. Mean numbers of partners and proportion reporting unprotected anal sex (UAS) declined during follow-

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Conflicts of Interest
For the remaining authors, no conflicts of interest were declared.

Disclaimers:
The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention. In addition, the views expressed herein do not necessarily reflect the official policies of the City and County of San Francisco; nor does mention of the San Francisco Department of Public Health imply its endorsement.

A portion of the results of this paper was presented as a poster presentation at the 6th International AIDS Society Conference on HIV Pathogenesis, Treatment, and Prevention, Rome Italy 2011: Liu A, Vittinghoff E, Chillag C, et al. No evidence of sexual risk compensation among HIV-uninfected men who have sex with men (MSM) participating in a tenofovir pre-exposure prophylaxis (PrEP) trial. (MOPE381)

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up ($p<0.05$), and mean UAS episodes remained stable. During the initial 9 months, changes in risk practices were similar in the group that began pills immediately vs. those in the delayed arm. These indices of risk did not differ significantly after initiation of pill-use in the delayed arm or continuation of study medication in the immediate arm. Use of poppers, amphetamines, and sexual performance-enhancing drugs were independently associated with one or more indices of sexual risk.

Conclusions—There was no evidence of risk compensation among HIV-uninfected MSM in this clinical trial. Monitoring for risk compensation should continue now that PrEP has been shown to be efficacious in MSM and other populations and will be provided in open-label trials and other contexts.

Keywords

risk compensation; behavioral disinhibition; sexual risk behavior; PrEP; MSM

INTRODUCTION

Pre-exposure prophylaxis (PrEP), or the use of antiretroviral medicines by HIV-uninfected individuals, is a rapidly emerging prevention strategy that could help reduce HIV incidence globally. In 2010, the iPrEx trial demonstrated a 44% reduction in HIV infections among men who have sex with men (MSM) who received daily oral emtricitabine/tenofovir (FTC/TDF) vs. a placebo pill [1]. More recently, data on PrEP in heterosexual populations have been reported [2]. While the FEM-PrEP trial evaluating daily oral FTC/TDF and the oral/topical tenofovir arms of the VOICE study, both in African women, were terminated early because of futility [3–5], the Partners PrEP study [6] in Kenya and Uganda and the CDC Botswana PrEP trial [7] found PrEP to be over 60% efficacious in heterosexual men and women at risk for HIV infection. Based on these results, the Centers for Disease Control and Prevention (CDC) issued interim guidance on PrEP use among MSM and heterosexually active adults in the United States (US) [8, 9], and the Food and Drug Administration approved FTC/TDF as PrEP in July 2012 [10]. In all trials to date, participants have been provided a comprehensive package of prevention services including risk-reduction counseling, regular HIV testing, and management of sexually transmitted infections.

While there is enthusiasm for PrEP as a novel HIV prevention approach, some have expressed concerns that the availability of a pill or gel for prevention could increase risk behavior, leading to increased HIV infections and undermine PrEP's protective benefits [11–13]. Conversely, daily PrEP could promote safer-sex behaviors by reminding people of their vulnerability to HIV and/or fostering a "preventionist" identity (e.g., one who cares about reducing one's HIV risk) [13]. Several mathematical models show that the beneficial impact of PrEP may be offset by small increases in risk behavior and could lead to an increase in new infections, particularly in scenarios of low effectiveness and coverage [14–16], while decreases in risk behavior associated with a biomedical prevention intervention could lead to synergistic reductions on population-level HIV incidence [14],[17].

The evidence for risk compensation in previous trials of HIV prevention interventions is mixed. Chesney et al. demonstrated an increase in unprotected anal sex among HIV vaccine trial recipients, and in two male circumcision trials, mean sexual contacts [18] and rates of unprotected sex [19] were higher in the circumcised vs. uncircumcised group. Conversely, Bartholow et al. observed a decrease in unprotected anal sex among MSM in the Vax004 trial [20], and Guest and colleagues found a decrease in number of sexual partners and rates of unprotected sex in a PrEP trial among high-risk women in West Africa [21]. Reported risk behaviors also declined in CAPRISA 004 [22], iPrEx [1], and Partners PrEP [6].

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One limitation of these trials is that both the control and intervention arm participants receive a pill, gel, or vaccine. Without a comparison group receiving no product, it is difficult to assess the direct effect of the intervention on risk behavior, since risk often declines as individuals enroll in a prevention trial and are provided frequent risk-reduction counseling and HIV testing. Therefore, in designing the US CDC Safety Study of daily TDF among MSM, we incorporated a wait-list control design in which half of the study cohort initiated pill use at enrollment, and the other half after a 9-month delay. This study design allowed for a more direct evaluation of the effect of pill-taking on sexual practices. We evaluate the effect of daily pill-taking on risk practices through a comparison of risk behavior in the immediate vs. delayed arms during the first 9 months of the study and describe how risk patterns changed within arms over the remainder of this 24 month study. We also evaluate correlates of reported risk behavior in this cohort, including substance use which has been associated with increased HIV risk among HIV-uninfected MSM in other studies. [23–25]

METHODS

Clinical trial

The US CDC Safety Study was a phase-2 randomized, double-blind, placebo-controlled extended safety trial of TDF in MSM in the US. The trial was conducted at sites in Atlanta (n=121 enrolled), Boston (n=79), and San Francisco (n=200). Participants were randomized 1:1:1:1 to one of 4 arms: 1) daily TDF beginning at enrollment; 2) daily placebo beginning at enrollment; 3) daily TDF beginning 9 months after enrollment; 4) daily placebo beginning 9 months after enrollment (figure 1). The sample size was chosen to provide >80% power to detect ≥12% differences in outcomes between groups assuming ≥28% reported this behavior in the delayed arm.

MSM at risk for HIV infection were enrolled from February 2005 to July 2007. Eligibility criteria included being male at birth, 18–60 years old, HIV-1 negative, healthy (no serious or life-threatening diseases or conditions and adequate hematologic, biochemical, hepatic, and pancreatic function by laboratory testing), able to understand English and provide written informed consent at screening, and reporting any anal sex with or without a condom with a man in the last 12 months (including main or casual partners). Men in a mutually monogamous relationship for ≥ 1 year with a known HIV-negative partner were excluded. Transgender women who met eligibility criteria were included in the study.

Volunteers were tested for HIV antibody at screening using a rapid HIV test kit; HIV seropositive men were not enrolled and were referred to medical care. Enrolled participants attended study visits every 3 months over a 2-year period and received HIV testing, risk-reduction counseling, free condoms and lubricants, and assessments of biomedical and behavioral safety, adherence, and acceptability. Study staff regularly counseled men that the efficacy of TDF for prevention was unknown, reminded participants they might be receiving a placebo, and reinforced the importance of maintaining safer-sex practices.

Structured Interview

All participants were administered a structured questionnaire using Audio-Computer Assisted Self-Interview (ACASI) at enrollment and each quarterly follow-up visit.

Sexual behavior and substance use—At baseline and every 3 months, participants were asked about their number of male sexual partners (including oral or anal sex) in the past 3 months for each of 3 partner types: known HIV-positive and HIV–negative partners and partners of unknown HIV serostatus. Study participants were also asked about the

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number of times they engaged in insertive and receptive anal sex with and without using condoms during the prior 3 months, grouped by HIV serostatus of the partner. At baseline and quarterly follow-up visits, participants were also asked about their substance use in the past 3 months, including alcohol, poppers, cocaine, amphetamines, sedatives, and Ecstasy.

Perceived Treatment assignment—At semi-annual visits beginning at the 6-month visit for the immediate arms and the 12-month visit for the delayed arms, participants were asked which treatment group they believed they were in using the following worded choices: "I strongly think I am in the TDF (or placebo) group"; "I somewhat think I am in the TDF (or placebo) group"; and "don't know." The two TDF and two placebo categories (strongly/somewhat think) were grouped together for analysis. Consistency of responses was assessed by constructing a single variable indicating that participants consistently thought they had received TDF or placebo; consistently reported they didn't know their treatment assignment; or inconsistently perceived treatment assignment across all visits when treatment assignment was assessed and data were non-missing.

Perceived PrEP efficacy—At baseline and every 6 months, perception of PrEP efficacy was evaluated by the question, "How good do you think tenofovir is in preventing HIV infection?" Responses were based on a 0–10 scale where 10 means it prevents HIV infection all the time, 0 means it doesn't prevent HIV infection at all, and 5 means it prevents HIV half of the time. For multivariable analyses, this variable was collapsed into 4 a priori categories: 0–3 (low), 4–6 (moderate), 7–10 (high), and "didn't know." Data on perceived PrEP efficacy were collected before the release of efficacy data from other PrEP trials (e.g. iPrEx, Partners PrEP, CDC Botswana Study) and were not influenced by those results.

Data Analyses

To take advantage of our study design with pill use initiation deferred in the delayed arm, we analyzed risk practices reported at baseline, during months 3–9, when delayed arm participants were off study drug, and during months 12–24, when all subjects were given study drug. Finding no evidence in preliminary analysis of unblinding (see results section), we pooled data for the subgroups assigned to TDF and placebo within the immediate and delayed arms.

Primary outcome measures included numbers of partners and unprotected anal sex (UAS) with either a primary or casual partner in the past 3 months, both overall and by partner serostatus. We first estimated overall trends across groups (immediate vs. delayed arms) for each of these risk practices during months 3–9 and months 12–24 of follow-up. We then evaluated group-specific trends as well as baseline differences between the immediate and delayed arms using a model adjusting for period (months 3–9 vs. 12–24) and interaction between period and study arm (immediate vs. delayed). To assess risk compensation due to initiation of study drug, we compared changes in risk behavior from baseline to months 3–9 in the immediate vs. delayed arms using this model. We also assessed within-group changes in risk practices between months 3–9 and months 12–24 to assess the effects of initiating pill use in the delayed arm at the 9 month visit, and of continuing pill use (months 9–24) in the immediate arm. All these analyses were by intention-to-treat, without regard to study drug adherence during periods of assigned use.

We used negative binomials models for numbers of partners and UAS episodes and logistic regression for any UAS. To account for within-subject correlation as well as over-dispersion of the count outcomes, these models were fitted using generalized estimating equations (GEE) with exchangeable working correlation matrix and robust standard errors.

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Finally, we identified independent risk factors for risky behavior using multivariable negative binomial and logistic GEE models. In these analyses, potential risk factors were first screened using models controlling for treatment group and period, keeping variables with $p<0.1$; final models were then selected using backward deletion with a retention criterion of $p<0.2$. All analyses were conducted using Stata Version 12.

RESULTS

Participant haracteristics

Four hundred sexually active MSM enrolled. Over a quarter of participants were non-white (African-American, Asian/Pacific-Islander, or other race) and 9% Hispanic/Latino (table 1). Almost half (45%) reported moderate or heavy alcohol use, over a quarter reported use of poppers (27%) or sexual enhancing drugs (28%), and 11% reported amphetamine use in the past 3 months. Demographics and the proportion of men reporting alcohol/drug use were similar between the immediate vs. delayed arms. Overall study retention was high, with 16% (16.5% in the immediate and 15.5% in the delayed arm) lost to follow-up; rates of early study discontinuation were similar between arms.

Perceived Treatment Assignment and PrEP Efficacy

Perceptions of treatment assignment by study visit are shown in Figure 2a. At the 6-month visit (immediate arm only), a quarter (25%) of men believed they were assigned to TDF, about a quarter (23%) believed they were assigned to placebo, and approximately half (52%) reported that they did not know their treatment assignment. At the 12-month visit (including both immediate/delayed arms), 26% perceived they were assigned to TDF, 26% placebo, and 46% didn't know. Overall, about a quarter (24%) of study participants consistently stated that they did not know their treatment assignment, 12% consistently thought they had been assigned to TDF, and 11% consistently believed they had been assigned to placebo. Perceptions were not consistent for the remaining 53% participants. Participants assigned to TDF were equally or more likely to predict they were assigned to placebo than to TDF; the opposite was true for placebo participants, suggesting that there was no substantial degree of unblinding.

Perceptions of PrEP efficacy increased over time (Figure 2b). At baseline, 11% believed TDF had high efficacy, 19% believed TDF had moderate efficacy, 31% believed that TDF had low efficacy, and 39% reported they didn't know the efficacy of PrEP. At the 24-month visit, 31% believed that TDF had high efficacy, 33% moderate efficacy, 23% low efficacy, and 13% reporting they didn't know (p-value for trend < 0.00005).

Numbers of male sex partners

At baseline, there were no significant differences in self-reported numbers of male sex partners in the past 3 months between the immediate vs. delayed arms ($p=0.68$). Overall, mean numbers of sex partners (per subject, in the past 3 months) decreased significantly from 7.25 at baseline to 6.02 during months 3–9 and 5.71 during months 12–24 ($p<0.001$). These declines were similar between the immediate vs. delayed arms during months 3–9 (p for interaction=0.67) (see figure 3a). Furthermore, the mean number of partners did not differ in months 12–24 vs. months 3–9 with initiation of study drug in the delayed arm (IRR 0.93, $p=0.22$) or continuation of drug in the immediate arm (IRR 0.96, $p=0.56$).

When analyzed separately by partner HIV serostatus, the mean number of partners reported in the last 3 months also decreased from baseline or remained stable. Mean numbers of positive or unknown HIV-status partners declined from 4.17 at baseline to 3.51 during months 3–9 ($p=0.04$) and 3.37 during months 12–24 ($p=0.01$). The mean number of HIV-

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negative partners decreased significantly from baseline (3.11) to months 3–9 (2.52, p=0.03) and months 12–24 (2.32, p=0.002). Furthermore, the proportion of participants reporting an HIV-positive sex partner decreased during follow-up (30% at baseline vs. 25% during months 3–9 (p=0.006) and 27% during months 12–24, p<0.03). There was a greater decrease in mean HIV-negative partners in the immediate vs. delayed arms during months 3–9 (IRR 0.64, p for interaction=0.01); changes from baseline to months 3–9 did not differ significantly by immediate vs. delayed arms for positive/unknown status partners (p=0.14) or proportion reporting an HIV-positive partner (p=0.73).

Correlates of number of partners in the past 3 months are shown in table 2 (left side of table). Use of poppers and sexual-enhancing drugs such as sildenafil and higher perception of PrEP efficacy were associated with higher number of partners after controlling for study period, being assigned to take pills, site, age, race/ethnicity, education, and perception of treatment assignment; amphetamine use was marginally associated with a greater number of partners (p=0.07).

Unprotected anal sex (UAS)

At baseline, over half (57%) of men reported engaging in any UAS in the past 3 months (table 1). These proportions were similar between the immediate vs. delayed arm (p = 0.29). Overall, the proportion of men engaging in UAS decreased from baseline (57%) to months 3–9 (48%, p=0.001) and months 12–24 (52%, p=0.03). The change in proportion of men reporting UAS from baseline to months 3–9 was similar between the immediate vs. delayed arms (p for interaction = 0.15)(see figure 3b). The proportion of men reporting UAS did not change significantly after initiation of study drug in the delayed arm (p=0.41) but may have increased slightly with continuation of drug in the immediate arm (IRR 1.17, 95% CI 0.98–1.39, p=0.09).

The proportions reporting any unprotected anal sex with an HIV-positive or unknown HIV-status partner (UASPU) also declined during study follow-up (29% at baseline, vs. 21% during months 3–9 and 22% during months 12–24, p<0.001). Declines in UASPU from baseline did not differ by immediate vs. delayed arms during follow-up (overall p for interaction=0.43). The proportion of men reporting UASPU did not significantly change after initiation of study medication in the delayed arm (p=0.55) or continuation of study medication in the immediate arm (p=0.60).

In the multivariable analysis (table 2, middle columns), correlates of reporting any UAS included younger age and use of poppers, amphetamines, or sexual performance enhancing drugs, after adjusting for being on pills, site, race/ethnicity, education, and perception of treatment assignment and PrEP efficacy. UAS significantly declined during the first 3–9 months after adjustment for these factors.

Episodes of unprotected anal sex

At baseline, the mean number of episodes of UAS (per subject, in the past 3 months) reported at baseline was 4.78, with a marginally significantly greater number of episodes in the immediate vs. delayed arms (5.79 vs. 3.78 episodes respectively, p=0.08). Overall, mean episodes of UAS did not change significantly from baseline during months 3–9 (p=0.98) and months 12–24 (p=0.28). Furthermore, UAS episodes did not differ significantly between immediate vs. delayed arms during months 3–9 (p=0.10) and did not change significantly after initiation of study drug in the delayed group (p=0.42) or with continuation of drug in the immediate arm (p=0.22).

Mean UAS episodes with a positive or unknown HIV status partner (UASPU episodes) remained stable or decreased during follow-up (2.02 at baseline vs. 1.51 during months 3–9

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(p=0.22) and 1.37 during months 12–24 (p=0.05)). Overall, UASPU episodes were similar in the immediate vs. delayed arms during months 3–9 (p value for interaction=0.29). In contrast, numbers of UAS episodes with HIV-negative partners increased during follow-up, especially during months 12–24 (2.75 episodes at baseline vs. 4.00 at 12–24 months, p=0.01), but the patterns were similar in the immediate vs. delayed arms (p for interaction=0.42).

In multivariable analyses, greater mean numbers of UAS episodes was associated with use of sexual-enhancing drugs. Fewer UAS episodes were reported in African American men, at the Boston site, and among those who believed they were taking TDF.

DISCUSSION

We found no evidence of risk compensation among at-risk MSM initiating PrEP in this trial. In particular, mean numbers of partners and proportion of men reporting UAS decreased significantly from baseline during 24 months of follow-up, and declines were similar in the immediate vs. delayed arms. Episodes of UAS remained stable over time. Furthermore, there was little or no increase in these risk indices after initiation of study drug. These findings are consistent with other studies showing a similar reduction of risk practices with initiation of a biomedical prevention strategy within a clinical trial [1],[22],[21]. As in previous trials, men in this study received risk-reduction counseling, condoms and lubricants, regular HIV/STI testing, and linkage to prevention services (including substance use treatment) which may explain the observed risk declines and could mitigate any potential for risk compensation.

We also analyzed changes in risk practices by HIV serostatus of the participants' partners. For positive and unknown HIV-status partners, all risk indices decreased during follow-up. These declines were similar in the immediate vs. delayed arms during months 3–9 and did not increase in the delayed arm with drug initiation. For HIV-negative partners, mean numbers of partners declined significantly during follow-up. Episodes of UAS with HIV-negative partners increased during follow-up, especially during months 12–24, in both immediate and delayed arms. Given that episodes of UAS with HIV-negative partners began increasing in the delayed arm prior to pill initiation and increased in both arms during months 12–24, these findings most likely represent secular behavioral trends in this cohort, rather than risk compensation due to pill initiation; these changes may reflect a possible increase in seroadaptive practices, in which men preferentially have more episodes of UAS with assumed HIV-negative partners.

In our multivariable analyses, we found that substance use (including poppers, amphetamines, and sexual-enhancing drugs) was associated with increased reported risk. Drug use remained stable throughout the study (data not shown) and therefore did not explain overall decreases in overall partner number and UAS in this cohort. Services to link substance-using MSM into counseling and treatment should be considered in future PrEP programs. Future trials focusing on substance-using MSM should be conducted to provide additional clinical and behavioral safety data on PrEP use in this group. We also found younger men were more likely to engage in UAS. Young MSM, particularly African American MSM, have recently experienced significant increases in HIV incidence [26] and may be a target population for PrEP; counseling and other strategies to help reduce risk and support PrEP adherence will be important in this population. Our finding that African-American MSM reported fewer UAS episodes compared with white MSM in our cohort is consistent with reports from other studies finding lower reported risk behaviors among African-American MSM [27, 28] and suggests other factors, including social/sexual networks [29] and undiagnosed HIV infection [30, 31], may place this population at elevated

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risk for HIV infection. While a higher perception of PrEP efficacy was associated with a small increase in total partners, this was not associated with increases in UAS or UAS episodes; perception of treatment assignment to TDF was associated with fewer UAS episodes.

Our findings are subject to several limitations. Participants were counseled that they may be receiving a placebo, and that there was no known efficacy of PrEP. Therefore, risk behavior changes in this trial may not reflect changes that may occur with open-label PrEP administration in the setting of known efficacy. Also, our sexual behavior measures recorded participants' self-report of risk practices over the prior 3 months, which may be subject to social desirability (although likely mitigated with ACASI) and recall difficulties over this period. Our risk behavior analysis included multiple comparisons of various sexual behaviors, so any significant associations should be interpreted with appropriate caution. Finally, this trial was conducted in 3 large metropolitan US cities (San Francisco, Boston, and Atlanta) and just over one-quarter of participants were men of color; results may not generalize to other populations of MSM who may use PrEP.

Despite these limitations, our data provide important information on changes in risk practices among MSM in the US initiating PrEP in a clinical trial setting. A major strength is the unique study design incorporating randomization of a comparison group in which participants did not receive study pills during the first 9 months, allowing for a direct comparison of the magnitude of behavior change in the immediate vs. delayed arms. Other strengths of this study include the intention-to-treat analysis, thus minimizing confounding factors, and good retention rates.

Now that PrEP has been shown to be efficacious in MSM [1], it will be important for future studies and programs to monitor for changes in sexual practices as PrEP is provided in an open-label context. Behavioral measures in open-label extension phases of successful PrEP trials as well as upcoming PrEP demonstration projects will provide important information on changes in sexual practices in more real-world settings. Data from these programs will also help inform the development of optimal behavioral interventions that can be coupled with PrEP delivery as part of a comprehensive prevention package. Our findings suggest the importance of addressing substance use issues and providing counseling about the relative benefits and harms of seroadaptive practices as part of PrEP support interventions [32]; this combination of prevention strategies will likely have the largest public health impact.

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REFERENCES

1. Grant RM, Lama JR, Anderson PL, McMahan V, Liu AY, Vargas L, et al. Preexposure Chemoprophylaxis for HIV Prevention in Men Who Have Sex with Men. N Engl J Med. 2010
2. Celum C, Baeten JM. Tenofovir-based pre-exposure prophylaxis for HIV prevention: evolving evidence. Curr Opin Infect Dis. 25:51–57. [PubMed: 22156901]
3. Van Damme L, Corneli A, Ahmed K, Agot K, Lombaard J, Kapiga S, et al. Preexposure prophylaxis for HIV infection among African women. N Engl J Med. 2012; 367:411–422. [PubMed: 22784040]
4. Microbicide Trials Network. MTN Statement on Decision to Discontinue Use of Oral Tenofovir Tablets in VOICE, a Major HIV Prevention Study in Women. [press release]. 28 September 2011 Available at www.mtnstopshiv.org/node/3619.
5. Microbicide Trials Network. MTN Statement on Decision to Discontinue Use of Tenofovir Gel in VOICE, a Major HIV Prevention Study in Women. [press release]. 25 November 2011. Available at www.mtnstopshiv.org/node/3909.
6. Baeten JM, Donnell D, Ndase P, Mugo NR, Campbell JD, Wangisi J, et al. Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. N Engl J Med. 367:399–410. [PubMed: 22784037]
7. Thigpen MC, Kebaabetswe PM, Paxton LA, Smith DK, Rose CE, Segolodi TM, et al. Antiretroviral preexposure prophylaxis for heterosexual HIV transmission in Botswana. N Engl J Med. 2012; 367:423–434. [PubMed: 22784038]
8. Smith D, Grant R, Weidle P, Lansky A, Mermin J, Fenton KA. Interim Guidance: Preexposure Prophylaxis for the Prevention of HIV Infection in Men Who Have Sex with Men. MMWR. 2011; 60
9. Interim Guidance for Clinicians Considering the Use of Preexposure Prophylaxis for the Prevention of HIV Infection in Heterosexually Active Adults. MMWR Morb Mortal Wkly Rep. 2012; 61:586–589. [PubMed: 22874836]
10. Holmes D. FDA paves the way for pre-exposure HIV prophylaxis. Lancet. 380:325. [PubMed: 22852138]
11. Cassell MM, Halperin DT, Shelton JD, Stanton D. Risk compensation: the Achilles' heel of innovations in HIV prevention? Bmj. 2006; 332:605–607. [PubMed: 16528088]
12. Eaton LA, Kalichman S. Risk compensation in HIV prevention: implications for vaccines, microbicides, and other biomedical HIV prevention technologies. Curr HIV/AIDS Rep. 2007; 4:165–172. [PubMed: 18366947]
13. Golub SA, Operario D, Gorbach PM. Pre-exposure prophylaxis state of the science: empirical analogies for research and implementation. Curr HIV/AIDS Rep. 7:201–209. [PubMed: 20809218]
14. Vissers DC, Voeten HA, Nagelkerke NJ, Habbema JD, de Vlas SJ. The impact of pre-exposure prophylaxis (PrEP) on HIV epidemics in Africa and India: a simulation study. PLoS ONE. 2008; 3:e2077. [PubMed: 18461185]
15. Desai K, Sansom SL, Ackers ML, Stewart SR, Hall HI, Hu DJ, et al. Modeling the impact of HIV chemoprophylaxis strategies among men who have sex with men in the United States: HIV infections prevented and cost-effectiveness. AIDS. 2008; 22:1829–1839. [PubMed: 18753932]
16. Paltiel AD, Freedberg KA, Scott CA, Schackman BR, Losina E, Wang B, et al. HIV preexposure prophylaxis in the United States: impact on lifetime infection risk, clinical outcomes, and cost-effectiveness. Clin Infect Dis. 2009; 48:806–815. [PubMed: 19193111]
17. Hallett TB, Singh K, Smith JA, White RG, Abu-Raddad LJ, Garnett GP. Understanding the impact of male circumcision interventions on the spread of HIV in southern Africa. PLoS ONE. 2008; 3:e2212. [PubMed: 18493593]
18. Auvert B, Taljaard D, Lagarde E, Sobngwi-Tambekou J, Sitta R, Puren A. Randomized, controlled intervention trial of male circumcision for reduction of HIV infection risk: the ANRS 1265 Trial. PLoS Med. 2005; 2:e298. [PubMed: 16231970]

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19. Bailey RC, Moses S, Parker CB, Agot K, Maclean I, Krieger JN, et al. Male circumcision for HIV prevention in young men in Kisumu, Kenya: a randomised controlled trial. Lancet. 2007; 369:643–656. [PubMed: 17321310]
20. Bartholow BN, Buchbinder S, Celum C, Goli V, Koblin B, Para M, et al. HIV sexual risk behavior over 36 months of follow-up in the world's first HIV vaccine efficacy trial. J Acquir Immune Defic Syndr. 2005; 39:90–101. [PubMed: 15851919]
21. Guest G, Shattuck D, Johnson L, Akumatey B, Clarke EE, Chen PL, MacQueen KM. Changes in sexual risk behavior among participants in a PrEP HIV prevention trial. Sex Transm Dis. 2008; 35:1002–1008. [PubMed: 19051397]
22. Abdool Karim Q, Abdool Karim SS, Frohlich JA, Grobler AC, Baxter C, Mansoor LE, et al. Effectiveness and safety of tenofovir gel, an antiretroviral microbicide, for the prevention of HIV infection in women. Science. 2010; 329:1168–1174. [PubMed: 20643915]
23. Koblin BA, Husnik MJ, Colfax G, Huang Y, Madison M, Mayer K, et al. Risk factors for HIV infection among men who have sex with men. Aids. 2006; 20:731–739. [PubMed: 16514304]
24. Colfax G, Santos GM, Chu P, Vittinghoff E, Pluddemann A, Kumar S, Hart C. Amphetamine-group substances and HIV. Lancet. 376:458–474. [PubMed: 20650520]
25. Buchbinder SP, Vittinghoff E, Heagerty PJ, Celum CL, Seage GR 3rd, Judson FN, et al. Sexual Risk, Nitrite Inhalant Use, and Lack of Circumcision Associated With HIV Seroconversion in Men Who Have Sex With Men in the United States. J Acquir Immune Defic Syndr. 2005; 39:82–89. [PubMed: 15851918]
26. Prejean J, Song R, Hernandez A, Ziebell R, Green T, Walker F, et al. Estimated HIV incidence in the United States, 2006–2009. PLoS One. 6:e17502. [PubMed: 21826193]
27. Golden MR, Dombrowski JC, Kerani RP, Stekler JD. Failure of serosorting to protect African American men who have sex with men from HIV infection. Sex Transm Dis. 39:659–664. [PubMed: 22902660]
28. Millett GA, Flores SA, Peterson JL, Bakeman R. Explaining disparities in HIV infection among black and white men who have sex with men: a meta-analysis of HIV risk behaviors. Aids. 2007; 21:2083–2091. [PubMed: 17885299]
29. Hurt CB, Beagle S, Leone PA, Sugarbaker A, Pike E, Kuruc J, et al. Investigating a sexual network of black men who have sex with men: implications for transmission and prevention of HIV infection in the United States. J Acquir Immune Defic Syndr. 61:515–521. [PubMed: 22972020]
30. Nelson KM, Thiede H, Hawes SE, Golden MR, Hutcheson R, Carey JW, et al. Why the wait? Delayed HIV diagnosis among men who have sex with men. J Urban Health. 87:642–655. [PubMed: 20186493]
31. Prevalence and awareness of HIV infection among men who have sex with men --- 21 cities, United States, 2008. MMWR Morb Mortal Wkly Rep. 59:1201–1207.
32. Vallabhaneni S, Li X, Vittinghoff E, Donnell D, Pilcher CD, Buchbinder SP. Seroadaptive practices: association with HIV acquisition among HIV-negative men who have sex with men. PLoS One. 7:e45718. [PubMed: 23056215]

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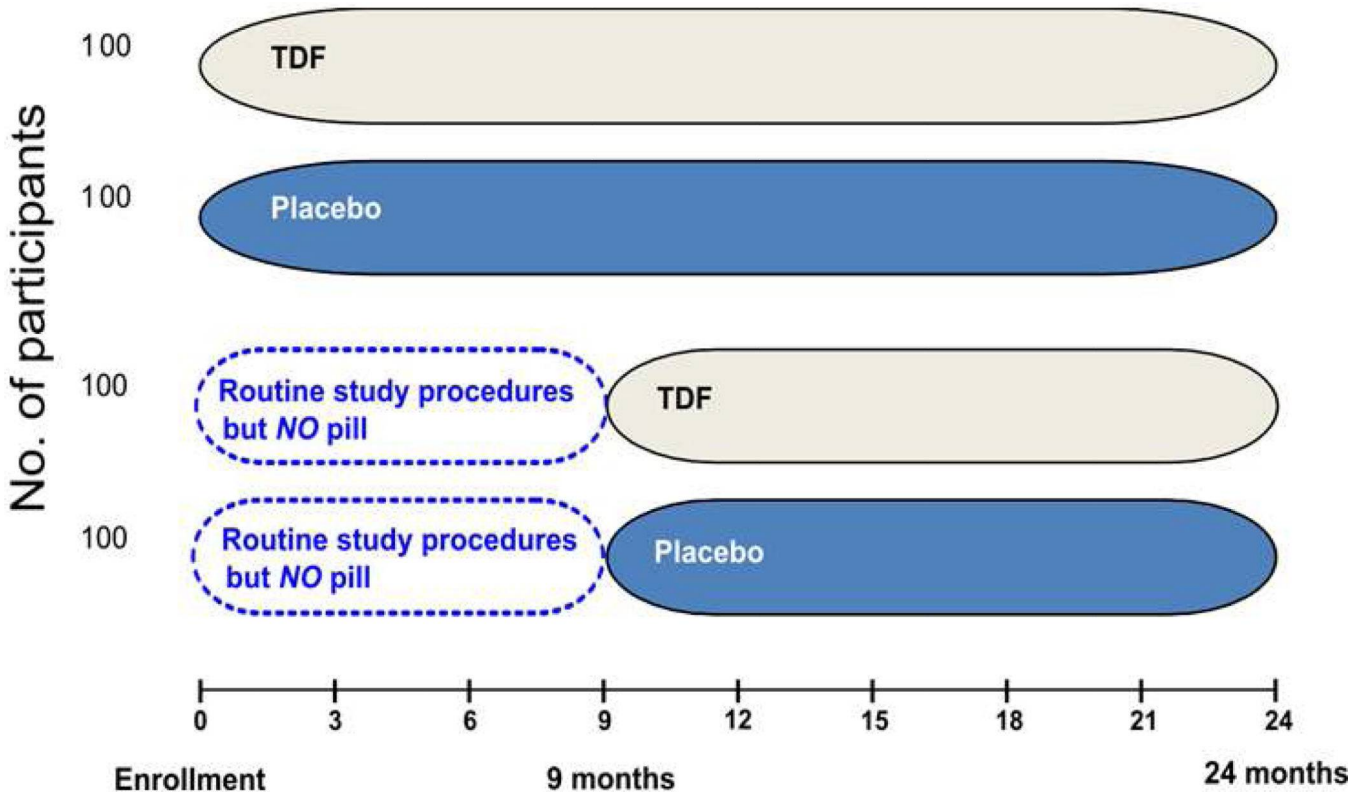


Figure 1. Study design diagram with 4 arms

Participants were randomly assigned to one of four arms. Participants in the 2 immediate arms (TDF vs. placebo) initiated study drug at enrollment; those in the 2 delayed arms (TDF vs. placebo) initiated study drug at the 9 month visit.

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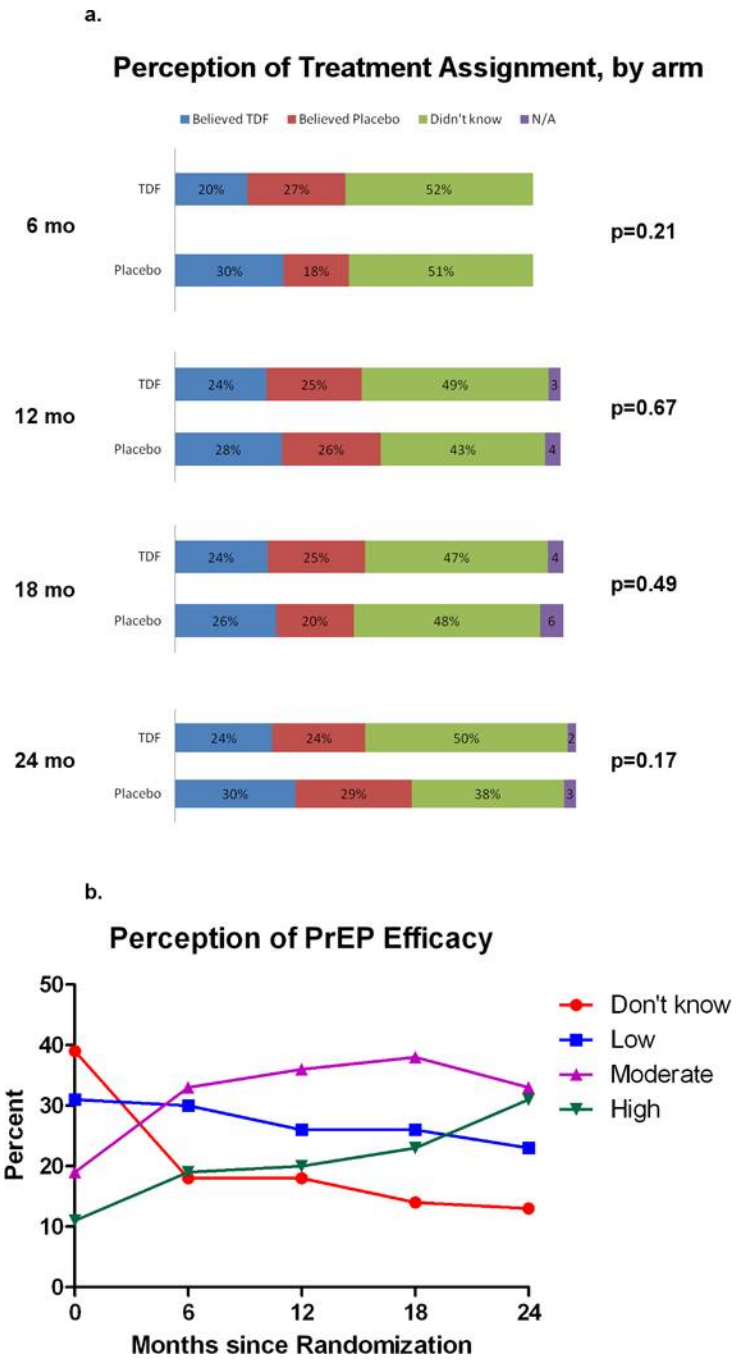


Figure 2. a and 2b. Perception of Treatment Assignment and PrEP efficacy, by treatment arm

Bar graphs in Figure 2a show the proportion of participants who believed they were taking either TDF, placebo, or didn't know, by the participant's actual treatment assignment. At 6 months, only data from the immediate arm are included; other time points include data from both immediate and delayed arms. P value represents Fisher's exact test for differences in perception of treatment assignment by actual treatment arm.

Graph in figure 2b shows the perception of PrEP efficacy by months of follow-up since randomization in the trial.

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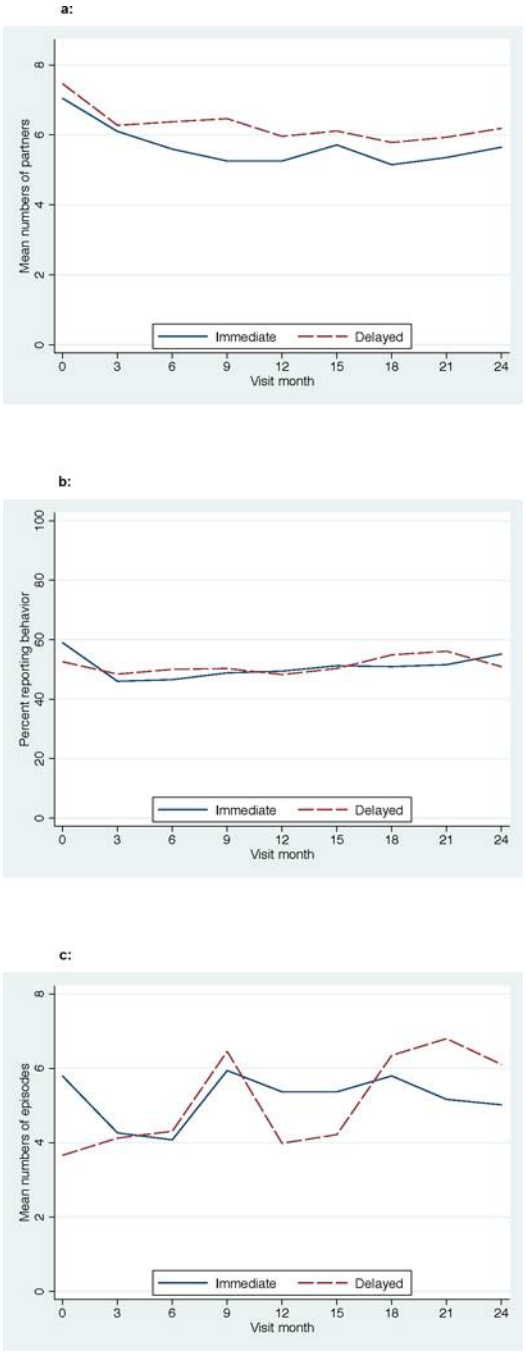


Figure 3. a–c. Mean number of sex partners, proportion reporting UAS, and mean number of UAS episodes, by immediate vs. delayed arms

Figure 3a shows mean number of male sex partners in the past 3 months, by immediate vs. delayed arms. Figure 3b shows proportion of men reporting unprotected anal sex (UAS) in the past 3 months, by immediate vs. delayed arms. Figure 3c shows mean number of UAS episodes in the past 3months, by immediate vs. delayed arms.

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Table 1

Participant Demographics and Risk Characteristics at Baseline (%)

Characteristic	Immediate arm (n=200)	Delayed arm (n=200)	*P*
Age, years (median, range)	38 (18–60)	38.5 (18–59)	0.82
Race n (%)			
White	144 (72)	149 (75)	
African-American	32 (16)	28 (14)	0.63
Asian/Pacific-Islander	9 (5)	5 (3)	
Other	15 (8)	18 (9)	
Hispanic n (%)	20 (10)	16 (8)	0.60
Education n (%)			
Never graduated from high school	5 (3)	4 (2)	
High school graduate or GED	18 (9)	16 (8)	0.94
Some college	65 (33)	69 (35)	
College graduate	112 (56)	111 (56)	
Site n (%)			
San Francisco	100 (50)	100 (50)	1.00
Atlanta	61 (31)	60 (30)	
Boston	39 (20)	40 (20)	
Number of male partners in past 3 months n (%)			
0	4 (2)	6 (3)	
1	28 (14)	25 (13)	0.81
2–5	105 (53)	96 (48)	
6–9	26 (13)	28 (14)	
≥10	37 (19)	44 (22)	
Steady male partner (overall) n (%)	82 (41)	78 (39)	0.68
With an HIV-negative partner	56 (28)	54 (27)	0.82
With an HIV-positive or unknown status partner	26 (13)	24 (12)	0.77
Any unprotected anal sex (overall) n (%)	117 (59)	107 (54)	0.27
With an HIV-negative partner	80 (41)	61 (31)	0.06
With an HIV-positive or unknown status partner	52 (26)	62 (32)	0.27
Any unprotected receptive anal sex (overall) n (%)	67 (34)	58 (29)	0.33
With an HIV-negative partner	50 (25)	36 (18)	0.09
With an HIV-positive or unknown status partner	26 (13)	27 (14)	0.88
Alcohol use* in past 3 months n (%)			
None	33 (17)	30 (15)	0.78
Light	75 (38)	82 (41)	

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Characteristic	Immediate arm (n=200)	Delayed arm (n=200)	*P*
Moderate	83 (42)	82 (41)	
Heavy	9 (5)	6 (3)	
Any non-injection drug use, past 3 months n (%)			
Poppers, amyl nitrate	52 (26)	54 (27)	0.91
Crack/powder cocaine	35 (18)	30 (15)	0.59
Amphetamines	23 (12)	20 (10)	0.75
Sedatives	26 (13)	20 (10)	0.43
Ecstasy	20 (10)	18 (9)	0.74
Use of sexual enhancing drugs, past 3 months n (%)	58 (29)	53 (27)	0.58

*Alcohol use was categorized as none, light (1–2 drinks/occasion on no more than 1–2 days/week, or 3–4 drinks/occasion, no more than once a month), moderate (1–2 drinks/occasion on a daily basis or 3–4 drinks/occasion at least 2–3 times/month), or heavy (5–6 drinks/occasion on a daily basis or 6 or more drinks on any one occasion)

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Table 2

Multivariable models for Total Sex Partners, UAS, and UAS episodes

Characteristic	Total Partners		Any UAS		UAS episodes	
	IRR (95% CI)	P value	OR (95% CI)	P value	IRR (95% CI)	P value
Period (relative to baseline)		**0.02***		**0.003***		0.33*
Months 3–9	**0.85 (0.76–0.95)**	**0.005**	**0.76 (0.60–0.98)**	**0.03**	1.00 (0.70–1.42)	0.98
Months 12–24	**0.82 (0.70–0.97)**	**0.02**	0.95 (0.69–1.30)	0.74	1.17 (0.76–1.81)	0.48
Assigned pills†	0.93 (0.82–1.06)	0.28	0.88 (0.69–1.11)	0.27	0.91 (0.64–1.30)	0.61
Age (per 10 year increase)¥	1.09 (0.96–1.25)	0.20	**0.81 (0.69–0.95)**	**0.01**	0.85 (0.66–1.08)	0.18
Site		0.12*		0.23*		0.08*
Atlanta	(ref)		(ref)		(ref)	
San Francisco	1.24 (0.89–1.74)	0.21	0.96 (0.67–1.39)	0.85	0.95 (0.66–1.38)	0.80
Boston	0.91 (0.67–1.24)	0.55	0.73 (0.50–1.08)	0.12	**0.66 (0.45–0.96)**	**0.03**
Race		0.13*		0.46*		0.15*
White	(ref)		(ref)		(ref)	
African-American	0.80 (0.59–1.08)	0.14	0.72 (0.47–1.11)	0.14	**0.56 (0.34–0.92)**	**0.02**
Asian/Pacific Islander	0.78 (0.38–1.62)	0.51	0.86 (0.41–1.79)	0.69	1.00 (0.50–2.00)	1.00
Other	1.49 (0.96–2.31)	0.07	0.80 (0.45–1.43)	0.46	1.08 (0.59–2.00)	0.80
Ethnicity						
Non-Hispanic	(ref)		(ref)		(ref)	
Hispanic	1.22 (0.80–1.86)	0.36	1.09 (0.67–1.78)	0.74	1.34 (0.79–2.29)	0.28
Education		0.05*		0.91*		0.53*
High school graduate or less	(ref)		(ref)		(ref)	
Some college	0.98 (0.65–1.47)	0.92	0.96 (0.57–1.62)	0.87	0.88 (0.46–1.70)	0.71
College graduate	1.30 (0.89–1.90)	0.18	0.90 (0.53–1.53)	0.71	1.07 (0.57–2.03)	0.83
Drug use (time-dependent)						
Poppers	**1.34 (1.16–1.54)**	**<0.001**	**1.27 (1.04–1.54)**	**0.02**	1.15 (0.88–1.52)	0.31

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Characteristic	Total Partners		Any UAS		UAS episodes	
	IRR (95% CI)	P value	OR (95% CI)	P value	IRR (95% CI)	P value
Amphetamines	1.18 (0.98–1.41)	0.07	**1.75 (1.31–2.35)**	**<0.001**	1.23 (0.90–1.69)	0.19
Sexual-enhancing drugs	**1.32 (1.19–1.48)**	**<0.001**	**1.74 (1.43–2.11)**	**<0.001**	**1.40 (1.14–1.72)**	**0.002**
Perception of treatment assignment						
Placebo	(ref)		(ref)		(ref)	
TDF	0.91 (0.81–1.03)	0.14	0.88 (0.70–1.09)	0.23	**0.77 (0.65–0.91)**	0.002
Perception of PrEP efficacy‡	**1.04 (1.00–1.08)**	**0.04**	0.99 (0.93–1.05)	0.79	1.03 (0.97–1.10)	0.32

UAS=unprotected anal sex; IRR=incident rate ratio (ratio of mean effects); ref=reference group

*Test for overall effects of categorical variables

†Assigned pills variable set to 1 for immediate group starting at month 3 and delayed group starting at month 12

‡Per 1-unit increase in perception of PrEP efficacy coded as a 4-level variable (0 for don't know or N/A, 1=low, 2=moderate, 3=high)

¥Interpreted as the IRR or OR for each 10 year increase in age

ADDRESSING STIGMA

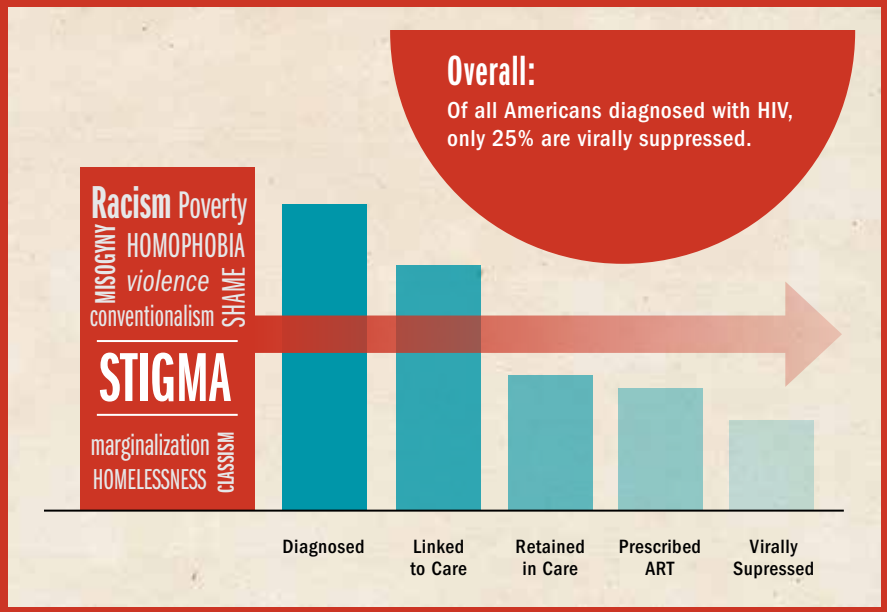
A Blueprint for Improving HIV/STD Prevention and Care Outcomes for Black & Latino Gay Men

NASTAD™
NATIONAL ALLIANCE OF STATE & TERRITORIAL AIDS DIRECTORS

NCSD
National Coalition of STD Directors
Promoting Sexual Health Through STD Prevention



THE BAR BEFORE THE BARS



Stigma and other social determinants influence the HIV care continuum before a diagnosis is even made.

ADDRESSING STIGMA

BACKGROUND

Stigma and epidemics of sexually transmitted diseases (STDs), notably HIV, have long been intertwined in the United States and countries around the globe. Stigma refers to the social devaluation of people who are different, whether due to conditions that do not affect the majority of a population (e.g., homosexuality, HIV/AIDS, mental illness), or more ordinary conditions that affect many or all in a population (e.g., demographic features tied to age, race/ethnicity, gender). Stigma, in its varying forms, serves to fuel the propagation of STDs, notably within marginalized and stigmatized communities.

> "Disentangling stigma from HIV risk, infection, and treatment is one of the greatest public health challenges of the 21st century.[2,16]"

Governments and non-government entities[2] have called for interventions to reduce stigma and its impacts on risk for HIV/STDs and uptake of prevention and treatment for HIV. In the summer of 2010, the White House released the National HIV/AIDS Strategy (NHAS). In response to the NHAS, the U.S. Centers for Disease Control and Prevention (CDC) made significant changes to its plan for providing funding to state and local health departments for HIV programs and services. A key component of this change was a focus on High Impact Prevention (HIP). HIP encourages health departments to implement programs and other scalable interventions that have demonstrated the potential to reduce new HIV infections in the most impacted populations in order to yield a greater impact on the HIV epidemic[6].

The release of the NHAS and changes to the way health departments are funded for HIV prevention represent unique opportunities for public health leaders, HIV/AIDS and sexual health practitioners, and community stakeholders to reassess and evaluate public health efforts to reduce HIV infection. Specifically, efforts to prevent and treat HIV/STDs among Black and Latino gay men and other men who have sex with men (MSM)—populations that are most significantly impacted by HIV/AIDS in the U.S.—must be critically evaluated.

In reflecting on past successes and failures, we must acknowledge that stigma is a central challenge that remains inadequately addressed in attempts to promote sexual health and reduce HIV/STDs among Black and Latino gay men/MSM. The National Alliance of State and Territorial AIDS Directors (NASTAD) and the National Coalition of STD Directors (NCSD) have been engaged in a multi-pronged effort to reduce stigma in public health practice and promote access to HIV and STD prevention and treatment among gay men/MSM. The actions facilitate the implementation of the NHAS and the achievement of the goals of HIP, as well as respond to important gaps in the NHAS and CDC's revised prevention strategy.

The complex role stigma plays in poor sexual health outcomes among gay men/MSM – and the resulting disproportionate rates of HIV and STDs among the population – are largely overlooked in the NHAS. Throughout the NHAS, only stigma surrounding HIV (and not specifically targeting/affecting gay men/MSM) is addressed. Likewise, the prevention programs prioritized in the CDC funding strategy are primarily focused on strategies such as HIV testing and condom distribution, but not necessarily the personal-, community-, and institution-level factors that reduce uptake of these interventions.

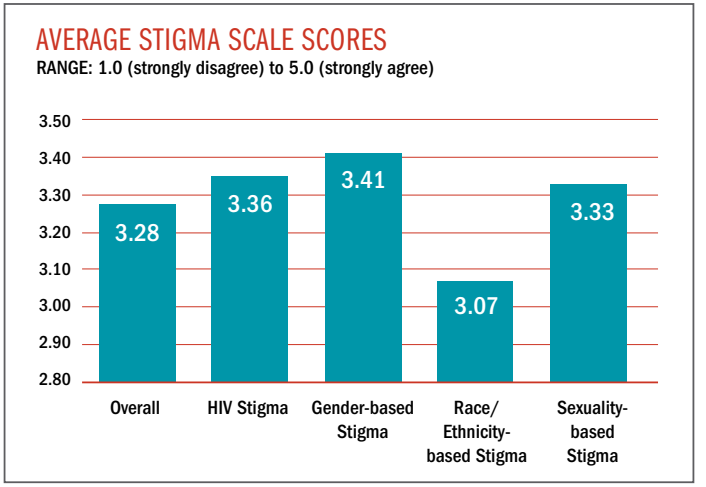


Figure 1. Average scores on stigma scale and sub-scales based on survey conducted by NASTAD and NCSD.

> "Research has shown that in order to effectively respond to the HIV and STD epidemics affecting Black and Latino gay men/MSM, stigma tied to homosexuality, race, and gender nonconformity must be addressed.[11, 15, 18, 33]"

The recent advances made in HIV prevention, including the use of antiretroviral therapies as pre-exposure prophylaxis (PrEP) and treatment as prevention, will fail to put a significant dent in the epidemic affecting Black and Latino gay men/MSM without robust, multi-level interventions to reduce stigma across a variety of domains.

NASTAD and NCSD have partnered to engage in activities aimed at (a) understanding stigma within public health practice, (b) arming health departments and communities with the information and resources they need to effectively combat stigma, and (c) increasing comprehensive access to unfettered HIV and STD prevention and treatment services that respects gay men/MSM from diverse backgrounds.

As a part of these efforts, NASTAD and NCSD have advanced three key activities:

- First, the organizations conducted a stigma survey to explore perceptions of institution-level stigma impacting Black and Latino gay men/MSM.
- Second, two "Optimal Care Checklists" were developed with the goals of (1) providing Black and Latino gay men/MSM with comprehensive sexual health information and (2) educating health care providers on the unique sexual health needs of Black and Latino gay men/MSM.
- Third, a stigma toolkit was developed in an effort to provide tools that health departments and communities across the U.S. can use to engage in stigma reduction efforts and improve health outcomes among Black and Latino gay men/MSM.

THE STIGMA SURVEY

The stigma survey was designed and implemented in an attempt to explore how community- and institution-level stigma within public health practice negatively affect HIV- and STD-related outcomes. The survey,

which was completed by more than 1,300 health department and community-based organization (CBO) staff, health providers, and community members representing 54 different U.S. states and territories, showed high levels of perceived community-level and institutional stigma targeting Black and Latino gay men/MSM (see Figure 1). Higher levels of gender-, HIV-, and sexuality-based stigma were reported compared to levels of race/ethnicity-based stigma. Also, perceptions of institutional stigma varied by geographic region and state, race/ethnicity, gender, sexual orientation, and occupation.

Subsequent analyses showed that state polices related to HIV criminalization, immigration, and LGBT rights were shown to be related to HIV incidence and prevalence, as well as state-level perceptions of community/institutional stigma. Findings showed that states with HIV criminalization policies had higher HIV incidence and prevalence than states without criminalization policies. Also, states with employee non-discrimination policies focused on sexual orientation and/or gender, those with a hate crimes law, and those allowing for same-sex marriage or civil unions showed lower average levels of stigma across several domains. NASTAD and NCSD have been disseminating findings from the stigma survey and using the data to provide technical assistance (TA) to health departments and CBOs.

OPTIMAL CARE CHECKLISTS

Two interrelated factors that help explain HIV and STD disparities affecting Black and Latino gay men/MSM are access to health care and institutionalized stigma in health care settings[20]. The stigma survey showed that Black/African-American and sexual minority participants expressed higher levels of race-, sexual orientation-, gender, and HIV status-based institutionalized stigma compared to White and heterosexual participants, respectively. With the implementation of the Affordable Care Act (ACA), the country has an unprecedented opportunity to ensure that populations that have previously lacked access to routine medical care, such as lower income and minority individuals, receive such care.

In order to capitalize on the opportunity the ACA will provide, we must make efforts to reduce stigma in health care settings and improve Black and Latino gay men's experiences receiving health care.

In response to the need to address stigma within health care settings and empower Black and Latino gay men/MSM with the knowledge they need to have about sexual health, NASTAD and NCSD developed patient and provider "Optimal Care Checklists" (OCCs). The checklists are meant to be guides for Black and Latino gay men/MSM to use when seeking and engaging in health care and for providers who treat Black and Latino gay men/MSM.

The OCCs were developed via a series of activities, including:

- A review of research literature to identify barriers to sexual health care among gay men/MSM.
- One-on-one consultations with providers who treat patients who are Black and Latino and/or gay men/MSM.
- A national Blue Ribbon Panel of clinicians and sexual health experts to discuss best practices and provider needs.

The patient-focused OCC informs Black and Latino gay men/MSM about how to choose a doctor and effectively communicate needs, provides information on sexual health and HIV/STD prevention, symptoms, and treatment, and includes information on hepatitis A and B vaccinations and PrEP. The provider-focused OCC educates health care providers on the role of stigma in contributing to poor health outcomes among gay men/MSM, explains the need for providing patient-centered care, taking a detailed sexual history, and conducting MSM-specific health screenings. Together, the OCCs are resources for patients and providers, and the health departments that support them.

THE STIGMA TOOLKIT

The stigma survey and OCCs represent NASTAD's and NCSD's attempts to describe stigma targeting Black and Latino gay men/MSM as it influences public health practice, and to reduce the impact of stigma on the provision and uptake of clinical care. These activities are only the start of robust and progressive steps that must be taken to reduce stigma and mitigate its effects on HIV and STD vulnerability among Black and Latino gay men/MSM.

Stigma-focused interventions must be implemented by health departments and the communities that they serve in order to improve health outcomes and reduce disparities. This Stigma Toolkit represents a primer that health departments, communities, and advocacy organizations can use to develop and implement novel approaches to addressing stigma and its impacts on prevention efforts targeting Black and Latino gay men/MSM. It is designed to stimulate conversations about approaches to reduce stigma in public health practice. It also describes innovations in community-level, institutional, and structural interventions to reduce stigma. These efforts will enhance opportunities to reduce disparities in HIV and STD diagnoses affecting Black and Latino gay men/MSM, and realize the goals of the NHAS and HIP.

WHY BLACK AND LATINO GAY MEN/MSM?

Black and Latino men's increased vulnerability to HIV is exemplified by national epidemiological data. The CDC indicates that in 2009, men accounted for the majority



(77%) of new HIV diagnoses in the United States. Within this group, Black and Latino men were disproportionately impacted[28]. That same year, HIV incidence among Black and Latino men was six and a half and two and a half times greater, respectively, than it was among White men.

In some U.S. cities, HIV prevalence among men of color rivals prevalence in countries with generalized HIV epidemics[10]. Likewise, Black and Latino men account for a disproportionate number of STD diagnoses in the U.S.[22]. Notably, throughout the last decade there have been outbreaks of syphilis and gonorrhea[7, 29, 31], two STDs that enhance the transmission of HIV and fuel the epidemic.

The continuing HIV crisis among Black and Latino MSM suggests that public health interventions are greatly needed in order to control the epidemic in these groups. However, there are very few HIV prevention interventions tailored to the unique needs of Black and Latino MSM. For example, of the 74 interventions currently included in the CDC's Compendium of Evidence-Based HIV Behavioral Interventions, the primary source of HIV/AIDS interventions used by community-based organizations (CBOs), only one was specifically developed for Black MSM (i.e., Many Men, Many Voices) while two have been adapted for use with Black and/or Latino MSM (i.e., MPowerment, Popular Opinion Leader (POL)).

Though other interventions targeting Black and Latino MSM, such as *dUp!*, *Hermanos de Luna y Sol*, and *SOMOS*, are being disseminated, there are still too few programs that are culturally sensitive to the unique prevention and treatment needs of Black and Latino MSM. Moreover, existing interventions do not focus on the many barriers at the community, institutional, and structural levels that increase risk in this population[9, 33]. This oversight must be addressed in order to reduce disparities[22]. The critical factor that influences and perpetuates barriers at each level is stigma.

DEFINING AND CONCEPTUALIZING STIGMA

Stigma encompasses a wide-ranging and complex assortment of attitudes and behaviors. It refers to personal experiences, interactions and stereotyping experiences among marginalized and non-marginalized groups, and broader social and cultural factors including power relations, community values, and historical practices[31].

There have been several different and useful conceptualizations of stigma put forth over the last several decades. Erving Goffman[13], one of the pioneers of stigma research and theory, noted that:

> "[Stigma is] an attribute that links a person to an undesirable stereotype, leading other people to reduce the bearer from a whole and usual person to a tainted, discounted one."

Thus, stigma is understood as devaluing a person or group of people based on the way society views a particular attribute or characteristic. Individuals who are stigmatized have higher levels of stress due to both the anticipation of negative treatment by non-marginalized/non-stigmatized individuals, and the internalization of stigma. This stress has direct and indirect impacts on the health of stigmatized individuals.
Recently, stigma has been increasingly acknowledged as a critical process for maintaining systems of power and dominant societal norms. As Parker & Aggleton[25] note:

> "Stigma plays a key role in producing and reproducing relations of power and control. It causes some groups to be devalued and others to feel that they are superior in some way. Ultimately, therefore, stigma is linked to the workings of social inequality and to properly understand issues of stigmatization and discrimination, whether in relation to HIV and AIDS or any other issue, requires us to think more broadly about how some individuals and groups come to be socially excluded, and about the forces that create and reinforce social exclusion in different settings."

Previous understandings of stigma were limited to thinking of stigma in terms of individual-level and inter-group processes. The recent shift takes a more systemic approach that incorporates social, economic, political and cultural forces tied to power and privilege. Thus, while our focus on the prejudicial beliefs, stereotypes, and discriminatory actions of individuals and groups is important when examining stigma and its effects on health, we must also describe and intervene upon systems of power and social processes that aim to legitimize and reinforce social hierarchies and inequities. These inequities are a driving factor in explaining HIV and STD disparities affecting Black and Latino gay men/MSM.

Camara Jones[17], a well-known family physician and epidemiologist whose work has aimed to describe the effects of racism on health, has a frequently referred to metaphor that helps to explain the complex process by which stigma becomes institutionalized and a part of dominant social forces. The work, which uses the story of a gardener that finds differential outcomes in flowers planted in two different flower boxes, helps to simplify the explanation of a complex process.

Upon moving into a new house, the gardener finds two flower boxes, one empty and one with existing soil. She adds new soil to the empty flower box, adding seeds for red flowers, her favorite. She uses the existing soil to plants seeds for pink flowers, which she does not like as much. The gardener notices that the red flowers quickly sprout and flourish, while the pink flowers were slow to sprout and did not appear to be strong.

As seasons pass, the flowers in the boxes repeatedly go to seed, dropping their progeny into the soil in which they are planted. Over time, the gardener sees the red flowers thrive while the pink ones struggle; she sees this as an endorsement of her preference for red flowers. The red flowers simply do better than pink ones and thus should be preferred. Others may see the flowers and the differences in how they grow over time and come to the same conclusion.

This story highlights how stigma perpetuates from inequality – in this case, fertile soil for the red flowers and poor soil for the pink flowers. This feature is easy to overlook, particularly as you see the different flowers develop over time. The difference in how well the flowers thrive is mistakenly attributed to innate characteristics of the flowers, instead of the different soils in which they are planted, which do not offer the same opportunities for growth, though they may appear to look the same. In this way, the differential outcomes of the flowers serve to support the gardener's preference for red flowers, just as pervasive stigma related to race, sexual orientation, gender, and HIV status serves to support societal beliefs and practices that keep non-marginalized groups dominant to those who are marginalized.

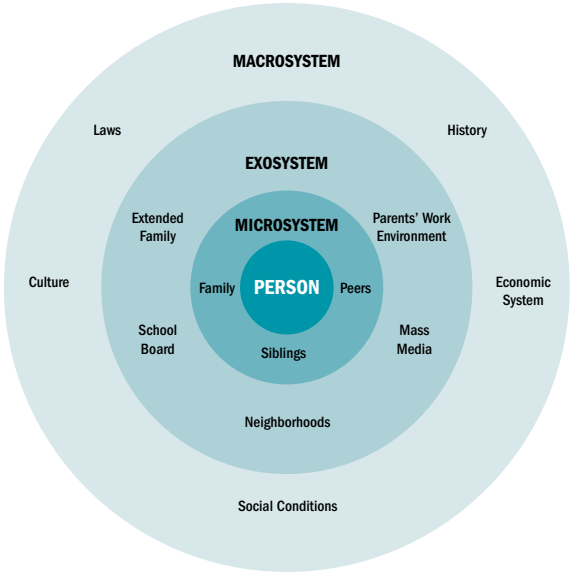


Figure 2. Bronfenbrenner's (1995) Ecological Model

STIGMA AND THE ECOLOGICAL FRAMEWORK

The dominant frameworks used to explore stigma highlight the importance of conceptualizing stigma as a phenomenon that exists and is practiced at multiple levels, including individual, group, and institutional levels. Examining stigma through an ecological framework may facilitate understanding the social forces that perpetuate stigma and targets for intervention.

The ecological model, developed by Uri Bronfenbrenner[3, 4, 5] is a frequently used method to examine the varying degrees of social influence in human development. As Figure 2 shows, human development is influenced by overlapping and concentric social factors at various levels. These levels include parents and peers (i.e., microsystem influences), neighborhoods and mass media (i.e., exosystem influences), and laws, culture and history (i.e., macrosystem influences). At each of these levels, and across time periods, stigma may exist and be enacted in such a way to exacerbate race/ethnicity-, gender-, sexual orientation-, and class-based disparities in HIV and STDs.

The ecological model exemplifies the way that stigma can take many forms and can be understood as layered—or stemming from a multitude of sources and attached to different personal characteristics and/or behaviors—within the lives of gay men/MSM. It is affected by powerful historical, political, and cultural factors in the U.S.

In order to effectively reduce stigma targeted toward Black and Latino gay men/MSM, and improve sexual health outcomes in this population, we must develop interventions and approaches to reduce stigma as it exists within multiple levels of influence.

TYPES OF STIGMA IMPACTING BLACK AND LATINO GAY MEN/MSM

Community- and institutional-level stigma has a profound impact on the health of Black and Latino gay men/MSM. In this toolkit, we focus on four interrelated types of stigma:

1. Stigma related to HIV/AIDS (i.e., community-level and/or institutional attitudes or practices that devalue or discriminate against people living with or affected by HIV)
2. Stigma related to same-sex sexuality/homophobia (i.e., community-level and/or institutional attitudes or practices that devalue or discriminate against people who engage in same-sex sexual behavior)
3. Stigma tied to gender performance/femininity (i.e., community-level and/or institutional attitudes or practices that devalue or discriminate against effeminate men, transgender women, and other gender queer individuals)
4. Race/ethnicity-related stigma/racism (i.e., community-level and/or institutional attitudes or practices that devalue or **oddslot** discriminate against persons from minority racial, ethnic, and immigrant groups).

These types of stigma affect Black and Latino gay men/MSM via multiple spheres, including individual (i.e., through internalization of stigma), group/community (i.e., through experiences of prejudice and discrimination), and institutional (i.e., through exclusionary policies and programs, systematic discrimination, and norms that perpetuate social hierarchies). The impacts of these types of stigma may vary from level to level, and over the life course.

In the stigma toolkit, we aim to provide information and recommendations for health departments and communities that are comprehensive and account for the complexities of stigma in its varied forms. As noted in the introduction, solving the problem of stigma and its effects on HIV and STDs is one of the most difficult challenges of the century. While no one document can solve this problem, we endeavor to use it to facilitate stigma-reduction actions at multiple levels and within various contexts in order to achieve the structural changes necessary to reduce the impact of HIV and STDs on Black and Latino gay men/MSM.



THINGS TO CONSIDER

WHEN IMPLEMENTING THESE RECOMMENDATIONS

CONSIDERATION

Have you engaged both internal and external partners who might assist in implementing these recommendations? If so who?

Has your AIDS/STD Director/supervisor signed off?

IMPLEMENTATION

Do you have a plan for diffusing these recommendations among staff?

Have you considered concrete ways to gauge whether these recommendations are decreasing stigma for your health department?

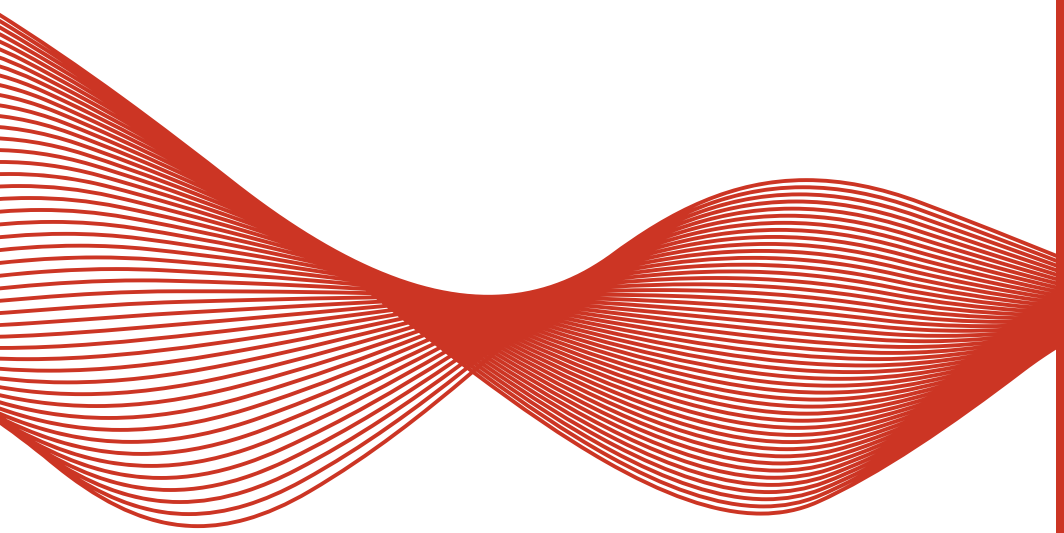
FOLLOW-UP

Do you have a 6-month and annual benchmark to assess effectiveness of the recommendations?

List three possible evaluation benchmarks.

BIBLIOGRAPHY

1. Bartlett, J. A. (2002). Addressing the challenges of adherence. JAIDS Journal of Acquired Immune Deficiency Syndromes, 29, S2-S10.
2. Breyer, C., Sullivan, P. S., Sanchez, J., Dowdy, D., Altman, D., Trapence, G., ... & Mayer, K. H. (2012). A call to action for comprehensive HIV services for men who have sex with men. The Lancet, 380 (9839), 424–438.
3. Bronfenbrenner, U. (1977). Toward an experimental ecology of human development. American psychologist, 32(7), 513-531.
4. Bronfenbrenner, U. (1994). Ecological models of human development. In T. Husen & T. N. Postlethwaite (Eds.), International Encyclopedia of Education, 2nd Ed. (pp. 1643–1647). Oxford, England: Elsevier Science.
5. Bronfenbrenner, U. (1995). Developmental ecology through space and time: A future perspective. In P. Moen, G. H. Elder Jr., & K. Lüscher (Eds.), Examining lives in context: Perspectives on the ecology of human development (pp. 619–648). Washington, DC: American Psychological Association.
6. Centers for Disease Control and Prevention (2012). High-Impact HIV Prevention: CDC's Approach to Reducing HIV Infections in the United States. CDC DHAP: Atlanta: U.S. Department of Health and Human Services.
7. Centers for Disease Control and Prevention (2009). Sexually transmitted disease surveillance 2007 supplement: Gonococcal Isolate Surveillance Project (GISP) Annual Report 2007. Atlanta: U.S. Department of Health and Human Services.
8. Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, Hakim J, Kumwenda J, Grinsztejn B, Pilotto JH, Godbole SV, Mehendale S, Chariyalertsak S, Santos BR, Mayer KH, Hoffman IF, Eshleman SH, Piwowar-Manning E, Wang L, Makhema J, et al. Prevention of HIV-1 infection with early antiretroviral therapy. NEJM. 2011, 365: 493-505.
9. Earnshaw, V. A., Bogart, L. M., Dovidio, J. F., & Williams, D. R. (2013). Stigma and racial/ethnic HIV disparities: Moving toward resilience. American Psychologist, 68(4), 225-236.
10. El-Sadr, W. M., Mayer, K. H., & Hodder, S. L. (2010). AIDS in America—forgotten but not gone. New England Journal of Medicine, 362(11), 967.
11. Fullilove, M. T., & Fullilove, R. E. (1999). Stigma as an obstacle to AIDS action. American Behavioral Scientist, 42(7), 1117-1129.
12. Gardner, E. M., McLees, M. P., Steiner, J. F., del Rio, C., & Burman, W. J. (2011). The spectrum of engagement in HIV care and its relevance to test-and-treat strategies for prevention of HIV infection. Clinical infectious diseases, 52(6), 793-800
13. Goffman E. (1963) Stigma: Notes on the Management of Spoiled Identity. Simon & Schuster Inc.: New York.
14. Hall, H. I., Frazier, E. L., Rhodes, P., Holtgrave, D. R., Furlow-Parmley, C., Tang, T., ... & Skarbinski, J. (2013). Differences in human immunodeficiency virus care and treatment among subpopulations in the United States. JAMA internal medicine, 173(14), 1337-1344.
15. Harawa, N. T., Williams, J. K., Ramamurthi, H. C., & Bingham, T. A. (2006). Perceptions towards condom use, sexual activity, and HIV disclosure among HIV-positive African American men who have sex with men: Implications for heterosexual transmission. Journal of Urban Health, 83(4), 682-694.
16. Joint United Nations Programme on HIV/AIDS (2012). Key Programmes to Reduce Stigma and Discrimination and Increase Access to Justice in National HIV Responses. UNAIDS: Geneva, Switzerland.
17. Jones, C. P. (2000). Levels of racism: a theoretic framework and a gardener's tale. American Journal of Public Health, 90(8), 1212-1215.
18. Kraft, J. M., Beeker, C., Stokes, J. P., & Peterson, J. L. (2000). Finding the "community" in community-level HIV/AIDS interventions: Formative research with young African American men who have sex with men. Health Education & Behavior, 27(4), 430-441.
19. Magnus, M., Jones, K., Phillips, G., Binson, D., Hightow-Weidman, L., Richards-Clarke, C….& Hidalgo, J. (2010). Characteristics associated with retention among African American and Latino adolescent HIV-positive men: results from the outreach, care, and prevention to engage HIV-seropositive young MSM of color special project of national significance initiative. Journal of Acquired Immune Deficiency Syndromes, 53(4), 529-536.
20. Malebranche, D. J., Peterson, J. L., Fullilove, R. E., & Stackhouse, R. W. (2004). Race and sexual identity: Perceptions about medical culture and healthcare among Black men who have sex with men. Journal of the National Medical Association, 96(1), 97-107.
21. Maulsby, C., Millett, G., Lindsey, K., Kelley, R., Johnson, K., Montoya, D., & Holtgrave, D. (2013). HIV Among Black Men Who Have Sex with Men (MSM) in the United States: A Review of the Literature. AIDS and Behavior, 18, 10-25.
22. Millett, G. A., Peterson, J. L., Flores, S. A., Hart, T. A., Jeffries, W. L., Wilson, P. A., ... & Remis, R. S. (2012). Comparisons of disparities and risks of HIV infection in black and other men who have sex with men in Canada, UK, and USA: a meta-analysis. The Lancet, 380 (9839), 341–348.
23. Millett, G. A., Ding, H., Marks, G., Jeffries IV, W. L., Bingham, T., Lauby, J., ... & Stueve, A. (2011). Mistaken assumptions and missed opportunities: correlates of undiagnosed HIV infection among black and Latino men who have sex with men. JAIDS Journal of Acquired Immune Deficiency Syndromes, 58(1), 64-71.
24. Mimiaga, M. J., Reisner, S. L., Bland, S., Skeer, M., Cranston, K., Isenberg, D., ... & Mayer, K. H. (2009). Health system and personal barriers resulting in decreased utilization of HIV and STD testing services among at-risk black men who have sex with men in Massachusetts. AIDS Patient Care and STDs,23(10), 825-835.
25. Parker, R., & Aggleton, P. (2003). HIV and AIDS-related stigma and discrimination: a conceptual framework and implications for action. Social Science & Medicine, 57(1), 13-24.
26. Penniman Dyer, T., Shoptaw, S., Guadamuz, T. E., Plankey, M., Kao, U., Ostrow, D., ... & Stall, R. (2012). Application of syndemic theory to black men who have sex with men in the Multicenter AIDS Cohort Study. Journal of Urban Health, 89(4), 697-708.
27. Singh, N., Berman, S. M., Swindells, S., Justis, J. C., Mohr, J. A., Squier, C., & Wagener, M. M. (1999). Adherence of Human Immunodeficiency Virus—Infected Patients to Antiretroviral Therapy. Clinical Infectious Diseases, 29(4), 824-830.
28. Prejean, J., Song, R., Hernandez, A., Ziebell, R., Green, T., Walker, F., ... & Hall, H. I. (2011). Estimated HIV incidence in the United States, 2006–2009.PloS one, 6(8), e17502.
29. Seña, A. C., Torrone, E. A., Leone, P. A., Foust, E., & Hightow-Weidman, L. (2008). Endemic early syphilis among young newly diagnosed HIV-positive men in a southeastern US state. AIDS Patient Care and STDs, 22(12), 955-963.
30. Spire, B., Duran, S., Souville, M., Leport, C., Raffi, F., & Moatti, J. P. (2002). Adherence to highly active antiretroviral therapies (HAART) in HIV-infected patients: from a predictive to a dynamic approach. Social science & medicine, 54(10), 1481-1496.
31. Stuber, J., Meyer, I., & Link, B. (2008). Stigma, prejudice, discrimination and health. Social Science & Medicine, 67(3), 351-357.
32. Torian, L. V., Makki, H. A., Menzies, I. B., Murrill, C. S., & WEISFUSE, I. B. (2002). HIV infection in men who have sex with men, New York City Department of Health sexually transmitted disease clinics, 1990-1999: a decade of serosurveillance finds that racial disparities and associations between HIV and gonorrhea persist. Sexually Transmitted Diseases, 29(2), 73-78.
33. Wilson, P. A., & Moore, T. E. (2009). Public Health responses to the HIV epidemic among Black men who have sex with men: A qualitative study of health departments and communities in the U.S. American Journal of Public Health, 99(6), 1013-1022
34. Wilson, P. A., Nanin, J., Amesty, S., Wallace, S., Cherenack, E. M., & Fullilove, R. E. (2013). Using syndemic theory to understand vulnerability to HIV infection among Black and Latino men in New York City. Submitted to Journal of Urban Health.



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NASTAD represents the nation's chief state health agency staff who have programmatic responsibility for administering HIV/AIDS and viral hepatitis health care, prevention, education and support service programs funded by state and federal governments. As the only national organization with a constituency that provides frontline STD programs and services, NCSD works toward the development of systemic change and promotion of national awareness in the policies that govern STDs.

Julie M. Scofield,
NASTAD Executive Director

Bill Smith,
NCSD Executive Director

May 2014

BACKGROUND

After more than three decades of the HIV epidemic, there is little evidence that HIV prevention efforts have been effective in decreasing rates of HIV infection among Black and Latino gay men and other men who have sex with men (MSM) in the U.S. Indeed, seroprevalence data show that, since 2006, HIV incidence has increased among Black and Latino gay men/MSM, notably those aged 13 to 24 years[28]. Investments in tools that can be used to prevent HIV transmission and acquisition across populations, such as condom dissemination programs, behavioral interventions, post-exposure prophylaxis (PEP), and pre-exposure prophylaxis (PrEP), have not paid off for Black and Latino gay men/MSM.

The goal of this component is to provide summaries of how stigma impedes the implementation of prevention programs, and, most importantly, offer recommendations and action steps for addressing stigma in HIV prevention programs implemented by health departments and their community partners.

1. BEHAVIORAL INTERVENTIONS

Since the beginning of the HIV epidemic, behavioral interventions have been a critical component of the public health response to reducing HIV incidence and prevalence. Behavioral interventions have targeted a variety of HIV-related health behaviors, including promoting condom use and promoting social norms around safer sex, among others.

Public health practitioners and researchers have noted the dearth of culturally-tailored behavioral interventions for Black and Latino gay men/MSM. For example, a recently conducted review of behavioral interventions for Black MSM identified only eight studies conducted to test the efficacy of interventions for Black MSM21. The limited number of behavioral interventions targeting Black and Latino gay men/MSM has direct implications on the level of exposure these men have to appropriate interventions that can otherwise improve health outcomes.

Institutional and community-level stigma have impeded the development of potentially effective, culturally-tailored HIV testing and prevention interventions for Black and Latino gay men/MSM. Institutional stigma contributes to the lack of practitioners and researchers with the knowledge needed to develop behavioral interventions, and limits public health's focus on the rapid development, testing, and dissemination of behavioral interventions designed for diverse groups of Black and Latino gay men/MSM.

2. PEP & PREP

For years medical personnel and those with accidental exposures to HIV have used post-exposure prophylaxis (PEP) as a resource to prevent HIV infection. With data showing its efficacy in preventing infection after accidental exposure, PEP has been offered to those with non-occupational exposures since just before 2000. It is now available from private providers, emergency rooms, and HIV/sexual health clinics to all who need it. Pre-exposure prophylaxis (PrEP), or use of antiretroviral drugs (currently, Truvada) prior to exposure to HIV in order to prevent infection, came to the forefront as a prevention strategy for gay men after the iPrEX trial demonstrated a 44% reduction in the incidence of HIV among gay men who used PrEP8. Demonstration trials (i.e., HPTN 073, Project PrEPARE) are currently underway to explore the feasibility and acceptability of using PrEP to prevent HIV among HIV-negative Black gay men/MSM.

While feasibility and acceptability data are still pending, insights from community-based organizations and clinics let us know that PEP and PrEP appear to have had limited uptake by Black and Latino gay men/MSM, two at-risk populations that could greatly benefit from it. Just as in the development of behavioral interventions, community-level stigma targeting Black and Latino gay men/MSM impedes the implementation of potentially effective PEP and PrEP programs. Likewise, stigma exacerbates disparities in accessing health care, and, given that PEP and PrEP tend to be administered in health care settings, limits access to these HIV prevention interventions.

3. HOME HIV TESTING

Another important HIV prevention tool that has not been explored for feasibility and acceptability, but is available for use by the public is home HIV testing. In 2012, the Food and Drug Administration (FDA) approved use of an over-the-counter HIV test designed by OraSure. The home HIV test is marketed as a way to reach those who will not get an HIV test, and help to reduce the relatively large number of people in the U.S. who are unaware of their HIV status, potentially due to stigma around HIV testing. Moreover, while many individuals seek treatment once learning of their HIV status, Black and Latino gay men/MSM may avoid or delay treatment due to stigma related to being HIV-positive. Thus, it seems clear that for home HIV testing to be truly effective in preventing new HIV infections, stigma associated with being HIV-positive must be explored and addressed.

RECOMMENDED STEPS
FOR REMOVING *STIGMA* FROM PUBLIC HEALTH PRACTICE

In order to enhance the potential for behavioral interventions, PEP and PrEP, and home HIV testing to successfully address and reduce HIV risk among Black and Latino gay men/MSM, there are several steps that can be taken:

☐ ROUTINIZE HIV AND OTHER STD TESTING (IN PUBLIC AND PRIVATE SETTINGS).

Testing is central to prevention-focused behavioral interventions and is usually a marker to decide whether PEP/PrEP is an option based on an individual circumstance.

- Health departments and providers should increase public education for home testing.
- In conjunction with the National HIV/AIDS Strategy (NHAS) imperative to reduce stigma, stakeholders (e.g., CDC and health departments and communities) should consider the efficacy of approaches and/or messages to remove stigma not just from initial testing events, but from life-long repeat testing.
- The public health community should encourage regular testing for Black and Latino gay men/MSM (every 3-6 months, if necessary), based on risk.

☐ ASSESS CURRENT INDICATORS AND INTEGRATE TESTING.

We should not let imperfect data stop us from determining whether our efforts are impacting progress. In addition, any increase in testing must be accompanied by home-grown community-level stigma reduction efforts that empower Black and Latino gay men/MSM to routinize testing.

Federal agencies, health departments, community based organizations and private physicians should analyze key testing indicators among Black and Latino gay men/MSM. For example, how many new Black and Latino gay men/MSM need to be tested in order to identify new cases that can be linked into care? What are the best ways to integrate HIV/STD testing into non-medical settings? These are just a few of the questions that need to be addressed with regard to accelerating goals of the NHAS.

☐ INCREASE LEARNING AND SKILL-BUILDING OPPORTUNITIES TO ENSURE BLACK AND LATINO GAY MEN/MSM RECEIVE OPTIMAL CARE.

As HIV prevention interventions, including behavior change programs and adherence interventions, become more routinely implemented in medical settings and/or medical care homes, it is important that those working within these settings are well-equipped to deliver HIV prevention services to Black and Latino gay men/MSM.

- Talk to the men that you are serving and ask them what they need and how you can assist them in meeting shared goals.
- Robust, comprehensive sexuality and health curricula need to be integrated into medical student/provider training programs.
- The implementation of these curricula need to be mandated as a part of medical training, and specific attention should be paid to those disproportionately affected by negative sexual health outcomes, namely Black and Latino gay men/MSM.

☐ CREATE AN ENVIRONMENT OF ACCEPTANCE.

Healthcare providers need to obtain continuing education in delivering culturally appropriate interventions and understanding the concept of "cultural humility."

Cultural humility is a concept that builds upon the idea of cultural competency. Cultural humility suggests that, in order to be effective in delivering care, providers need to possess a lifelong commitment to self-evaluation and critique, to redressing the power imbalances in the physician-patient dynamic, and to developing mutually beneficial and non-paternalistic partnerships with communities on behalf of individuals and defined populations. Cultural humility is an important characteristic that all health care providers, health educators and counselors, and patient navigators that work with Black and Latino gay men/MSM should possess.

☐ FOCUS STIGMA-REDUCTION EFFORTS AND BEHAVIORAL INTERVENTIONS TO INTERRUPT HIV/STD ACQUISITION.

Addressing stigma that impedes prevention can have a profound impact on the HIV care continuum, which must be addressed to see reductions in new infections.

As we determine how to allocate resources and the best ways to address the epidemic among Black and Latino gay men/MSM, prevention should be at the forefront of our minds.

BACKGROUND

Screening for HIV and STDs (that can facilitate the transmission of HIV and exacerbate poor health outcomes) is a hallmark of HIV prevention. Without access to testing for the diagnosis of HIV and other STDs, prevention and treatment programs cannot work effectively. Community-level and institutional stigma can keep Black and Latino gay men/MSM from getting tested for HIV, and from asking medical providers about additional tests to diagnose STDs for which they may be at risk (e.g., syphilis, gonorrhea, and HPV/anal cancer).

Placing STD testing and HIV testing into separate silos within the national and local public health systems may enhance stigma that Black and Latino gay men/MSM experience around HIV testing by encouraging them to believe that HIV is different from other STDs, or that other STDs are unimportant (or at least not as important relative to HIV) for their health. Given what we know about the interplay between HIV and STDs in promoting poor HIV-related health outcomes, it is essential to remove these separated screenings from their current siloes and couple them as one combined sexual health promotion intervention.

This component of the blueprint focuses on routine HIV and STD screening in clinic and community settings. Our goal is to provide a summary of the ways stigma impedes the implementation and uptake of HIV and STD screening, and, most importantly, offer recommendations and action steps for addressing stigma in HIV and STD screening activities implemented by health departments and their community partners.

HIV AND STD SCREENING

HIV and STD screening are critical activities in the fight against HIV. While HIV testing and diagnosis aligns squarely with the HIV treatment continuum, the role of screening in the HIV care continuum is less clear (in that it is not explicitly mentioned). For Black and Latino gay men/MSM, STD screening is perhaps just as profound for the continuum as HIV testing. This is because these men are far more likely to have an STD compared to the general population[22]. Since 2002, there have been outbreaks of syphilis and gonorrhea that have been documented among gay men/MSM throughout the country[7, 29, 32]. These two STDs have a particular impact on HIV, as they facilitate both the acquisition of HIV (by those who are HIV-negative), and the transmission of HIV (by those who are HIV-positive) to uninfected others. Moreover, STDs such as syphilis and gonorrhea also increase viral shedding and impede the effectiveness of antiretroviral treatments, making viral suppression – the critical "endpoint" of the treatment continuum – much more difficult.

Syphilis and gonorrhea are only two of several STDs that disproportionately affect Black and Latino gay men/MSM. The CDC recommends that gay men/MSM who are sexually active be tested for the following STDs on an annual basis: HIV (at least annually), syphilis, hepatitis B and C, chlamydia and gonorrhea of the rectum, chlamydia and gonorrhea of the penis (urethra), and gonorrhea of the throat.

Tests for some of these STDs can be invasive (e.g., involving anal or urethra swabs), and require both providers to be comfortable asking and hearing about sensitive sexual health information, and patients to be comfortable requesting STD testing and disclosing behaviors which are often stigmatized (e.g., engaging in receptive oral and/or anal intercourse). Research suggests that neither behavior from providers or Black and Latino gay/MSM patients occurs as regularly as needed.

For example, one study of 197 sexually active Black MSM in Massachusetts found that 33% had not tested for HIV in the last two years, and 60% had not tested for STDs in the same timeframe[24]. Community-level and institutional stigmas are at play in reducing patient-provider discussion surrounding sexual health. Without addressing the underlying issues that keep providers from having frank discussions with their gay/MSM patients and that keep Black and Latino gay men/MSM from accessing health care and disclosing sexual behaviors, improved outcomes as they relate to the treatment continuum will not improve for this population.

> The **CDC recommends** that gay men/MSM who are sexually active be tested for the following STDs on an annual basis:
>
> - HIV (at least annually)
> - syphilis
> - hepatitis B and C
> - chlamydia and gonorrhea of the rectum
> - chlamydia and gonorrhea of the penis (urethra)
> - gonorrhea of the throat

RECOMMENDED STEPS
FOR REMOVING *STIGMA* FROM PUBLIC HEALTH PRACTICE

In order to harness the great potential for HIV and STD screening to reduce HIV incidence among Black and Latino gay men/MSM, there are several steps that can be taken:

☐ IMPLEMENT STRATEGIES TO INTEGRATE HIV TESTING AND STD SCREENING.

When Black and Latino gay men/MSM are offered HIV testing, they should also be offered an STD screen.

Integrating HIV and STD testing will require actions on the parts of state and local health departments, as well as within public and private health clinics and medical practices. While bureaucracies and policies must be considered in this process, coupling HIV and STD testing is critically important in terms of improving outcomes across the HIV treatment continuum, but also for de-stigmatizing and normalizing HIV and STD screening behaviors.

☐ OFFER SEXUAL HEALTH VACCINATIONS FOR BLACK AND LATINO GAY MEN/MSM.

Vaccinations such as HPV and hepatitis A and B need to be targeted as pivotal areas for physicians and health providers, as well as Black and Latino gay/MSM patients, to address.

Health providers and clinicians should offer these potentially life-saving vaccinations to all of their gay/MSM patients. Health department policies and medical provider trainings can facilitate the exchange of information regarding why these vaccinations are critically important for Black and Latino gay men/MSM.

☐ EXAMINE EFFORTS TO BREAKDOWN "HIV TESTING AND STD SCREENING" STIGMA.

State and local health departments must engage in community-level stigma reduction efforts that specifically address Black and Latino gay men/MSM's negative perceptions of HIV and STD screening.

These efforts should focus on reducing the discomfort in having frank discussions about sexuality, behaviors that place one at risk for various STDs, and testing/treatment actions to take if a possible exposure occurs. Testing for HIV and other STDs needs to be considered as "routine" as any test for a chronic disease or condition (such as high blood pressure, diabetes, and cancer).

☐ PHYSICIANS, NURSES AND KEY STAKEHOLDERS WORKING WITH BLACK AND LATINO GAY MEN/MSM, AND BLACK AND LATINO GAY MEN/MSM THEMSELVES, SHOULD SEEK THE KNOWLEDGE AND TOOLS TO EDUCATE THEMSELVES AROUND HIV AND STD PREVENTION.

Stigma around HIV and sexuality serves as a barrier for Black and Latino gay men/MSM to equip themselves with knowledge about STDs and available treatments and feel empowered to have honest and open discussions with their health care providers about their sexual behaviors.

NASTAD and the National Coalition of STD Directors (NSCD) have developed Optimal Care Checklists (OCCs) for patients and providers that can facilitate these actions and reduce the stigma around testing for STDs and protecting one's sexual health. Multi-pronged, iterative approaches, including social marketing campaigns that demystify sexual health and promote "knowing your body" are paramount.

Addressing stigma that hinders routine HIV and STD screening can have a profound impact on the health outcomes of Black and Latino gay men/MSM. Focused, multi-level interventions aimed at reducing stigma around HIV and STD testing, and improving access to and utilization of STD screening (that includes HIV), can potentially improve treatment outcomes at many points across the HIV care continuum.

BACKGROUND

Two recent major advances in HIV research and intervention have highlighted the importance of linkages to and retention in care. First, in 2011, Dr. Edward Gardner and colleagues published work exploring the spectrum of engagement in HIV care in the U.S., ranging from HIV testing and diagnosis, to linkage and engagement in care, receipt of antiretroviral therapy, and, finally, achievement of viral suppression. In this work it was estimated that of all HIV-infected individuals in the U.S., only 19% were virally suppressed (i.e., had an undetectable HIV load)[12]. It should be noted that, because Gardner analyzed the estimated proportion of those virally suppressed out of all HIV infected individuals in the U.S. (including those unaware of their infection/not diagnosed as HIV-positive), his estimate is lower than the CDC's estimate of 25% virally suppressed. The CDC based their estimate off the number of HIV diagnosed individuals in the U.S.

Gardner's model has become the standard in terms of understanding the complexities and various meanings of "engagement in care." It has also highlighted the inadequacies of current approaches to linkages to and retention in care by highlighting the drastic drops in the number of individuals engaged in care.

A second key advance was a six-year, global research trial conducted by the HIV Prevention Trials Network (i.e., HPTN 052) that showed the effectiveness of consistent adherence to antiretroviral treatment (ART) in: (1) improving health outcomes among HIV-positive individuals, and (2) significantly reducing their ability to transmit the virus to uninfected partners[8]. The work highlights the importance of people living with HIV to be actively engaged in care, which is necessary for the continuous receipt of ART and monitoring its effects on viral load and other health outcomes.

This component of the blueprint focuses on linkages to and retention in care among Black and Latino gay men/MSM. The goal is to provide a summary of the ways stigma thwarts efforts to link and retain HIV-positive Black and Latino gay men/MSM, and, most importantly, offer recommendations and action steps for addressing stigma in linkage and retention activities implemented by health departments and their community partners.

LINKAGE TO AND RETENTION IN CARE

It is essential to improve linkages to and retention in care among HIV-positive Black and Latino gay men/MSM. In 2013, Dr. H. Irene Hall and colleagues published results from a comprehensive analysis looking at the HIV care continuum within specific demographic groups[14]. The analysis demonstrated that Blacks and Latinos are markedly less likely to be engaged in care across the spectrum. Racial and ethnic minorities who are HIV-positive are less likely to have ongoing care and be virally suppressed. Moreover, there have been several studies documenting HIV-positive Black and Latino gay men's reduced engagement in care compared to HIV-positive White gay men/MSM.

When comparing HIV-positive Black and Latino MSM to other HIV-positive MSM, it is clear that there are glaring differences in HIV care access. Black and Latino MSM are less likely to have access to health insurance, attend clinical visits to receive treatment, and have access to ART[19, 22]. Other work has shown similar disparities affecting HIV-positive Latino MSM, notably those who are under the age of 24.

Both institutional and community-level stigma strongly influence the existence and persistence of these disparities in linkage to and retention in care. Stigma related to HIV prevents Black and Latino gay men/MSM who are HIV-positive from disclosing their status to providers and accessing treatment facilities and resources that may be available to them. Fear of being seen at an HIV treatment/sexual health clinic prevents these men from setting up and consistently attending medical appointments to receive treatment. Many treatment facilities, including those catering to lower-income and racial/ethnic minority HIV-positive individuals, have ostracized Black and Latino gay men/MSM due in large part to institutional stigma and structural homophobia. These treatment facilities are often perceived to be unwelcoming toward racial/ethnic minority patients.

Similarly, HIV care providers are often unaware of the unique health and treatment needs of HIV-positive Black and Latino gay men/MSM, and are perceived as uncaring and not focused on treating the whole person. The lack of culturally appropriate care provided at health clinics and from providers exacerbates disparities in linkages to and retention in care. Thus, it is clear that in order to redress these disparities, structural and community-level interventions are needed to reduce stigma in public health practice.

> "Black and Latino MSM are less likely to have access to health insurance, attend clinical visits to receive treatment, and have access to ART.

RECOMMENDED STEPS
FOR REMOVING *STIGMA* FROM PUBLIC HEALTH PRACTICE

In order to improve engagement in care among Black and Latino gay men/MSM and improve linkage to care and retention in care, there are several steps that can be taken:

☐ **EXPAND ACCREDITED, CONTINUING EDUCATION OPPORTUNITIES FOR MEDICAL PROVIDERS SERVING BLACK AND LATINO GAY MEN/MSM.**

A critical action step is improving provider education and competence in providing culturally appropriate and holistic HIV care to Black and Latino gay men/MSM.

Currently, most medical providers do not receive consistent, continuing education training on the unique health concerns and issues affecting racial/ethnic minorities and lesbian, gay, bisexual and transgender (LGBT) persons. Medical schools and continuing education programs rarely include courses on LGBT and minority health. This oversight has meant that providers working with patients who are Black and Latino gay men have to learn about these populations on the job, if they learn about them at all. Greater efforts must be made to change the way healthcare providers are educated and to make training on racial/ethnic minority and LGBT health a mandatory component of medical education.

☐ **IMPROVE ACCESS TO MENTAL HEALTH SERVICES FOR BLACK AND LATINO GAY MEN/MSM TO INCREASE THEIR ABILITY TO STAY ENGAGED IN CARE OVER TIME.**

HIV testing and treatment clinics should integrate mental health counseling both at the time of diagnosis and in the months following, as newly diagnosed Black and Latino gay men/MSM are linked to care and begin to make decisions with their health providers about their course of treatment.

Similarly, mental health treatment should be accessible to HIV-positive Black and Latino gay men/MSM who are actively engaged in care and may need resources to stay engaged, especially as they are likely to experience high levels of stigma within their communities and have personal difficulties maintaining their treatment regimens.

☐ **INCREASE ACCESS TO SUBSTANCE USE TREATMENT FOR BLACK AND LATINO GAY MEN/MSM TO FACILITATE LINKAGES AND RETENTION IN CARE.**

Clinics that work with HIV-positive Black and Latino gay men/MSM must integrate substance use treatment services (along with mental health counseling, as previously noted) into HIV care.

☐ **CONSIDER WAYS TO IMPROVE THE EXPERIENCES THAT BLACK AND LATINO GAY MEN/MSM HAVE WHEN RECEIVING HIV TREATMENT.**

Healthcare providers should go beyond provider training to focusing on institutional settings.

From the clinic receptionist to the medical director, all staff at HIV and sexual health clinics must be mindful of the needs of Black and Latino gay men/MSM and respectful of these men's experiences and cultures. Including health care materials that feature gay men of color, hiring staff who are Black and Latino, and creating comfortable spaces in which men can speak with their providers are all strategies that can improve the healthcare experiences of HIV-positive Black and Latino gay men/MSM.

Addressing institutional and community-level stigma that intensifies the persistence of racial/ethnic group disparities in linkages to and retention in care is critical in order to see reductions in new HIV infections among Black and Latino gay men/MSM in the U.S. Structural interventions that seek to improve access to and utilization of culturally-appropriate HIV treatment services, enhance medical provider education and motivate Black and Latino gay men/MSM to stay engaged in HIV care can potentially increase treatment outcomes across the treatment cascade and reduce HIV incidence and AIDS mortality in this population.

BACKGROUND

Treatment adherence has become one of the most important topics in HIV prevention and treatment programming, clinical practice, and research. This is due to a landmark six-year, global research trial conducted by the HIV Prevention Trials Network. The trial, called HPTN 052, showed that early treatment and consistent adherence to antiretroviral treatment (ART) among HIV-positive individuals reduced transmission of HIV to uninfected sex partners by 96%[8]. This work, which the journal *Science* named its 2011 Breakthrough of the Year, gave rise to the current "Treatment as Prevention" era. HPTN 052 demonstrated the critical importance of treatment adherence in managing our current epidemic in the U.S. and promoting reduction in future incidence.

This final component focuses on treatment adherence among Black and Latino gay men/MSM. This part of the blueprint provides a summary of the ways stigma impedes treatment adherence among HIV-positive Black and Latino gay men/MSM, and, most importantly, offers recommendations and action steps that can be implemented by health departments and their community partners.

TREATMENT ADHERENCE

Treatment adherence—which involves consistent, as-scheduled, daily use of ART—is critically important to improving health outcomes and reducing new infections among Black and Latino gay men/MSM.

Adherence to ART leads to viral suppression and decreased morbidity and mortality in people living with HIV. However, research has shown that adherence is a challenge for most HIV-positive individuals, as ART medications need to be taken consistently and correctly (90-95% of prescribed doses) for adequate viral suppression to occur. Maintaining 95% adherence to prescribed doses equates to missing no more than three doses of a twice-daily HIV medication over the course of a 30-day period.

In one study, between 57% and 77% of HIV-positive individuals failed to meet the high standard of ART adherence[27, 30]. For HIV-positive Black and Latino gay men/MSM, rates of treatment adherence are much lower than they are for other groups. Of note, research suggests that HIV-positive Black MSM are half as likely to be adherent to ART than White MSM.

Reasons for non-adherence include:

- Forgetting to take the medication.
- Changes in a daily routine.
- Feeling depressed or overwhelmed.
- Dealing with side effects[1].

Key barriers to treatment adherence among HIV-positive Black and Latino gay men/MSM include institutional and community-level stigma. Stigma that men experience within their families and social networks, neighborhoods, jobs, health care institutions, and other institutional settings (e.g., churches, prisons and detention facilities, etc.) could strongly influence treatment adherence disparities affecting Black and Latino gay men/MSM. Stigma around HIV and homosexuality creates contexts in which these men feel that they have to hide their medication and their use of it. This means they may have fewer, less reliably occurring, and consistent daily occasions to take medications, compared to other populations.

Unstable living situations, joblessness, incarceration experiences and other traumatic life experiences—each of which Black and Latino gay men/MSM experience at greater rates than other MSM—exacerbates struggles with daily adherence. Both community-level and institutional stigma are internalized among many Black and Latino gay men/MSM, and through direct and indirect ways influence men's desires to take ART and their abilities to consistently adhere to treatment. The stigma that Black and Latino gay men/MSM experience must be addressed in order to improve health outcomes.



In one study, between **57% & 77%** of HIV-positive individuals failed to meet the high standard of ART adherence.

RECOMMENDED STEPS
FOR REMOVING *STIGMA* FROM PUBLIC HEALTH PRACTICE

In order to improve treatment adherence among Black and Latino gay men/MSM there are several steps that can be taken by health departments and the communities they serve:

☐ DEVELOP EFFORTS TO REDUCE STIGMA AROUND HIV AND HOMOPHOBIA, IN BLACK AND LATINO COMMUNITIES ACROSS THE U.S.

Anti-stigma campaigns need to be developed, and those in existence need to be evaluated, and, if shown effective, taken to scale.

Additionally, greater alliances among public health departments, community-based organizations, and private sector companies need to be developed. These alliances can help to create norm changes within and across community and institutional settings. The CDC's Act Against AIDS Leadership Initiative, a partnership between CDC and leading national organizations representing the populations hardest hit by HIV, including Blacks, Latinos, and gay men/MSM, needs to be replicated on the state and local levels.

Similarly, efforts such as Kaiser Family Foundation's Speak Out initiative, which involves young gay men telling their own stories and experiences about HIV/AIDS, need to be leveraged. These alliances should make their missions, at least in part, to reduce stigma around HIV and homosexuality. Lastly, greater numbers of HIV-positive Black and Latino gay men/MSM need to be empowered to publicly disclose their HIV status. Attempts to normalize HIV, promote community perceptions of HIV as a manageable disease, and highlight the presence of HIV-positive Black and Latino gay men/MSM in all parts of the community, from churches to corporate offices, will aid in reducing stigma and negative perceptions around HIV.

☐ DEVELOP TREATMENT REGIMENS THAT DO NOT REQUIRE DAILY USE AND/OR HAVE TREATMENTS THAT CAN BE DELIVERED LESS FREQUENTLY.

Because many Black and Latino gay men/MSM must conceal their HIV status and use of ART, and due to the lack of private spaces these men have to take ART, treatments that do not require frequent use may greatly enhance treatment adherence in this population.

Efforts to develop such regimens are currently underway. When the opportunity presents itself, health departments, researchers, and pharmaceutical companies should work together to promote the dissemination of these treatment regimens, and ensure uptake by patients. These regimens will provide greater options to HIV-positive Black and Latino gay men/MSM and, when implemented with robust efforts to improve access to care, will allow many of these men to experience greater levels of adherence.

☐ PROMOTE KNOWLEDGE OF TREATMENT ADVANCES AND EMPOWER HIV-POSITIVE BLACK AND LATINO GAY MEN/MSM TO BE EDUCATED CONSUMERS OF HIV CARE.

Men need to be made aware of the different treatments available to them, their efficacy, toxicity level, and side effects, and the frequency with which they need to be used in order to be effective.

Tools such as pill boxes, cell phone reminders, and text messaging tools need to be provided in HIV treatment and sexual health clinics, as well as in primary care settings and emergency rooms in which Black and Latino gay men/MSM may access health care. Promoting greater access to these tools will allow men to have more resources that can increase the likelihood of them getting to the 90-95% adherence level that is necessary for most ART in order for viral suppression to occur.

☐ PROMOTE MESSAGES ON THE AVAILABILITY OF PREP FOR HIV-NEGATIVE BLACK AND LATINO GAY MEN/MSM BUT ALSO THE NEED TO BE ADHERENT AMONG THOSE WHO USE IT AS AN HIV PREVENTION STRATEGY.

While our focus on treatment adherence has been targeted to HIV-positive Black and Latino gay men/MSM, it should be noted that adherence is important for at-risk HIV-negative men who may use Pre-Exposure Prophylaxis (PrEP).

While PrEP has shown promise as an HIV prevention tool, like ART, its efficacy is dependent on consistent use as prescribed.

From a Family Planning client's perspective…

My partner is HIV positive and I am HIV negative. Is PrEP right for me?

PrEP may be one HIV prevention strategy for you to consider to reduce your HIV risk, and can be used with other HIV prevention methods. We're all about being proactive about your sexual health choices.
For example, if your HIV-positive partner is already taking HIV medications to treat his/her HIV and reduce viral load to undetectable levels, it reduces his/her chance of transmitting the virus to you. If you add PrEP to the equation, then you would add another layer of protection to reduce your HIV risk. As a disclaimer, remember that PrEP does not protect you against other STIs, like gonorrhea or syphilis, or prevent pregnancy.
It's important for you to have open communication with your partner and your doctor about whether PrEP may be a good option for you to consider.

I'm the HIV negative partner in a heterosexual relationship, serodiscordant relationship and we're trying to get pregnant and start a family. Can PrEP help us do this safely?

Yes, PrEP is one of many options available to you as you make decisions about how to safely conceive and have a family. While there is research showing that PrEP works for HIV prevention for adult heterosexual women and men, more research needs to be done on women using PrEP *during* pregnancy.
As the hopeful soon-to-be dad or soon-to-be mom, there are many things to consider that you should discuss with your partner and doctor— general health, fertility, STIs, HIV viral load of the HIV-positive partner, and risk of HIV transmission—before trying to get pregnant. For example, research shows if your partner has an undetectable viral load with effective HIV treatment and you limit sex without a condom to the woman's most fertile days, then PrEP may not have additional protective benefits. It is essential to discuss with your partner and doctor what HIV prevention strategy works best for you to ensure a healthy pregnancy and minimize your risk of acquiring HIV.
When considering PrEP, it is important to remember that medications used for HIV treatment and prevention are different, so it is not as simple as sharing medications between partners. Do not try this on your own; sharing medications with each other is a big no-no. While using PrEP, the HIV-negative partner will need to work closely with a doctor for monitoring.

I'm using hormone based birth control. Does it interact with PrEP?

To date, research shows that hormone-based birth control drugs do NOT interact with PrEP. As advocated by the U.S. Women and PrEP Working Group, a coalition of more than 50 women from leading HIV and women's health organizations, more research needs to be done studying women and their prevention choices to avoid both HIV infection and pregnancy.

Can I still take PrEP if I have my period?

From what we know so far, being on your period should not impact the effectiveness of PrEP.

If I take PrEP while pregnant or breastfeeding, how will it affect the baby?

While PrEP reduces the HIV risk of the HIV-negative mother and baby, more research is needed to figure out the long-term health effects for children whose mothers use PrEP during pregnancy and/or breastfeeding.

Preconception Counseling and Care for Women of Childbearing Age Living with HIV

Reproductive Options for Couples with the Same or Differing HIV Status

Last Updated: November 14, 2017; Last Reviewed: November 14, 2017

Panel's Recommendations Regarding Reproductive Options for Couples with the Same or Differing HIV Status

Panel's Recommendations

For Couples Who Want to Conceive When One or Both Partners are Living with HIV:

- Expert consultation is recommended so that approaches can be tailored to couples' specific needs **(AIII)**.
- Partners should be screened and treated for genital tract infections before attempting to conceive **(AII)**.
- Partners living with HIV infection should attain maximum viral suppression before attempting conception to prevent HIV sexual transmission **(AI)** and, for women living with HIV, to minimize the risk of HIV transmission to the infant **(AII)**.
- For couples with differing HIV status, when the woman is living with HIV, assisted insemination at home or in a provider's office with a partner's semen during the peri-ovulatory period is recommended as a conception strategy that eliminates the risk of HIV transmission to the partner without HIV **(AIII)**.
- For couples with differing HIV status, when the man is living with HIV, the use of donor sperm from a man who is HIV-uninfected can be used as a conception strategy that eliminates the risk of HIV transmission to the partner without HIV **(BIII)**.
- For couples with differing HIV status, when the partner living with HIV is on ART and has achieved sustained viral suppression, sexual intercourse without a condom limited to the 2 to 3 days before and the day of ovulation (peak fertility) is an approach to conception with very low risk of sexual HIV transmission to the partner without HIV **(BII)**.
- For couples with differing HIV status who attempt conception via sexual intercourse without a condom (despite counseling) when the partner living with HIV has not been able to achieve viral suppression or when the viral suppression status is not known, administration of antiretroviral pre-exposure prophylaxis (PrEP) to the partner without HIV is recommended to reduce the risk of sexual transmission of HIV **(AI)**. Couples should still be counseled to limit sex (without condoms) to the period of peak fertility **(AIII)**.
- For couples with differing HIV status who attempt conception (sexual intercourse without a condom limited to peak fertility) when the partner living with HIV has achieved viral suppression, it is unclear whether administering PrEP to the partner without HIV further

Panel's Recommendations Regarding Reproductive Options for Couples with the Same or Differing HIV Status

Panel's Recommendations

reduces the risk of sexual transmission **(CIII)**.

Rating of Recommendations: *A = Strong; B = Moderate; C = Optional*
Rating of Evidence: *I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

The objective of this section is to provide guidance for safe conception and pregnancy while maximizing efforts to prevent HIV transmission to partners and infants.

For couples in which one or both partners are living with HIV, optimal health should be attained before attempting conception; couples should be counseled to only attempt conception after the partners living with HIV have initiated antiretroviral therapy (ART) and have achieved sustained suppression of plasma viral load below the limits of detection. For couples with the same or differing HIV status who want to conceive, expert consultation is recommended so that approaches can be tailored to their specific needs.

Before attempting to conceive, both partners should be screened for genital tract infections. Treatment of such infections is important because genital tract inflammation is associated with genital tract shedding of HIV.[1-5]

Couples with Differing HIV Status

Before conception is attempted, the partner living with HIV should be receiving ART and have achieved sustained suppression of plasma viral load below the limits of detection. HPTN 052 was a randomized clinical trial designed to evaluate whether immediate versus delayed initiation of ART by persons living with HIV with CD4 T lymphocyte (CD4) cell counts of 350 to 550 cells/mm^3 could prevent sexual transmission of HIV among couples with differing HIV status. Most of the participants were from Africa (54%), with 30% from Asia and 16% from North and South America. This study showed that earlier initiation of ART led to a 93% reduction in sexual transmission of HIV to the partner. Of 46 cases of HIV infection documented to be genetically linked to the partner living with HIV, 43 occurred in the 877 couples in which the partner living with HIV delayed initiation of ART until the CD4 cell count fell below 250 cells/mm^3, whereas 3 cases of HIV infection occurred in the 886 couples with a partner living with HIV who began immediate ART. The majority of transmissions (82%) were observed in participants from Africa. Thus, this randomized

trial clearly demonstrated that provision of treatment to persons living with HIV can reduce the risk of transmission of HIV to their sexual partners.[6] In addition, the PARTNERS trial—which studied 1,166 serodiscordant couples (both heterosexual and men who have sex with men) where the partner with HIV was on suppressive ART and had sex without using a condom—had no cases of transmission after 1.3 years.[7]

In 161 serodiscordant couples (133 with a male partner living with HIV) where the partner living with HIV received suppressive ART, and the couple opted for natural conception, a total of 144 natural pregnancies occurred and 107 babies were born. No case of sexual (to partner) or vertical (to infant) transmission occurred.[8]

It is important to recognize that no single method (including treatment of the partner living with HIV) is fully protective against transmission of HIV, though the risk appears to approach zero when the partner living with HIV maintains consistently undetectable plasma viral load on ART.[9] Effective ART that decreases plasma viral load to undetectable levels is also associated with decreased concentration of virus in genital secretions. However, discordance between plasma and genital viral loads has been reported, and individuals with an undetectable plasma viral load may have detectable genital tract virus.[10-12] In addition, antiretroviral (ARV) drugs vary in their ability to penetrate the genital tract.[13] In a prospective study of 2,521 African couples with differing HIV status, higher genital HIV RNA concentrations were associated with greater risk of heterosexual HIV-1 transmission and this effect was independent of plasma HIV concentrations.[14] Each $\log_{10}$ increase in genital HIV-1 RNA levels increased the risk of female-to-male or male-to-female HIV transmission by 1.7-fold.[14] However, there was no case of transmission in the context of undetectable plasma viral load but detectable genital tract HIV.

In addition to reducing the risk of HIV transmission between partners, starting ART before conception in women living with HIV may also further reduce the risk of perinatal transmission.[15] Early and sustained control of HIV viral replication may be associated with decreasing residual risk of perinatal transmission,[16,17] but did not completely eliminate the risk of perinatal transmission.[17] In addition, reports are mixed on the possible effects of ART on prematurity and low birthweight, with some but not all data suggesting that such outcomes may be more frequent in women on ARV drugs at conception.[18-20]

The implications of initiating therapy before conception and the need for strict adherence to achieve plasma viral load below the limits of detection should be discussed with the couple. Consultation with an expert in HIV care is strongly recommended.

Strategies for Safer Conception

For serodiscordant couples where the woman is living with HIV, assisted insemination at home or in a provider's office with a partner's semen during the periovulatory period is recommended as a conception strategy that eliminates the risk of HIV transmission to the partner without HIV. For serodiscordant couples where the man is living with HIV, the use of donor sperm from a man who is HIV-uninfected can be used as a conception strategy that eliminates the risk of HIV transmission to the partner without HIV.

However, as described above, studies have shown that the risk of HIV infection to the partner without HIV is very low when the partner living with HIV is on ART and has demonstrated sustained plasma viral load below the limits of detection. For serodiscordant couples where the partner living with HIV is on ART and has achieved sustained viral suppression, sexual intercourse without a condom limited to the 2 to 3 days before and the day of ovulation (peak fertility) is an approach to conception with low risk of sexual HIV transmission to the partner without HIV. The use of an ovulation kit would be optimal to identify the most fertile time of the cycle.

The use of sperm preparation techniques coupled with either intrauterine insemination or *in vitro* fertilization with intracytoplasmic sperm injection has been reported. However, the appropriate role of semen preparation techniques in the current context is unclear, particularly given their expense and technical requirements. These sperm preparation techniques were largely developed prior to the studies demonstrating the efficacy of PrEP and ART in decreasing transmission to sexual partners without HIV. Sperm preparation techniques may be useful in cases of male infertility.

Semen analysis is recommended for men living with HIV before conception is attempted because HIV, and possibly ART, may be associated with a higher prevalence of sperm abnormalities such as low sperm count, low motility, higher rate of abnormal forms, and low semen volume. If such abnormalities are present, the female partner without HIV may be exposed unnecessarily and for prolonged periods to her partner's infectious genital fluids when the likelihood of conceiving naturally is low or nonexistent.[21-24]

For serodiscordant couples who attempt conception via sexual intercourse without a condom (despite counseling), when the partner living with HIV has not been able to achieve viral suppression or when viral suppression status is not known, administration of antiretroviral PrEP to the partner without HIV is recommended to reduce the risk of sexual transmission of HIV. PrEP is the use of ARV medications by an individual who is HIV negative to maintain blood and genital drug levels sufficient to prevent acquisition of HIV. Only daily dosing of combination tenofovir disoproxil fumarate (TDF) and emtricitabine is currently Food and Drug Administration-approved for use as PrEP. Adherence is critical. Couples should still be counseled to limit sex without a condom to the period of peak fertility.

One study evaluated timed intercourse with PrEP in 46 heterosexual couples of differing HIV status where the female partner was HIV negative. The male partners living with HIV were receiving ART and had undetectable plasma HIV RNA levels. One dose of oral TDF was taken by the women at luteinizing hormone peak and a second oral dose was taken 24 hours later. None of the women contracted HIV and pregnancy rates were high, reaching a plateau of 75% after 12 attempts.[25] Another study from England reported the use of TDF with or without emtricitabine for PrEP by the female partner who was HIV negative with timed intercourse in 13 couples of differing HIV status; PrEP was well tolerated and no HIV transmissions occurred.[26]

Sun et al. reported on 91 serodiscordant couples (43 with men living with HIV and 48 with women living with HIV) with effective ART being used in the partner with HIV, with PrEP (or post-exposure prophylaxis) administered to the partner without HIV, and with intercourse timed to maximally reduce the risk of HIV transmission. There were 196 acts of intercourse with a condom, 100 natural conceptions, and 97 live births. There were no cases of HIV seroconversion in the sexual partner without HIV.[27]

Among 1,013 Kenyan and Ugandan, high-risk HIV serodiscordant couples (67% of couples where the woman was living with HIV), where an integrated ART and PrEP strategy for HIV prevention was implemented, there were no HIV tranmissions to male partners. Only 2 incident infections were observed in the women (HIV incidence of 0.2 per 100 person years). These 2 infections occurred in the absence of use of ART or PrEP.[28]

Many studies have demonstrated that PrEP reduces the risk of HIV acquisition in both men and women, with minimal risk of incident ARV resistance. Other trials failed to demonstrate PrEP efficacy, likely related to suboptimal levels of adherence[6,29-34] Table 4 summarizes clinical trials of PrEP.[35]

Table 4. Clinical Trials of Pre-Exposure Prophylaxis

Trial	Study Population	Location	Intervention	Outcome	Comments
TDF2	1,219 sexually active adults; 55% male, 45% female; 94 % unmarried; approximately	Botswana	Daily oral TDF/FTC	63% protection	>30% did not complete study; cannot draw definitive conclusions for women and men separately.

Table 4. Clinical Trials of Pre-Exposure Prophylaxis

Trial	Study Population	Location	Intervention	Outcome	Comments
	90% aged 21–29				
PIP	4,758 serodiscordant heterosexual couples; 38% HIV-negative female, 68% HIV-negative male partner; 98% married; median age 33	Botswana, Kenya, Rwanda, South Africa, Tanzania, Uganda, Zambia	Daily oral TDF or TDF/FTC	67% protection with TDF alone; 75% protection with TDF/FTC	Serodiscordant couples may be a distinct, unique population.
FEM-PrEP	1,951 heterosexual women aged 18–35 at high risk of infection	Kenya, South Africa, Tanzania	Daily oral TDF/FTC	Trial discontinued for futility in April 2011.	Adherence assessment with monthly clinical samples to measure drug concentration is pending.
VOICE MTN-003	5,029 heterosexual women aged 18–45 in high-prevalence areas	Uganda, South Africa, Zimbabwe	Daily oral TDF or daily oral TDF/FTC or daily topical TFV gel	No study drug significantly reduced the risk of HIV acquisition. Estimates of effectiveness were less than 0 for TDF and TDF/FTC daily oral dosing (negative 48.8% and negative 4.2% TDF/FTC respectively), and reduced risk of HIV	Adherence to study drugs was low; TFV was detected in 30% of the oral TDF arm, 29% in the oral TDF/FTC arm, and 25% in the TDF gel arm.

Table 4. Clinical Trials of Pre-Exposure Prophylaxis

Trial	Study Population	Location	Intervention	Outcome	Comments
				infection of 14.7% for TDF gel.	

Key to Acronyms: FTC = emtricitabine; TDF = tenofovir disoproxil fumarate; TFV = tenofovir

Source
Adapted from: Kashuba et al., Pre-exposure prophylaxis for HIV prevention: how to predict success: Table Antiretroviral-based HIV prevention studies. Lancet. 2012;379(9835): 2409-2411.

Pregnancy and breastfeeding are not contraindications to PrEP.[36-40] There is no evidence of an increase in congenital anomalies among children born to women exposed to TDF or to emtricitabine during the first trimester.[41] Data from studies of infants born to mothers living with HIV and exposed to TDF through breast milk suggest limited drug exposure.[42-44] Condom use should be encouraged in pregnancy because several studies have reported increased incidence of HIV acquisition during pregnancy, which may also lead to increased perinatal transmission.

For couples with differing HIV status who attempt conception (sexual intercourse without a condom limited to peak fertility) when the partner living with HIV has achieved viral suppression, it is unclear if administration of PrEP for the partner without HIV further reduces the risk of sexual transmission. A modeling study analyzed the utility of PrEP under different conditions. Hoffman's analysis shows that PrEP provides little added benefit when the male partner is on ART with suppressed viral load, sex without a condom is limited to the ovulation window, and other modifiable transmission risks are optimized.[45]

Pre-Exposure Prophylaxis Provision and Monitoring in Couples with Differing HIV Status

If clinicians elect to use PrEP in couples with differing HIV status, the couples should be educated about the potential risks and benefits and all available alternatives for safer conception. The Centers for Disease Control and Prevention (CDC) has issued guidelines for the use of PrEP in sexually active heterosexual adults.[46] The CDC recommends that an individual who does not have HIV and is planning pregnancy with a partner living with HIV start daily oral TDF plus emtricitabine beginning 1 month before conception is attempted and continued for 1 month after conception is attempted.[46] Recommended laboratory testing should include HIV diagnostic testing at baseline then every 3 months, renal function testing at baseline and then every 6 months, and pregnancy testing at baseline

and every 3 months. Testing for hepatitis B virus (HBV) infection should be performed when initiating PrEP. Individuals without HBV infection should be vaccinated if they have not received HBV vaccination or they lack immunity to HBV. Individuals receiving PrEP should be educated about symptoms associated with acute HIV infection and advised to contact their providers immediately for further evaluation, should symptoms occur. Partners who are HIV negative should undergo frequent HIV testing to detect HIV infection quickly. If HIV infection is documented, the PrEP ARV agents should be discontinued to minimize selection of drug-resistant virus, measures should be instituted to prevent perinatal transmission if pregnancy has occurred and attempts at conception stopped if pregnancy has not occurred, and the patient should be referred to an HIV specialist immediately. Individuals with chronic HBV should be monitored for possible hepatitis flares when PrEP is stopped.[47] Clinicians are strongly encouraged to register women who become pregnant while receiving PrEP with the Antiretroviral Pregnancy Registry.

Couples Where Both Partners are Living with HIV

Both partners should be on ART with maximum viral suppression before attempting conception. Periovulatory unprotected intercourse (with use of condoms at all other times) is a reasonable option. The risk of HIV superinfection or infection with a resistant virus is negligible when both partners are on ART and have fully suppressed plasma viral loads.[48]

Monitoring of Pregnant Women Without HIV who have Partners with HIV

Women without HIV who present during pregnancy and indicate that their partners are living with HIV, like all pregnant women, should be notified that HIV screening is recommended, and they will receive an HIV test as part of the routine panel of prenatal tests unless they decline. Pregnant women without HIV should also be counseled to always use condoms to reduce the risk of HIV acquisition and their partners living with HIV should be virologically suppressed on ART. These women should be tested for HIV, at least once per trimester, or more often if the partner's viral load is not known. Furthermore, pregnant women who present in labor without results of third-trimester testing should be screened on the labor and delivery unit with an expedited serum HIV test, preferably a fourth-generation antigen/antibody expedited HIV test. If at any time during pregnancy a clinician suspects that a pregnant woman may be in the "window" period of seroconversion (i.e., she has signs or symptoms consistent with acute HIV infection), then a plasma HIV RNA test should be used in conjunction with an HIV antigen/antibody fourth-generation test. If the plasma HIV RNA is negative, it should be repeated in 2 weeks. Pregnant women without HIV with partners living with HIV should be counseled on methods to prevent acquisition of HIV, including suppressive ART for her partner, PrEP, and condom use. Women should be counseled regarding the symptoms of acute

retroviral syndrome (i.e., fever, pharyngitis, rash, myalgia, arthralgia, diarrhea, and headache) and the importance of seeking medical care and testing if they experience such symptoms.

Women who test HIV seropositive on either conventional or rapid HIV tests should receive appropriate evaluation and interventions to reduce perinatal transmission of HIV, including immediate initiation of appropriate ART and consideration of elective cesarean delivery according to established guidelines (see Transmission and Mode of Delivery). In cases where confirmatory test results are not readily available, such as with rapid testing during labor, it is still appropriate to initiate interventions to reduce perinatal transmission (see Intrapartum Care and Infant Antiretroviral Prophylaxis).

Women with partners living with HIV who test HIV seronegative should continue to be regularly counseled regarding consistent condom use to decrease their risk of sexual transmission of HIV. They should also be counseled on the importance of their partners' adherence to ART and the need for achievement of sustained virologic suppression to reduce the risk of sexual transmission of HIV. Women with primary HIV infection during pregnancy or lactation are at high risk of transmitting HIV to their infants.[49,50]

Coordination of care across multiple disciplines including HIV primary care, Ob/Gyn, family planning, case management and peer support is advised. Integration of reproductive health counseling including pregnancy desires and/or prevention are all recommended.

The National Perinatal HIV Hotline (1-888-448-8765) is a resource for a list of institutions offering reproductive services for HIV concordant/serodiscordant couples.

Updated Guidelines for Antiretroviral Postexposure Prophylaxis After Sexual, Injection Drug Use, or Other Nonoccupational Exposure to HIV—United States, 2016

from the
Centers for Disease Control and Prevention,
U.S. Department of Health and Human Services

Update: Interim Statement Regarding Potential Fetal Harm from Exposure to Dolutegravir – Implications for HIV Post-exposure Prophylaxis (PEP). Please see attached file.

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This report describes use of certain drugs and tests for some indications that do not reflect labeling approved by the Food and Drug Administration at the time of publication. Use of trade names and commercial sources is for identification only and does not imply endorsement by the U.S. Department of Health and Human Services.

CONTENTS

I. List of Tables and Figures 5

II. Abbreviations and Acronyms 6

III. Disclosure of Potential Competing Interest 8

IV. Summary 8

IV-A. What Is New in This Update 8

IV-B. Summary of Guidelines 8

V. Introduction 10

VI. Evidence Review 11

VI-A. Possible Effectiveness of nPEP 11

V1-A1. oPEP Studies 11

V1-A2. Observational and Case Studies of nPEP 11

VI-A3. Postnatal Prophylaxis of Infants Born to HIV-infected Mothers 14

VI-A4. Animal Studies 14

VI-B. Possible Risks Associated with nPEP 15

VI-B1. Antiretroviral Side Effects and Toxicity 15

V1-B2. Selection of Resistant Virus 17

VI-B3. Effects of nPEP on Risk Behaviors 17

VI-C. Antiretroviral Use During Pregnancy 18

VI-D. Behavioral Intervention to Support Risk Reduction During nPEP Use 19

VI-E. Adherence to nPEP Regimens and Follow-up Visits 19

VI-F. nPEP Cost-effectiveness 21

VI-G. Attitudes, Policies, and Knowledge About nPEP Use Among Health Care Providers and Candidates for nPEP 21

VII. Patient Management Guidelines 23

VII-A. Initial Evaluation of Persons Seeking Care After Potential Nonoccupational Exposure to HIV 23

VII-A1. HIV Status of the Potentially Exposed Person 23

VII-A2. Timing and Frequency of Exposure 24

VII-A3. HIV Acquisition Risk from the Exposure 24

VII-A4. HIV Status of the Exposure Source 26

VII-B. Laboratory Testing 26

VII-B1. HIV Testing 28

VII-B2. Recognizing Acute HIV Infection at Time of HIV Seroconversion 28

VII-B3. STI Testing 29

VII-B4. HBV Testing 29

VII-B5. Pregnancy Testing 30
VII-B6. Baseline and Follow-up Testing to Assess Safety of Antiretroviral Use for nPEP 30
VII-C. Recommended Antiretroviral nPEP Regimens 30
VII-D. Prophylaxis for STIs and Hepatitis 38
VII-E. Considerations for All Patients Treated with Antiretroviral nPEP 39
VII-E1. Provision of nPEP Starter Packs or a 28-day Supply at Initiation 39
VII-E2. Expert Consultation 39
VII-E3. Facilitating Adherence 39
VII-E4. HIV Prevention Counseling 40
VII-E5. Providing PrEP After nPEP Course Completion 40
VII.E6. Providing nPEP in the Context of PrEP 40
VII-E7. Management of Source Persons with HIV Infection 41
VII-F. Additional Considerations 41
VII-F1. Reporting and Confidentiality 41
VII-F2. Special Populations 41
VII-F3. Special Legal and Regulatory Concerns 44
VII-F4. Potential Sources of Financial Assistance for nPEP Medication 44
VIII. Conclusion 45
VIII-A. Plans for Updating These Guidelines 46
IX. References 47
X. Appendices 59
Appendix 1A. Summary of Methods for nPEP Guidelines Development and Roles of Teams and Consultants 60
Appendix 1B. nPEP Guidelines Development Teams and Consultants 62
Appendix 1C. Financial Disclosures of Potential Competing Interest nPEP Guidelines Consultants and Working Group 64
Appendix 2. Literature Search Methods for the nPEP Guidelines 67
Appendix 3. Studies Reviewed for the nPEP Guidelines 68
Appendix 4. Consideration of Other Alternative HIV nPEP Antiretroviral Regimens 91

I. List of Tables and Figures

Figure 1. Algorithm for evaluation and treatment of possible nonoccupational HIV exposures 23

Table 1. Estimated per-act risk for acquiring human immunodeficiency virus (HIV) from an infected source, by exposure act 25

Table 2. Recommended schedule of laboratory evaluations of source and exposed persons for providing nPEP with preferred regimens 27

Table 3. Clinical signs and symptoms of acute (primary) human immunodeficiency virus infection 28

Table 4. Hepatitis B virus screening serology 29

Table 5. Preferred and alternative antiretroviral medication 28-day regimens for nPEP 31

Table 6. Formulations, cautions, and dose adjustments for antiretroviral medications in preferred and alternative nPEP regimens 33

Table 7. Antiretroviral medications that should not be used for nPEP among pregnant women 42

Figure 2. nPEP considerations summary 45

II. Abbreviations and Acronyms

3TC	lamivudine
Ab	antibody
Ag	antigen
Ag/Ab	antigen/antibody combination test
AIDS	acquired immunodeficiency syndrome
Anti-HBc	hepatitis B core antibody
Anti-HBs	hepatitis B surface antibody
aOR	adjusted odds ratio
ATV	atazanavir
ATV/r	ritonavir-boosted atazanavir
CAI	condomless anal intercourse
CA-NSI	community-acquired needlestick injury
CD4	CD4 T lymphocyte
CDC	Centers for Disease Control and Prevention
CI	confidence interval
d4T	stavudine
DDI	didanosine
DNA	deoxyribonucleic acid
DRV	darunavir
DRV/r	ritonavir-boosted darunavir
DTG	dolutegravir
DHHS	U.S. Department of Health and Human Services
ED	emergency department
EFV	efavirenz
ELISA	enzyme-linked immunosorbent assay
FDA	Food and Drug Administration
FTC	emtricitabine
HBsAg	hepatitis B surface antigen
HBV	hepatitis B virus
HIV	human immunodeficiency virus
IDV	indinavir
IDV/r	ritonavir-boosted indinavir
IFA	indirect fluorescent antibody
LPV	lopinavir

LPV/r	ritonavir-boosted lopinavir
MSM	gay, bisexual, and other men who have sex with men
NAAT	nucleic acid amplification test
NFV	nelfinavir
NIH	National Institutes of Health
NNRTI	non-nucleoside reverse transcriptase inhibitors
NRTI	nucleoside reverse transcriptase inhibitors
NVP	nevirapine
nPEP	nonoccupational postexposure prophylaxis
oPEP	occupational postexposure prophylaxis
PCR	polymerase chain reaction
PI	protease inhibitor
PrEP	preexposure prophylaxis
PWID	persons who inject drugs
OR	odds ratio
PCR	polymerase chain reaction
PEP	postexposure prophylaxis
PrEP	preexposure prophylaxis
QALY	quality-adjusted life year
RAL	raltegravir
RNA	ribonucleic acid
RPV	rilpivirine
RTV	ritonavir
SANE	Sexual Assault Nurse Examiner
SD	standard deviation
SIV	simian immunodeficiency virus
SHIV	simian human immunodeficiency virus
STI	sexually transmitted infection
TDF	tenofovir disoproxil fumarate
ZDV	zidovudine

III. Disclosure of Potential Competing Interest

nPEP Guidelines Consultants and Working Group Potential Competing Interest. The federal government employees who prepared this report have no competing interests with the manufacturers of the products discussed herein. See Appendixes 1A, 1B, and 1C for the definition of competing interests for persons involved in guidelines development and procedures for managing conflicts of interest, lists of names and affiliations of the nPEP guidelines development teams and consultants, and financial disclosures of potential competing interests.

IV. Summary

The purpose of these guidelines is to provide health care providers in the United States with updated guidelines to the 2005 U.S. Department of Health and Human Services nonoccupational postexposure prophylaxis (nPEP) recommendations[1] on the use of antiretroviral nPEP and other aspects of case management for persons with isolated exposure outside health care settings to blood, genital secretions, or other potentially infectious body fluids that might contain human immunodeficiency virus (HIV). The use of occupational PEP (oPEP) for case management for persons with possible HIV exposures occurring in health care settings are not addressed in this guideline; updated oPEP guidelines have been published separately.[2]

IV-A. What Is New in This Update

This update incorporates additional evidence regarding use of nonoccupational postexposure prophylaxis (nPEP) from animal studies, human observational studies, and consideration of new antiretroviral medications that were approved since the 2005 guidelines, some of which have improved tolerability. New features are inclusion of guidelines for the use of rapid antigen/antibody (Ag/Ab) combination HIV tests, for revised preferred and alternative 3-drug antiretroviral nPEP regimens, an updated schedule of laboratory evaluations of source and exposed persons, updated antimicrobial regimens for prophylaxis of sexually transmitted infections and hepatitis, and a suggested procedure for transitioning patients between nPEP and HIV preexposure prophylaxis (PrEP), as appropriate.

IV-B. Summary of Guidelines

- Health care providers should evaluate persons rapidly for nPEP when care is sought ≤72 hours after a potential nonoccupational exposure that presents a substantial risk for HIV acquisition.[a] [VI-A4] [VII-A2][b]
    - All persons considered for nPEP should have determination of their HIV infection status by HIV testing, preferably by using rapid combined Ag/Ab, or antibody blood tests. [VII-A1] [VII-B1]
    - If rapid HIV blood test results are unavailable, and nPEP is otherwise indicated, it should be initiated without delay and can be discontinued if the patient is later determined to have HIV infection already or the source is determined not to have HIV infection. [VII-A1]

[a] See Figure 1.

[b] Numbers in brackets refers readers to the section in these guidelines that provides the basis for the recommendation.

- nPEP is recommended when the source of the body fluids is known to be HIV-positive and the reported exposure presents a substantial risk for transmission. [VII-A]

- nPEP is not recommended when the reported exposure presents no substantial risk of HIV transmission. [VII-A]

- nPEP is not recommended when care is sought > 72 hours after potential exposure. [VI-A4] [VII-A] [VII-A2]

- A case-by-case determination about the nPEP is recommended when the HIV infection status of the source of the body fluids is unknown and the reported exposure presents a substantial risk for transmission if the source did have HIV infection. [VII-A]

- All persons offered nPEP should be prescribed a 28-day course of a 3-drug antiretroviral regimen.[a] [VII-B1] [VII-C]

    - The preferred regimen for otherwise healthy adults and adolescents
        - tenofovir disoproxil fumarate (tenofovir DF or TDF) (300 mg) with emtricitabine (200 mg) once daily ***plus***

          raltegravir (RAL) 400 mg twice daily or dolutegravir (DTG) 50 mg daily. [VI-A2ci] [VII-C]

    - Alternative regimen for otherwise healthy adults and adolescents is
        - tenofovir DF (300 mg) with emtricitabine (FTC) (200 mg) once daily ***plus***

          darunavir (DRV) (800 mg) and ritonavir[a] (RTV) (100 mg) once daily. [VII-C]

    - Regimens are also provided for children, persons with decreased renal function, and pregnant women (see Table 6). [VII-C]

    - Health care providers considering using antiretroviral regimens for nPEP other than those listed in these guidelines as preferred or alternative are encouraged to consult with other health care providers who have expertise in antiretroviral medication use for similar patients (e.g., children, pregnant women, or those with such comorbid conditions as impaired renal function). [VII-C] [VII-E2]

- All persons evaluated for possible nPEP should be provided any indicated prevention, treatment, or supportive care for other exposure-associated health risks and conditions (e.g., bacterial sexually transmitted infections, traumatic injuries, hepatitis B virus and hepatitis C virus infection, or pregnancy). [VII] [VII-B3] [VII-B4] [VII-B5] [VII-D]

- All persons who report behaviors or situations that place them at risk for frequently recurring HIV exposures (e.g., injection drug use, or sex without condoms) or who report receipt of ≥ 1 course of nPEP in the past year should be provided risk-reduction counseling and intervention services, including consideration of preexposure prophylaxis. [VII-E4] [VII-E5]

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[a] Ritonavir is used in clinical practice as a pharmacokinetic enhancer to increase the trough concentration and prolong the half-life of darunavir and other protease inhibitors; it was not considered an additional drug when enumerating drugs in a regimen.

V. INTRODUCTION

The most effective methods for preventing human immunodeficiency virus (HIV) infection are those that protect against exposure. Antiretroviral therapy cannot replace behaviors that help avoid HIV exposure (e.g., sexual abstinence, sex only in a mutually monogamous relationship with an HIV-uninfected partner, consistent and correct condom use, abstinence from injection drug use, and consistent use of sterile equipment by those unable to cease injection drug use). Provision of antiretroviral medication after isolated sexual, injection drug use, or other nonoccupational HIV exposure, known as nonoccupational postexposure prophylaxis (nPEP), is less effective at preventing HIV infection than avoiding exposure.

In 2005, the U.S. Department of Health and Human Services (DHHS) released its first recommendations for nPEP use to reduce the risk for HIV infection after nonoccupational exposures to blood, genital secretions, and other body fluids that might contain HIV.[1] In 2012, updated guidelines on the use of occupational PEP (oPEP) for case management for persons with possible HIV exposures occurring in health care settings were published and are not addressed in this guideline.[2] Other organizations, including health departments, professional medical societies, and medical institutions, have developed guidelines, recommendations, and protocols for nPEP delivered to adults and children.[3-10]

This document updates the 2005 DHHS nPEP recommendations in response to new information regarding clinical experience for delivering nPEP, including using newer antiretroviral regimens and their side-effect profiles and cost-effectiveness of nPEP to prevent HIV infection for different exposure types. We describe in more detail the goals for the new guidelines, funding source of the guidelines, persons involved in guidelines development, definition of competing interest for persons involved in guidelines development and procedures for managing competing interest (Appendix 1A).

CDC scientists selected nPEP subject matter experts from the Food and Drug Administration (FDA), the National Institutes of Health (NIH), hospitals, clinics, health departments, and professional medical societies to participate as panelists to discuss recent developments in nPEP practice by CDC teleconferences in December 2011, and April 2012 (Appendix 1B). Any potential conflicts of interests reported by persons involved in developing the guidelines and the determination made for each of those potential conflicts are listed in Appendix 1C.

A working group of CDC HIV prevention scientists and other CDC scientists with expertise pertinent to the nPEP guidelines conducted nPEP-related systematic literature reviews. Appendix 2 summarizes the methods used to conduct that review, including databases queried, topics addressed, search terms, search dates, and any limitations placed on the searches (i.e., language, country, population, and study type). All studies identified through the literature search were reviewed and included in the body of evidence. Appendix 3 includes a summary of the key observational and case studies among humans that comprise the main body of evidence.

These nPEP guidelines are not applicable for occupational exposures to HIV; however, we attempted to standardize the selection of preferred drugs for nPEP and occupational postexposure prophylaxis (oPEP).[2] These guidelines also do not apply to continuous daily oral antiretroviral prophylaxis that is initiated before potential exposures to HIV as a means of reducing the risk for HIV infection among persons at high risk for its sexual acquisition (preexposure prophylaxis or PrEP[11]).

Among the limitations of these guidelines is that they are based on a historical case-control study related to occupational PEP among hospital workers, observational and case studies examining nPEP's effectiveness among humans, animal studies related to PEP's efficacy among primates, and expert opinion on clinical practice among humans related to nPEP. Because of concerns about the ethics and feasibility of conducting large-scale prospective randomized placebo-controlled nPEP clinical trials, no such studies have been

conducted. Additionally, although nPEP failures were rare in the observational studies we reviewed, those studies often have inadequate follow-up testing rates for HIV infection; therefore, nPEP failures might be underestimated. Because these guidelines represent an update of previous guidelines about a now established clinical practice, we elected not to use a formal grading scheme to indicate the strength of supporting evidence.

VI. Evidence Review

VI-A. Possible Effectiveness of nPEP

No randomized, placebo-controlled clinical trial of nPEP has been conducted. However, data relevant to nPEP guidelines are available from animal transmission models, perinatal clinical trials, observational studies of health care workers receiving prophylaxis after occupational exposures, and observational and case studies of nPEP use. Although the working group mainly systematically reviewed studies conducted after 2005 through July 2015, we also include findings from seminal studies published before 2005 that help define key aspects of nPEP guidelines. Newer data reviewed in this document continue to support the assertion that nPEP initiated soon after exposure and continued for 28 days with sufficient medication adherence can reduce the risk for acquiring HIV infection after nonoccupational exposures.

V1-A1. oPEP Studies

A case-control study demonstrating an 81% (95% confidence interval [CI] = 48%–94%) reduction in the odds of HIV transmission among health care workers with percutaneous exposure to HIV who received zidovudine (ZDV) prophylaxis was the first to describe the efficacy of oPEP.[12] Because of the ethical and operational challenges, no randomized controlled trials have been conducted to test the efficacy of nPEP directly. In the absence of a randomized controlled trial for nPEP, this case-control study reports the strongest evidence of benefit of antiretroviral prophylaxis initiated after HIV exposure among humans.

V1-A2. Observational and Case Studies of nPEP

The following is a synopsis of domestic and international observational studies and case reports that have been published since the 2005 U.S. nPEP guidelines were issued. In the majority of studies, failure of nPEP, defined as HIV seroconversion despite taking nPEP as recommended, was typically confirmed by a seronegative HIV enzyme-linked immunosorbent assay (ELISA) at baseline visit, followed by a positive ELISA and Western blot or indirect fluorescent antibody (IFA) during a follow-up visit.

VI-A2a. Men Who Have Sex with Men

Based on 1 case report[13] and 6 studies[14-19] reporting results exclusively or separately among men who have sex with men (MSM), 49 seroconversions were reported after nPEP use. The case report from Italy described an nPEP failure in an MSM despite self-reported 100% adherence to his 3-drug medication regimen consisting of ZDV, lamivudine (3TC), and indinavir (IDV) and denial of ongoing HIV risk transmission behaviors after completing nPEP; concomitant hepatitis C virus (HCV) seroconversion was also diagnosed.[13] In the 6 studies, 48 of 1,535 (31.3 seroconverions/1,000 persons) MSM participants became HIV infected despite nPEP use. At least 40 of the 48 seroconversions likely resulted from ongoing risk behavior after completing nPEP. Thirty-five of these 40 seroconversions occurred ≥ 180 days subsequent to nPEP initiation and are unlikely to constitute nPEP failures.[16,18] The remaining 8 seroconverters among 1,535 MSM participants (5.2 seroconverions/1,000 persons) may be classified as potential nPEP failures. This included 1 recipient with an indeterminate HIV test result and isolation of an M184 mutation resistant virus on the last day of his 28-day regimen despite initiating

nPEP ≤ 48 hours after exposure,[20] indicating that seroconversion was occurring during the 28-day period of nPEP administration. Another 4 patients seroconverted at 91 days, 133 days, 160 days, and 168 days after nPEP initiation, including 3 who reported completing the 28-day regimen; however, there was no description of the presence or lack of ongoing sexual risk behaviors after nPEP completion.[18] Among the remaining 3 men who seroconverted after taking nPEP, taking nPEP was not associated with any suggestion of change in seroconversion risk, although no information was reported regarding the nPEP regimen prescribed, adherence to nPEP, delay in nPEP initiation or timing of HIV-positive results.[15]

In a 2-year prospective study in Brazil, investigators provided 200 seronegative MSM at high risk with education regarding nPEP and a 4-day starter pack with instructions to initiate its use for a suspected eligible exposure.[16] A follow-up 24-day pack (to complete a 28-day course) was provided only for those men with eligible exposures. Sixty-eight of 200 MSM initiated nPEP. Adherence to nPEP medications was estimated on the basis of questions at the 28-day visit and remaining pill counts. The entire 28-day nPEP regimen was completed by 89% of men with eligible exposures including 1 participant who seroconverted. Ten of 11 seroconversions occurred among men who did not initiate nPEP.[16]

VI-A2b. Sexual Assault

VI-A2bi. General Population (all ages). Globally, 3 systematic reviews[20-22] and 1 prospective *cohort* study[23] spanning childhood through adulthood reported wide-ranging proportions of participants being eligible for nPEP (range, 6%–94%), being offered nPEP (range, 5%–94%), accepting nPEP (range, 4%–100%), or completing nPEP (range, 9%–65%). Among the 3 systematic reviews, none reported HIV screening results or the number of nPEP failures.[20-22]

VI-A2bii. Adults and Adolescents. Although nPEP use for sexual assault survivors has been widely encouraged both in the United States and elsewhere,[24-27] documented cases of HIV infection resulting from sexual assault of women or men rarely have been published.[25,28,29] Of 5 individual retrospective studies of nPEP limited to adult and/or adolescent sexual assault survivors that the working group reviewed, 3 reported no seroconversions at baseline or at follow-up among those sexual assault survivors who completed nPEP,[30-32] and 2 did not report any information about HIV screening results or the number of nPEP failures.[33,34]

VI-A2biii. Children and Adolescents. Studies of nPEP also have focused on children or adolescents evaluated for sexual assault. In a pooled analysis based on 10 studies of 8,336 children or adolescents evaluated for sexual assault or abuse, at least 1,362 were determined to be nPEP eligible. Twenty-four of the remaining 6,974 (3.4 seroconversions/1,000 persons) children or adolescents who were not eligible for nPEP were found to be HIV infected at baseline testing.[35-44] Among 672 children or adolescents reported to have been offered nPEP, 472 were known to have initiated nPEP, and 126 were reported to have completed a 28-day nPEP course. No new HIV infections were documented among these 472 (0.0 seroconversions/1,000 persons) children/adolescents in the pooled analysis who initiated nPEP. New HIV infections might have been underestimated as return rates for children or adolescents attending at least 1 follow-up visit during which an HIV test might have been conducted after initiating nPEP ranged from 10%[40] to 76%.[44]

VI-A2c. Mixed or Other Populations

VI-A2ci. Mixed populations. Eighteen studies, including 9 international studies[45-54] and 9 domestic studies[55-63] examined multiple routes of HIV risk exposure among adults, adolescents, and children with sexual and nonsexual exposures, including consensual sexual relations, sexual assault, injection drug use, and needlestick exposures.

Fifteen of the 19 studies reported both the number of participants who completed 28 days of nPEP and the number of participants who HIV seroconverted after initiating nPEP.[46-58,62,63] In these 15 studies, 2,209 participants completed 28 days of nPEP, of whom, at least 19 individuals HIV seroconverted,[45-48,52,54,56,62,63] but

only 1 seroconversion[47] (8.6/1,000) was attributed to nPEP failure. This seroconversion occurred 6 weeks after nPEP initiation in a sexually assaulted female who presented ≤ 4 hours after assault and completed nPEP.[47] She had a positive HIV RNA polymerase chain reaction (PCR) test but no confirmatory HIV ELISA test documented during the 5–6 week follow-up HIV testing period after initiating nPEP. Among the other 18 seroconversions that occurred during follow-up HIV testing among participants who completed 28 days of nPEP, 5 occurred ≥6 months after nPEP completion and were likely associated with ongoing sexual risk behavior after nPEP completion.[45,54] One seroconversion occurred after a participant reported poor adherence to nPEP, ongoing sexual risk behavior, and multiple nPEP courses after the initial course of nPEP, however, the timing of seroconversion was not clearly specified.[63] One seroconversion occurred in an MSM presenting with acute retroviral syndrome 3 weeks after condomless anal sex with an anonymous partner and no receipt of nPEP.[48] One seroconversion occurred in a woman during the 6-month follow-up period after completing nPEP and it was attributed to ongoing sharing of injection drug use equipment.[48] One seroconversion occurred in a patient who started nPEP > 72 hours after a high-risk exposure.[46] Additional seroconversions occurred at various time periods after initiation of nPEP without detailed information about ongoing sexual exposure or adherence to nPEP (2 and 5 months [n=2 participants][62]; 3 and 6 months [n=2 participants][52]; 5 months [n=1 participant][62]; and 12 months [n=1 participant]).[62] Among 3 participants who seroconverted while taking or shortly after taking ZDV-containing nPEP regimens, there was a lack of information about ongoing sexual exposure or detailed information about strict adherence to the full 28-day nPEP regimen.[56] However, only 33.8%–42.1% of all patients who were administered ZDV-containing nPEP regimens in this study completed their regimens as prescribed.[56]

In the remaining 4 of 19 studies, 2 studies did not report rates of HIVseroconversion[59,60] and 2 studies did not report rates of completion of the 28-day nPEP regimen,[45,61] including a study that reported 7 seroconversions that occurred at unspecified time periods during the 6 months after nPEP initiation among 649 users of nPEP.[61]Of all nPEP clients in this study, 18.5% had previously used nPEP between 1 and 5 times.[61]

In 3 domestic studies, participants who were administered tenofovir (TDF)-containing nPEP regimens were substantially more likely than historical control subjects in studies consisting of ZDV-containing regimens to complete their prophylaxis as prescribed and less likely to experience common side effects.[49,56,57,60] In two studies, the highest completion rates were observed for the TDF-3TC (87.5%) and TDF-emtricitabine (FTC) (72.7%) arms followed by the TDF-FTC-raltegravir (RAL) (57%) and ZDV-3TC-3rd drug arms (the 3rd drug was mainly a protease inhibitor [PI]) (38.8 %).[57] In addition to the 57% of patients who completed all 3 drugs of the TDF-FTC-RAL arm, 27% of patients took their TDF-FTC and first RAL dose daily, but sometimes missed the second dose of RAL.[57] In another study, the completion rates were highest in the TDF-FTC-ritonavir (RTV)-boosted lopinavir (LPV/r) arm (88.3%) compared with the TDF-3TC-RTV-boosted atazanavir (ATV/r) arm (79%), ZDV-3TC-LPV/r arm (77.5%), or ZDV-3TC-nelfinavir (NFV) arm (65.5%).[49] In the last domestic study, TDF-containing compared with ZDV-containing regimens were associated with significantly higher completion rates in the bivariate analysis (OR 2.80 [95% CI = 1.69–1.18]) but not in the multivariate analysis (OR 1.96 [95% CI = 0.73–5.28]).[60]

VI-A2cii. Other Populations. Data for 438 persons with unintentional nonoccupational needlestick or other sharps exposures described in 7 published reports were reviewed, including data for 417 children and 21 adults.[64-70] Childhood and adolescent exposures were characterized as community-acquired exposures occurring in public outdoor places (e.g., playgrounds, parks, or beaches) or by reaching into needle disposal boxes at home or in a hospital. Adult exposures were often similar to occupational exposures occurring while handling needles or disposing of needles in a sharps container. In all cases, the HIV status of the source person was unknown except in 1 report[64] involving multiple percutaneous exposures with lancets among 21 children while playing with discarded needles in a playground. Some of the lancets had been used multiple times to stick different children. One of the children stuck with a lancet was known to be HIV infected before the incident, not receiving antiretroviral therapy, and documented to have an HIV-1 plasma viral load of 5,250,000 copies/mL; the other 20 children were considered potentially exposed to HIV.[64] Additionally, in 1 of the studies, 2 children

were hepatitis B surface antigen (HBsAg)-positive at baseline before starting prophylaxis.[66] Among 155 children offered nPEP, 149 accepted and initiated nPEP, and 93 completed their 28-day nPEP course.[64-70] Antiretroviral prophylaxis with either ZDV and 3TC or ZDV, 3TC plus a PI (IDV, NFV, LPV/r) or a non-nucleoside reverse transcriptase inhibitor (NNRTI) (nevirapine [NVP]) was used for those 149 children or adults accepting and initiating nPEP. No seroconversions for HIV, hepatitis B virus (HBV), or HCV were reported among those receiving or not receiving nPEP.[64-70]

In the case report of a 12-year old girl in Saudi Arabia with sickle-cell disease who was inadvertently transfused with a large volume of packed red blood cells, the use of a 13-week, 4-drug nPEP regimen of TDF, FTC, ritonavir-boosted darunavir (DRV/r) (later changed to LPV) and RAL resulted in loss of presence of detectable HIV-1 antibodies.[71] No HIV-1 DNA or plasma HIV-1 RNA was detected by PCR testing during the 8-month follow-up period.

VI-A3. Postnatal Prophylaxis of Infants Born to HIV-infected Mothers

Data regarding the efficacy of infant PEP to prevent mother-to-child HIV transmission provides only limited, indirect information about the efficacy of antiretroviral medications for nPEP. Postpartum antiretroviral prophylaxis is designed to prevent infection after contact of mucosal surfaces (ocular, oral, rectal, or urethral) or broken skin in the infant with maternal blood or other fluids that are present at time of labor and delivery, especially during vaginal births. Trials in which the infant was provided postpartum prophylaxis but the mother received neither prepartum or intrapartum antiretroviral prophylaxis provide the most relevant indirect data regarding nPEP after exposure to a source who did not have suppressed viral load secondary to antiretroviral therapy. Although a combination of prophylaxis during the prenatal, intrapartum, and postpartum periods offers the most effective reduction of perinatal transmission, postpartum prophylaxis alone also offers reduction.[72-75]

A randomized open-label clinical trial of antiretrovirals provided to infants born to breastfeeding HIV-infected women demonstrated an overall reduction in postnatal HIV infection at 14 weeks (the end of the period of prophylaxis) by approximately 70% (95% CI unreported). The trial compared a control group receiving a short-arm postnatal prophylaxis regimen and 2 comparison groups, each receiving different extended-arm postnatal prophylaxis regimens.[76] The control group received the short-arm regimen consisting of single-dose NVP plus 1-week ZDV and the 2 comparison groups received the control regimen and either 1) extended daily NVP for 14 weeks or 2) extended daily NVP and ZDV for 14 weeks. The corresponding HIV infection rates at 14 weeks were 8.5% in the control group, and 2.6% and 2.5% in the 2 extended arms comparison groups, respectively.

An observational study documented a potential effect of ZDV prophylaxis initially started postnatally compared with the prepartum and intrapartum periods. A review of 939 medical records of HIV-exposed infants in New York State indicated that the later the prophylaxis was started after the prepartum period, the higher the likelihood of perinatal transmission and that a benefit existed to postnatal prophylaxis alone (without maternal intrapartum or prepartum medication). Perinatal prophylaxis started during the prepartum, intrapartum, early postpartum ($\leq$48 hours after birth), and late postpartum (3 days–42 days) periods resulted in corresponding transmission rates of 6.1%, 10.0%, 9.3%, and 18.4%, respectively.[77] A perinatal transmission rate of 31.6% was observed when no perinatal prophylaxis was provided; the study included data from patients who had pregnancies early in the epidemic when HIV perinatal prophylaxis was first being implemented, and it was uncertain whether using intrapartum and/or postnatal prophylaxis alone was beneficial among mothers without prenatal care.

VI-A4. Animal Studies

Macaque models have been used to assess potential PEP efficacy. These studies examined artificial exposures to simian immunodeficiency virus (SIV) which varied by modes of exposure, virus innocula, and drug

regimens. The parameters imposed by those animal studies might not reflect human viral exposures and drug exposures, and those differences should be considered when interpreting their findings. Nevertheless, macaque models have provided important proof-of-concept data regarding PEP efficacy. More recent animal studies have tested the effectiveness of newer antiretrovirals and alternate routes of PEP administration. Subcutaneous tenofovir was reported to block SIV infection after intravenous challenge among long-tailed macaques if initiated ≤ 24 hours after exposure and continued for 28 days.[78] All 10 macaques initiated on PEP at 4 or 24 hours post inoculation were documented to be SIV-uninfected at 36–56 weeks post inoculation compared with all 10 macaques that failed to receive any prophylaxis and became SIV infected within 20–36 weeks post-inoculation. In a study of 24 macaques, TDF was less effective if initiated 48 or 72 hours post-exposure or if continued for only 3 or 10 days.[79] In contrast, all 11 macaques became SIV infected in a study involving 3 control macaques receiving no prophylaxis and 8 macaques receiving a combination of ZDV, 3TC, and IDV administered orally through nasogastric catheter after intravenous virus inoculation at 4 or 72 hours post-SIV inoculation.[80] High virus innocula and drug exposures that are lower than those achieved among humans as a result of inadequate interspecies adjustment of drug dosing might have contributed to the lack of protection reported for that study. However, a macaque study designed to model nPEP for vaginal HIV exposure demonstrated that a combination of ZDV, 3TC and a high dose of IDV protected 4 of 6 animals from vaginal SIV infection when initiated ≤ 4 hours after vaginal exposure and continued for 28 days, whereas 6 of 6 animals in the control group receiving a placebo became SIV infected.[81] In another study, after 20 vaginal simian/human immunodeficiency virus infection (SHIV) challenges and a 10-week follow-up period, 5 of 6 macaques were protected when treated with topically applied gel containing 1% RAL 3 hours after each virus exposure compared with none of four macaques treated with placebo gel.[82] Likewise, macaques administered subcutaneous TDF for 28 days, beginning 12 hours (4 animals) or 36 hours (4 animals) after vaginal HIV-2 exposure, were protected from infection. Three of 4 animals treated 72 hours after exposure were also protected.[83] Three of 4 untreated animals in the control group became infected with HIV-2. Overall, data from these macaque studies demonstrate that PEP might be effective among humans if initiated ≤ 72 hours and continued daily for 28 days. In a systematic review and meta-analysis of 25 nonhuman primate studies, including rhesus macaques in10 studies and cynomolgus monkeys in 5 studies, use of PEP was associated with an 89% lower risk of seroconversion compared with nonhuman primates who did not use PEP. Also, use of tenofovir compared with other drugs was associated with lower seroconversion.[84]

VI-B. Possible Risks Associated with nPEP

Concerns regarding potential risks associated with nPEP as a clinical HIV prevention intervention include the occurrence of serious adverse effects from the short-term use of antiretroviral medications by otherwise healthy persons without HIV infection, and potential selection for drug-resistant strains of virus among those who become HIV infected despite nPEP use (particularly if medication adherence is inconsistent during the 28-day course or if the source transmits resistant virus). An additional concern is that persons engaging in consensual sex or nonsterile injection drug use may rely solely on PEP instead of adopting more long-term risk-reduction behaviors such as safer sexual and drug-injecting behaviors.

VI-B1. Antiretroviral Side Effects and Toxicity

In a meta-analysis[20] of 24 nPEP-related studies, including 23 cohort studies and 1 randomized clinical trial (behavioral intervention to improve nPEP adherence), of 2,166 sexually assaulted persons, clinicians prescribed 2-drug regimens,[36,38,40,42,85-88] 3-drug regimens,[23,31,58,89-92] 2- and 3-drug regimens,[30,32,50,93,94] or an unknown number of drugs.[46,95-97] ZDV was a part of all the regimens and all 2-drug regimens contained ZDV and 3TC, except 1 study in which ZDV and zalcitabine were prescribed.[88] Antiretrovirals provided as a part of 3-drug regimens included ZDV, 3TC, NFV, IDV, LPV/r, NVP, efavirenz (EFV), or co-formulated FTC/TDF with co-formulated LPV/r. Nausea, vomiting, diarrhea, and fatigue were the most commonly reported side effects.[20]

Serious side effects have been reported occasionally (e.g., nephrolithiasis and hepatitis) in the literature.[98-100] Rarely, severe hepatotoxicity has been observed among patients administered NVP-containing regimens for both oPEP and nPEP, including a female health care worker who required a liver transplantation after taking oPEP[101]; therefore, CDC advises against use of NVP forPEP.[1,99] Also, since January 2001, product labeling for NVP states that using it as part of a PEP regimen is contraindicated.[102]

A retrospective study in western Kenya involved 296 patients who were eligible for and initiated nPEP, including 104 who completed a 28-day course of nPEP; patients received either stavudine (d4T), 3TC and NVP or ZDV, 3TC, and LPV/r.[47] Neither the proportion of patients reporting side effects (14% [LPV-containing arm] and 21% [NVP-containing arm]) nor antiretroviral therapy completion rates differed substantially between the 2 arms. The most commonly reported side effects included epigastric pain, skin rash, and nausea among patients receiving NVP-containing regimens and diarrhea, dizziness, and epigastric pain among those receiving LPV/r-containing regimens. However, 1 hepatitis-related death of a sexual assault survivor taking a NVP-containing regimen prompted investigators to change to a new PEP regimen containing ZDV, 3TC, and LPV/r. Inclusion of NVP and d4T were initially included in nPEP regimens because of availability and cost but were discontinued in 2005 as a result of adverse events and toxicities among healthy patients. This change was also influenced by a black box warning in the drug labeling for NVP describing increased toxicity among patients on NVP with higher CD4 T lymphocyte (CD4) cell counts.

Commonly used medications in the observational studies of nPEP published after 2005 included ZDV, 3TC, LPV/r, TDF, FTC, and RAL. The majority of regimens involved using 3 drugs (range, 2–4 drugs) with a daily 2-pill burden (range, 1–3 pills). The side-effect profile that included fatigue, nausea, headache, diarrhea, and other gastrointestinal complaints was similar across studies of MSM having mainly consensual sex and studies of sexual assault survivors, including mainly women, children, and a limited proportion of men.[20,23,31,44,55-57,103]

Two trials, including a total of 602 participants, compared TDF- versus ZDV-containing nPEP regimens; both reported better medication tolerability among participants taking TDF-containing regimens.[49,56] Another study reported fewer side effects among 100 adult participants prescribed a 3-drug nPEP regimen that included RAL, TDF, and TDF compared to historical controls using a 3-drug PEP regimen including ZDV, 3TC, and a RTV-boosted PI.[57]

In an open-label, nonrandomized, prospective cohort study comparing RAL-FTC-TDF in 86 MSM and FTC-TDF in 34 MSM, 92% and 91% of participants completed 28 days of treatment, respectively, with mean adherences of 89% and 90%, respectively.[17] Use of RAL rather than a PI was associated with the avoidance of 8 prescribed drug, and 37 potential illicit drug, interactions. However, in the RAL arm, 8 recipients (9%) developed mild myalgias, and 4 recipients developed grade 4 elevations in creatinine kinase. Both the myalgias and creatinine kinase elevations improved to grade 2 or less by week 4 without RAL discontinuation.

Among 100 MSM in an open-label, single-arm study at 2 public health clinics and 2 hospital EDs in urban areas in Australia, a once daily 28-day nPEP single-pill combination regimen of FTC-rilpivirine (RPV)-TDF was well tolerated with 98.5% adherence by self-report and 92% completion of the 28-day regimen.[19] However, within 1 week of completing nPEP, 1 patient developed acute abdominal pain, vomiting, and grade 4 laboratory evidence of acute pancreatitis (lipase 872 IU/L). The pancreatitis resolved ≤ 21 days without need for hospitalization.[19]

In a 2-arm open label randomized multicenter clinical trial in EDs in 6 urban hospitals in Barcelona, Spain, comparing ZDV/3TC + LPV/r with ZDV/3TC + atazanavir (ATV), 64% of nPEP recipients in both arms completed the 28-day course and 92% of patients reported taking > 90% of scheduled doses (without difference between arms).[53] Adverse events were reported in 46% of patients overall (49%, LPV/r arm; 43%, ATV arm). Gastrointestinal problems were more common in the LPV/r arm.

A pooled series of case reports revealed that 142 (67%; range, 0%–99%) of 213 children and adolescents who initiated nPEP and who had ≥1 follow-up visit, reported adverse effects and 139 of 465 (30%; range, 0%–64.7%) children and adolescents who initiated nPEP, completed their course of nPEP.[32,35-44] Most commonly reported nPEP regimens included ZDV + 3TC or ZDV + 3TC + (NFV or IDV or LPV/r). Most common adverse events among the 213 participants included nausea (n = 83; 39%), fatigue (n = 58; 27%), vomiting (n = 38; 18%), headache (n = 26; 12%), diarrhea (n = 25; 12%), and abdominal pain (n = 15; 7%).

V1-B2. Selection of Resistant Virus

In instances where nPEP fails to prevent infection, selection of resistant virus by the antiretroviral drugs is theoretically possible. However, because of the paucity of resistance testing in documented nPEP failures, the likelihood of resistance occurring is unknown.

A case report from Brazil documented a 3TC-resistance mutation on day 28 of therapy in a man treated with ZDV and 3TC who subsequently underwent HIV seroconversion.[16] Although the patient was noted to have taken nPEP, detailed information regarding adherence was unreported. Because the source-person could not be tested, whether the mutation was present at the time of transmission or whether it emerged during nPEP use is unknown.

Rationale for the concern regarding acquiring resistant virus from the exposure that leads to nPEP prescription includes data from an international meta-analysis of 287 published studies of transmitted HIV-1 drug resistance among 50,870 individuals during March 1, 2000–December 31, 2013, including 27 studies and 9,283 individuals from North America.[104] The study-level estimate of transmitted drug resistance in North America was 11.5% (resistance to any antiretroviral drug class), 5.8% (resistance to NRTIs), 4.5% (resistance to NNRTIs, and 3.0% (resistance to PIs).

VI-B3. Effects of nPEP on Risk Behaviors

The majority of studies examining the association between use and availability of nPEP and sexual risk behaviors during or after its use have been conducted in developed countries, primarily among MSM; no studies related to risk compensation were conducted among persons with injection-related risk factors.[14,16,105-111] The majority of these studies did not report increases in high-risk sexual behaviors after receipt of nPEP[14,16,106,110,111] and participants sometimes reported a decrease in sexual risk-taking behavior.[16,106] However, in 3 studies, nPEP users were more likely than persons who did not use nPEP to report having multiple partners and engaging in condomless receptive or insertive anal sex with HIV-infected partners or partners with unknown serostatus after completing nPEP.[14,108,110] In 2 of these studies, nPEP users were also more likely to subsequently become HIV infected than patients who did not use nPEP.[108,110] During 2000–2009 in the Amsterdam Cohort Study, MSM who were prescribed nPEP, compared with a reference cohort of MSM, had an incidence of HIV infection approximately 4 times as high (6.4 versus 1.6/100 person-years).[108] During 2001–2007, MSM in a community cohort study in Sydney, Australia reported continued, but not increased, high-risk sexual behaviors among nPEP users; more specifically, no change in sexual behavior was reported at 6 months after 154 incident nPEP uses and after ≥18 months for 89 incident nPEP uses. Among those MSM who received nPEP, the hazard ratio of subsequent HIV infection was 2.67 (95% CI = 1.40, 5.08).[110] The authors did not attribute this elevated risk for HIV seroconversion among users of nPEP to nPEP failure but rather to a documented higher prevalence of condomless anal intercourse (CAI) with HIV-infected partners among users of nPEP, compared with persons who did not use nPEP. In summary, users of nPEP, compared with participants who did not use nPEP had a continued higher prevalence of ongoing CAI with HIV-infected persons resulting in a greater likelihood of HIV seroconversion during all periods, especially after completing nPEP. In another study, repeated courses of nPEP were unassociated with risk for subsequent HIV infection.[45] In a study of 99 patients who attended a clinic in Toronto to be evaluated for nPEP during January 1, 2013–September 30, 2014, 31 (31%) met CDC criteria for

PrEP initiation.[112] PrEP candidacy in this study was associated with sexual exposure to HIV, prior nPEP use, and lack of drug insurance. Those studies[14,108,110,112] demonstrate that certain nPEP users with ongoing high-risk sexual behaviors might need additional behavioral and biomedical prevention interventions, including PrEP, instead of nPEP.[11,113]

One U.S.-based study among 89 MSM that examined risk behavior during the 28-day course of nPEP reported that among participants, 21% reported having insertive or receptive CAI, and 43% reported engaging with ≥ 1 partner known to be HIV-positive or of unknown serostatus (i.e., a high-risk partner).[105] Ninety-four percent of participants reporting having high-risk partners also reported having insertive or receptive anal intercourse. Of participants with high-risk partners and who practiced insertive or receptive anal intercourse, 26% reported CAI with their high-risk partner while receiving nPEP. The strongest predictor of CAI during nPEP in that study was HIV engagement, defined as receiving services from an HIV-related organization, donating money to or volunteering for an HIV-related cause, or reading HIV-related magazines and online sites. A nearly 5-fold chance of reporting condomless sex with a high-risk partner during nPEP was associated with each standard deviation increase in HIV engagement (OR 4.7 [95% CI = 1.3–17.04]). Investigators hypothesized that persons who are more involved with HIV-related services or organizations might be more informed about the effectiveness of nPEP and more likely to perceive themselves to be at less risk for HIV transmission while receiving nPEP and therefore more likely to have CAI.[105]

Awareness of nPEP availability, defined as general knowledge of availability of nPEP as a tool for preventing HIV infection after a potential HIV exposure[107] or nPEP use more than once in 5 years,[103] was associated with condomless sex among MSM.[103,107] Additionally, a longitudinal study of MSM in the Netherlands reported no associations existed between any nPEP-related beliefs (e.g., perceiving less HIV or acquired immunodeficiency syndrome (AIDS) threat, given the availability of nPEP, or perceiving high effectiveness of nPEP in preventing HIV) and the incidence of sexually transmitted infections (STIs) or new HIV infection.[109]

VI-C. Antiretroviral Use During Pregnancy

No trials have been conducted to evaluate use or the maternal or fetal health effects of short-term (i.e., 28-day) antiretroviral use as nPEP among pregnant women without HIV infection. However, clinical trials have been conducted and extensive observational data exist regarding use of specific antiretrovirals during pregnancy among HIV-infected women both when initiated as treatment for health benefits to the women and when initiated to reduce mother-to-child HIV transmission. Although duration of antiretroviral use during pregnancy has varied in these trials, it often spans months of pregnancy. Only ZDV is specifically approved for use in pregnancy, but as a result of data from clinical trials, other antiretroviral drugs have been reported to have short-term safety for pregnant women and their fetuses, and therefore can be considered for nPEP in women who are or who might become pregnant. See *Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States* for information regarding use of specific antiretrovirals during pregnancy.[114] Additionally, results from ongoing surveillance of major teratogenic effects related to antiretroviral use during pregnancy are described in the Antiretroviral Pregnancy Registry International Interim Report every 6 months.[115]

Certain antiretrovirals have been associated with severe side effects, toxicity, potential for teratogenicity, or other untoward effects among pregnant and non-pregnant women with HIV infection[114] and therefore are not recommended for nPEP use (see section VII-F2b. Pregnant Women and Women of Childbearing Potential for a list of antiretroviral medications that should not be used for nPEP in pregnant women). These include EFV, NVP, and d4T plus didanosine (DDI).[114] Using IDV without RTV-boosting demonstrated altered drug metabolism during pregnancy.[116,117] No severe side effects, toxicity, or adverse pregnancy outcomes have been reported to occur among HIV-uninfected women taking antiretrovirals for oPEP or nPEP.

Reports are conflicting regarding whether an association exists of substantial malformations with use of EFV during the first trimester among humans. Studies using cynomolgus monkeys reported a potential association between neurologic congenital malformations and first-trimester use of EFV.[118] Although case reports exist of neurologic defects among infants of women receiving EFV,[119,120] no elevated risk for overall congenital malformations associated with first-trimester EFV exposure have been reported in either prospectively reported pregnancies from the Antiretroviral Pregnancy Registry[115] or from a meta-analysis of 23 studies with birth outcomes from 2,026 live births among women receiving EFV during the first trimester.[121]

HIV-infected pregnant women receiving combination antiretroviral regimens that included NVP have been reported to suffer severe hepatic adverse events, including death. However, whether pregnancy increases the risk for hepatotoxic events associated with NVP therapy is unknown. Use of NVP in HIV-infected women (regardless of pregnancy status) with high CD4 counts > 250 cells/mm^3[102] or elevated transaminase levels at baseline[122] has been associated with potentially life-threatening rash and hepatotoxicity. NVP use in 3 HIV-infected women with CD4 counts <100 cells/mm^3 at baseline has been associated with death among those also taking anti-tuberculosis therapy.[122]

Among antiretroviral medication combinations no longer recommended, regimens containing d4T with DDI have been associated with severe maternal lactic acidosis among pregnant HIV-infected women,[123,124] including severe necrotic pancreatic and hepatic steatosis and necrotic cellulitis of the abdominal wall in 1 woman,[123] 1 fetal demise (normal for gestational age) at 38 weeks gestation,[124] and 1 postnatal death at age 2 weeks in a 1,000 gram infant with trisomy 18.[123] Additionally, using IDV without RTV-boosting during pregnancy results in substantially lower antepartum exposures of IDV, compared with use of RTV-boosted IDV.[116,117]

VI-D. Behavioral Intervention to Support Risk Reduction During nPEP Use

Study findings from 2 randomized control trials underscore the importance of combining nPEP with behavioral interventions[125] to support continuing risk reduction. In a randomized controlled counseling intervention trial among nPEP recipients at a single U.S. site, investigators compared behavioral effects among those who received 2 (standard) versus 5 (enhanced) risk-reduction counseling sessions. Both interventions were based on social cognitive theory, motivational interviewing, and coping effectiveness. Compared with baseline, a reduction occurred at 12 months in the reported number of condomless sex acts for both intervention arms. The group reporting ≤ 4 condomless sex acts during the previous 6 months at baseline benefitted more from the 2-session intervention, while persons reporting ≥ 5 condomless sex acts during the previous 6 months at baseline revealed a greater reduction of condomless sex acts after receiving the 5-session intervention.[126] These findings demonstrate that more counseling sessions might be necessary for persons reporting higher levels of sexual risk behavior when initiating nPEP. In another randomized control trial, MSM who received contingency management, a substance abuse intervention providing voucher-based incentives for stimulant-use abstinence, had greater nPEP completion rates, greater reductions in stimulant use, and fewer acts of condomless anal intercourse compared with control participants who received incentives that were not contingent on their substance abstinence.[127]

VI-E. Adherence to nPEP Regimens and Follow-up Visits

Difficulties in adherence have been noted in both maintaining adherence to daily doses of antiretroviral medication for 28 days among the majority of populations and adherence to follow-up clinical visits for HIV testing and other care. Such adherence difficulties appear particularly severe in studies of nPEP for sexually assaulted persons. Methods for measuring completion of nPEP medication regimen differed across studies, and loss to follow-up was a major hindrance to assessing medication adherence for the majority of studies.

In a systematic review and meta-analysis of 34 nPEP studies not including sexual assault and 26 nPEP studies including only sexual assault, nPEP completion rates were lowest among persons who experienced sexual assault (40.2% [95% CI = 31.2%, 49.2%]) and highest among persons who had other nonoccupational exposures (65.6% [95% CI = 55.6%, 75.6%]).[128] In a separate meta-analysis of 24 nPEP-related studies, including 23 cohort studies and 1 randomized behavioral intervention to improve nPEP adherence, of 2,166 sexually assaulted persons receiving nPEP and pooled across the 24 studies, 40.3% (95% CI = 32.5%–48.1%; range, 11.8%–73.9%) adhered to a 28-day course of nPEP, and 41.2% (95% CI = 31.1%–51.4%; range, 2.9%–79.7%) did not return to pick up their prescribed medication or did not return for follow-up appointments.[20] Medication adherence was measured in 24 studies by using varying methodology, including pill count, volume of syrup remaining, self-report, counts of number of pharmacy visits, recall of number of doses taken by notation on a calendar, number of prescriptions filled, and number of weekly clinic appointments kept. Reported medication adherence was lower in developed countries (n=15 studies, 5 countries)[23,30-32,36,38,46,50,58,88-92,94,97] compared with developing countries (n=8 studies, three countries)[40,42,85-87,93,95,96] (33.3% versus 53.2%, respectively; *P*=0.007), possibly due to higher awareness of HIV transmission risk in countries with a high HIV prevalence.[20] Eight of the 24 (33%) studies[30,32,46,86-89,97] provided nPEP medications at time of initiation of prophylaxis as starter packs including 4–7 days of medication, and 1 study provided either a starter pack of medications or a full 28-day supply of nPEP at initiation.[96] In this latter study, the proportion who adhered to the 28 days of nPEP was 29% for patients initially receiving the starter pack and 71% for patients receiving a full 28-day supply.[96]

Although sexually assaulted persons are sometimes at risk for HIV transmission, they often decline nPEP, and many who do take it do not complete the 28-day course. This pattern has been reported in multiple countries and in programs in North America. In Ontario, for example, 798 of 900 eligible sexually assaulted persons were offered nPEP, including 69 and 729 at high or unknown risk for HIV transmission due to the factors associated with their sexual assault, respectively.[23] Forty-six (67%) of 69 persons at high risk for HIV transmission and 301 (41%) of 729 persons with unknown risk accepted and initiated nPEP. Twenty-four percent of patients at high risk and 33% of patients with unknown risk completed the 28-day course. Reasons for discontinuing treatment were documented in 96 cases and included adverse effects (81%), interference with routine (42%), inability to take time away from work or school (22%), and reconsideration of HIV risk (19%).

Of the observational studies of sexually assaulted persons provided nPEP, the majority identified similar challenges. Studies have demonstrated that early discontinuation of medication and a lack of follow-up pose challenges to providing nPEP to sexually assaulted persons.[31,33,47,50]

Four international studies examined adherence among both men and women with non-assault sexual and injection drug use risk exposures.[46,48,49,51] Full medication adherence in these studies ranged from 60%–88%; 60%[48] and 79%[51] completed therapy (without specifying how completion was defined) and 67%[48] and 88%[49] completed 28 days or 4 weeks of nPEP. The proportion of MSM who adhered to nPEP medication for 28 days reported in those studies ranged from 42%–91%.

Studies that used a fixed dose combination of ZDV/3TC and LPV/r as primary components in the nPEP drug regimen reported low medication adherence for 28 days (24%–44%).[23,44,47] A study among MSM compared use of a fixed-dose combination regimen containing TDF/FTC with or without RAL (an integrase inhibitor) with ZDV/3TC and a RTV-boosted PI; adherence rates were superior for the TDF-containing regimens (57% [with RAL]–72.7% [without RAL]) compared with the PI-containing regimen (46%). Although 57% of the TDF/FTC/RAL arm reported taking their medications as directed, an additional 27% took their once daily medication, but sometimes missed their second daily dose of RAL.[57]

VI-F. nPEP Cost-effectiveness

Estimates of cost-effectiveness of nPEP as an HIV prevention method reported in the literature vary by HIV exposure route and estimated prevalence of infection among source persons. A study using data from the San Francisco nPEP program estimated the cost-effectiveness of hypothetical nPEP programs in each of the 96 metropolitan statistical areas in the United States.[129] It included 3 different data sources, including data from clinical care and drug cost data from the San Francisco Department of Public Health nPEP program,[130] estimates of the per-act probability of HIV transmission associated with different modes of sexual and parenteral HIV exposure,[131-133] and HIV prevalence data from 96 U.S. metropolitan statistical areas.[134] Investigators estimated the cost-effectiveness of hypothetical nPEP programs as an HIV prevention method in each area compared with no intervention. By defining cost-effective programs as those costing <$60,000/quality-adjusted life year (QALY), that study found nPEP programs were cost-effective across the combined metropolitan statistical areas with a cost utility ratio of $12,567/QALY saved (range, $4,147–$39,101). nPEP was most cost-effective for MSM ($4,907/QALY). It was not cost-effective for needle-sharing persons who inject drugs (PWID) ($97,867/QALY), persons sustaining nonoccupational needlesticks ($159,687/QALY), and receptive female partners ($380,891/QALY) or insertive male partners ($650,792/QALY) in penile-vaginal sex. The hypothetical nPEP program would be cost-saving (cost-utility ratio, <$0) only for men and women presenting with receptive anal intercourse or if nPEP use was limited to clients with known HIV-infected partners.[129] In another study limited to San Francisco, the overall cost-utility ratio for the existing nPEP program was $14,449/QALY saved and for men experiencing receptive anal sex, the nPEP program was cost-saving.[130]

Studies in Australia and France reported similar results. For example, in Australia, using a threshold for cost-effectiveness of $50,000/QALY, nPEP was cost-effective among persons having CAI with an HIV-infected source ($40,673/QALY).[135] In France, using thresholds for cost-saving and cost-effectiveness of €0/QALY saved and <€50,000/QALY saved, respectively, nPEP was cost-saving among men and women who had receptive anal intercourse with an HIV-infected man (-€22,141/QALY saved [men]; and -€22,031/QALY saved [women]) and cost-saving among PWID having shared needles with an HIV-infected person (-€1,141/QALY saved).[136]

Additionally, these same French and Australian studies, and a Swiss study, reported that HIV testing to determine the status of the source person (when possible) was determined to reduce costs associated with nPEP programs by avoiding unnecessary prophylaxis.[48,135,136]

VI-G. Attitudes, Policies, and Knowledge About nPEP Use Among Health Care Providers and Candidates for nPEP

Since 1997, certain health care providers, health policy makers, and scientific investigators of nPEP have recommended wider availability and/or use of nPEP,[24,131,137-144] while others have been more cautious about implementing it in the absence of definitive evidence of efficacy or effectiveness.[145,146] Multiple public health jurisdictions in the U.S., including the New York State AIDS Institute, the San Francisco County Health Department, the Massachusetts Department of Public Health, the Rhode Island Department of Health, and the California State Office of AIDS, have issued policies or advisories for nPEP use.[3,4,147,148]

Surveys of health care providers and facilities indicate a low level of awareness and capacity to provide nPEP as well as a lack of access for nPEP for those for whom it is recommended need for more widespread dissemination and implementation of guidelines and protocols for nPEP use and a need for improved access. In a study of 181 patients presenting to the emergency department (ED) who had been sexually assaulted, lack of insurance, older patient age, and acquaintance rape were factors associated with not being offered nPEP.[30] A study evaluating access to nPEP services in 117 health care sites in Los Angeles County through use of Internet

searches and telephone surveys, determined that only 14% offered nPEP to clients regardless of insurance status, and an even lower percentage, 8%, offered nPEP to uninsured clients, indicating the need to improve access to such services.[149] A survey in New York State (NYS) reported that among 184 EDs, 88% reported evaluating patients with possible nonoccupational exposures to HIV in accordance with NYS guidelines, however, full implementation of NYS nPEP guidelines was incomplete with 4% neither supplying nor prescribing antiretroviral drugs in the ED and only 22% confirming whether linkage to follow-up care was successful.[150] Screening of STIs, risk-reduction counseling, and education about symptoms of acute HIV seroconversion were not consistently performed according to the NYS guidelines.[150] Additionally, in a survey of 142 HIV health care providers in Miami and the District of Columbia, prescribing nPEP was associated with having patients request nPEP, or having a written nPEP protocol, although most providers reported not having a written nPEP protocol and that patients rarely or never requested nPEP.[151] Lack of prescribing nPEP was associated with believing that nPEP would lead to antiretroviral resistance.[151] More health care providers in the District of Columbia compared with those in Miami, prescribed nPEP (59.7% versus 39.5%, respectively $P < 0.048$).[152] In a cross-sectional study describing program practices related to HIV testing and nPEP among 174 sexual assault nurse examiner (SANE)/forensic nurse examiner (FNE) programs in the U.S. and Canada, 75% had nPEP policies, 31% provided HIV testing, and 63% offered nPEP routinely or based on patient request.[153] Medication cost was the most important barrier to providing nPEP in these programs.

Awareness, knowledge, and use of nPEP has been described among MSM.[14,15,106,108,110,154] Evidence indicates awareness of nPEP and interest in its use among potential patients. When nPEP studies were established in San Francisco, approximately 400 persons sought treatment during December 1997–March 1999.[106,154] In an HIV prevention trial of 4,295 MSM in 6 U.S. cities during 1999–2003, a total of 2,037 (47%) had heard of nPEP at baseline and 315 (7%) reported using nPEP on ≥1 occasion.[14] Predictors of nPEP use included having multiple partners, engagement in condomless sex with a known HIV-infected partner or with a partner of unknown HIV status, and use of illicit drugs. Among 1,427 MSM in a community cohort of HIV-negative men in Sydney, Australia, during 2001–2007, knowledge of nPEP increased from 78.5% at baseline to 97.4% by the fifth annual interview, and nPEP use increased from 2.9/100 person-years in 2002 to 7.1/100 person-years in 2007.[110] During 2006–2009, knowledge of nPEP among MSM from urban areas in the Netherlands increased from 46% to 73%.[108] Also, the annual number of PEP prescriptions to MSM in Amsterdam increased 3-fold, from 19 in 2000 to 69 in 2007.[15]

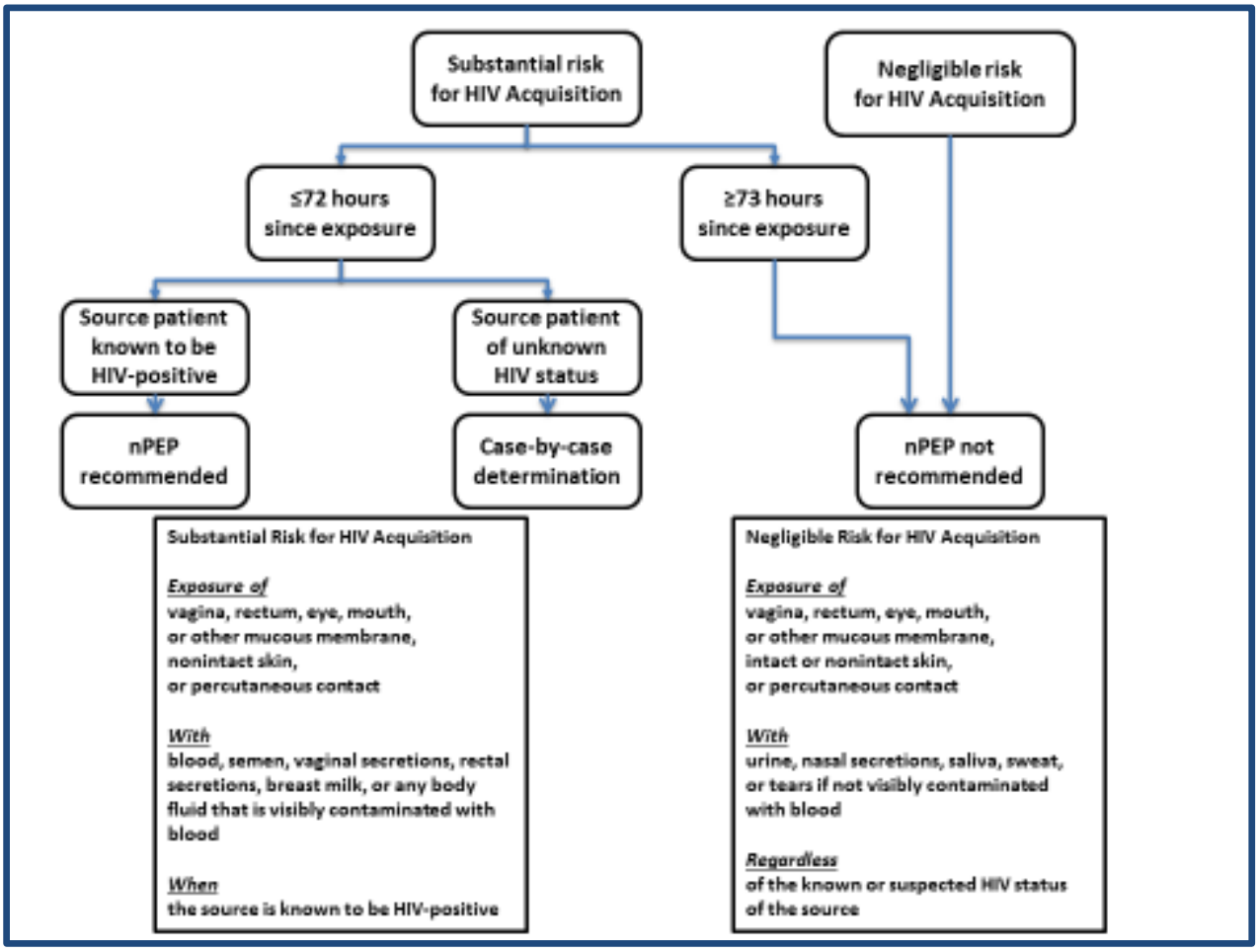
In a study of 227 pediatric and adolescent patients aged 9 months–18 years who were evaluated for sexual assault in Atlanta, Georgia, 40% of patients were examined ≤ 72 hours after the sexual assault, of whom 81% reported a history of genital or anal trauma.[41] In that study, patients aged 13–18 years and those who reported sexual assault by a stranger were more likely to present to the ED ≤ 72 hours after the sexual assault. Health care providers in the hospital's ED where this nPEP study was conducted expressed reluctance to prescribe nPEP to pre-pubertal children. For example, of 87 children and adolescents seen in the ED ≤ 72 hours after the assault, 23 had anogenital trauma or bleeding, and 5 were offered nPEP.

VII. Patient Management Guidelines

VII-A. Initial Evaluation of Persons Seeking Care After Potential Nonoccupational Exposure to HIV

Effective delivery of nPEP after exposures that carry a substantial risk for HIV infection requires prompt evaluation of patients and consideration of biomedical and behavioral interventions to address current and ongoing health risks. The initial evaluation provides the information necessary for determining if nPEP is indicated (Figure 1).

Figure 1. Algorithm for evaluation and treatment of possible nonoccupational HIV exposures



Procedures at the evaluation visit include determining the HIV infection status of the potentially exposed person and the source person (if available), the timing and characteristics of the exposure for which care is being sought, and the frequency of possible HIV exposures. Additionally, to determine whether other treatment or prophylaxis is indicated, health care providers should assess the likelihood of STIs, infections efficiently transmitted by injection practices or needlesticks (e.g., hepatitis B or hepatitis C virus), and pregnancy for women.

VII-A1. HIV Status of the Potentially Exposed Person

nPEP is only indicated for potentially exposed persons without HIV infection. Because potentially exposed persons might have acquired HIV infection already and be unaware of it, routine HIV antibody testing should

be performed on all persons seeking evaluation for potential nonoccupational HIV exposure. If possible, this should be done with an FDA-approved rapid antibody or Ag/Ab blood test kit with results available within an hour. If HIV blood test results will be unavailable during the initial evaluation visit, a decision whether nPEP is indicated should be made based on the initial assumption that the potentially exposed patient is not infected. If medication of HIV prophylaxis is indicated by the initial evaluation and started, it can be discontinued if the patient is later determined to already have HIV infection.

VII-A2. Timing and Frequency of Exposure

Available data from animal studies indicate that nPEP is most effective when initiated as soon as possible after HIV exposure; it is unlikely to be effective when instituted > 72 hours after exposure.[83] Therefore, persons should seek nPEP as soon as possible after an exposure that might confer substantial risk and health care providers should evaluate such patients rapidly and initiate nPEP promptly when indicated.

nPEP should be provided only for infrequent exposures. Persons who engage in behaviors that result in frequent, recurrent exposures that would require sequential or near-continuous courses of antiretroviral medications (e.g., HIV-discordant sex partners who inconsistently use condoms or PWID who often share injection equipment) should not be prescribed frequent, repeated courses of nPEP. Instead, health care providers should provide persons with repeated HIV exposure events (or coordinate referrals for) intensive sexual or injection risk-reduction interventions, and consider the prescription of daily oral doses of the fixed-dose combination of TDF and FTC (Truvada, Gilead Sciences, Inc., Foster City, California) for PrEP.[11] However, if the most recent recurring exposure is within the 72 hours prior to an evaluation, nPEP may be indicated with transition of the patient to PrEP after completion of 28 days of nPEP medication.

In the special case of children with evidence of chronic sexual abuse who come to the attention of a health care provider ≤ 72 hours after their most recent exposure, nPEP can be considered on a case-by-case basis. In addition, child protective services should be engaged for consideration of removal of the child from exposure to the perpetrator of the sexual abuse.

VII-A3. HIV Acquisition Risk from the Exposure

In addition to determining when the potential exposure occurred, determining whether nPEP is indicated requires assessing if the reported sexual, injection drug use, or other nonoccupational exposure presents a substantial risk for HIV acquisition. Health care providers should consider 3 main factors in making that determination: (1) whether the exposure source is known to have HIV infection, (2) to which potentially infected body fluid(s) the patient was exposed, and (3) the exposure site or surface.

The highest level of risk is associated with exposure of susceptible tissues to potentially infected body fluid(s) from persons known to have HIV infection, particularly those who are not on antiretroviral treatment. Persons with exposures to potentially infectious fluids from persons of unknown HIV status are at unknown risk for acquiring HIV infection. When the source of exposure is known to be from a group with a high prevalence of HIV infection (e.g., a man who has sex with men or a PWID who shares needles or other injection equipment), the risk for unrecognized HIV infection in the source is increased.

The estimated per-act transmission risk, when exposed to infectious fluid(s) from a person with HIV infection, varies considerably by exposure route (Table 1).[155] The highest estimated per-act risks for HIV transmission are associated with blood transfusion, needle sharing during injection drug use, receptive anal intercourse, and percutaneous needlestick injuries. Insertive anal intercourse, insertive penile-vaginal intercourse, and oral sex represent substantially lower per-act transmission risk.

Table 1. Estimated per-act risk for acquiring human immunodeficiency virus (HIV) from an infected source, by exposure act[a]

Exposure type	Rate for HIV acquisition per 10,000 exposures
Parenteral	
Blood transfusion	9,250
Needle sharing during injection drug use	63
Percutaneous (needlestick)	23
Sexual	
Receptive anal intercourse	138
Receptive penile-vaginal intercourse	8
Insertive anal intercourse	11
Insertive penile-vaginal intercourse	4
Receptive oral intercourse	Low
Insertive oral intercourse	Low
Other[b]	
Biting	Negligible
Spitting	Negligible
Throwing body fluids (including semen or saliva)	Negligible
Sharing sex toys	Negligible

Source: http://www.cdc.gov/hiv/policies/law/risk.html

[a] Factors that may increase the risk of HIV transmission include sexually transmitted diseases, acute and late-stage HIV infection, and high viral load. Factors that may decrease the risk include condom use, male circumcision, antiretroviral treatment, and preexposure prophylaxis. None of these factors are accounted for in the estimates presented in the table.

[b] HIV transmission through these exposure routes is technically possible but unlikely and not well documented.

A history should be taken of the specific sexual, injection drug use, or other exposure events that can lead to acquiring HIV infection. Eliciting a complete description of the exposure and information about the HIV status of the partner(s) can substantially lower (e.g., if the patient was exclusively the insertive partner or a condom was used) or increase (e.g., if the partner is known to be HIV-positive) the estimate of risk for HIV transmission resulting from a specific exposure.

Percutaneous injuries from needles discarded in public settings (e.g., parks and buses) sometimes result in requests for nPEP. Although no HIV infections from such injuries have been documented, concern exists that syringes discarded by PWID might pose a substantial risk. However, such injuries typically involve small-bore needles that contain only limited amounts of blood, and the infectiousness of any virus present might be low.[156,157] Saliva that is not contaminated with blood contains HIV in much lower titers and constitutes a negligible exposure risk,[158] but saliva that is contaminated with HIV-infected blood poses a substantial exposure risk. HIV transmission by this route has been reported in ≥ 4 cases.[159-162]

VII-A4. HIV Status of the Exposure Source

When the exposure source's HIV status is unknown, that person's availability for HIV testing should be determined. When the source person is available and consents to HIV testing, a clinical evaluation visit should be arranged that includes HIV testing by using a fourth-generation combined Ag/Ab test. The risk for transmission might be especially great if the source person has been infected recently because the viral burden in blood and semen might be particularly high.[163,164] However, ascertaining this in the short time available for the initial nPEP evaluation might not be possible. If the risk associated with the exposure is high, starting nPEP and then making a decision whether to continue nPEP after the source's HIV status is determined is recommended.

If the exposure source is known to have HIV infection at the time of the nPEP evaluation visit and consents, the health care provider should attempt to interview that person or that source person's health care provider to determine the history of antiretroviral use and most recent viral load. That information might help guide the choice of nPEP medications to avoid prescribing antiretroviral medications to which the source-virus is likely to be resistant. If the person with HIV infection is willing, the clinician might consider drawing blood for viral load and resistance testing, the results of which might be useful in modifying the initial nPEP medications if the results can be obtained promptly.[165]

VII-B. Laboratory Testing

Laboratory testing is required to (1) document the HIV infection status of the person presenting for nPEP evaluation (and the exposure source when available and consent has been granted), (2) identify and clinically manage any other conditions potentially resulting from sexual- or injection-related exposure to potentially infected body fluids, (3) identify any conditions that would affect the nPEP medication regimen, and (4) monitor for safety or toxicities related to the regimen prescribed (Table 2).

Table 2. Recommended schedule of laboratory evaluations of source and exposed persons for providing nPEP with preferred regimens

Test	Source	Exposed persons			
	Baseline	Baseline	4–6 weeks after exposure	3 months after exposure	6 months after exposure
		For all persons considered for or prescribed nPEP for any exposure			
HIV Ag/Ab testing[a] (or antibody testing if Ag/Ab test unavailable)	✓	✓	✓	✓	✓[b]
Hepatitis B serology, including: hepatitis B surface antigen hepatitis B surface antibody hepatitis B core antibody	✓	✓	—	—	✓[c]
Hepatitis C antibody test	✓	✓	—	—	✓[d]
		For all persons considered for or prescribed nPEP for sexual exposure			
Syphilis serology[e]	✓	✓	✓	—	✓
Gonorrhea[f]	✓	✓	✓[g]	—	—
Chlamydia[f]	✓	✓	✓[g]	—	—
Pregnancy[h]	—	✓	✓	—	—
		For persons prescribed tenofovir DF+ emtricitabine + raltegravir or tenofovir DF+ emtricitabine + dolutegravir			
Serum creatinine (for calculating estimated creatinine clearance[i])		✓	✓	—	—
Alanine transaminase, aspartate aminotranferase		✓	✓	—	—
	For all persons with HIV infection confirmed at any visit				
HIV viral load	✓	✓[j]			
HIV genotypic resistance	✓	✓[j]			

Abbreviations: Ag/Ab, antigen/antibody combination test; HIV, human immunodeficiency virus; nPEP, nonoccupational postexposure prophylaxis; tenofovir DF, tenofovir disoproxil fumarate.

[a] Any positive or indeterminate HIV antibody test should undergo confirmatory testing of HIV infection status.

[b] Only if hepatitis C infection was acquired during the original exposure; delayed HIV seroconversion has been seen in persons who simultaneously acquire HIV and hepatitis C infection.

[c] If exposed person susceptible to hepatitis B at baseline.

[d] If exposed person susceptible to hepatitis C at baseline.

[e] If determined to be infected with syphilis and treated, should undergo serologic syphilis testing 6 months after treatment

[f] Testing for chlamydia and gonorrhea should be performed using nucleic acid amplification tests. For patients diagnosed with a chlamydia or gonorrhea infection, retesting 3 months after treatment is recommended.

- For men reporting insertive vaginal, anal, or oral sex, a urine specimen should be tested for chlamydia and gonorrhea.
- For women reporting receptive vaginal sex, a vaginal (preferred) or endocervical swab or urine specimen should be tested for chlamydia and gonorrhea.
- For men and women reporting receptive anal sex, a rectal swab specimen should be tested for chlamydia and gonorrhea.
- For men and women reporting receptive oral sex, an oropharyngeal swab should be tested for gonorrhea. (http://www.cdc.gov/std/tg2015/tg-2015-print.pdf)

[g] If not provided presumptive treatment at baseline, or if symptomatic at follow-up visit.

[h] If woman of reproductive age, not using effective contraception, and with vaginal exposure to semen.

[i] eCrCl = estimated creatinine clearance calculated by the Cockcroft-Gault formula; eCrClCG = [(140 − age) x ideal body weight] ÷ (serum creatinine x 72) (x 0.85 for females).

[j] At first visit where determined to have HIV infection.

VII-B1. HIV Testing

All patients initiating nPEP after potential HIV exposure should be tested for the presence of HIV-1 and HIV-2 antigens and antibodies in a blood specimen at baseline (before nPEP initiation), preferably using a rapid test. Patients with baseline rapid tests indicating existing HIV infection should not be started on nPEP. Patients for whom baseline HIV rapid test results indicate no HIV infection or rapid HIV test results are not available should be offered nPEP. There should be no delay in initiation of nPEP while awaiting baseline HIV test results. Repeat HIV testing should occur at 4–6 weeks and 3 months after exposure to determine if HIV infection has occurred. See http://www.cdc.gov/hiv/testing/laboratorytests.html regarding information on approved HIV tests. Oral HIV tests are not recommended for use among persons being evaluated for nPEP.

Additionally, persons whose sexual or injection-related exposures results in concurrent acquisition of HCV and HIV infection might have delayed HIV seroconversion. This has been documented among MSM with sexual exposure[13] and health care personnel receiving oPEP for needlestick exposures.[166,167] Therefore, for any person whose HCV antibody test is negative at baseline but positive at 4–6 weeks after the exposure, HIV antibody tests should be conducted at 3 and 6 months to rule out delayed seroconversion (see Table 2).

VII-B2. Recognizing Acute HIV Infection at Time of HIV Seroconversion

Persons initiating nPEP, if it fails, may experience signs and symptoms of acute HIV infection while on nPEP. At the initial visit, patients should be instructed about the signs and symptoms associated with acute (primary) HIV infection (Table 3), especially fever and rash,[168] and asked to return for evaluation if these occur during the 28 days of prophylaxis or anytime within a month after nPEP concludes.

Table 3. Clinical signs and symptoms of acute (primary) human immunodeficiency virus infection[169,170]

		Sex		Mode of HIV acquisition	
Features	**Overall (n = 375), %**	**Male (n = 355), %**	**Female (n = 23), %**	**Sexual (n = 324), %**	**Injection drug use (n = 34), %**
Fever	75	74	83	77	50
Fatigue	68	67	78	71	50
Myalgia	49	50	26	52	29
Skin rash	48	48	48	51	21
Headache	45	45	44	47	30
Pharyngitis	40	40	48	43	18
Cervical adenopathy	39	39	39	41	27
Arthralgia	30	30	26	28	26
Night sweats	28	28	22	30	27
Diarrhea	27	27	21	28	23

Acute HIV infection is associated with high viral load. However, health care providers should be aware that available assays might yield low viral-load results (e.g., <3,000 copies/ml) among persons without HIV infection (i.e., false-positives). Without confirmatory tests, such false-positive results can lead to misdiagnoses of HIV infection.[171] Transient, low-grade viremia has been observed among persons exposed to HIV who were

administered antiretroviral nPEP[172] and did not become infected. In certain cases, this outcome might represent aborted infection rather than false-positive test results, but this can be determined only through further testing.

All patients who have begun taking nPEP and for whom laboratory evidence later confirms acute HIV infection at baseline or whose follow-up antibody testing indicates HIV infection, should be transferred rapidly to the care of an HIV treatment specialist (if nPEP was provided by another type of health care provider). If the patient is taking a 3-drug antiretroviral regimen for nPEP at the time of HIV infection diagnosis, the 3-drug regimen should not be discontinued by the nPEP provider until the patient has been evaluated and a treatment plan initiated by an experienced HIV care provider.[173]

VII-B3. STI Testing

Any sexual exposure that presents a risk for HIV infection might also place a person at risk for acquiring other STIs.[174] For all persons evaluated for nPEP because of exposure during sexual encounters, STI-specific nucleic acid amplification (NAAT) testing is recommended for gonorrhea and chlamydia,[174] by testing first-catch urine or with swabs collected from each mucosal site exposed to potentially infected body fluids (oral, vaginal, cervical, urethral, rectal).[174,175] Additionally, blood tests for syphilis should be conducted for all persons evaluated for nPEP.

VII-B4. HBV Testing

HBV infection is of specific concern when considering nPEP for 2 reasons. First, multiple medications used for nPEP, including 2 in the preferred regimen (TDF and FTC) are active against HBV infection. For safety reasons, health care providers need to know if a patient has active HBV infection (positive hepatitis B surface antigen [HBsAg]) so that the patient can be closely monitored for reactivation "flare ups" when nPEP is stopped, and treatment for HBV infection is discontinued. Although this is rare, it can result in substantial hepatic dysfunction if not detected and treated early. Additionally, obtaining hepatitis serology (HBsAg, hepatitis B surface antibody [anti-HBs], and hepatitis B core antibody [anti-HBc]) will identify nonimmune persons who should be provided hepatitis B vaccination Table 4).[176]

Table 4. Hepatitis B virus screening serology[177]

HBsAg	Anti-HBc	Anti-HBs	IgM Anti-HBc	Interpretation	Action
Negative	Negative	Negative	—	Susceptible	Vaccinate
Negative	Positive	Positive	—	Immune (natural infection)	Document
Negative	Negative	Positive	—	Immune (prior vaccination)	Document
Positive	Positive	Negative	Negative	Chronic hepatitis B virus infection	Evaluate for treatment
Positive	Positive	Negative	Positive	Acute hepatitis B virus infection	Follow and evaluate for treatment
Negative	Positive	Negative	—	Unclear—might be: • resolved infection (most common) • false-positive anti-HBc; susceptible • "low level" chronic infection • resolving acute infection	Case-by-case evaluation
Abbreviations: HBsAg, hepatitis B surface antigen; anti-HBc, hepatitis B core antibody; anti-HBs, hepatitis B surface antibody.					

VII-B5. Pregnancy Testing

nPEP is not contraindicated for pregnant women. Moreover, because pregnancy has been demonstrated to increase susceptibility to sexual HIV acquisition,[178] nPEP can be especially important for women who are pregnant at the time of sexual HIV exposure.

For women of reproductive capacity who have had genital exposure to semen and a negative pregnancy test when evaluated for possible nPEP, current contraception use should be assessed, and if a risk for pregnancy exists, emergency contraception should be discussed with the patient.

VII-B6. Baseline and Follow-up Testing to Assess Safety of Antiretroviral Use for nPEP

All patients who will be prescribed nPEP should have serum creatinine measured and an estimated creatinine clearance calculated at baseline to guide selection of a safe and appropriate antiretroviral regimen for nPEP. Also, health care providers treating patients with nPEP should monitor liver function, renal function, and hematologic parameters when indicated by the prescribing information for the antiretrovirals prescribed. Drug-specific recommendations are available at the online AIDS*Info* Drugs Database at: http://aidsinfo.nih.gov/drugs or the antiretroviral treatment guidelines.[114,173,179]

Unusual or severe toxicities from antiretroviral drugs should be reported to the manufacturer or FDA (http://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm, or 1-800-FDA-1088 [1-800-332-1088]).

If nPEP is prescribed to a woman who is pregnant at the time of exposure or becomes pregnant while on nPEP, health care providers should enter the patient's information (anonymously) into the Antiretroviral Pregnancy Registry (http://www.apregistry.com).

VII-C. Recommended Antiretroviral nPEP Regimens

A 28-day course of nPEP is recommended for HIV-uninfected persons who seek care ≤ 72 hours after a nonoccupational exposure to blood, genital secretions, or other potentially infected body fluids of persons known to be HIV infected or of unknown HIV status when that exposure represents a substantial risk for HIV acquisition. Since adherence is critical for nPEP efficacy, it is preferable to select regimens that minimize side effects, number of doses per day and the number of pills per dose.

No strong evidence exists, based on randomized clinical trials, that any specific combination of antiretroviral medication is optimal for nPEP use. Although a limited number of studies have evaluated the penetration of antiretroviral medications into genital tract secretions and tissues,[180-182] evidence is insufficient for recommending a specific antiretroviral medication as most effective for nPEP for sexual exposures. Therefore, the recommended regimens for nPEP in these guidelines are based on expert opinion from the accumulated experience with antiretroviral combinations that effectively suppress viral replication among HIV-infected persons for the purpose of HIV treatment and mainly observational studies of the medication tolerance and adherence when these same drugs are taken for nPEP.

The recommendation for a 3-drug antiretroviral regimen is based on extrapolation of data demonstrating that the maximal suppression of viral replication occurs among persons with HIV infection when combination antiretroviral therapy with ≥3 drugs is provided. Also, the likelihood of protection against acquiring resistant virus would be greater with a 3-drug regimen compared with a 2-drug regimen. Recommending a 3-drug regimen for all patients who receive nPEP will increase the likelihood of successful prophylaxis in light of potential exposure to virus with resistance mutation(s) and will provide consistency across PEP guidelines for

both nPEP and oPEP.[2] Additionally, if infection occurs despite nPEP, a 3-drug regimen will more likely limit emergence of resistance than a 2-drug regimen.

Table 5. Preferred and alternative antiretroviral medication 28-day regimens for nPEP[a,b]

Age group	Preferred/ alternative	Medication
Adults and adolescents aged ≥ 13 years, including pregnant women, with normal renal function (creatinine clearance ≥ 60 mL/min)	**Preferred**	A 3-drug regimen consisting of tenofovir DF 300 mg ***and*** fixed dose combination emtricitabine 200 mg (Truvada[c]) once daily ***with*** raltegravir 400 mg twice daily ***or*** dolutegravir 50 mg once daily
	Alternative	A 3-drug regimen consisting of tenofovir DF 300 mg ***and*** fixed dose combination emtricitabine 200 mg (Truvada) once daily ***with*** darunavir 800 mg (as 2, 400-mg tablets) once daily ***and*** ritonavir[b] 100 mg once daily
Adults and adolescents aged ≥ 13 years with renal dysfunction (creatinine clearance ≤59 mL/min)	**Preferred**	A 3-drug regimen consisting of zidovudine ***and*** lamivudine, with both doses adjusted to degree of renal function ***with*** raltegravir 400 mg twice daily ***or*** dolutegravir 50 mg once daily
	Alternative	A 3-drug regimen consisting of zidovudine ***and*** lamivudine, with both doses adjusted to degree of renal function ***with*** darunavir 800 mg (as 2, 400-mg tablets) once daily ***and*** ritonavir[b] 100 mg once daily
Children aged 2–12 years	**Preferred**	A 3-drug regimen consisting of tenofovir DF, emtricitabine, and raltegravir, with each drug dosed to age and weight[d]
	Alternative	A 3-drug regimen consisting of zidovudine ***and*** lamivudine ***with*** raltegravir ***or*** lopinavir/ritonavir[b], with raltegravir and lopinavir/ritonavir dosed to age and weight[d]
	Alternative	A 3-drug regimen consisting of tenofovir DF ***and*** emtricitabine ***and*** lopinavir/ritonavir[b], with each drug dosed to age and weight[d]

Age group	Preferred/ alternative	Medication
Children aged 3–12 years	Alternative	A 3-drug regimen consisting of tenofovir DF **and** emtricitabine **and** darunavir[e]/ritonavir[b], with each drug dosed to age and weight[d]
Children aged 4 weeks[f]–< 2 years	**Preferred**	A 3-drug regimen consisting of zidovudine oral solution ***and*** lamivudine oral solution ***with*** raltegravir ***or*** lopinavir/ritonavir[b] oral solution (Kaletra[g]), with each drug dosed to age and weight[d]
Children aged 4 weeks[f]–< 2 years	Alternative	A 3-drug regimen consisting of zidovudine oral solution ***and*** emtricitabine oral solution ***with*** raltegravir ***or*** lopinavir/ritonavir[b] oral solution (Kaletra), with each drug adjusted to age and weight[d]
Children aged birth–27 days	Consult a pediatric HIV-specialist	

Abbreviations: HIV, human immunodeficiency virus; nPEP, nonoccupational postexposure prophylaxis; tenofovir DF, tenofovir disoproxil fumarate.

[a] These recommendations do not reflect current Food and Drug Administration-approved labeling for antiretroviral medications listed in this table.

[b] Ritonavir is used in clinical practice as a pharmacokinetic enhancer to increase the trough concentration and prolong the half-life of darunavir, lopinavir, and other protease inhibitors. Ritonavir is not counted as a drug directly active against HIV in the above "3-drug" regimens.

[c] Gilead Sciences, Inc., Foster City, California.

[d] See also Table 6.

[e] Darunavir only FDA-approved for use among children aged ≥ 3 years.

[f] Children should have attained a postnatal age of ≥ 28 days and a postmenstrual age (i.e., first day of the mother's last menstrual period to birth plus the time elapsed after birth) of ≥ 42 weeks.

[g] AbbVie, Inc., North Chicago, Illinois.

Table 6. Formulations, cautions, and dose adjustments for antiretroviral medications in preferred and alternative nPEP regimens[a]

Drug	Formulation	Side effects, contraindications, and cautions	Dose adjustments
Tenofovir disoproxil fumarate (TDF) (Viread, Gilead Sciences, Inc., Foster City, California) Also available as component of fixed-dose combination, Truvada (Gilead Sciences, Inc., Foster City, California) (emtricitabine + TDF)	150-mg tablet 200-mg tablet 250-mg tablet 300-mg tablet 40-mg/gm powder	**Side effects:** Asthenia, headache, diarrhea, nausea, vomiting **Contraindications:** Nephrotoxicity; for nPEP, should not be administered to persons with acute or chronic kidney injury or those with eCrCl < 60 mL/min **Cautions:** TDF can be used in nPEP regimens for patients with chronic hepatitis B infection, but hepatic function tests should be closely monitored when regimen is stopped because withdrawal of this drug may cause an acute hepatitis exacerbation.	**Children aged 2–11 years (powder)** • 8 mg/kg body weight • Not to exceed adult dose (300 mg qd) **Children aged 2–11 years (tablet), per body weight** • 17 to < 22 kg, 150 mg-tablet once daily • 22 to < 28 kg, 200 mg-tablet once daily • 28 to < 35 kg, 250-mg tablet once daily • ≥ 35 kg, 300-mg tablet once daily • Not to exceed adult dose (300 mg once daily)
Emtricitabine (FTC) (Emtriva, Gilead Sciences, Inc., Foster City, California) Also available as component of fixed-dose combination, Truvada (FTC + TDF)	200-mg capsule 10-mg/mL oral solution	**Side effects:** Hyperpigmented rash or skin discoloration **Cautions:** FTC can be used in nPEP regimens for patients with chronic hepatitis B infection, but hepatic function tests should be closely monitored when regimen is stopped because withdrawal of this drug might cause an acute hepatitis exacerbation. **Contraindications:** Do not administer with lamivudine	**Children aged 0–3 months (oral solution)** • 3 mg/kg once daily • Not to exceed 240 mg once daily **Children aged 3 months–17 years, per body weight** • 6 mg/kg once daily (oral solution) • ≥ 33 kg 200-mg tablet once daily • Not to exceed 240 mg once daily
Raltegravir (RAL) (Isentress, Merck & Co., Inc., Kenilworth, New Jersey)	400-mg tablet 100-mg chewable, scored tablet 25-mg chewable tablet	**Side effects:** Insomnia, nausea, fatigue, headache; severe skin and hypersensitivity reactions have been reported **Cautions:** Dosage adjustment required if co-administered with rifampin (800 mg twice daily for adults). Co-administration with antacids, laxatives, or other products containing polyvalent cations (Mg, Al, Fe, Ca, Zn), including iron, calcium, or magnesium supplements; sucralfate; buffered medications; and certain oral multivitamins can reduce absorption of RAL. RAL should be administered ≥ 2 hours before or ≥ 6 hours after administration of cation-containing medications or products, however, RAL can be co-administered with calcium carbonate-containing antacids.[154] **Contraindications:** None	**Children aged 6–12 years and weighing > 25 kg** • 400 mg-tablet twice daily **Or** • Chewable tablets twice daily. See table below for chewable tablet dose. **Children aged 2–12 years (chewable tablets), per body weight** • 11 to < 14 kg, 75-mg twice daily • 14 to < 20 kg, 100-mg twice daily • 20 to < 28 kg, 150-mg twice daily • 28 to < 40 kg, 200-mg twice daily • ≥ 40 kg, 300-mg twice daily

Drug	Formulation	Side effects, contraindications, and cautions	Dose adjustments
Dolutegravir (DTG) (Tivicay, ViiV Healthcare, Brentford, Middlesex, United Kingdom)	50-mg tablet	**Side effects:** Insomnia, headache **Cautions:** Dosage adjustment required if co-administered with rifampin, fosamprenavir/ritonavir, tipranvir/ritonavir, or efavirenz (50 mg twice daily for adults). Co-administration with antacids, laxatives, or other products containing polyvalent cations (Mg, Al, Fe, Ca, Zn), including iron, calcium, or magnesium supplements; sucralfate; buffered medications; and some oral multivitamins can reduce absorption of DTG. DTG should be administered ≥ 2 hours before or at ≥ 6 hours after administration of cation-containing medications or products.[151] **Contraindications:** Do not administer with dofetilide.	**Children aged 12 years old and older and weighing ≥ 40 kg** • 50-mg tablet once daily
Darunavir (DRV)/ritonavir(RTV) (Prezista, Janssen Therapeutics, Titusville, New Jersey)	75-mg tablet 150-mg tablet 400-mg tablet 600-mg tablet 100-mg/mL oral suspension	**Side effects:** Rash (sulfonamide allergy), diarrhea, nausea, headache **Cautions:** Must be administered with food; must be co-administered with ritonavir; can cause hepatotoxicity. Use with caution with persons with known allergy to sulfonamide medications **Contraindications:** Co-administration of ritonavir with certain sedative hypnotics, antiarrhythmics, sildenafil, or ergot alkaloid preparations is contraindicated and might result in potentially life-threatening adverse events.	**Children aged 3 to < 18 years and weight > 10 kg** WEIGHT (KG) — DOSE (TWICE DAILY WITH FOOD) 10 to < 11 kg* — darunavir 200 mg (2.0 mL) plus ritonavir 32 mg (0.4 mL†) 11 to < 12 kg* — darunavir 220 mg (2.2 mL) plus ritonavir 32 mg (0.4 mL†) 12 to < 13 kg* — darunavir 240 mg (2.4 mL) plus ritonavir 40 mg (0.5 mL†) 13 to < 14 kg* — darunavir 260 mg (2.6 mL) plus ritonavir 40 mg (0.5 mL†) 14 to < 15 kg* — darunavir 280 mg (2.8 mL) plus ritonavir 48 mg (0.6 mL†) 15 to < 30 kg — darunavir 375 mg (combination of tablets or 3.8 mL‡) plus ritonavir 48 mg (0.6 mL†) 30 to < 40 kg — darunavir 450 mg (combination of tablets or 4.6 mL‡) plus ritonavir 100 mg (tablet or 1.25 mL†) ≥ 40 kg — darunavir 600 mg (tablet or 6 mL) plus ritonavir 100 mg (tablet or 1.25 mL†) * The dose in children weighing 10–15 kg is 20 mg/kg darunavir and 3 mg/kg ritonavir per kg body weight per dose, which is higher than the weight-adjusted dose in children with higher weight. † Ritonavir 80 g/mL oral solution ‡ The 375-mg and 450-mg darunavir doses are rounded for suspension-dose convenience.

Drug	Formulation	Side effects, contraindications, and cautions	Dose adjustments
Lopinavir (LPV)/ritonavir (RTV) (Kaletra, AbbVie Inc., North Chicago, Illinois)	200/50-mg tablets 100/25-mg tablets 80/20-mg/mL oral solution	**Side effects:** Nausea, vomiting, diarrhea **Cautions:** PR and QT interval prolongation have been reported. Use with caution with patients at risk for cardiac conduction abnormalities or receiving other drugs with similar effect. Do not administer to neonates before a postmenstrual age (first day of the mother's last menstrual period to birth plus the time elapsed after birth) of ≥ 42 weeks and a postnatal age of ≥ 14 days. **Contraindications:** Co-administration of ritonavir with certain sedative hypnotics, antiarrhythmics, sildenafil, or ergot alkaloid preparations is contraindicated and might result in potentially life-threatening adverse events.	**Children aged 14 days–12 months, per body weight** Suspension (lopinavir/ritonavir) • 16/4 mg/kg or 300/75 mg/m^2 twice daily **Children aged > 12 months–18 years, per body weight** Suspension (lopinavir/ritonavir) • < 15 kg, 12/3 mg/kg twice daily • ≥ 15 kg to 40 kg, 10/2.5 mg/kg twice daily • > 40 kg, 400/100 mg twice daily • not to exceed the recommended adult dose (400/100 mg [5 mL] twice daily **Children aged > 12 months–18 years** Tablet, weight-based dosing (lopinavir/ritonavir) • 15 to 25 kg, 2 100/25-mg tablets twice daily • > 25 to 35 kg, 3 100/25-mg tablets twice daily • > 35 kg, 4 100/25-mg tablets twice daily or 2 200/50-mg tablets twice daily
Ritonavir[b](RTV) (Norvir, AbbVie, Inc., North Chicago, Illinois)	100-mg tablets 100-mg soft gelatin capsules 80-mg/mL oral solution	**Side effects:** Abdominal pain, asthenia, headache, malaise, anorexia, diarrhea, dyspepsia, nausea, vomiting, circumoral paresthesia, peripheral paresthesia, dizziness, and taste perversion. **Cautions:** PR and QT interval prolongation have been reported. Use with caution with patients at risk for cardiac conduction abnormalities or receiving other drugs with similar effect. Can cause hepatotoxicity, pancreatitis, or hyperglycemia **Contraindications:** Co-administration of ritonavir with certain sedative hypnotics, antiarrhythmics, sildenafil, or ergot alkaloid preparations is contraindicated and might result in potentially life-threatening adverse events.	• See pediatric dosage for use as a boosting agent with darunavir or lopinavir in respective darunavir and lopinavir sections of this table.

Drug	Formulation	Side effects, contraindications, and cautions	Dose adjustments
Zidovudine (ZDV; AZT) (Retrovir, ViiV Healthcare, Brentford, Middlesex, United Kingdom)	100-mg capsule 300-mg tablet 10-mg/mL oral syrup 10-mg/mL intravenous infusion	**Side effects:** Nausea, vomiting, headache, insomnia, and fatigue **Cautions:** Can cause anemia and neutropenia	**Infants aged birth–41 days** **Full term (aged ≥ 35 weeks gestation at birth), per body weight** Syrup • 4 mg/kg orally twice daily Intravenous[c] • 3.0 mg/kg, infused over 30 minutes, every 12 hours **Premature (aged ≥ 30 to 35 weeks gestation at birth; from birth through day 14 of life; switch to full term infant dose at 15 days of life), per body weight** Syrup • 2 mg/kg orally twice daily Intravenous[c] • 1.5 mg/kg, infused over 30 minutes, every 12 hours **Premature (aged < 30 weeks gestation at birth; day 14–28 of life; switch to full term infant dose at 29 days* of life), per body weight** Syrup • 2 mg/kg orally twice daily Intravenous[c] • 1.5 mg/kg, infused over 30 minutes, every 12 hours **Infants and children aged ≥35 weeks post-conception and at least 4 weeks post-delivery, per body weight** Syrup or Capsules • 4 to < 9 kg, 12 mg/kg twice daily • 9 to < 30 kg, 9 mg/kg twice daily Tablet • ≥ 30 kg, 300-mg tablet twice daily * Note: Premature infants exposed to HIV after day 1 of life are switched to full-term infant dose at 29 days of life.

Drug	Formulation	Side effects, contraindications, and cautions	Dose adjustments
Lamivudine (3TC) (Epivir, ViiV Healthcare, Brentford Middlesex, United Kingdom)	150-mg scored tablet 100-mg tablet 300-mg tablet 10-mg/mL oral solution	**Side effects:** Headache, nausea, malaise and fatigue, nasal signs and symptoms, diarrhea, and cough **Cautions:** 3TC may be used in nPEP regimens for patients with chronic hepatitis B infection, but hepatic function tests should be closely monitored when regimen is stopped since withdrawal of this drug may cause an acute hepatitis exacerbation. **Contraindications:** Do not administer with emtricitabine	**Neonates and infants, aged ≤ 27 days** Oral solution • 2 mg/kg twice daily **Children, aged ≥ 4 weeks** Oral solution • 4 mg/kg (maximum dose 150 mg) twice daily **Children aged < 16 years and weighing ≥ 14 kg** Scored 150-mg tablet • 14 to < 20 kg, 75 mg (1/2 tablet) AM + 75 mg (1/2 tablet) PM • 20 to < 25 kg, 75 mg (1/2 tablet) AM + 150 mg (1 tablet) PM • ≥ 25 kg, 150 mg tablet twice daily **Adolescents (aged ≥ 16 years) and adults, per body weight** • < 50 kg, 4 mg/kg (up to 150 mg) twice daily • ≥ 50 kg, 150 mg twice daily or 300 mg once daily

Abbreviations: eCrCl = estimated creatinine clearance calculated by the Cockcroft-Gault formula; eCrClCG = [(140 − age) x ideal body weight] ÷ (serum creatinine x 72) (x 0.85 for females); nPEP, nonoccupational postexposure prophylaxis.

[a] For most current dosing regimens for treatment naïve children, see 1) AIDSInfo Drugs Database at http://aidsinfo.nih.gov/drugs, 2) Drugs@FDA (FDA approved drug products index) at http://www.accessdata.fda.gov/scripts/cder/drugsatfda/, 3) Pediatric ARV treatment guidelines at http://aidsinfo.nih.gov/guidelines/html/2/pediatric-treatment-guidelines/0#, and 4) Perinatal guidelines at http://aidsinfo.nih.gov/guidelines/html/3/perinatal-guidelines/0

[b] Ritonavir is used in clinical practice as a pharmacokinetic enhancer to increase the trough concentration and prolong the half-life of darunavir, lopinavir, and other protease inhibitors

[c] Infants unable to receive oral dosing may receive intravenous dosing

Health care providers might consider using antiretroviral regimens for nPEP other than those listed as preferred or alternative because of patient-specific information (e.g., an HIV-infected exposure source with known drug-resistance or contraindications to ≥1of the antiretrovirals in a preferred regimen). In those cases, health care providers are encouraged to seek consultation with other health care providers knowledgeable in using antiretroviral medications for similar patients (e.g., children, pregnant women, those with comorbid conditions) (Appendix 4).

> Providers should be aware that abacavir sulfate (Ziagen, ViiV Healthcare, Brentford, Middlesex, United Kingdom) should not be prescribed in any nPEP regimen. Prompt initiation of nPEP does not allow time for determining if a patient has the *HLA-B*5701* allele, the presence of which is strongly associated with a hypersensitivity syndrome that can be fatal.[183]

Health care providers and patients who are concerned about potential adherence and toxicity or the additional cost associated with a 3-drug antiretroviral regimen might consider using a 2-drug regimen (i.e., a combination of 2 NRTIs or a combination of a PI and a NNRTI). However, this DHHS guideline recommends a 3-drug regimen in all cases when nPEP is indicated.

VII-D. Prophylaxis for STIs and Hepatitis

All adults and adolescents with exposures by sexual assault should be provided with prophylaxis routinely for STIs and HBV,[174] as follows:

- For gonorrhea, (male and female adults and adolescents),
  - ceftriaxone 250 mg intermuscular, single dose;
  - ***plus*** azithromycin, 1 g, orally, single dose;
- For chlamydia (male and female adults and adolescents),
  - azithromycin, 1 g, orally, single dose
  - ***or*** doxycycline, 100 mg, orally, twice a day for 7 days.
- For trichomonas (female adults and adolescents),
  - metronidazole, 2 g, orally, single dose
  - ***or*** tinidazole, 2 g, orally, single dose

All persons not known to be previously vaccinated against HBV, should receive hepatitis B vaccination (without hepatitis B immune globulin),[174] with the first dose administered during the initial examination. If the exposure source is available for testing and is HBsAg-positive, unvaccinated nPEP patients should receive both hepatitis B vaccine and hepatitis B immune globulin during the initial evaluation. Follow-up vaccine doses should be administered during 1–2 months and at 4–6 months after the first nPEP dose. Previously vaccinated sexually assaulted persons who did not receive postvaccination testing should receive a single vaccine booster dose.

HPV vaccination is recommended for female survivors aged 9–26 years and male survivors aged 9–21 years. For MSM with who have not received HPV vaccine or who have been incompletely vaccinated, vaccine can be

administered through age 26 years. The vaccine should be administered to sexual assault survivors at the time of the initial examination, and follow-up dose administered at 1–2 months and 6 months after the first dose.[174]

Routine use of STI prophylaxis is not recommended for sexually abused or assaulted children.[174]

VII-E. Considerations for All Patients Treated with Antiretroviral nPEP

The patient prescribed nPEP should be counseled regarding potential associated side effects and adverse events specific to the regimen prescribed. Any side effects or adverse events requiring immediate medical attention should be emphasized.

VII-E1. Provision of nPEP Starter Packs or a 28-day Supply at Initiation

Patients might be under considerable emotional stress when seeking care after a potential HIV exposure and might not be attentive to, or remember, all the information presented to them before making a decision regarding nPEP. Health care providers should consider giving an initial prescription for 3–7 days of medication (i.e., a starter pack) or an entire 28-day course and scheduling an early follow-up visit. Provision of the entire 28-day nPEP medication supply at the initial visit rather than a starter pack of 3–7 days has been reported to increase likelihood of adherence, especially when patients find returning for multiple follow-up visits difficult.[96,184] Routinely providing starter packs or the entire 28-day course requires that health care providers stock nPEP drugs in their practice setting or have an established agreement with a pharmacy to stock, package and urgently dispense nPEP drugs with required administration instructions. At the patient's second visit, health care providers can discuss the results of baseline HIV blood testing (if rapid tests were not used), provide additional counseling and support, assess medication side effects and adherence, or provide an altered nPEP medication regimen if indicated by side effects or laboratory test results. nPEP starter packs or 28-day supplies might also include such medications as antiemetics to alleviate recognized side effects of the specific medications prescribed, if they occur. Health care providers should counsel patients regarding which side effects might occur (Table 6), how to manage them, and when to contact the provider if they do not resolve.[173]

VII-E2. Expert Consultation

When health care providers are inexperienced with prescribing or managing patients on antiretroviral medications or when information from persons who were the exposure source indicates the possibility of antiretroviral resistance, consultation with infectious disease or other HIV-care specialists, if available immediately, is warranted before prescribing nPEP to determine the correct regimen. Similarly, consulting with specialists with experience using antiretroviral drugs is advisable when considering prescribing nPEP for certain persons—pregnant women (infectious disease specialist or obstetrician), children (pediatrician), or persons with renal dysfunction (infectious disease specialist or nephrologist). However, if such consultation is not available immediately, nPEP should be initiated promptly and, if necessary, revised after consultation is obtained. Expert consultation can be obtained by calling the PEPline at the National Clinician's Consultation Center at 888-448-4911 (additional information is available at http://nccc.ucsf.edu/clinician-consultation/pep-post-exposure-prophylaxis/).

VII-E3. Facilitating Adherence

Observational studies have reported that adherence to nPEP regimens is often inadequate and has been especially so among sexual assault survivors. Medication adherence can be facilitated by (1) prescribing medications with fewer side effects, fewer doses per day, and fewer pills per dose; (2) educating the patient

regarding potential side effects of the specific medications prescribed and providing medications to assist if side effects occur (e.g., antiemetics); (3) recommending medication adherence aids (e.g., pill boxes); (4) helping patients incorporate doses into their daily schedules; and (5) providing a flexible and proactive means for patient–health care provider contact during the nPEP period.[185,186] Also, establishing a trusting relationship and maintaining good communication about adherence can help to improve completion of the nPEP course. Adherence to the nPEP medications prescribed to children will depend on the involvement of and support provided to parents and guardians.

VII-E4. HIV Prevention Counseling

The majority of persons who seek care after a possible HIV exposure do so because of failure to initiate or maintain effective risk-reduction behaviors. Notable exceptions are sexual assault survivors and persons with community-acquired needlestick injuries.

Although nPEP can reduce the risk for HIV infection, it is not always effective. Therefore, patients should practice protective behaviors with sex partners (e.g., consistent condom use) or drug-use partners (e.g., avoidance of shared injection equipment) throughout the nPEP course to avoid transmission to others if they become infected and after nPEP to avoid future HIV exposures.

At follow-up visits, when indicated, health care providers should assess their patients' needs for behavioral intervention, education, and services. This assessment should include frank, nonjudgmental questions about sexual behaviors, alcohol use, and illicit drug use. Health care providers should help patients identify ongoing risk concerns and develop plans for improving their use of protective behaviors.[187]

To help patients obtain indicated interventions and services, health care providers should be aware of local resources for high-quality HIV education and ongoing behavioral risk reduction, counseling and support, inpatient and outpatient alcohol and drug-treatment services, family and mental health counseling services, and support programs for HIV-infected persons. Information regarding publicly funded HIV prevention programs can be obtained from state or local health departments.

VII-E5. Providing PrEP After nPEP Course Completion

Persons who engage in behaviors that result in frequent, recurrent exposures that would require sequential or near-continuous courses of nPEP should be offered PrEP[11] at the conclusion of their 28-day nPEP medication course. Because no evidence exists that prophylactic antiretroviral use delays seroconversion and nPEP is highly effective when taken as prescribed, a gap is unnecessary between ending nPEP and beginning PrEP. Upon documenting HIV-negative status, preferably by using an Ag/Ab test, daily use of the fixed dose combination of TDF (300mg) and FTC (200 mg) can begin immediately for patients for whom PrEP is indicated. Clinicians with questions about prescribing PrEP, are encouraged to call the PrEPline 855-448-7737 at the National Clinician Consultation Center or go to their website (http://nccc.ucsf.edu/clinician-consultation/prep-pre-exposure-prophylaxis/).

VII.E6. Providing nPEP in the Context of PrEP

Patients fully adhering to a daily PrEP regimen as recommended by their health care practitioner are not in need of nPEP if they experience a potential HIV exposure while on PrEP. PrEP is highly effective when taken daily or near daily.[11,188] For patients who report that they take their PrEP medication sporadically and those who did not take it within the week before the recent exposure, initiating a 28-day course of nPEP might be indicated. In

that instance, all nPEP baseline and follow-up laboratory evaluations should be conducted. After the 28-day nPEP regimen is completed, if confirmed to be HIV uninfected, the daily PrEP regimen can be reinitiated.

VII-E7. Management of Source Persons with HIV Infection

When persons who were the exposure source are present during the course of evaluating a patient for potential HIV exposure, health care providers should also assess that person's access to relevant medical care, behavioral intervention, and social support services. If needed care cannot be provided directly, health care providers should help HIV-infected source persons obtain care in the community (http://locator.aids.gov/).

VII-F. Additional Considerations

VII-F1. Reporting and Confidentiality

As with all clinical care, health care providers should handle nPEP evaluations with confidentiality. Confidential reporting of STIs and newly diagnosed HIV infections to health departments should occur as indicated by that jurisdiction's local laws and regulations.

For cases of sexual assault, health care providers should document their findings and assist patients with notifying local authorities.[174] How health care providers should document and report their findings is beyond the scope of these guidelines. Laws in all 50 states strictly limit the evidentiary use of a survivor's previous sexual history, including evidence of previously acquired STIs, to avoid efforts to undermine the credibility of the survivor's testimony. Evidentiary privilege against revealing any aspect of the survivor's examination or medical treatment also is enforced in the majority of most states.

Certain states and localities have special programs that provide reimbursement for medical therapy, including antiretroviral medication after sexual assault, and those areas might have specific reporting requirements. In all states, sexually assaulted persons are eligible for reimbursement of medical expenses through the U.S. Department of Justice Victim's Compensation Program in cases where the sexual assault is reported to the police (http://www.ojp.usdoj.gov/ovc/map.html).When the sexual abuse of a child is suspected or documented, the clinician should report it in compliance with that jurisdiction's laws and regulations.

VII-F2. Special Populations

VII-F2a. Sexually Assaulted Persons

Eighteen percent of a national sample of adult women in the United States reported having ever been raped, and approximately 1 in 10 women (9.4%) has been raped by an intimate partner during her lifetime.[189] Sexual assault also occurs among men. Approximately 1 in 71 men (1.4%) in the United States has been raped at some time in his life.[189] In 1 series from an ED, 5% of reported rapes involved men sexually assaulted by men.[190]

Sexual assault typically has multiple characteristics that increase the risk for HIV transmission if the assailant is infected. In 1 prospective study of 1,076 sexually assaulted person, 20% had been attacked by multiple assailants, 39% had been assaulted by strangers, 17% had had anal penetration, and 83% of females had been penetrated vaginally. Genital trauma was documented among 53% of those assaulted, and sperm or semen was detected in 48%.[191] Often, in both stranger and intimate-partner rape, condoms are not used[192,193] and STIs are frequently contracted.[194-197] In the largest study[198] examining prevalence of HIV infection among sexual assailants, 1% of men convicted of sexual assault in Rhode Island were HIV infected when they entered prison, compared with 3% of all prisoners and 0.3% of the general male population.

Persons provided nPEP after sexual assault or child sexual abuse should be examined and co-managed by professionals specifically trained in assessing and counseling patients and families during these circumstances (e.g., Sexual Assault Nurse Examiner [SANE] program staff). Local SANE programs can be located at http://www.sane-sart.com/. Patients who have been sexually assaulted will benefit from supportive services to improve adherence to nPEP if it is prescribed, and from crisis, advocacy, and counseling services provided by sexual assault crisis centers.

VII-F2b. Pregnant Women and Women with Childbearing Potential

Information is being collected regarding safe use of antiretroviral drugs for pregnant and breastfeeding women who do not have HIV infection, particularly those whose male partners have HIV infection and who use antiretrovirals as PrEP.[114] Because considerable experience has been gained in recent years in the safe and recommended use of antiretroviral medications during pregnancy and breastfeeding among women with HIV infection—either for the benefit of the HIV-infected woman's health or to prevent transmission to newborns—and because of the lack of similar experience in HIV-uninfected pregnant women, nPEP drug recommendations (Table 5) rely on those used for HIV-infected women during pregnancy and breastfeeding.

Health care providers should be aware that certain medications are contraindicated for use as nPEP among potentially or actually pregnant women as follows (Table 7):

- Efavirenz (EFV) is classified as FDA pregnancy Category D because of its potential teratogenicity when used during the first 5–6 weeks of pregnancy.[199] It should be avoided in nPEP regimens for HIV-uninfected women during the first trimester and should not be used for women of childbearing age who might become pregnant during an antiretroviral prophylaxis course. For all women with childbearing potential, pregnancy testing must be done before the EFV initiation, and women should be counseled regarding potential risks to the fetus and the importance of avoiding pregnancy while on an EFV-containing regimen.[114]

- Prolonged use of stavudine (d4T) in combination with didanosine (DDI) for HIV-infected pregnant women has been associated with maternal and fetal morbidity attributed to lactic acidosis; therefore, this combination is not recommended for use in an nPEP regimen during pregnancy.[123,124]

- Because using indinavir (IDV) is associated with increased risk for nephrolithiasis among pregnant women and its use without co-administration of a ritonavir as a boosting agent can result in substantially decreased plasma levels of IDV (the active agent) among pregnant women, IDV should not be used as nPEP for pregnant women.

- Severe hepatotoxicity has been observed among patients administered nevirapine (NVP)-containing nPEP regimens (regardless of pregnancy status); therefore, NVP is contraindicated for nPEP, including for pregnant women.[83]

Table 7. Antiretroviral medications that should not be used for nPEP among pregnant women

Antiretroviral	Risk in pregnancy	Concern
Efavirenz	Teratogenicity	Fetal safety
Nevirapine	Hepatotoxicity	Maternal safety
Stavudine and didanosine	Mitochondrial toxicity and lactic acidosis	Maternal safety
Indinavir (without co-administration with ritonavir) during second or third trimester	Substantially decreased plasma concentration; risk for nephrolithiasis	Efficacy and maternal safety
Abbreviation: nPEP, nonoccupational postexposure prophylaxis.		

If nPEP is prescribed to a woman who is pregnant at the time of exposure or becomes pregnant while on nPEP, health care providers should enter the patient's information (anonymously) into the Antiretroviral Pregnancy Registry (http://www.apregistry.com).

VII-F2c. Incarcerated Persons

Approximately 2 million persons are incarcerated in jails and prisons and can be at risk for HIV infection acquisition during incarceration. Studies have indicated that the risk for becoming infected while incarcerated is probably less than the risk outside a facility[200-202]; nevertheless, correctional facilities should develop protocols for nPEP to help reduce the legal, emotional and medical problems associated with an exposure event for this vulnerable population. As foundation for nPEP provision when it is indicated, correctional facilities should provide HIV education, voluntary HIV testing, systems to assist in identifying potential HIV exposures without repercussion for inmates, and provision of nPEP evaluation and medication. Sexual assaults in particular can put inmates at risk for HIV acquisition and inmates may engage in behaviors that put them at risk for HIV acquisition both prior to being incarcerated and upon reentry into the community. A 15-minute interactive educational program designed to educate inmates about nPEP resulted in a 40% increase in knowledge compared to baseline regardless of inmate-related demographics or HIV-risk characteristics.[203]

The federal Bureau of Prisons has published a clinical practice guideline that integrates guidance for nonoccupational and occupational HIV-related exposures.[204] Those guidelines specific to nPEP represent an adaptation of the 2005 CDC nPEP guidelines and outline HIV postexposure management recommendations for the different exposure types. The federal Bureau of Prisons nPEP recommendations can be modified for use in correctional facilities of varying sizes and resources. The Bureau of Prisons guidelines provide practical materials for both correctional health care providers and inmates and include worksheets to assist health care providers in systematically documenting HIV exposures and nPEP therapy management, and sample patient consent forms. They recommend that each correctional facility develop its own postexposure management protocol. The CDC recommends that health care providers should make every effort to use of current CDC guidelines related to selection of nPEP antiretrovirals.

VII-F2d. PWID

A history of injection drug use should not deter health care providers from prescribing nPEP if the exposure provides an opportunity to reduce the immediate risk for acquisition of HIV infection. A survey of health care providers who treat PWID determined a high degree of willingness to provide nPEP after different types of potential HIV exposure.[202]

When evaluating whether exposures are isolated, episodic, or ongoing, health care providers should assess whether persons who continue to engage in injecting or sexual HIV risk behaviors are practicing risk reduction (e.g., not sharing syringes, using a new sterile syringe for each injection, and using condoms with every partner or client). For certain persons, a high-risk exposure might be an exceptional occurrence and merit nPEP despite their ongoing general risk behavior. For other persons, the risk exposures might be frequent enough to merit consideration of PrEP either instead of nPEP or after a 28-day nPEP course.

PWID should be assessed for their interest in substance abuse treatment and their knowledge and use of safe injecting and sexual practices. Patients desiring substance abuse treatment should be referred for such treatment. Persons who continue to inject or who are at risk for relapse to injection drug use should be instructed regarding use of a new sterile syringe for each injection and the importance of avoiding sharing injection equipment. In areas where programs are available, health care providers should refer such patients to sources of sterile injection equipment. When sexual practices can result in ongoing risk for HIV acquisition, referral for sexual risk-reduction interventions is recommended.

None of the preferred or alternative antiretroviral drugs recommended for nPEP in Table 5 have substantial interactions with methadone or buprenorphine. However, other antiretrovirals might decrease or increase methadone levels; therefore, health care providers electing to use antiretrovirals not specifically recommended for nPEP should check for interactions before prescribing to persons on opiate substitution therapy.
For example, RTV-boosted DRV can decrease methadone levels marginally (within acceptable clinical range), and careful monitoring for signs and symptoms of withdrawal is advised.[205]

VII-F3. Special Legal and Regulatory Concerns

VII-F3a. HIV Testing of Exposure Source Patients

When approaching persons who were the exposure source for patients being considered for nPEP, health care providers should be aware of potential legal concerns related to requesting them to undergo HIV testing. During 2011, a total of 33 states had ≥ 1 HIV-specific criminal exposure laws.[206] These laws focus explicitly on persons living with HIV. HIV-specific criminal laws criminalize or impose additional penalties on certain behaviors (e.g., sexual activity or needle-sharing without disclosure of HIV-positive status) and sex offenses. In jurisdictions where consent to HIV testing might invoke legal repercussions (see http://www.cdc.gov/hiv/policies/law/states/), the exposure source person should be made aware of possible legal jeopardies. Health care providers can opt instead to make nPEP treatment decisions without HIV testing of the source.

VII-F3b. Adolescents and Clinical Preventive Care

Health care providers should be aware of local laws and regulations that govern which clinical services adolescent minors can access with or without prior parental consent. In certain jurisdictions, minors of particular ages can access contraceptive services, STI diagnosis and treatment, or HIV testing without parental or guardian consent. In fewer settings, minors can access clinical preventive care (e.g. vaccines, nPEP, or PrEP).[207] To provide and coordinate care when a minor presents for possible nPEP, health care providers should understand their local regulations and institutional policies guiding provision of clinical preventive care to adolescent minors.

VII-F4. Potential Sources of Financial Assistance for nPEP Medication

Antiretroviral medications are expensive, and certain patients are unable to cover the out-of-pocket costs. When public, privately purchased, or employer-based insurance coverage is unavailable, health care providers can assist patients with obtaining antiretroviral medications through the medication assistance programs of the pharmaceutical companies that manufacture the prescribed medications. Applications are available online that can be faxed to the company or certain companies can be called on an established phone line. Requests for assistance often can be handled urgently so that accessing medication is not delayed. Information for specific medications and manufacturers is available at http://www.pparx.org/en/prescription_assistance_programs/list_of_participating_programs.

Additionally, persons being prescribed nPEP after sexual assault can be reimbursed for medications and clinical care costs through state Crime Victim's Compensation Programs funded by the U.S. Department of Justice. Contact information for each state is available at http;//www.ojp.usdoj.gov/ovc/map.html or http;//www.nacvcb.org/index.asp?bid=16.

VIII. CONCLUSION

Accumulated data from human clinical and observational studies, supported by data from animal studies, indicate that using antiretroviral medication initiated as soon as possible ≤72 hours after sexual, injection drug use, or other substantial nonoccupational HIV exposure and continued for 28 days might reduce the likelihood of HIV acquisition. Because of these findings, DHHS recommends prompt initiation of nPEP with a combination of antiretroviral medications when persons seek care ≤72 hours after exposure, the source is known to be HIV infected, and the exposure event presents a substantial risk for HIV acquisition by an exposed, uninfected person. When the HIV status of the source is unknown and the patient seeks care ≤72 hours after exposure, DHHS does not recommend for or against nPEP, but encourages health care providers and patients to weigh the risks and benefits on a case-by-case basis. When the HIV acquisition risk is negligible or when patients seek care > 72 hours after a substantial exposure, nPEP is not recommended. A 3-drug nPEP regimen is recommended for all persons for whom nPEP is indicated. Providing a 28-day nPEP supply or a 3–7 day nPEP starter pack at initiation of nPEP might improve adherence. Providing medications to ameliorate specific side effects for the antiretrovirals prescribed might improve adherence to the nPEP regimen. Figure 2 includes a summary of key nPEP considerations.

Figure 2. nPEP considerations summary

Initial nPEP Evaluation

- Obtain history of potential exposure event
  - HIV and HBV status of exposed person and source person, if available
  - Timing of most recent potential exposure
  - Type of exposure event and risk for HIV acquisition
  - Make determination if nPEP is indicated
- If nPEP is indicated
  - Conduct laboratory testing
    - HIV blood test (rapid combined Ag/Ab test, if available)
    - STIs, HBV, HCV, pregnancy, and chemistries, as indicated
  - Prescribe 28-day nPEP course
    - Educate patient about potential regimen-specific side effects and adverse events
    - Counsel patient about medication adherence
    - Provide patient with nPEP prescription or full 28-day nPEP course or nPEP starter pack and prescription
  - When necessary, assist patients with obtaining nPEP medication through a medication assistance program for the prescribed regimen
- For all persons evaluated
  - Prescribe prophylaxis for STIs and HBV infection, if indicated
  - Provide counseling related to HIV prevention strategies, as appropriate
  - Document sexual assault findings and fulfill local reporting requirements
  - Conduct confidential reporting of newly diagnosed STIs and HIV infection to health department
  - Link HIV-infected persons to relevant medical and psychosocial support services

Follow-up evaluations for persons prescribed nPEP

- Conduct HIV and any other indicated laboratory testing
- Consider changing nPEP regimen if indicated by side effects or results of initial testing
- Provide additional counseling and support for medication adherence and HIV prevention, if indicated

Abbreviations: Ag/Ab, antigen/antibody combination test; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; nPEP, nonoccupational postexposure prophylaxis; STI, sexually transmitted infection.

VIII-A. Plans for Updating These Guidelines

These guidelines are intended to assist U.S. health care providers in reducing the occurrence of new HIV infections through the effective delivery of nPEP to the patients most likely to benefit. As new medications and new information regarding nPEP become available, these guidelines will be revised and published.

IX. REFERENCES

1. Smith DK, Grohskopf LA, Black RJ, et al. Antiretroviral postexposure prophylaxis after sexual, injection-drug use, or other nonoccupational exposure to HIV in the United States: recommendations from the U.S. Department of Health and Human Services. *MMWR Recomm Rep.* 2005;54(No. RR-2):1-20.

2. Kuhar DT, Henderson DK, Struble KA, et al. Updated US Public Health Service guidelines for the management of occupational exposures to human immunodeficiency virus and recommendations for postexposure prophylaxis. *Infect Control Hosp Epidemiol.* 2013;34(9):875-892.

3. New York State Department of Health AIDS Institute. HIV Prophylaxis Following Non-Occupational Exposure Including Sexual Assault New York, NY: New York State Department of Health AIDS Institute; 2014: available at http://www.hivguidelines.org/clinical-guidelines/post-exposure-prophylaxis/hiv-prophylaxis-following-non-occupational-exposure/. Accessed October 2, 2015.

4. Nonoccupational HIV PEP Task Force, Brown University AIDS Program, Rhode Island Department of Health. Nonoccupational human immunodeficiency virus postexposure prophylaxis guidelines for Rhode Island healthcare practitioners. Providence, Rhode Island,2002: available at http://www.health.state.ri.us/publications/guidelines/provider/NonoccupationalHIVPostexposureProphalaxis.pdf.

5. The California Task Force on Non-Occupational PEP, the California Department of Health Services, Office of AIDS. Offering HIV Post-Exposure Prophylaxis (PEP) Following Non-Occupational Exposures Recommendations for Health Care Providers in the State of California Sacramento, California,2004: available at http://www.cdph.ca.gov/programs/aids/Documents/RPT2004OfferingPEPFollowingNonOccupExp2004-06.pdf.

6. Havens PL, American Academy of Pediatrics Committee on Pediatric AIDS. Postexposure prophylaxis in children and adolescents for nonoccupational exposure to human immunodeficiency virus. *Pediatrics.* 2003;111(6):1475-1489.

7. 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.

8. Ford N, Mayer KH, World Health Organization Postexposure Prophylaxis Guideline Development Group. World Health Organization Guidelines on Postexposure Prophylaxis for HIV: Recommendations for a Public Health Approach. *Clin Infect Dis.* 2015;60 Suppl 3:S161-164.

9. Tolle MA, Schwarzwald HL. Postexposure prophylaxis against human immunodeficiency virus. *Am Fam Physician.* 2010;82(2):161-166.

10. American College of Emergency Physicians. Emergency Management of the Sexually Assaulted or Sexually Abused Patient In: Riviello RJ, Rozzi H, eds. 2nd Edition ed. Irving, Texas: American College of Emergency Physicians; 2013: http://www.acep.org/workarea/DownloadAsset.aspx?id=93246. Accessed 12/10/2015.

11. Centers for Disease Control and Prevention (CDC), US Public Health Service. Preexposure Prophylaxis for the Prevention of HIV Infection in the United States-2014-A Clinical Practice Guideline. Atlanta, GA: US Department of Health and Human Services, CDC; 2014: available at http://www.cdc.gov/hiv/pdf/PrEPguidelines2014.pdf. Accessed October 5, 2015.

12. Cardo DM, Culver DH, Ciesielski CA, et al. A case-control study of HIV seroconversion in health care workers after percutaneous exposure. *New Engl J Med.* 1997;337(21):1485-1490.

13. Terzi R, Niero F, Iemoli E, Capetti A, Coen M, Rizzardini G. Late HIV seroconversion after non-occupational postexposure prophylaxis against HIV with concomitant hepatitis C virus seroconversion. *AIDS.* 2007;21(2):262-263.

14. Donnell D, Mimiaga MJ, Mayer K, Chesney M, Koblin B, Coates T. Use of non-occupational post-exposure prophylaxis does not lead to an increase in high risk sex behaviors in men who have sex with men participating in the EXPLORE trial. *AIDS Behav.* 2010;14(5):1182-1189.

15. Sonder GJB, 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.

16. Schechter M, do Lago RF, Mendelsohn AB, et al. Behavioral impact, acceptability, and HIV incidence among homosexual men with access to postexposure chemoprophylaxis for HIV. *J Acquir Immune Defic Syndr.* 2004;35(5):519-525.

17. McAllister J, Read P, McNulty A, Tong WW, Ingersoll A, Carr A. Raltegravir-emtricitabine-tenofovir as HIV nonoccupational post-exposure prophylaxis in men who have sex with men: safety, tolerability and adherence. *HIV Med.* 2014;15(1):13-22.

18. Jain S, Oldenburg CE, Mimiaga MJ, Mayer KH. Subsequent HIV infection among men who have sex with men who used non-occupational post-exposure prophylaxis at a Boston community health center: 1997-2013. *AIDS Patient Care STDS.* 2015;29(1):20-25.

19. Foster R, McAllister J, Read TR, et al. Single-tablet emtricitabine-rilpivirine-tenofovir as HIV postexposure prophylaxis in men who have sex with men. *Clin Infect Dis.* 2015:1-5.

20. Chacko L, Ford N, Sbaiti M, Siddiqui R. Adherence to HIV post-exposure prophylaxis in victims of sexual assault: a systematic review and meta-analysis. *Sex Transm Infect.* 2012;88(5):335-341.

21. Draughon JE, Sheridan DJ. Nonoccupational postexposure prophylaxis for human immunodeficiency virus in Sub-Saharan Africa: a systematic review. *J Forensic Nurs.* 2011;7(2):89-96.

22. Draughon JE, Sheridan DJ. Nonoccupational postexposure prophylaxis following sexual assault in industrialized low-HIV-prevalence countries: a review. *Psychol Health Med.* 2012;17(2):235-254.

23. Loutfy MR, Macdonald S, Myhr T, et al. Prospective cohort study of HIV post-exposure prophylaxis for sexual assault survivors. *Antivir Ther.* 2008;13(1):87-95.

24. Lurie P, Miller S, Hecht F, Chesney M, Lo B. Postexposure prophylaxis after nonoccupational HIV exposure: clinical, ethical, and policy considerations. *JAMA.* 1998;280(20):1769-1773.

25. Claydon E, Murphy S, Osborne EM, Kitchen V, Smith JR, Harris JR. Rape and HIV. *Int J STD AIDS.* 1991;2(3):200-201.

26. Myles JE, Hirozawa A, Katz MH, Kimmerling R, Bamberger JD. Postexposure prophylaxis for HIV after sexual assault. *JAMA.* 2000;284(12):1516-1518.

27. Fong C. Post-exposure prophylaxis for HIV infection after sexual assault: when is it indicated? *Emerg Med J.* 2001;18(4):242-245.

28. Albert J, Wahlberg J, Leitner T, Escanilla D, Uhlen M. Analysis of a rape case by direct sequencing of the human immunodeficiencey virus type-1 *pol* and *gag* genes. *J Virol.* 1994;68(9):5918-5924.

29. Murphy S, Kitchen V, Harris JRW, Forster SM. Rape and subsequent seroconversion to HIV. *BMJ.* 1989;299(6701):718-718.

30. Linden JA, Oldeg P, Mehta SD, McCabe KK, LaBelle C. HIV postexposure prophylaxis in sexual assault: current practice and patient adherence to treatment recommendations in a large urban teaching hospital. *Acad Emerg Med.* 2005;12(7):640-646.

31. Griffith WF, Ackerman GE, Zoellner CL, Sheffield JS. Sexual assault: a report on human immunodeficiency virus postexposure prophylaxis. *Obstet Gynecol Int.* 2010;2010(196963):1-6.

32. Olshen E, Hsu K, Woods ER, Harper M, Harnisch B, Samples CL. Use of human immunodeficiency virus postexposure prophylaxis in adolescent sexual assault victims. *Arch of Pediat Adolesc Med.* 2006;160(7):674-680.

33. Carrieri MP, Bendiane MK, Moatti JP, Rey D. Access to HIV prophylaxis for survivors of sexual assault: the tip of the iceberg. *Antivir Ther.* 2006;11(3):391-392.

34. Krause KH, Lewis-O'Connor A, Berger A, et al. Current practice of HIV postexposure prophylaxis treatment for sexual assault patients in an emergency department. *Women Health Iss.* 2014;24(4):e407-412.

35. Girardet RG, Lemme S, Biason TA, Bolton K, Lahoti S. HIV post-exposure prophylaxis in children and adolescents presenting for reported sexual assault. *Child Abuse Negl.* 2009;33(3):173-178.

36. Schremmer RD, Swanson D, Kraly K. Human immunodeficiency virus postexposure prophylaxis in child and adolescent victims of sexual assault. *Pediatr Emerg Care.* 2005;21(8):502-506.

37. Ellis JC, Ahmad S, Molyneux EM. Introduction of HIV post-exposure prophylaxis for sexually abused children in Malawi. *Arch Dis Child.* 2006;90(12):1297-1299.

38. Neu N, Heffernan-Vacca S, Millery M, Stimell M, Brown J. Postexposure prophylaxis for HIV in children and adolescents after sexual assault: a prospective observational study in an urban medical center. *Sex Transm Dis.* 2007;34(2):65-68.

39. Merchant RC, Keshavarz R, Low C. HIV post-exposure prophylaxis provided at an urban paediatric emergency department to female adolescents after sexual assault. *Emerg Med J.* 2004;21(4):449-451.

40. Speight CG, Klufio A, Kilonzo SN, et al. Piloting post-exposure prophylaxis in Kenya raises specific concerns for the management of childhood rape. *Trans R Soc Trop Med Hyg.* 2006;100(1):14-18.

41. Fajman N, Wright R. Use of antiretroviral HIV post-exposure prophylaxis in sexually abused children and adolescents treated in an inner-city pediatric emergency department. *Child Abuse Negl.* 2006;30(8):919-927.

42. Collings SJ, Bugwandeen SR, Wiles WA. HIV post-exposure prophylaxis for child rape survivors in KwaZulu-Natal, South Africa: who qualifies and who complies? *Child Abuse Negl.* 2008;32(4):477-483.

43. Chesshyre ELD, Molyneux EM. Presentation of child sexual abuse cases to Queen Elizabeth Central Hospital following the establishment of an HIV post-exposure prophylaxis programme. *Malawi Med J.* 2009;21(2):54-58.

44. Du Mont J, Myhr TL, Husson H, Macdonald S, Rachlis A, Loutfy MR. HIV postexposure prophylaxis use among Ontario female adolescent sexual assault victims: a prospective analysis. *Sex Transm Dis.* 2008;35(12):973-978.

45. Pierce AB, Yohannes K, Guy R, et al. HIV seroconversions among male non-occupational post-exposure prophylaxis service users: a data linkage study. *Sex Health.* 2011;8(2):179-183.

46. Rey D, Bendiane MK, Bouhnik A-D, Almeda J, Moatti JP, Carrieri MP. Physicians' and patients' adherence to antiretroviral prophylaxis after sexual exposure to HIV: results from South-Eastern France. *AIDS Care.* 2008;20(5):537-541.

47. Siika AM, Nyandiko WM, Mwangi A, et al. The structure and outcomes of a HIV postexposure prophylaxis program in a high HIV prevalence setup in Western Kenya. *J Acquir Immune Defic Syndr.* 2009;51(1):47-53.

48. Tissot F, Erard V, Dang T, Cavassini M. Nonoccupational HIV post-exposure prophylaxis: a 10-year retrospective analysis. *HIV Med.* 2010;11(9):584-592.

49. Tosini W, Muller P, Prazuck T, et al. Tolerability of HIV postexposure prophylaxis with tenofovir/emtricitabine and lopinavir/ritonavir tablet formulation. *AIDS.* 2010;24(15):2375-2380.

50. Wong K, Hughes CA, Plitt S, et al. HIV non-occupational postexposure prophylaxis in a Canadian province: treatment completion and follow-up testing. *Int J STD AIDS.* 2010;21(9):617-621.

51. Olowookere SA, Fatiregun AA. Human immunodeficiency virus postexposure prophylaxis at IBadan, Nigeria. *J Int Assoc Physicians AIDS Care (Chic).* 2010;9(3):187-190.

52. Chan AC, Gough K, Yoong D, Dimeo M, Tan DH. Non-occupational post-exposure prophylaxis for HIV at St Michael's Hospital, Toronto: a retrospective review of patient eligibility and clinical outcomes. *Int J STD AIDS.* 2013;24(5):393-397.

53. Diaz-Brito V, Leon A, Knobel H, et al. Post-exposure prophylaxis for HIV infection: a clinical trial comparing lopinavir/ritonavir versus atazanavir each with zidovudine/lamivudine. *Antivir Ther.* 2012;17(2):337-346.

54. Gulholm T, Jamani S, Poynten IM, Templeton DJ. Non-occupational HIV post-exposure prophylaxis at a Sydney metropolitan sexual health clinic. *Sex Health.* 2013;10(5):438-441.

55. Shoptaw S, Rotheram-Fuller E, Landovitz RJ, et al. Non-occupational post exposure prophylaxis as a biobehavioral HIV-prevention intervention. *AIDS Care* 2008;20(3):376-381.

56. Mayer KH, Mimiaga MJ, Cohen D, et al. Tenofovir DF plus lamivudine or emtricitabine for nonoccupational postexposure prophylaxis (NPEP) in a Boston community health center. *J Acquir Immune Defic Syndr.* 2008;47(4):494-499.

57. Mayer KH, Mimiaga MJ, Gelman M, Grasso C. Raltegravir, tenofovir DF, and emtricitabine for postexposure prophylaxis to prevent the sexual transmission of HIV: safety, tolerability, and adherence. *J Acquir Immune Defic Syndr.* 2012;59(4):354-359.

58. Babl FE, Cooper ER, Damon B, Louie T, Kharasch S, Harris JA. HIV postexposure prophylaxis for children and adolescents. *Am J Emerg Med.* 2000;18(3):282-287.

59. Bogoch II, Scully EP, Zachary KC, et al. Patient attrition between the emergency department and clinic among individuals presenting for HIV nonoccupational postexposure prophylaxis. *Clin Infect Dis.* 2014;58(11):1618-1624.

60. Jain S, Oldenburg CE, Mimiaga MJ, Mayer KH. Longitudinal trends in HIV nonoccupational postexposure prophylaxis use at a Boston community health center between 1997 and 2013. *J Acquir Immune Defic Syndr.* 2015;68(1):97-101.

61. Beymer MR, Bolan RK, Flynn RP, et al. Uptake and repeat use of postexposure prophylaxis in a community-based clinic in Los Angeles, California. *AIDS Res Hum Retrov.* 2014;30(9):848-855.

62. McDougal SJ, Alexander J, Dhanireddy S, Harrington RD, Stekler JD. Non-occupational post-exposure prophylaxis for HIV: 10-year retrospective analysis in Seattle, Washington. *PLoS One.* 2014;9(8):e105030.

63. Fletcher JB, Rusow JA, Le H, Landovitz RJ, Reback CJ. High-risk sexual behavior is associated with post-exposure prophylaxis non-adherence among men who have sex with men enrolled in a combination prevention intervention. *J Sex Transm Dis.* 2013;2013:210403.

64. Thomas HL, Liebeschuetz S, Shingadia D, Addiman S, Mellanby A. Multiple needle-stick injuries with risk of human immunodeficiency virus exposure in a primary school. *Pediatr Infect Dis J.* 2006;25(10):933-936.

65. Papenburg J, Blais D, Moore D, et al. Pediatric injuries from needles discarded in the community: epidemiology and risk of seroconversion. *Pediatrics.* 2008;122(2):e487-e492.

66. de Waal N, Rabie H, Bester R, Cotton MF. Mass needle stick injury in children from the Western Cape. *J of Trop Pediatr.* 2006;52(3):192-196.

67. Russell FM, Nash MC. A prospective study of children with community-acquired needlestick injuries in Melbourne. *J Paediatr Child Health.* 2002;38(3):322-323.

68. Makwana N, Riordan FAI. Prospective study of community needlestick injuries. *Arch Dis Child.* 2005;90(5):523-524.

69. Butsashvili M, Kamkamidze G, Kajaia M, Kandelaki G, Zhorzholadze N. Circumstances surrounding the community needle-stick injuries in Georgia. *J Commun Health.* 2011;36(6):1050-1052.

70. Babl FE, Cooper ER, Kastner B, Kharasch S. Prophylaxis against possible human immunodeficiency virus exposure after nonoccupational needlestick injuries or sexual assaults in children and adolescents. *Arch of Pediatr Adolesc Med.* 2001;155(6):680-682.

71. Al-Hajjar SH, Frayha HH, Al-Hazmi M, et al. Prevention of HIV-1 transmission with postexposure prophylaxis after inadvertent infected blood transfusion. *AIDS.* 2014;28(10):1539-1541.

72. Shaffer N, Chuachoowong R, Mock PA, et al. Short-course zidovudine for perinatal HIV-1 transmission in Bangkok, Thailand: a randomised controlled trial. *Lancet.* 1999;353(9155):773-780.

73. Guay LA, Musoke P, Fleming T, et al. Intrapartum and neonatal single-dose nevirapine compared with zidovudine for prevention of mother-to-child transmission of HIV-1 in Kampala, Uganda: HIVMET 012 randomised trial. *Lancet.* 1999;354(9181):795-802.

74. Moodley D, Moodley J, Coovadia H, et al. A multicenter randomized controlled trial of nevirapine versus a combination of zidovudine and lamivudine to reduce intrapartum and early postpartum mother-to-child transmission of human immunodeficiency virus type 1. *J Infect Dis.* 2003;187(5):725-735.

75. Sperling RS, Shapiro DE, Coombs RW, et al. Maternal viral load, zidovudine treatment, and the risk of transmission of human immunodeficiency virus type 1 from mother to infant. *N Engl J Med.* 1996;335(22):1621-1629.

76. Taha TE, Li Q, Hoover DR, et al. Postexposure prophylaxis of breastfeeding HIV-exposed infants with antiretroviral drugs to age 14 weeks: updated efficacy results of the PEPI-Malawi trial. *J Acquir Immune Defic Syndr.* 2011;57(4):319-325.

77. Wade NA, Birkhead GS, Warren BL, et al. Abbreviated regimens of zidovudine prophylaxis and perinatal transmission of the human immunodeficiency virus. *New Engl J Med.* 1998;339(20):1409-1414.

78. Tsai CC, Follis KE, Sabo A, et al. Prevention of SIV infection in macaques by (R)-9-(2-phosphonylmethoxypropyl)adenine. *Science.* 1995;270(5239):1197-1199.

79. Tsai CC, Emau P, Follis KE, et al. Effectiveness of postinoculation (R)-9-(2-phosphonylmethoxypropyl) adenine treatment for prevention of persistent simian immunodeficiency virus SIVmne infection depends critically on timing of initiation and duration of treatment. *J Virol.* 1998;72(5):4265-4273.

80. Le Grand R, Vaslin B, Larghero J, et al. Post-exposure prophylaxis with highly active antiretroviral therapy could not protect macaques from infection with SIV/HIV chimera. *AIDS.* 2000;14(12):1864-1866.

81. Bourry O, Brochard P, Souquiere S, et al. Prevention of vaginal simian immunodeficiency virus transmission in macaques by postexposure prophylaxis with zidovudine, lamivudine and indinavir. *AIDS.* 2009;23(4):447-454.

82. Dobard C, Sharma S, Parikh UM, et al. Postexposure protection of macaques from vaginal SHIV infection by topical integrase inhibitors. *Sci Transl Med.* 2014;6(227):1-9.

83. Otten RA, Smith DK, Adams DR, et al. Efficacy of postexposure prophylaxis after intravaginal exposure of pig-tailed macaques to a human-derived retrovirus (human immunodeficiency virus type 2). *J Virol.* 2000;74(20):9771-9775.

84. Irvine C, Egan KJ, Shubber Z, Van Rompay KK, Beanland RL, Ford N. Efficacy of HIV postexposure prophylaxis: systematic review and meta-analysis of nonhuman primate studies. *Clin Infect Dis.* 2015;60 Suppl 3:S165-169.

85. Carries S, Muller F, Muller FJ, Morroni C, Wilson D. Characteristics, treatment, and antiretroviral prophylaxis adherence of South African rape survivors. *J Acquir Immune Defic Syndr.* 2007;46(1):68-71.

86. Abrahams N, Jewkes R, Lombard C, Mathews S, Campbell J, Meel B. Impact of telephonic psycho-social support on adherence to post-exposure prophylaxis (PEP) after rape. *AIDS.* 2010;22(10):1173-1181.

87. Roland ME, Myer L, Martin LJ, et al. Preventing human immunodeficiency virus infection among sexual assault survivors in Cape Town, South Africa: an observational study. *AIDS Behav.* 2012;16(4):990-998.

88. Wiebe ER, Comay SE, McGregor M, Ducceschi S. Offering HIV prophylaxis to people who have been sexually assaulted: 16 months' experience in a sexual assault service. *CMAJ.* 2000;162(5):641-645.

89. Bani-Sadr F, Teissiere F, Curie I, et al. [Anti-infection prophylaxis after sexual assault. Experience of the Raymond Poincare-Garches Hospital]. *Presse medicale.* 2001;30(6):253-258.

90. Limb S, Kawsar M, Forster GE. HIV post-exposure prophylaxis after sexual assault: the experience of a sexual assault service in London. *Int J STD AIDS.* 2002;13(9):602-605.

91. Masanzu R, Ajayi C, Sibly E, Forster G. Post-exposure prophylaxis following sexual assault. *HIV Med.* 2010;11(Suppl. 1):53.

92. Lunding S, Katzenstein TL, Kronborg G, et al. The Danish PEP registry: experience with the use of postexposure prophylaxis (PEP) following sexual exposure to HIV from 1998 to 2006. *Sex Transm Dis.* 2010;37(1):49-52.

93. Garcia MT, Figueiredo RM, Moretti ML, Resende MR, Bedoni AJ, Papaiordanou PMO. Postexposure prophylaxis after sexual assaults: a prospective cohort study. *Sex Transm Dis.* 2005;32(4):214-219.

94. Lacombe K, Daguenel-Nguyen A, Lebeau V, Fonquernie L, Girard PM, Meyohas MC. Determinants of adherence to non-occupational post HIV exposure prophylaxis. *AIDS.* 2006;20(2):291-294.

95. Diniz NM, de Almeida LC, dos S. Ribeiro BC, de Macêdo VG. Women victims of sexual violence: adherence to chemoprevention of HIV. *Rev Lat Am Enfermagem.* 2007;15(1):6.

96. Kim JC, Askew I, Muvhango L, et al. Comprehensive care and HIV prophylaxis after sexual assault in rural South Africa: the Refentse Intervention Study. *BMJ.* 2009;338:b515.

97. MacDonald R. HIV post-exposure prophylaxis prescribing after sexual assault in a sexual assault referral centre. *HIV Med.* 2010;11(Suppl 1):51.

98. Henry K, Acosta EP. Hepatotoxicity and rash associated with zidovudine and zalcitabine chemoprophylaxis. *Ann Intern Med.* 1996;124(9):855-855.

99. Centers for Disease Control and Prevention (CDC). Serious adverse events attributed to nevirapine regimens for postexposure prophylaxis after HIV exposures--worldwide, 1997-2000. *Morb Mortal Wkly Rep.* 2001;49(51):1153-1156.

100. Postma MJ, Bos JM, de Jong-van den Berg LTW, Tramarin A, van Bergen JEAM. HIV post-exposure prophylaxis: enhancing its pharmaco-economic profile by discriminate prescribing. *AIDS.* 2002;16(8):1177-1179.

101. Johnson S, Baraboutis JG. Adverse effects associated with use of nevirapine in HIV postexposure prophylaxis for 2 health care workers. *JAMA.* 2000;284(21):2722-2723.

102. National Institutes of Health. *Viramune Drug Label*. Bethesda, MD: US Department of Health and Human Services; 2014: available at http://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=5ec05500-6333-4bd0-ac83-464fad0d5162.

103. Sonder GJB, Van den Hoek A, Regez RM, et al. Trends in HIV postexposure prophylaxis prescription and compliance after sexual exposure in Amsterdam, 2000-2004. *Sex Transm Dis.* 2007;34(5):288-293.

104. Rhee SY, Blanco JL, Jordan MR, et al. Geographic and temporal trends in the molecular epidemiology and genetic mechanisms of transmitted HIV-1 drug resistance: an individual-patient- and sequence-level meta-analysis. *PloS Med.* 2015;12(4):1-29.

105. Golub SA, Rosenthal L, Cohen DE, Mayer KH. Determinants of high-risk sexual behavior during post-exposure prophylaxis to prevent HIV infection. *AIDS Behav.* 2008;12(6):852-859.

106. Martin JN, Roland ME, Neilands TB, et al. Use of postexposure prophylaxis against HIV infection following sexual exposure does not lead to increases in high-risk behavior. *AIDS.* 2004;18(5):787-792.

107. Waldo CR, Stall RD, Coates TJ. Is offering post-exposure prevention for sexual exposures to HIV related to sexual risk behavior in gay men? *AIDS.* 2000;14(8):1035-1039.

108. Heuker J, Sonder GJB, 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.

109. van Der Snoek EM, de Wit JB, Mulder PG, van Der Meijden WI. Incidence of sexually transmitted diseases and HIV infection related to perceived HIV/AIDS threat since highly active antiretroviral therapy availability in men who have sex with men. *Sex Transm Dis.* 2005;32(3):170-175.

110. Poynten IM, Jin F, Mao L, et al. Nonoccupational postexposure prophylaxis, subsequent risk behaviour and HIV incidence in a cohort of Australian homosexual men. *AIDS.* 2009;23(9):1119-1126.

111. Loke WC, Conway K, Kulasegaram R. The impact of taking HIV post-exposure prophylaxis after sexual exposure (PEPSE) on sexual behaviour. *HIV Med.* 2010;11(Suppl 1):52.

112. Siemieniuk RA, Sivachandran N, Murphy P, et al. Transitioning to HIV pre-exposure prophylaxis (PrEP) from non-occupational post-exposure prophylaxis (nPEP) in a comprehensive HIV prevention clinic: a prospective cohort study. *AIDS Patient Care STDS.* 2015;29(8):431-436.

113. Centers for Disease Control and Prevention (CDC), Health Resources and Services Administration, National Institutes of Health, et al. Recommendations for HIV Prevention with Adults and Adolescents with HIV in the United States, 2014. Atlanta, GA: CDC; 2014: available at http://stacks.cdc.gov/view/cdc/26062. Accessed October 9, 2015.

114. Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission. Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States. Bethesda, MD: US Department of Health and Human Services, National Institutes of Health.; 2014: available at https://aidsinfo.nih.gov/contentfiles/lvguidelines/perinatalgl.pdf. Accessed October 5, 2015.

115. Antiretroviral Pregnancy Registry Steering Committee. Antiretroviral Pregnancy Registry International Interim Report for 1 January 1989 through 31 July 2014. Wilmington, NC: Registry Coordinating Center; 2014: available at http://www.apregistry.com/forms/interim_report.pdf. Accessed October 5, 2015.

116. Unadkat JD, Wara DW, Hughes MD, et al. Pharmacokinetics and safety of indinavir in human immunodeficiency virus-infected pregnant women. *Antimicrob Agents Chemother.* 2007;51(2):783-786.

117. Hayashi S, Beckerman K, Homma M, Kosel BW, Aweeka FT. Pharmacokinetics of indinavir in HIV-positive pregnant women. *AIDS.* 2000;14(8):1061-1062.

118. Food and Drug Administration (FDA). Sustiva: prescribing information. Rockville, MD: US Department of Health and Human Services, FDA; 2010: available at http://www.accessdata.fda.gov/drugsatfda_docs/label/2010/02136s024lbl.pdf. Accessed October 9, 2015.

119. Brogly SB, Abzug MJ, Watts DH, et al. Birth defects among children born to human immunodeficiency virus-infected women: pediatric AIDS clinical trials protocols 219 and 219C. *Pediatr Infect Dis J.* 2010;29(8):721-727.

120. Knapp KM, Brogly SB, Muenz DG, et al. Prevalence of congenital anomalies in infants with in utero exposure to antiretrovirals. *Pediatr Infect Dis J.* 2012;31(2):164-170.

121. Ford N, Mofenson L, Shubber Z, et al. Safety of efavirenz in the first trimester of pregnancy: an updated systematic review and meta-analysis. *AIDS.* 2014;28 Suppl 2:S123-131.

122. Peters PJ, Stringer J, McConnell MS, et al. Nevirapine-associated hepatotoxicity was not predicted by CD4 count >= 250 cells/mu L among women in Zambia, Thailand and Kenya. *HIV Med.* 2010;11(10):650-660.

123. Mandelbrot L, Kermarrec N, Marcollet A, et al. Case report: nucleoside analogue-induced lactic acidosis in the third trimester of pregnancy. *AIDS.* 2003;17(2):272-273.

124. Luzzati R, Del Bravo P, Di Perri G, Luzzani A, Concia E. Riboflavine and severe lactic acidosis. *Lancet.* 1999;353(9156):901-902.

125. Centers for Disease Control and Prevention. Compendium of Evidence-Based Interventions and Best Practices for HIV Prevention. 2015; http://www.cdc.gov/hiv/prevention/research/compendium/index.html. Accessed December, 15, 2015.

126. Roland ME, Neilands TB, Krone MR, et al. A randomized noninferiority trial of standard versus enhanced risk reduction and adherence counseling for individuals receiving post-exposure prophylaxis following sexual exposures to HIV. *Clin Infect Dis.* 2011;53(1):76-83.

127. Landovitz RJ, Fletcher JB, Shoptaw S, Reback CJ. Contingency management facilitates the use of postexposure prophylaxis among stimulant-using men who have sex with men. *Open Forum Infect Dis.* 2015;2(1):1-9.

128. Ford N, Irvine C, Shubber Z, et al. Adherence to HIV postexposure prophylaxis: a systematic review and meta-analysis. *AIDS.* 2014;28(18):2721-2727.

129. Pinkerton SD, Martin JN, Roland ME, Katz MH, Coates TJ, Kahn JO. Cost-effectiveness of HIV postexposure prophylaxis following sexual or injection drug exposure in 96 metropolitan areas in the United States. *AIDS.* 2004;18(15):2065-2073.

130. Pinkerton SD, Martin JN, Roland ME, Katz MH, Coates TJ, Kahn JO. Cost-effectiveness of postexposure prophylaxis after sexual or injection-drug exposure to human immunodeficiency virus. *Arch Intern Med.* 2004;164(1):46-54.

131. Gerberding JL, Katz MH. Post-exposure prophylaxis for HIV. In: Mills J, Volberding PA, Corey L, eds. *Antiviral Chemotherapy 5: New Directions for Clinical Application and Research.* Vol 45. New York, NY: Springer; 1999:213-222.

132. Royce RA, Sena A, Cates W, Jr., Cohen MS. Sexual transmission of HIV. *New Engl J Med.* 1997;336(15):1072-1078.

133. Vittinghoff E, Douglas J, Judson F, McKirnan D, MacQueen K, Buchbinder SP. Per-contact risk of human immunodeficiency virus transmission between male sexual partners. *Am J Epidemiol.* 1999;150(3):306-311.

134. Holmberg SD. The estimated prevalence and incidence of HIV in 96 large US metropolitan areas. *Am J Public Health.* 1996;86(5):642-654.

135. Guinot D, Ho MT, Poynten IM, et al. Cost-effectiveness of HIV nonoccupational post-exposure prophylaxis in Australia. *HIV Med.* 2009;10(4):199-208.

136. Herida M, Larsen C, Lot F, Laporte A, Desenclos JC, Hamers FF. Cost-effectiveness of HIV post-exposure prophylaxis in France. *AIDS.* 2006;20(13):1753-1761.

137. Katz MH, Gerberding JL. The care of persons with recent sexual exposure to HIV. *Ann Intern Med.* 1998;128(4):306-312.

138. Katz MH, Gerberding JL. Postexposure treatment of people exposed to the human immunodeficiency virus through sexual contact or injection-drug use. *New Engl J Med.* 1997;336(15):1097-1100.

139. Mayer KH, Kwong J, Singal R, Boswell S. Non-occupational postexposure HIV prophylaxis: clinical issues and public health questions. *Med health RI.* 2000;83(7):210-213.

140. Desmond NM, Coker RJ. Should preventive antiretroviral treatment be offered following sexual exposure to HIV? The case for. *Sex Transm Infect.* 1998;74(2):144-145.

141. Desmond NM, King ECJ, Dawson SG. Sexual exposure to HIV infection: Is there a role for emergency prophylaxis? *Int J STD AIDS.* 1998;9(1):51-52.

142. Sultan B, Benn P, Waters L. Current perspectives in HIV post-exposure prophylaxis. *HIV AIDS (Auckl).* 2014;6:147-158.

143. Doblecki-Lewis S, Kolber MA. Preventing HIV infection: pre-exposure and postexposure prophylaxis. *IUBMB life.* 2014;66(7):453-461.

144. Kaplan JE, Dominguez K, Jobarteh K, Spira TJ. Postexposure prophylaxis against human immunodeficiency virus (HIV): new guidelines from the WHO: a perspective. *Clin Infect Dis.* 2015;60 Suppl 3:S196-199.

145. Evans B, Darbyshire J, Cartledge J. Should preventive antiretroviral treatment be offered following sexual exposure to HIV? Not yet! *Sex Trans Infect.* 1998;74(2):146-148.

146. Mackie NE, Coker RJ. Post-exposure prophylaxis following non-occupational exposure to HIV: risks, uncertainties, and ethics. *Int J STD AIDS.* 2000;11(7):424-427.

147. Myles JE, Bamberger JD. *Offering HIV prophylaxis following sexual assault: recommendations for the State of California.* Sacramento, CA: California Department of Health Services;2001.

148. Commonwealth of Massachusetts Department of Public Health. Clinical Advisory: HIV prophylaxis for non-occupational exposures. Boston, MA: Massachusetts Department of Public Health; 2000: Available at http://www.mass.gov/dph/aids/guidelines/ca_exposure_nonwork.htm

149. Landovitz RJ, Combs KB, Currier J. Availability of HIV post-exposure prophylaxis services in Los Angeles County *Clin Infect Dis.* 2009;48(11):1624-1627.

150. Fitzpatrick LJ, Egan DJ, Cowan E, et al. Nonoccupational post-exposure prophylaxis for HIV in New York State emergency departments. *J Int Assoc Provid AIDS Care.* 2014;13(6):539-546.

151. Rodriguez AE, Castel AD, Parish CL, et al. HIV medical providers' perceptions of the use of antiretroviral therapy as nonoccupational postexposure prophylaxis in 2 major metropolitan areas. *J Acquir Immune Defic Syndr.* 2013;64 Suppl 1:S68-79.

152. Kearney S, Sharathkumar A, Rodriguez V, et al. Neonatal circumcision in severe haemophilia: a survey of paediatric haematologists at United States Hemophilia Treatment Centers. *Haemophilia.* 2015;21(1):52-57.

153. Draughon JE, Anderson JC, Hansen BR, Sheridan DJ. Nonoccupational postexposure HIV prophylaxis in sexual assault programs: a survey of SANE and FNE program coordinators. *J Assoc Nurses AIDS Care.* 2014;25(1 Suppl):S90-S100.

154. Kahn JO, Martin JN, Roland ME, et al. Feasibility of postexposure prophylaxis (PEP) against human immunodeficiency virus infection after sexual or injection drug use exposure: the San Francisco PEP Study. *J Infect Dis.* 2001;183(5):707-714.

155. Patel P, Borkowf CB, Brooks JT, Lasry A, Lansky A, Mermin J. Estimating per-act HIV transmission risk: a systematic review. *AIDS.* 2014;28(10):1509-1519.

156. Abdala N, Reyes R, Carney JM, Heimer R. Survival of HIV-1 in syringes: effects of temperature during storage. *Substance Use Misuse.* 2000;35(10):1369-1383.

157. Rich JD, Dickinson BP, Carney JM, Fisher A, Heimer R. Detection of HIV-1 nucleic acid and HIV-1 antibodies in needles and syringes used for non-intravenous injection. *AIDS.* 1998;12(17):2345-2350.

158. Richman KM, Rickman LS. The potential for transmission of human immunodeficiency virus through human bites. *J Acquir Immune Defic Syndr.* 1993;6(4):402-406.

159. Anonymous. Transmission of HIV by a human bite. *Lancet.* 1987;2(8557):522.

160. Vidmar L, Poljak M, Tomazic J, Seme K, Klavs I. Transmission of HIV-1 by human bite. *Lancet.* 1996;347(9017):1762-1763.

161. Deshpande AK, Jadhav SK, Bandivdekar AH. Possible transmission of HIV infection due to human bite. *AIDS Res Ther.* 2011;8(1):16.

162. Andreo SMS, Barra LAC, Costa LJ, Sucupira MCA, Souza IEL, Diaz RS. Short communication: HIV type 1 transmission by human bite. *AIDS Res Hum Retroviruses.* 2004;20(4):349-350.

163. Pilcher CD, Eron JJ, Jr., Vemazza PL, et al. Sexual transmission during the incubation period of primary HIV infection. *JAMA.* 2001;286(14):1713-1714.

164. Chakraborty H, Sen PK, Helms RW, et al. Viral burden in genital secretions determines male-to-female sexual transmission of HIV-1: a probabilistic empiric model. *AIDS.* 2001;15(5):621-627.

165. Hirsch MS, Günthard HF, Schapiro JM, et al. Antiretroviral drug resistance testing in adult HIV-1 infection: 2008 recommendations of an International AIDS Society-USA panel. *Clin Infect Dis.* 2008;47(2):266-285.

166. Ridzon R, Gallagher K, Ciesielski C, et al. Simultaneous transmission of human immunodeficiency virus and hepatitis C virus from a needle-stick injury. *N Engl J Med.* 1997;336(13):919-922.

167. Ciesielski CA, Metler RP. Duration of time between exposure and seroconversion in healthcare workers with occupationally acquired infection with human immunodeficiency virus. *Am J Med.* 1997;102(5B):115-116.

168. Hecht FM, Busch MP, Rawal B, et al. Use of laboratory tests and clinical symptoms for identification of primary HIV infection. *AIDS.* 2002;16(8):1119-1129.

169. Daar ES, Pilcher CD, Hecht FM. Clinical presentation and diagnosis of primary HIV-1 infection. *Curr Opin HIV AIDS.* 2008;3(1):10-15.

170. Vanhems P, Routy JP, Hirschel B, et al. Clinical features of acute retroviral syndrome differ by route of infection but not by gender and age. *J Acquir Immune Defic Syndr.* 2002;31(3):318-321.

171. Rich JD, Merriman NA, Mylonakis E, et al. Misdiagnosis of HIV infection by HIV-1 plasma viral load testing: A case series. *Ann Intern Med.* 1999;130(1):37-39.

172. Puro V, Calcagno G, Anselmo M, et al. Transient detection of plasma HIV-1 RNA during postexposure prophylaxis. *Infect Control and Hosp Epidemiol.* 2000;21(8):529-531.

173. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents. Bethesda, MD: Department of Health and Human Services, National Institutes of Health 2015: Available at http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf Accessed October 6, 2015.

174. Workowski KA, Bolan G. Sexually Transmitted Diseases Treatment Guidelines. *MMWR Recomm Rep.* Vol 64. Atlanta: Centers for Disease Control and Prevention; 2015: available at http://www.cdc.gov/std/tg2015/tg-2015-print.pdf. Accessed October 6, 2015.

175. Centers for Disease Control and Prevention. Recommendations for the Laboratory-Based Detection of *C. trachomatis* and *N. gonorrhoeae* — 2014. 2014; http://www.cdc.gov/std/laboratory/2014labrec/recommendations2.htm. Accessed January 13, 2016.

176. Centers for Disease Control and Prevention (CDC). Recommendations for Routine Testing and Follow-Up for Chronic Hepatitis B Virus (HBV) Infection. Atlanta, GA: US Department of Health and Human Services, CDC; 2008: available at http://www.cdc.gov/hepatitis/hbv/PDFs/ChronicHepBTestingFlwUp.pdf. Accessed October 6, 2015.

177. Centers for Disease Control and Prevention (CDC). Hepatitis B FAQs for Health Professionals. Atlanta, GA: US Department of Health and Human Services, CDC; 2015: available at http://www.cdc.gov/hepatitis/HBV/HBVfaq.htm#general.

178. Mugo NR, Heffron R, Donnell D, et al. Increased risk of HIV-1 transmission in pregnancy: a prospective study among African HIV-1-serodiscordant couples. *AIDS.* 2011;25(15):1887-1895.

179. Panel on Antiretroviral Therapy and Medical Management of HIV-Infected Children. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection. Bethesda, MD: US Department of Health and Human Services, National Institutes of Health; 2015: available at https://aidsinfo.nih.gov/contentfiles/lvguidelines/pediatricguidelines.pdf. Accessed October 6, 2015.

180. Chaudry NI, Eron JJ, Naderer OJ, et al. Effects of formulation and dosing strategy on amprenavir concentrations in the seminal plasma of human immunodeficiency virus type 1-infected men. *Clin Infect Dis.* 2002;35(6):760-762.

181. Reddy YS, Gotzkowsky SK, Eron JJ, et al. Pharmacokinetic and pharmacodynamic investigation of efavirenz in the semen and blood of human immunodeficiency virus type 1-infected men. *J Infect Dis.* 2002;186(9):1339-1343.

182. Patterson KB, Prince HA, Kraft E, et al. Penetration of tenofovir and emtricitabine in mucosal tissues: implications for prevention of HIV-1 transmission. *Sci Transl Med.* 2011;3(112):1-8.

183. Food and Drug Adminstration (FDA). Information for health care professional: Abacavir (marketed as Ziagen) and abacavir-containing medications. Rockville, MD: US Department of Health and Human Services, FDA; 2013: available at http://www.fda.gov/drugs/drugsafety/postmarketdrugsafetyinformationforpatientsandproviders/ucm123927.htm. Accessed October 8, 2015.

184. Ford N, Venter F, Irvine C, Beanland RL, Shubber Z. Starter packs versus full prescription of antiretroviral drugs for postexposure prophylaxis: a systematic review. *Clin Infect Dis.* 2015;60 Suppl 3:S182-186.

185. Chandwani S, Koenig LJ, Sill AM, Abramowitz S, Conner LC, D'Angelo L. Predictors of antiretroviral medication adherence among a diverse cohort of adolescents with HIV. *J Adolescent Health.* 2012;51(3):242-251.

186. Koenig LJ, Lyles C, Smith DK. Adherence to antiretroviral medications for HIV pre-exposure prophylaxis: lessons learned from trials and treatment studies. *Am J Prev Med.* 2013;44(1 (S2)):S91-S97.

187. Peterson J, Di Clemente R. *The Handbook of HIV Prevention.* New York, NY: Kluwer Academic/Plenum; 2000.

188. Grant RM, Anderson PL, McMahan V, et al. Uptake of pre-exposure prophylaxis, sexual practices, and HIV incidence in men and transgender women who have sex with men: a cohort study. *Lancet Infect Dis.* 2014;14(9):820-829.

189. Black MC, Basile KC, Breiding MJ, et al. The National Intimate Partner and Sexual Violence Survey (NISVS): 2010 Summary Report Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Injury Prevention and Control; 2011: Available at http://www.cdc.gov/violenceprevention/pdf/nisvs_report2010-a.pdf. Accessed October 8, 2015.

190. Lipscomb GH, Muram D, Speck PM, Mercer BM. Male victims of sexual assault. *JAMA.* 1992;267(22):3064-3066.

191. Riggs N, Houry D, Long G, Markovchick V, Feldhaus KM. Analysis of 1,076 cases of sexual assault. *Ann Emerg Med.* 2000;35(4):358-362.

192. Swan H, O'Connell DJ. The impact of intimate partner violence on women's condom negotiation efficacy. *J Interpers Violence.* 2012;27(4):775-792.

193. Raj A, Santana MC, La Marche A, Amaro H, Cranston K, Silverman JG. Perpetration of intimate partner violence associated with sexual risk behaviors among young adult men. *Am J Public Health.* 2006;96(10):1873-1878.

194. Wingood GM, DiClemente RJ, Raj A. Adverse consequences of intimate partner abuse among women in non-urban domestic violence shelters. *Am J Prev Med.* 2000;19(4):270-275.

195. Wingood GM, DiClemente RJ, Raj A. Identifying the prevalence and correlates of STDs among women residing in rural domestic violence shelters. *Women Health.* 2000;30(4):15-26.

196. Gielen AC, Ghandour RM, Burke JG, Mahoney P, McDonnell KA, O'Campo P. HIV/AIDS and intimate partner violence—Intersecting women's health issues in the United States. *Trauma Violence Abuse.* 2007;8(2):178-198.

197. Campbell JC, Soeken K. Forced sex and intimate partner violence: effects on women's health *Violence Against Women.* 1999;5:1017-1035.

198. Digiovanni C, Berlin F, Casterella P, et al. Prevalence of HIV antibody among a group of paraphilic sex offenders. *J Acquir Immune Defic Syndr.* 1991;4(6):633-637.

199. Bristol-Myers Squibb. Efavirenz (Sustiva) [package insert]. New York, NY: Bristol-Myers Squibb; 2015: available at http://packageinserts.bms.com/pi/pi_sustiva.pdf. Accessed October 8, 2015.

200. Wohl AR, Johnson D, Jordan W, et al. High-risk behaviors during incarceration in African-American men treated for HIV at three Los Angeles public medical centers. *J Acquir Immune Defic Syndr.* 2000;24(4):386-392.

201. Mutter RC, Grimes RM, Labarthe D. Evidence of intraprison spread of HIV infection. *Arch Intern Med.* 1994;154(7):793-795.

202. Brewer TF, Vlahov D, Taylor E, Hall D, Munoz A, Polk BF. Transmission of HIV-1 within a statewide prison system. *AIDS.* 1988;2(5):363-367.

203. Gupta N, Schmidt H, Buisker T, et al. After the fact: a brief educational program on HIV postexposure prophylaxis for female detainees in a local jail. *J Correct Health Care.* 2015;21(2):140-151.

204. Federal Bureau of Prisons. Medical Management of Exposures: HIV, HBV, HCV, Human Bites, and Sexual Assaults. Bureau of Prisons Clinical Practice Guidelines, March 2014. Washington, DC: US Department of Justice, Federal Bureau of Prisons; 2014: available at http://www.bop.gov/resources/pdfs/exposures.pdf. Accessed October 8, 2015.

205. Gruber VA, McCance-Katz EF. Methadone, buprenorphine, and street drug interactions with antiretroviral medications. *Curr HIV/AIDS Rep.* 2010;7(3):152-160.

206. Lehman JS, Carr MH, Nichol AJ, et al. Prevalence and public health implications of state laws that criminalize potential HIV exposure in the United States. *AIDS Behav.* 2014;18(6):997-1006.

207. Culp L, Caucci L. State adolescent consent laws and implications for pre-exposure prophylaxis (PrEP). *Am J Prev Med.* 2012;44(1S2):S119-S124.

X. APPENDICES

Appendix 1A

Summary of Methods for nPEP Guidelines Development and Roles of Teams and Consultants

Topic	Comment
The guidelines' goal	Provide guidance for medical practitioners regarding nPEP use for persons in the United States.
nPEP Working Group	The nPEP Working Group is composed of 13 members from the Centers for Disease Control and Prevention (CDC) with expertise in nPEP or other subject areas pertinent to the guidelines (e.g., cost-effectiveness, sexual assault, or nPEP adherence), including certain members who were involved in the writing of the previous version(s) of the CDC nPEP guidelines.
nPEP Writing Group	The nPEP Writing Group is composed of 12 members from CDC with expertise in nPEP or other subject areas pertinent to the guidelines (e.g., cost-effectiveness, sexual assault, or nPEP adherence, etc.), including 1 member who was involved in the writing of the previous version of CDC's nPEP guidelines.
nPEP external consultants	External consultants were selected from government, academia, and the health care community by CDC to participate in 2 consultations by telephone conference call regarding nPEP on the basis of the member's area of subject matter expertise. Each consultation was chaired by 1 of the CDC nPEP co-chairs. The list of the external consultants is available in Appendix 2B.
Competing interests and management of conflicts of interest	All internal CDC staff and external consultants involved in developing the guidelines or who served in the external consultations submitted a written financial disclosure statement reporting any potential conflicts of interest related to questions discussed during the consultations or concerns involved in developing of the nPEP guidelines. A list of these disclosures and their last update is available in Appendix 2C. The nPEP co-chairs reviewed each reported association for potential competing interest and determined the appropriate action, as follows: disqualification from the panel, disqualification/recusal from topic review and discussion; or no disqualification needed. A *competing interest* is defined as any direct financial interest related to a product addressed in the section of the guideline to which a panel member contributes content. *Financial interests* include direct receipt by the panel member of payments, gratuities, consultancies, honoraria, employment, grants, support for travel or accommodation, or gifts from an entity having a commercial interest in that product. *Financial interest* also includes direct compensation for membership on an advisory board, data safety monitoring board, or speakers bureau. Compensation and support that filters through a panel member's university or institution (e.g., grants or research funding) is not considered a competing interest.

Topic	Comment
OMB Peer Review and OMB Public Engagement	As recommended by the Office of Management and Budget for scientific documents fitting the classification of Influential Scientific Information, during Oct. 2014–December 2015, the draft nPEP guidelines underwent peer review by independent scientific and technical experts. They were asked to review the scientific and technical evidence that provides the basis for the nPEP guidelines and to provide input on the draft guidelines before they were finalized. Peer reviewers were asked whether any recommendations are based on studies that were inappropriate as supporting evidence or were misinterpreted, whether there are significant oversights, omissions, or inconsistencies that are critical for the intended audience of clinicians, and whether the recommendations for the intended audience of health care providers are justified and appropriate. In addition, the recommendations from the draft nPEP guidelines were presented to the public through 2 public engagement webinars on November 14 and 17, 2014. Based on the responses from both peer review and public engagement, updates were made to the nPEP guidelines prior to their publication. CDC's responses to the comments were also posted on the CDC/ATSDR Peer Review Agenda website at http://www.cdc.gov/od/science/quality/support/peer-review.htm and the CDC Division of HIV/AIDS Prevention Program Planning Scientific Information Quality—Peer Review Agenda website at http://www.cdc.gov/hiv/policies/planning.html.
Guidelines users	Health care providers
Developer	The CDC nPEP Working Group
Funding source	Epidemiology Branch, Division of HIV/AIDS Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, TB Prevention, CDC
Recommendation ratings	Because none of the evidence is based on randomized clinical trials, but rather observational studies or expert opinion, we have elected not to provide graded recommendations for these guidelines.
Abbreviations: AIDS, acquired immunodeficiency virus; CDC, Centers for Disease Control and Prevention; HIV, human immunodeficiency virus; nPEP, nonoccupational postexposure prophylaxis.	

Appendix 1B

nPEP Guidelines Development Teams and Consultants

CDC nPEP Guidelines Writing Team

Kenneth L. Dominguez, MD, MPH (lead author), Dawn K. Smith, MD, MS, MPH, Vasavi Thomas, RPh, MPH; Nicole Crepaz, PhD; Karen S. Lang, MSW; Walid Heneine, PhD; Janet McNicholl, MD; Laurie Reid, RN, MS; Brandi Freelon, MD; Steven Nesheim, MD; Ya-lin (Aileen) Huang, PhD; and Paul J. Weidle, PharmD, MPH.

CDC nPEP Working Group

Ken Dominguez, MD, MPH (Co-lead); Vasavi Thomas, RPh, MPH (Co-lead), Dawn K. Smith, MD, MS, MPH; Steve Nesheim, MD; Walid Heneine, PhD; Lauri Reed, Brandi Freelon, MD; Nicole Crepaz, PhD; Karen S. Lang, MSW; Ya-lin (Aileen) Huang, PhD; Kathleen Irwin, MD, MPH; Gema Dumitru, MD; David Kuhar, MD; and Lynn Paxton, MD, MPH.

Federal Consultants

CDC: Norma Harris, PhD; John Brooks, MD; Pragna Patel, MD, MPH; and Philip J. Peters, MD.

Other Federal Agencies

Holly Van Lew, PharmD, Indian Health Service; Newton Kendig, MD, Bureau of Prisons; David Burns, MD, National Institutes of Health; Laura Cheever, MD, Health Resources and Services Administration; Maggie Czarnogorski, MD, Department of Veterans Affairs; Heather Huentelman, PharmD, Indian Health Service; Kimberly Struble, PharmD, Food and Drug Administration; Rohan Hazra, MD, National Institutes of Health; Lynne Mofenson, MD, National Institutes of Health; and Steve George Siberry, MD, MPH, National Institutes of Health.

Nonfederal External Consultants

Jeffrey Beal, MD, Florida Department of Health; Ronald H. Goldschmidt, MD, University of California, San Francisco; Donna Greco, MSW, Pennsylvania Coalition Against Rape/National Sexual Violence Resource Center; Angela Kashuba, BScPhm, PharmD, University of Northern Carolina Center for AIDS Research, Chapel Hill; Sally Laskey, MA, National Sexual Violence Resource Center, Enola, Pennsylvania; Kenneth Mayer, MD, Fenway Health Center, Boston, Massachusetts; Thera Meehan, MS, MPH, Massachusetts Department of Public Health, Boston; Jennifer Sayles, MD, Los Angeles County Public Health Department, California; Barbara Sheaffer, MA, Pennsylvania Coalition Against Rape, Enola, Pennsylvania; Lyn Stevens, MS, ACRN, NP, New York State Department of Health, Albany; Elaine Abrams, MD, Columbia University College of Physicians & Surgeons, New York, New York; Michael Brady, MD, Columbus Children's Hospital, Ohio; Ellen Chadwick, MD, Northwestern University's Feinberg School of Medicine, Chicago, Illinois; Rana Chakraborty, MD, Emory University School of Medicine, Atlanta, Georgia; Ellen Cooper, MD, Boston University School of Medicine, Massachusetts; Peter Havens, MD, MPH, Children's Hospital of Wisconsin, Milwaukee; Daniel Johnson, MD, Comer Children's Hospital, University of Chicago, Illinois; Paul Krogstad, MD, University of California at Los Angeles–David Geffen School of Medicine; Natalie Neu, MD, MPH, Columbia University Medical Center, New York, New York; Vicki Peters, MD, New York City Department of Health and Mental Hygiene, New York; Russ van Dyke, MD, Tulane University School of Medicine. New

Orleans, Louisiana; and Geoffrey Weinberg, MD, University of Rochester Medical Center, School of Medicine and Dentistry, New York.

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CDC editor

C. Kay Smith, Med

Abbreviation: nPEP, nonoccupational postexposure prophylaxis.

Appendix 1C

Financial Disclosures of Potential Competing Interest
nPEP Guidelines Consultants and Working Group

Member (affiliation)	Role	Company	Relationship	Determination
Elaine Abrams, MD, Columbia University College of Physicians & Surgeons	Non-federal external consultant	None		
Jeffrey Beal, MD, Florida Department of Health	Non-federal external consultant	CDC Flow Through Money—Perinatal Transmission Project	Principal Investigator	No disqualification needed
Beverly Bohannon, RN, MS, CDC	CDC scientific support staff	None		
Michael Brady, MD, Columbus Children's Hospital	Non-federal external consultant	None		
John Brooks, MD, CDC	Other CDC consultant	None		
David Burns, MD, NIH	Other federal consultant	None		
Ellen Chadwick, MD, Northwestern University's Feinberg School of Medicine	Non-federal external consultant	Abbott Labs	Spouse—Abbott retiree; Spouse—owner of stocks and stock options	Recusal from topic review and discussion of selection of antiretrovirals for nPEP use
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Abbreviations: CDC, Centers for Disease Control and Prevention; nPEP, nonoccupational postexposure prophylaxis.

Appendix 2

Literature Search Methods for the nPEP Guidelines

Topic	Databases	Research Question	Keywords	Dates of Search	Search Limits
Animal Studies	PubMed	Which studies related to PEP involving animal models were published since 2005?	SIV post exposure prophylaxis, post-exposure prophylaxis, antiretroviral prophylaxis in macaques	January 2005 to July 2015	No limitations
Observational Studies, Case Reports	Web of Knowledge, PubMed, Google Scholar	Which are the results of latest nPEP observational and case studies since 2005 with a focus on populations studied, drug regimens used, completion rates, side effects of medications, number of breakthrough infections?	nPEP, nonoccupational postexposure or post-exposure prophylaxis, and HIV postexposure or post-exposure prophylaxis	January 2005 to July 2015	Excluded opinion pieces; no other limitations
Effects on Risk-Reduction Behaviors	MEDLINE, EMBASE, CINAHI [EBSCOhost]	What are the potential behavioral implications of offering nPEP?	HIV infections, acquired immune deficiency syndrome, seropositivity, serodiagnosis, HIV, AIDS, post exposure or post-exposure prophylaxis, post exposure or post-exposure prevention, non-occupational, non pep, NOPEP, nPEP, PEP	January 1996 to July 2015	No limitations
Cost Effectiveness	PubMed	The cost-effectiveness evaluation of nPEP in the United States and other resource-rich countries.	HIV, post exposure post-exposure prophylaxis, PEP, nPEP, economic evaluation, cost utility, cost-benefit analysis, cost benefit, cost effectiveness	January 2005 to July 2015	English only; excluded occupational exposure; not an economic evaluation; no other limitations
Pregnant Women, Women of Childbearing Potential	PubMed	Which nPEP studies involving pregnant women and women of childbearing potential were conducted since 2005?	pregnant women, women of reproductive age, PEP, nPEP, postexposure or post-exposure HIV prophylaxis	January 2005 to July 2015	No limitations
Children/Adolescents	PubMed	Which nPEP studies involving children or adolescents were conducted since 2005?	Children, pediatrics, adolescents, PEP, nPEP, postexposure or post-exposure HIV prophylaxis	January 2005 to July 2015	No limitations
Sexual Assault Survivors	PubMed	Which nPEP studies involving sexual assault survivors were conducted since 2005?	Sexual assault, sexual abuse, PEP, nPEP, postexposure or post-exposure HIV prophylaxis	January 2005 to July 2015	No limitations
Incarcerated Populations	PubMed	Which nPEP studies involving incarcerated populations were conducted since 2005?	Incarcerated, jail, prison, correctional facility, nPEP, PEP	January 2005 to July 2015	No limitations

Abbreviations: AIDS, acquired immunodeficiency syndrome; HIV, human immunodeficiency virus; nPEP, non-PEP, or NOPEP, nonoccupational postexposure prophylaxis; PEP, postexposure prophylaxis.

Appendix 3

Studies Reviewed for the nPEP Guidelines

MSM Studies

Authors, year: Donnell et al, 2010[14]

Type of study: Randomized behavioral intervention trial to assess perceptions and nPEP use over a 4-year period

Location: 6 U.S. cities

Sample size: n=4,295 MSM

Risk: HIV uninfected men who reported unprotected anal sex in the past year

Intervention: Behavioral intervention vs. standard risk-reduction counseling (accompanying nPEP drug regimen not reported)

Drug regimen: Not reported

Time from exposure to nPEP: Not reported

Completion of nPEP: Not reported

HIV seroconversions: 3

Conclusion: Increased odds of nPEP use was observed in participants with multiple partners and participants who had unprotected anal sex with HIV infected and unknown status partners. The availability of nPEP did not lead to an increase in high-risk sex.

Authors, year: Foster et al, 2015[19]

Type of study: Open-label, single-arm nonrandomized trial at 2 public sexual health clinics and 2 hospital EDs during December 23, 2012–June 12, 2014.

Location: Melbourne, and Sydney, Australia

Sample size: n=100 MSM

Risk: Sexual 65% failed to use a condom after anal intercourse; 29% used a condom but it tore or slipped off; 6% source partner removed condom

Intervention: 3-drug single tablet once daily dose regimen

Drug regimen: RPV + FTC + TDF

Time from exposure to nPEP: ≤72 hours; presentation for nPEP initiation at a mean=30 hours; nPEP initiated at a mean of 2 hours after presentation

Completion of nPEP: 92%

HIV seroconversions: 0 seroconversions occurred through week 12 after initiation of nPEP. Adherence was 98.6% by pill count and 98.5% by self–report; 88% tested had plasma TDF levels suggesting full adherence. 88% experienced ≥1 clinical adverse events. Adverse events included mainly fatigue (34%) and nausea (23%); one participant developed acute abdominal pain and vomiting and grade 4 laboratory evidence of acute pancreatitis ≤1 week of completing nPEP.

Conclusion: A triple ARV regimen of RPV, FTC, and TDF administered once daily as a single combination tablet was well tolerated as nPEP with high levels of adherence and regimen completion.

Authors, year: Jain et al, 2015[18]

Type of study: Retrospective medical record review in a large community health center during July1997–August 2013

Location: Boston, Massachusetts

Sample size: n=788 MSM; median age=32.9 years; 21.2% presented for nPEP 2 or more times (range, 1–15 times)

Risk: Consensual unprotected sex most common n=726 (62.2%); n=425 (58.5%) receptive anal; n=277 (38.2%) insertive anal; n=157 (21.6%) receptive oral intercourse; n=351 (31.1%) condom failure or removal; (35.6%) HIV-positive partner

Intervention: nPEP (number of drugs not reported in this study, however, previous studies from this site have reported 2 or 3 drugs)

Drug regimen: Not reported

Time from exposure to nPEP: Not reported but assume 72 hours based on previously published studies from this site

Completion of nPEP: Not reported

HIV seroconversions: 39 seroconversions occurred at >90 days after initially presenting for nPEP; 4 occurred at <180 days: 91, 133, 160, 168 days; 3 of 4 reported completing 28-day regimen; adherence or ongoing sexual risk behavior not reported; 35 (89.7%) seroconversions occurred at ≥180 days after nPEP initiation; seroconversion associated with younger age and/or being African American or Latino; almost 90% of post-nPEP infections were probably due to subsequent risk-taking and not a failure of the initial nPEP regimen

Conclusion: Younger age, being Latino and/or being African American, but not repeated nPEP use, were associated with incident HIV infection. Younger MSM of color who are nPEP users may benefit from early HIV risk reduction and PrEP.

Authors, year: McAllister et al, 2014[17]

Type of study: Nonrandomized, open-label, prospective cohort study at two urban hospital centers

Location: Sydney, Australia

Sample size: n=125 MSM enrolled; n=91 prescribed 3-drug regimen; n=34 prescribed 2-drug regimen; mean age 32–34 years

Risk: Sexual

Intervention: 2-drug or 3-drug regimen

Drug regimen: TDF + FTC or RAL+ TDF + FTC; Mean Adherence to each arm: TDF + FTC (90%); RAL-FTC-TDF (89%); 8 patients reported myalgia on the 3-drug regimen vs. none on the 2-drug regimen; Grade 4 creatinine kinase elevations occurred in 5 subjects on the 3-drug regimen vs. none on the 2-drug regimen. All Grade 4 creatinine kinase elevations resolved to ≤grade 2 after desisting from exercise and increasing oral fluids intake

Time from exposure to nPEP: Not reported

Completion of nPEP: 86/91 (95%) participants prescribed a 3-drug regimen met criteria to stay on nPEP; 79/86 (92%) completed 28-day 3-drug regimen; 31/34 (91%) participants prescribed 2-drug regimen completed 28-day 2-drug regimen; overall 110/120 (91.7%) who met criteria to stay on nPEP completed 28-day regimen; overall 110/125 (88%) who were prescribed nPEP, completed the 28-day regimen

HIV seroconversions: 0

Conclusion: Although the 3-drug and 2-drug arms had similar percentages of patients completing their 28-day regimens, 9% of the 3-drug arm experienced grade 4 creatinine kinase elevations which subsequently resolved with increased fluid intake and desisting exercise. If a RAL-TDF-FTC regimen is used, a preferred nPEP regimen, authors recommend (1) asking patients about concomitant medications associated with rhabdomyolysis (i.e. statins); (2) patient education about possible association between RAL-containing nPEP, exercise, and rhabdomyolysis and the need to report myalgia; (3) laboratory monitoring of serum creatinine

kinase at baseline; if myalgia or weakness develops, conduct additional during treatment and clinical examination for proximal muscle weakness. Completion rates were higher for this study compared to those in other studies, including similar nPEP regimens. This may have been due to a high level of support provided by the study team including an experienced nPEP nurse, 24-hour contact with the nurse consultant, text reminders of appointments, proactive recall after missed appointments and frequent adherence education.

Authors, year: Schechter et al, 2004[16]

Type of study:

Location: Rio de Janeiro, Brazil

Sample size: n=200 participants; median age, 28 years; n=68 received nPEP

Risk: Sexual exposure (gay or bisexual)

Intervention: 2-drug regimen

Drug regimen: ZDV + 3TC

Time from exposure to nPEP: ≤48 hours

Completion of nPEP: 11 (1 among nPEP users, 10 among patients not using nPEP)

HIV seroconversions:

Conclusion: nPEP was safely tolerated and did not appear to be associated with either increases in reported high-risk behavior or HIV transmission; such findings may limit its impact as a public health intervention

Authors, year: Sonder et al, 2010[15]

Type of study: Observational study comparing 2 nPEP regimens

Location: Amsterdam

Sample size: n=309 MSM

Risk: Sexual exposure

Intervention: One 4-drug regimen and one 3-drug regimen; 2- or 3-pill burden

Drug regimen: Single-dose NVP + ZDV+ 3TC+ NFV or ZDV + 3TC + ATV

Time from exposure to nPEP: Seroconverters presented between 5–36 hours post exposure

Completion of nPEP: 237/261 (91%)

HIV seroconversions: 5 (likely due to ongoing risk behavior)

Conclusion: Common side effects were fatigue, nausea, and diarrhea (worse in regimen 1). There was no significant difference in completion rates of the two regimens. Strategies are needed to prevent subsequent HIV exposures in nPEP-treated individuals

Authors, year: Terzi et al, 2007[13]

Type of study: Case report

Location: Italy

Sample size: n=1 MSM
Risk: Receptive anal intercourse with HIV + male
Intervention: 3-drug regimen; 2-pill burden
Drug regimen: ZDV + 3TC (Combivir) + IDV
Time from exposure to nPEP: 30 hours
Completion of nPEP: Complete adherence
HIV seroconversions:
Conclusion: Sexual exposures to HIV and HCV require prolonged follow-up due to the risk of late seroconversion.

Sexual Assault Studies—Adults, Adolescents, and Children (combined)

Authors, year: Chacko et al, 2012[20]
Type of study: Systematic review of nPEP adherence among victims of sexual assault
Location: U.S. and International
Sample size: n=24 studies of adults, adolescents, and children
Risk: Sexual assault
Intervention: Various 2- and 3-drug regimens
Drug regimen: Most regimens included ZDV
Time from exposure to nPEP: Not reported
Completion of nPEP: 40%
HIV seroconversions: Not reported
Conclusion: Overall adherence was poor but was higher in developing countries compared to developed countries. Common side effects were: nausea and vomiting, diarrhea, and fatigue. More interventions are needed to improve adherence. Standard methods of conducting and reporting nPEP programs are needed.

Authors, year: Draughon and Sheridan, 2011[21]
Type of study: Systematic review spanning 10 years
Location: Sub-Saharan Africa (Kenya, Malawi, and South Africa)
Sample size: n=studies of adults, adolescents, and children
Risk: Sexual assault
Intervention: Not reported
Drug regimen: Not reported
Time from exposure to nPEP: Not reported
Completion of nPEP: 0%–65% (most studies reported >35%)

HIV seroconversions: Not reported

Conclusion: Overall adherence was low, but was higher in locations where the full 28-day PEP regimen was given up front.

Authors, year: Draughon and Sheridan, 2012[22]

Type of study: Systematic review

Location: Low HIV prevalence countries

Sample size: n=34 studies of adults, adolescents, and children

Risk: Sexual assault

Intervention: nPEP (number of drugs not reported by reviewers)

Drug regimen: Not reported

Time from exposure to nPEP: 24–96 hours

Completion of nPEP: 0%–63%

HIV seroconversions: Not reported

Conclusion: There was wide variation in the provision, acceptance, and adherence to nPEP programs. Anywhere from 5%–100% of eligible patients received nPEP across studies. Further research is needed to understand the experience of sexual assault survivors with the health care system and nPEP following an attack

Authors, year: Loutfy et al, 2008[23]

Type of study: Prospective cohort study

Location: Ontario, Canada

Sample size: n=798 sexual assault survivors presented to sexual assault treatment centers and offered nPEP; females (n=775 [97.1%]), age 4–17 years (n=190 [23.8%]), age 18–80 years (n=608 [77.2%]); 347 accepted nPEP

Risk: Sexual assault

Intervention: 3-drug regimen; 2-pill burden

Drug regimen: Combivir + Kaletra

Time from exposure to nPEP: ≤72 hours

Completion of nPEP: 111/347 (31.9%) completed nPEP including (11/46 [23.9%]) of participants at high risk completed therapy and (100/301 [33.2%]) of unknown risk participants completed therapy

HIV seroconversions: Not reported

Conclusion: The PEP program for sexual assault survivors in Ontario proved to be feasible and acceptable among participants. The most common side effects were fatigue, nausea, and diarrhea. Further research is needed to improve loss to follow-up and completion rates of nPEP.

Sexual Assault Studies—Adults and/or Adolescents

Authors, year: Carrieri et al, 2006[33]

Type of study: Retrospective survey of nPEP consultations

Location: Southeastern France

Sample size: n=94 persons, aged 18 years or older, presented to AIDS centers for nonoccupational HIV exposure (female n=88 [93.6%], male n=6 [6.4%]); nPEP prescribed to 86 persons

Risk: Sexual assault

Intervention: 2 and 3 drug regimens

Drug regimen: Not reported

Time from exposure to nPEP: 72% (n=77) ≤48 hours

Completion of nPEP: 25% (n=23) >3 months follow-up

HIV seroconversions: Not reported

Conclusion: Half of all participants were lost to follow-up after the first consultation. During the study period there were 600 additional sexual assaults that were reported to police but did not receive nPEP consultation. Prompt HIV medical assessment is needed for sexual assault survivors as well as strategies to improve nPEP adherence.

Authors, year: Griffith et al, 2010[31]

Type of study: Retrospective chart review in an urban county hospital from June 2007–June 2008

Location: Dallas, TX

Sample size: n=151 adolescent and adult women (151 prescribed nPEP, 62 received follow-up of which 58 self-reported taking nPEP); aged 13–17 years, n=43 (28%); 18–61 years, n=108 (72%)

Risk: Sexual assault

Intervention: 3-drug regimen; 2-pill burden

Drug regimen: Kaletra + Truvada or Combivir

Time from exposure to nPEP: ≤72 hours

Completion of nPEP: 62/151 (41%) of women presented for a follow-up visit. 37 of the 62 (60%) took nPEP for ≥21 days or completed prescribed course of therapy

HIV seroconversions: 0 (36 of 58 women who reported taking nPEP at follow-up were HIV screened at week 12 or 24 of follow-up)

Conclusion: Full medication compliance and follow-up counseling remain challenges for sexual assault survivors and providers. A detailed nPEP protocol and continuity of care promotes quality patient management.

Authors, year: Krause et al, 2014[34]

Type of study: Retrospective cohort study of medical records from a level 1 trauma center participating in the Sexual Assault Nurse Examiner (SANE) Program

Location: Northeastern, United States

Sample size: n=179 cases of sexual assault among 171 unique female patients, aged ≥16 years (median: 26 years); nPEP offered to 138 patients for whom PEP was appropriate within the 72-hour window period; an additional 5 patients outside the 72-hour window period were offered PEP; 86% or 124/143 cases who were offered PEP, accepted PEP

Risk: Sexual assault

Intervention: 2-drug or 3-drug regimen

Drug regimen: Either FTC/TDF and LPV/r) (n=85, 59.4%) or FTC/TDF alone (n=32, 22.4%)

Time from exposure to nPEP: ≤72 hours (for most cases; 5 cases were given nPEP outside the 72-hour window)

Completion of nPEP: 34 of 124 (27.4%) cases who followed up with an infectious disease specialist completed nPEP

HIV seroconversions: Not reported

Conclusion: All 138 sexual assault case patients who were eligible for nPEP were offered nPEP. Only a minority of those who were documented to have followed up with an infectious disease specialist completed nPEP. There is a need for a better system for post-assault follow-up.

Authors, year: Linden et al, 2005[30]

Type of study: Retrospective medical record review of female sexual assault survivors presenting to an urban ED during 10/1/99–9/30/2002

Location: Boston, MA

Sample size: n=292 charts reviewed; n=181 in final sample size; mean age 29.1 years (range, 18–82); n=89 patients offered nPEP; n=85 patients accepted

Risk: Sexual assault

Intervention: 2-drug or 3-drug regimen; 1- or 2-pill burden

Drug regimen: Initiated in ED, ZDV + 3TC (Combivir) (n=78); Combivir + NFV (n=4); Initiated in referral clinic: 2-drugs (unspecified) (n=2); 3-drugs (unspecified) (n=1)

Time from exposure to nPEP: Median time from assault to presentation in ED (10.1 hours; range, 0–24 hours)

Completion of nPEP: Overall 18 of 85 (21%), including 15 of 82 (18%) of those initiated on nPEP in ED and 3 of 3 initiated on nPEP after being referred to another clinical care site

HIV seroconversions: No seroconversions during follow-up period in 38 patients with at least 1 follow-up visit

Conclusion: A minority of sexual assault survivors were offered nPEP and few completed full nPEP course.

Authors, year: Olshen et al, 2006[32]

Type of study: Retrospective medical record review of adolescents presenting to urban pediatric EDs ≤72 hours of penetrating sexual assault in 2 academic medical centers during July 1, 2001 to June 30, 2003

Location: Boston, MA

Sample size: n=177 adolescents aged 12–22 years; n=145 adolescents with adequate documentation; n=129 eligible for nPEP; n=110 accepted nPEP; n=85 initiated nPEP

Risk: Sexual assault

Intervention: 2-drug or 3-drug regimen

Drug regimen: 3TC + ZDV (94%); 3TC +ZDV + NFV (3%); 3TC + ZDV + IDV (2%)

Time from exposure to nPEP: ≤72 hours

Completion of nPEP: 13/85 (15%) who initiated nPEP completed 28-day course; 37 returned for first follow-up visit

HIV seroconversions: No seroconversions among 23 tested for HIV

Conclusion: Poor rates of nPEP completion among adolescent sexual assault survivors. May be due to uncertainties regarding exposure, high rates of psychiatric comorbidity, and low rates of return for follow-up care.

Sexual Assault Studies Including Children and/or Adolescents

Authors, year: Chesshyre et al, 2009[43]

Type of study: Retrospective review of medical records from January 2005–February 2007

Location: Blantyre, Malawi

Sample size: n=217 children and adolescents presented with history of sexual abuse; ages: n=62 (29%)<5 years; n=113 (52%) 5–10 years; n=42 (19%) 11–16 years; n=92 children were eligible for and received nPEP; n=153 children were not offered nPEP because they presented >72 hours or had chronic history of abuse

Risk: Child sexual abuse

Intervention: 2-drug regimen

Drug regimen: ZDV + 3TC

Time from exposure to nPEP: ≤72 hours

Completion of nPEP: Not reported

HIV seroconversions: No HIV seroconversions in any of the 92 children initiated on nPEP; 7/153 (5%) children who were not offered nPEP tested HIV+

Conclusion: The initiation of an nPEP program for child victims of sexual abuse led to increased numbers of such children presenting for nPEP services and is likely to have resulted in decreased HIV acquisition in this population.

Authors, year: Collings et al, 2008[42]

Type of study: Prospective observational cohort of 200 consecutive cases of child rape referred for assessment to a state hospital, Oct–Dec 2004

Location: KwaZulu-Natal, South Africa

Sample size: n=200 children and adolescents presenting with history of child rape; mean age 10.6 years (range, 1–17 years); 120 children eligible and offered nPEP; n=64 children not eligible due to presentation >72 hours; n=113 followed by hospital; n=7 referred to another nPEP provider

Risk: Child sexual abuse

Intervention: 2-drug regimen

Drug regimen: ZDV + 3TC

Time from exposure to nPEP: ≤72 hours

Completion of nPEP: 40/113 (35.5%) followed by hospital completed 28-day course

HIV seroconversions: No seroconversions among 13/40 children returning for 3-month follow-up and 4/40 children returning at 6-month follow-up.

Conclusion: Poor nPEP adherence and return for follow-up existed; further research is needed to identify reasons for such nonadherence and identify interventions to improve adherence.

Authors, year: Du Mont et al, 2008[44]

Type of study: Retrospective analysis of data on female adolescent sexual assault survivors from the HIV PEP Project, an implementation and evaluation of a program of universal offering of nPEP to sexual assault victims of all ages in 18 hospital-based sexual treatment centers

Location: Ontario, Canada

Sample size: n=386 sexually assaulted female adolescents; mean age 16.7 years (range, 12–19 years); n=325 eligible for nPEP; 307 offered nPEP; n=131 accepted nPEP; the most common reason for declining nPEP was lack of concern about acquiring HIV; students, survivors with marked anxiety, and those encouraged by a health professional were more likely to accept PEP

Risk: Sexual assault

Intervention: 3-drug regimen; 2-pill burden

Drug regimen: Combivir and Kaletra

Time from exposure to nPEP: ≤72 hours

Completion of nPEP: 34% (44/131) completed 28-day course nPEP; 47% (61/131) adhered to day 14; the most common side effects were nausea, fatigue, vomiting, and diarrhea; survivors who were white and had known their assailant<24 hours were more likely to complete nPEP; most common reasons for stopping nPEP early: ARV side effects (73%), including most often nausea and fatigue

HIV seroconversions: Permission not obtained to provide results of HIV testing

Conclusion: Stronger health care provider recommendations needed for nPEP; need for training of health care providers to consistently offer and recommend nPEP to all those meeting established risk criteria.

Authors, year: Ellis et al, 2005[37]

Type of study: Prospective study of children presenting to hospital with history of child sexual abuse during January, 1 2004 through December 31, 2004

Location: Blantyre, Malawi

Sample size: n=64 children presented with history of sexual assault; median age 83 months (range, 22–180 months); n=17 children eligible for, offered, and accepted nPEP

Risk: Sexual assault

Intervention: 2-drug regimen

Drug regimen: AZT+3TC

Time from exposure to nPEP: ≤72 hours

Completion of nPEP: 11/17 (65%) accepting nPEP completed 28-day course

HIV seroconversions: Among nPEP users, no seroconversions among 11 who returned after 1 month, 7 who returned after 3 months, and 2 who returned at 6 months; 1 of 4 children who did not receive nPEP was screened for HIV and was HIV+

Conclusion: The study found nPEP to be safe, acceptable, and feasible. The authors recommend routine offering of nPEP to all eligible children.

Authors, year: Fajman et al, 2006[41]

Type of study: Retrospective study of medical records of children presenting with child sexual abuse to inner-city pediatric ED in 2002

Location: Atlanta, GA

Sample size: n=227 sexually assaulted children and adolescents with adequate data; age range, 9 months–18 years; n=87 presented ≤72 hours of assault; n=5 sexually assault adolescent survivors were prescribed nPEP; being assaulted by a stranger associated with receiving nPEP (PR=11.9, 95% CI=1.4, 100.2, *P*=0.02).

Risk: Sexual assault

Intervention: 3-drug regimen; 2-pill burden

Drug regimen: Combivir (ZDV + 3TC) + nelfinavir

Time from exposure to nPEP: Within 72 hours

Completion of nPEP: 0 completed 28-day course

HIV seroconversions: No seroconversions reported among the 3 nPEP recipients who were tested, or among the 82 patients who presented within 72 hours but did not receive nPEP

Conclusion: nPEP for pediatric HIV exposures was underutilized in a hospital in a large urban center with high HIV prevalence and underscores the need for physician education about nPEP for children.

Authors, year: Girardet et al, 2009[35]

Type of study: Retrospective medical record review of children and adolescents presenting at a sexual abuse clinic during a 38-month period (January 2001–March 2004)

Location: Houston, Texas

Sample size: Of 4,234 cases of child or adolescent sexual assault, 1,750 (41%) were tested for HIV; n=879 aged<13 years, n=871 adolescents; n=303 were nPEP eligible; 16/303 (5%) were offered nPEP (aged 3–17 years); n=15 accepted nPEP

Risk: Sexual assault

Intervention: 2- or 3-drug regimen

Drug regimen: ZDV + 3TC (14 cases); ZDV + 3TC +LPV/r (1 case of acute genital trauma)

Time from exposure to nPEP: ≤96 hours

Completion of nPEP: Inconsistent reporting; none of the children completed follow-up; no reported significant side effects among the 9 patients reporting for at least 1 follow-up visit

HIV seroconversions: No seroconversions among 9 children who returned for ≥1 follow-up visit

Conclusion: Only 5% of those children or adolescents who were eligible for nPEP were offered nPEP. Adherence was difficult to document based on limited adherence to follow-up visits. Need for research to better define nPEP efficacy in children and adolescents.

Authors, year: Merchant et al, 2004[39]

Type of study: Retrospective medical record review of female adolescents presenting at an urban pediatric ED (January 1999 to December 2000)

Location: New York, New York

Sample size: n=25 adolescent females aged 12–19 years presenting with history of sexual assault; n=15 eligible for and offered nPEP; n=14 accepted nPEP

Risk: Sexual assault

Intervention: 1- or 3-drug regimen

Drug regimen: 1 received ZDV in 1999; 13 received 3-drug regimen, ZDV + 3TC + 3rd drug (n=12); d4T + 3TC + 3rd drug (n=1); (3rd drug was NFV [n=9] or IDV [n=4])

Time from exposure to nPEP: ≤72 hours; nPEP ordered an average of 218 minutes after patient presented to the ED; patient received drugs on average 58 minutes after nPEP was ordered

Completion of nPEP: No patients completed 28-day course

HIV seroconversions: Not reported (efficacy not studied in this study)

Conclusion: There was a significant delay in ordering nPEP and administering nPEP in the emergency room. Highlights importance of expediting nPEP in that setting.

Authors, year: Neu et al, 2007[38]

Type of study: Prospective nonrandomized observational study of children and adolescents presenting to the pediatric ED during March 1999–September 2002

Location: New York City, New York

Sample size: n=70 patients (aged 11–19 years) evaluated for sexual assault; n=33 enrolled in the study (94% female; mean age 15.3 years)

Risk: Sexual assault

Intervention: 2-drug regimen; 1-pill burden

Drug regimen: Combivir

Time from exposure to nPEP: ≤72 hours

Completion of nPEP: 8/33 (24%); return rate for follow-up visits: 1st visit, 23/33 (70%); week 2, 20/33 (60%); week 4–6, 11/33 (33%); 12 weeks, 9/33 (27%); 24 weeks, 6/33 (18%)

HIV seroconversions: No seroconversions in those presenting for follow-up at 4–6 weeks (11/33), 12 weeks (9/33), or 24 weeks (6/33)

Conclusion: Inadequate adherence to medications and follow-up were significant problems in this nPEP program for sexually assaulted children and adolescents.

Authors, year: Schremmer et al, 2005[36]

Type of study: Retrospective medical record review of children presenting for evaluation of suspected sexual abuse who were provided nPEP during February 1999–March 2001.

Location: Kansas City, Missouri

Sample size: n=2,865 evaluated for suspected sexual abuse; n=34 children and adolescents received nPEP (aged 12 weeks to 18 years, mean age 13 years); nPEP use associated with stranger assault

Risk: Sexual abuse

Intervention: 1-, 2-, and 3-drug regimens

Drug regimen: ZDV (n=1); ZDV + 3TC (n=32); ZDV+3TC+NFV (n=1)

Time from exposure to nPEP: ≤73 hours (range, 2–73 hours)

Completion of nPEP: 8/34 (24%) patients completed 28-day course

HIV seroconversions: No seroconversions among 33 patients tested at initial evaluation or among the 16 patients who had at least 1 subsequent HIV test after initial evaluation

Conclusion: Inadequate adherence to medication regimen and follow-up in child and adolescent survivors of suspected sexual abuse who received nPEP were noted.

Authors, year: Speight et al, 2006[40]

Type of study: Retrospective medical record review of children presenting with suspected childhood rape to a sexual assault care center during July 2003–March 2004

Location: Thika, Kenya

Sample size: n=48 children aged<18 years (96.8% female) presenting with suspected rape; n=33 eligible for, offered, and accepted nPEP

Risk: Sexual assault

Intervention: 2-drug regimen

Drug regimen: ZDV + 3TC

Time from exposure to nPEP: ≤72 hours

Completion of nPEP: 15/33 (45%) completed 28-day course

HIV seroconversions: No seroconversions among 3 patients tested for HIV; 3 seroconversions among 15 who were not eligible for nPEP

Conclusion: Majority (86%) of children presented within the 72-hour window period. Providing post-rape care is feasible and acceptable but requires special training for counselors, and providers, including training related to pediatric dosing.

Pediatric and Adolescent Community-acquired Needlestick Injury (CA-NSI) Studies

Authors, year: de Waal et al, 2006[66]

Type of study: Case report of nPEP use among children involved in a mass needlestick injury (1999)

Location: Tygerberg, South Africa

Sample size: n=54 children involved in mass needlestick exposure from discarded needles on a soccer field; n=44 were administered nPEP

Risk: CA-NSI

Intervention: 2-drug regimen

Drug regimen: ZDV + 3TC

Time from exposure to nPEP: ≤72 hours

Completion of nPEP: ARV adherence declined from 64% at week 3 to 52% at week 4; 7 patients on nPEP experienced nausea at 3 weeks

HIV seroconversions: No seroconversions to HIV, HBV, or HCV were noted in 44 children tested at 6 months

Conclusion: Follow-up of patients after mass exposure was difficult and adherence to nPEP was poor. Fewer follow-up visits are probably adequate in a non-mobile community (might consider eliminating the 3-month follow-up visit).

Authors, year: Papenburg et al, 2008[65]

Type of study: Combination of prospective and retrospective case series describing community acquired needle stick injuries in children at 2 pediatric tertiary care teaching hospitals (1988–2006 for one hospital and 1995–2000 at another hospital)

Location: Montreal, Canada

Sample size: n=274 pediatric patients with community acquired needlestick injuries; 73% of patients sought care on day of injury; n=210 injuries occurred during an era when nPEP was available; n=87 patients offered nPEP; n=82 patients accepted nPEP

Risk: CA-NSI; blood reported on needle or syringe in 36 injuries; n=71 reported an injury that bled

Intervention: 2-drug or 3-drug regimen

Drug regimen: ZDV + 3TC (n=74); ZDV + 3TC + NFV (n=4); ZDV + 3TC + IDV (n=3); ZDV + 3TC + RTV (n=1)

Time from exposure to nPEP: Not specified

Completion of nPEP: 10/82 (12%) patients discontinued nPEP; unclear from report if remaining 72 completed the full 28-day course

HIV seroconversions: 0 HIV seroconversions occurred at 6 month follow-up visit among 189/274 (nPEP and non-nPEP) patients tested for HIV

Conclusion: There were no seroconversions for HIV, HBV, or HCV among the 274 pediatric, community-acquired needlestick injuries, adding evidence that suggests the risk of transmission of bloodborne viruses in these exposures is low.

Authors, year: Russell et al, 2002[67]

Type of study: Prospective study of children with community-acquired needlestick injuries (published 2002)

Location: Melbourne, Australia

Sample size: n=50 cases of CA-NSI; median age=6.9 years (range, 1.8–14.3 years)

Risk: CA-NSI

Intervention: No nPEP offered

Drug regimen: Not applicable

Time from exposure to nPEP: Not applicable

Completion of nPEP: Not applicable

HIV seroconversions: No seroconversions among 36 children tested for HIV, HBC, HBC

Conclusion: No seroconversions to HIV, HBV, or HCV occurred among 50 cases of CA-NSI; HBV prophylaxis and vaccination was administered and no nPEP for HIV was administered.

Authors, year: Thomas et al, 2006[64]

Type of study: Case report of CA-NSIs sustained by 21 children on primary school playground, including an HIV-infected source patient

Location: London, England

Sample size: n=20 children exposed and started on nPEP; 1 child already known to be HIV infected at baseline, not started on nPEP

Risk: CA-NSI

Intervention: 3-drug regimen

Drug regimen: ZDV + 3TC + NVP

Time from exposure to nPEP: Within 72 hours

Completion of nPEP: 10/20 (50%)

HIV seroconversions: None

Conclusion: Was logistically difficult to provide nPEP under such circumstances, however, it seemed to be effective.

Mixed Populations Studies

Authors, year: Babl et al, 2000[58]

Type of study: Retrospective medical record review of children and adolescents presenting with CA-NSI in to the pediatric emergency room of an urban hospital during June 1997–June 1998

Location: Boston, Massachusetts

Sample size: n=10 pediatric and adolescent patients offered nPEP; n=8 started on nPEP

Risk: Sexual assault (n=6); CA-NSI (n=4)

Intervention: 3-drug regimens

Drug regimen: ZDV + 3TC+ Indinavir (n=7); ZDV + 3TC+ NFV (n=1)

Time from exposure to nPEP:

Completion of nPEP: 2/8 (25%) completed 28-day course; financial concerns, side effects, additional psychiatric and substance abuse issues, degree of parental involvement influenced adherence to nPEP and follow-up

HIV seroconversions: No seroconversions among 5 tested at 4 to 28 weeks.

Conclusion: HIV nPEP presented medical and management challenges and requires coordinated effort. Need for written protocol, coordinated approach, and national guidelines.

Authors, year: Beymer et al, 2014[61]

Type of study: Retrospective medical record review of clients receiving PEP services at LGBT community-based clinic (May 2011–December 2012)

Location: Los Angeles

Sample size: n=649 nPEP clients (n=529 [81.5%] first PEP use, n=120 [18.5%] PEP use 1–5 times previous to current nPEP initiation); whites, Hispanics, and blacks made up 42.5%, 35.4%, and 8.8% of nPEP users, and 30.4%, 42.4%, and 16.7% of HIV-infected persons, respectively

Risk: Gay/homosexual 75.5%, bisexual 11.9%, heterosexual 10.6%, other 1.9%

Intervention: 2-drug regimen

Drug regimen: TDF/FTC

Time from exposure to nPEP: ≤72 hours; mean time from exposure to first PEP medication dose 38.5 hours (SD=19 h)

Completion of nPEP: 93% self-reported taking all 4 pills in the previous 4-day medication recall period at 2 weeks after nPEP initiation

HIV seroconversions: 7 seroconversions occurred during the 6-month study period after nPEP initiation (including the 5 months after completing nPEP; exact timing not described)

Conclusion: 18.5% repeat nPEP users may benefit from PrEP; racial/ethnic inequities found in nPEP use compared with corresponding HIV prevalence deserves attention.

Authors, year: Bogoch et al, 2014[59]

Type of study: Prospective longitudinal study of referrals to nPEP programs in 2 emergency rooms and 2 academic medical centers

Location: Boston, MA

Sample size: n=180 persons referred for nPEP; median age 28 years (interquartile range, 23–35 years); 65.6% women; n=98 (54.4%) attended first nPEP visit

Risk: Sexual (57.2%), 72% nonconsensual, 1% MSM; nonsexual (42.8%), 17.8% injecting-drug use, 40% accidental needlestick injuries, 42.2% accidental mucous membrane or non-needle percutaneous exposures

Intervention: 3-drug regimen

Drug regimen: First line regimen: co-formulated TDF and FTC (Truvada) and LPV/r (Kaletra); RAL was substituted for LPV/r with drug interactions or side effects preventing adherence

Time from exposure to nPEP: Not reported

Completion of nPEP: 43/177 (46%) patients had documented completion of a 28-day course of nPEP; women were less likely to complete a 28-day course of nPEP

HIV seroconversions: Not reported

Conclusion: There were significant attrition rates between the emergency department and nPEP follow-up clinic. Older patients and persons without insurance were significantly less likely to attend initial clinic for nPEP care after presenting to the emergency department. Individuals with exposure to a known HIV-positive source individual were more likely to attend their initial clinic appointment. Women accounted for the majority of nonconsensual sexual exposures and were less likely to have documented completion of their 28-day nPEP regimen.

Authors, year: Chan et al, 2013[52]

Type of study: Retrospective cohort study with medical record review at large urban hospital emergency room, January 1, 2008–December 31, 2010

Location: Toronto, Canada

Sample size: n=241 patients

Risk: All were sexual exposures; MSM 76.8%, heterosexual 23.2%, non-consensual 5.0% of 236 with documentation about whether sex was consensual; HIV-positive source n=102

Intervention: 2-drug regimen (for lower risk exposures), 3-drug regimen (for higher risk exposures)

Drug regimen: Not specified

Time from exposure to nPEP: ≤72 hours; among 205 with known timing of exposure: <24 hr, 70 (34.1%); 24–48 hr, 68 (33.2%); 48–72 hr, 28 (13.7%); >72 hr, 7 (3.4%); not documented, 32 (15.6%)

Completion of nPEP: Of 205 patients given nPEP, n=71 (34.6%) completed a 28-day course; n=20 (9.8%) stopped medications early due to patient preference, cost, low HIV risk, source patient tested HIV negative; n=114 (55.6%) unknown completion status; n=55 with adverse effects, diarrhea (n=20), nonspecific gastrointestinal upset (n=14), nausea (n=13)

HIV seroconversions: Two patients who initially tested HIV negative at baseline subsequently tested HIV-positive at 3-month and 6-month visits; data regarding ongoing sexual exposure was incomplete

Conclusion: While it was encouraging that 92.6% of patients presented within the 72-hour window period, only 34.6% were known to have completed the full 28-day course. It is unclear whether the 2 HIV seroconversions that occurred during the 3-month and 6-month follow-up visits were nPEP failures as sexual histories were incomplete during follow-up.

Authors, year: Diaz-Brito et al, 2012[53]

Type of study: Open label randomized multicenter clinical trial comparing 2 nPEP regimens in patients presenting to emergency rooms in 6 urban hospitals

Location: Barcelona, Spain

Sample size: n=255 patients presenting for nPEP evaluation randomized into ZDV/3TC + LPV/r twice daily arm (n=131) or ZDV/3TC + atazanavir (n=124)

Risk: n=200; nonoccupational n=170 (85%); sexual n=156 (78%); occupational n=30 (1%)

Intervention: 3-drug regimen

Drug regimen: ZDV/3TC + LPV/r or ZDV/3TC + atazanavir

Time from exposure to nPEP: Median interval between exposure and presentation=18h (IQR 5–32); nonoccupational (median=20 hours); occupational (median=5 hours)

Completion of nPEP: 64% completed 28-day course in both arms; 92% of patients reported taking >90% of scheduled doses (without difference between arms); adverse events reported in 46% of patients (49% LPV/r arm and 43% atazanavir arm); gastrointestinal problems more common in LPV/r arm

HIV seroconversions: 0

Conclusion: Rate of completion was similar for both arms; almost 50% of patients of both arms suffered side effects. Strategies to improve adherence are needed.

Authors, year: Fletcher et al, 2013[63]

Type of study: Prospective cohort study

Location: Los Angeles, California

Sample size: n=35 patients; gay n=30; not gay=5; mean age=34.1 years (SD 7.4)

Risk: Not clearly defined; however, participants reported mean of 11.9 (SD 26.5) episodes of unprotected anal intercourse in past 6 months

Intervention: 2-drug regimen

Drug regimen: TDF + FTC (Truvada)

Time from exposure to nPEP: ≤72 hours

Completion of nPEP: 25/35 (71.4%) completed the 28-day course; 48.6% took all 28 doses; 14.3% took > 90% of doses; at baseline, higher number of lifetime STDs and recent episodes of unprotected anal intercourse were associated with reductions in medication adherence

HIV seroconversions: 1 (participant reported nonadherence to nPEP and multiple subsequent sexual exposures)

Conclusion: There was a significant indirect association between sexual risk taking and nPEP adherence. Interventions to reduce sexual risk taking will reduce risk for HIV acquisition and may play a role in improving nPEP adherence.

Authors, year: Gulholm et al, 2013[54]

Type of study: Retrospective medical record review at urban hospital sexual health clinic (1/2008–12/2011)

Location: Sydney, Australia

Sample size: n = 282 patients on 319 occasions presented for nPEP; n = 262 (94.3%) male

Risk: n = 260 (99.2%) participants had homosexual exposure; of 319 presentations, 203 (63.6%) receptive unprotected anal intercourse, 87 (27.4%) insertive anal intercourse, 12 (3.8%) receptive vaginal intercourse, 5 (1.6%) penile-vaginal sexual assault, 5 (1.6%) receptive fellatio, 5 (1.6%) needlestick injuries, 4 (1.3%) needle-sharing episodes

Intervention: 2-drug or 3-drug regimen

Drug regimen: Mainly TDF/FTC-containing regimens; TDF + FTC (n = 136 [42.6%]), TDF + FTC + d4T (n = 149 [46.7%])

Time from exposure to nPEP: ≤ 72 hours; < 4 hours (16 [5.1%]), 4–12 hours (59 [19.0%]), 12–24 hours (82 [26.5%]), 24–48 hours (96 [31.0%]), 48–72 hours (57 [18.4%])

Completion of nPEP: 228/319 (71/%) completed nPEP; completion associated with reporting AEs and changing the nPEP regimen; adverse events associated with being prescribed a regimen other than TDF/FTC, younger age, earlier year of nPEP prescription, and changing the nPEP regimen

HIV seroconversions: 2 seroconversions more than 6 months after NPEP due to ongoing high-risk behavior

Conclusion: nPEP was appropriately targeted to highest risk patients. HIV seroconversions due to ongoing high-risk sexual behavior highlight importance of integrating counseling regarding safer sexual behaviors as an integral component of nPEP care.

Authors, year: Jain et al, 2015[60]

Type of study: Retrospective longitudinal study of electronic medical records of nPEP users (1999–2013)

Location: Boston, Massachusetts

Sample size: n = 894 patients; n = 1,244 nPEP courses; mean age at PEP enrollment = 33.9 years

Risk: MSM = 788; heterosexual = 91; sexual assault = 66; transgender = 15; injection drug use = 14; sexual exposure (non-assault) = 1,152

Intervention: n = 927 TDF-based treatment regimen; N = 592 3-drug regimen

Drug regimen: Either an AZT/3TC or TDF/FTC backbone with or without a third drug.

Time from exposure to nPEP: ≤ 72 hours

Completion of nPEP: 85.7% completion rate overall (463 of 540 with documented completion status); reasons for discontinuing: medication intolerance (48.1%) due to nausea (43.2%), diarrhea (13.5%), rash (13.5%), HIV negative partner (9.1%); increased completion rates associated with having HIV-infected partner or fewer drugs in regimen (2 vs.3)

HIV seroconversions: Not reported

Conclusion: nPEP use increased over time. nPEP users demonstrated recurrent high-risk behavior. A defined group of nPEP users may benefit from earlier, targeted HIV risk-reduction and PrEP counseling.

Authors, year: Mayer et al, 2008[56]

Type of study: Two phase 4 studies of TDF-containing regimens compared to historical controls who took ZDV-containing regimens

Location: Boston, Massachusetts

Sample size: n=353 enrollees; n=44 (TDF/FTC arm); n=68 (TDF/3TC arm); control arms: n=122 ZDV/3TC arm, n=119 ZDV/3TC + 3rd drug arm

Risk: Sexual exposure; TDF/FTC arm, n=41 (93.2%) male (MSM/bisexual), n=41 male (100%); TDF/3TC arm, n=66 (97.1 %) male, n=56 (82.4% MSM/bisexual); ZDV/3TC arm, n=98 (80.3%) male; ZDV/3TC + 3rd drug arm, n=88 (73.9%)

Intervention: 3 separate 2-drug regimens and one 3-drug regimen; 1-, 2-, or 3-pill burden

Drug regimen: TDF + 3TC, TDF + FTC, or ZDV + 3TC (with or w/o a PI)

Time from exposure to nPEP: ≤72 hours

Completion of nPEP: 42–87.5% completed nPEP (highest completion in TDF regimens): 72.7% (n=32 TDF/FTV arm), 87.5% (n=63 TDF/3TC arm), 42.1% (n=53 ZDV/3TC arm), 38.8% (n=50 ZDV/3TC + 3rd drug arm [3rd drug was mainly PI])

HIV seroconversions: In TDF arms, n=0 seroconversions; in AZT arms, n=3 (during or shortly after their course of nPEP); Note: Level of adherence in seroconverters not described.

Conclusion: Participants taking TDF-containing regimens for nPEP demonstrated greater adherence and tolerability, with milder side effects than those taking ZDV-containing regimens.

Authors, year: Mayer et al, 2012[57]

Type of study: Evaluation of a novel 3-drug nPEP regimen

Location: Boston, MA

Sample size: TDF-FTC-RAL arm (n=100); control arms: TDF/FTV arm, n=44; AZT/3TC +3rd drug arm, n=119; overall age range, 18–61 years; males (73.9%–100%—all arms); MSM/bisexual (70.5%–71.5% in TDF arms)

Risk: Sexual exposure to HIV-infected partner or partner of unknown HIV status

Intervention: 3-drug regimen; 2-pill burden

Drug regimen: RAL + fixed dose combination TDF and FTC (Truvada)

Time from exposure to nPEP: ≤72 hours

Completion of nPEP: 57% (n=57) completed TDF-FTC-RAL arm (an additional 27% completed a modified regimen.); 72.7% (n=32) completed TDF/FTV arm; 38.8% (n=46) completed AZT/3TC arm

HIV seroconversions: 0

Conclusion: Tolerability to the 3-drug regimen, with integrase inhibitor, RAL, was high. The most common side effects were nausea and vomiting, diarrhea, abdominal discomfort, headache, and fatigue.

Authors, year: McDougal et al, 2014[62]

Type of study: Retrospective medical record abstraction of patients attending a publicly funded HIV clinic between 2000 and 2010

Location: Seattle, Washington

Sample size: 360 evaluated for nPEP; 324 prescribed nPEP; median age 30 years (range, 14 years–68 years)

Risk: Among patients evaluated for nPEP: sexual exposures (928%), MSM (59%), sexual assault (22%)

Intervention: 66% (n=214) 3-drug regimen

Drug regimen:

Time from exposure to nPEP: 334/260 (93%) initiated ≤72 hours, 177/360 (49%) within 24 hours

Completion of nPEP: 287/324 (89%) completed nPEP

HIV seroconversions: n=4; 2 tested positive at 2 and 5 months; 1 tested negative at baseline and 11 days and positive at 5 months; 1 tested positive at 12 months after nPEP initiation; adherence to nPEP and history of ongoing sexual exposures not described

Conclusion: Must increase education and promotion of HIV prevention, including nPEP for populations who would benefit most. Established nPEP service sites may have added benefit of also serving as locations for HIV case-finding and PrEP referrals.

Authors, year: Olowookere et al, 2010[51]

Type of study: Retrospective medical record abstraction of clients presenting for HIV nPEP at an antiretroviral therapy clinic during January 2005–December 2006

Location: Ibadan, Nigeria

Sample size: n=48 clients received nPEP; mean age 27.9 years ± 12.3 years (n=6, <15 years); about 1/3 were children and adolescents

Risk: Nonoccupational exposures: sexual assault (50%); occupational exposures: needlesticks (25%), blood splash into mucous membranes (25%)

Intervention: 3-drug regimen

Drug regimen: Either ZDV + 3TC + 3rd drug or D4T + 3TC + 3rd drug; 3rd drug=EFV, IDV or LPV/r

Time from exposure to nPEP: Not reported

Completion of nPEP: 38/48 (79%) completed therapy

HIV seroconversions: No seroconversions among 40 clients at 6 months of follow-up

Conclusion: 24% of clients receiving nPEP could not complete therapy due to side effects.

Authors, year: Pierce et al, 2011[45]

Type of study: Data linkage study using an nPEP service database and an HIV surveillance registry

Location: Australia

Sample size: n=1,420 male nPEP recipients; age range, 14–78 years; median=34.5 years

Risk: Indirect data suggest most participants presenting for NPEP are MSM, but risk behaviors were not collected for these participants

Intervention: Number of drugs in nPEP regimen not reported.

Drug regimen: Not reported

Time from exposure to nPEP: ≤72 hours

Completion of nPEP: Not reported

HIV seroconversions: n=3 nPEP related failures; n=34 additional seroconversions >6 months after nPEP initiation and deemed related to ongoing risk behavior

Conclusion: Frequency of nPEP use was not associated with risk of HIV seroconversion. Note: Data on nPEP adherence and completion were not available, but may have provided an explanation for drug failure.

Authors, year: Rey et al, 2008[46]

Type of study: Retrospective medical record abstraction of all consultations for nPEP in three consultation centers January 2001–December 2002

Location: Southeastern France

Sample size: n=910 exposures; age range, 15–18 yr (5.9%), 19–35 yr (68.6%), 36–50 yr (21.4%), >50 yr (4.1%); men=60.4%; female=39.2%; transsexual=0.3%; n=800 given initial nPEP prescription; n=776 accepted nPEP; n=527 received remaining nPEP prescription to complete 28-day course

Risk: n=910 sexual exposures, including 108 sexual assaults, 220 homosexual contacts among men

Intervention: 2- or 3-drug regimen

Drug regimen: Not reported

Time from exposure to nPEP: nPEP given before and after the 72 hour window period

Completion of nPEP: 355/776 (44%) who accepted nPEP completed 28-day course

HIV seroconversions: 1 seroconversion occurred in a patient after completing nPEP but who presented >72 hours after a high-risk exposure (not considered an nPEP failure)

Conclusion: Follow-up rates were poor; strategies need to improve follow-up, including a tracking process and psychosocial support for youngest patients and survivors of sexual assault.

Authors, year: Shoptaw et al, 2008[55]

Type of study: Biobehavioral HIV prevention intervention

Location: Los Angeles

Sample size: n=100 enrollees

Risk: High-risk sexual or drug-related exposure; n=45 drug use, n=1 injection drug use, n=63 MSM, n=9 bisexual, n=9 heterosexual; mean age 31.8 years

Intervention: 2-drug regimen; 1-pill burden

Drug regimen: ZDV + 3TC

Time from exposure to nPEP: ≤72 hours

Completion of nPEP: n=84 individuals received the full 28-day supply of study drug; 63/84 (75%) completed nPEP

HIV seroconversions: 0

Conclusion: nPEP provision for persons at high risk for HIV is feasible and safe at the community level. The most common adverse events were fatigue, nausea, headache, and gastrointestinal complaints.

Authors, year: Siika et al, 2009[47]

Type of study: Retrospective cohort study of electronic medical records of patients enrolled for HIV nonoccupational and occupational PEP during November 2001–December 2006 (Note: Only results for nPEP patients summarized in this table)

Location: Eldoret, Kenya

Sample size: n=355 nPEP exposures among children, adolescents, and adults; 100% accepted nPEP; n=296 advised to continue nPEP after testing HIV negative at baseline

Risk: Sexual assault (n=292 [82%]; female adult [n=189], female child [n=91], male child [n=15]); unprotected consensual sex, condom malfunction, human bites, exposure to body fluids of individuals suspected to be HIV infected, and barber cuts (n=63 [18%])

Intervention: 3-drug regimen; 2- or 3-pill burden

Drug regimen: D4T + 3TC + NVP; ZDV + 3TC + LPV/r (Note: Authors do not distinguish between ARVs used for nPEP or oPEP)

Time from exposure to nPEP: Median time=19 hours (range, 1–672 hours; 86% <72 hours)

Completion of nPEP: 104/296 (35%) completed nPEP. No statistically significant difference in reported side effects between NVP arm (21%) and LPR/r arm (14%) (P=0.44). No difference in completion rates for two arms (P=0.91). 1 death related to ARV-associated acute hepatitis associated with NVP arm.

HIV seroconversions: 1 HIV seroconversion at 6 weeks after nPEP initiation using RNA PCR test among 129 patients; seroconversion occurred in sexually assaulted child who presented ≤4 hours of assault and completed nPEP. HIV ELISA tests were negative in 87 patients; however, child who seroconverted did not undergo ELISA testing as well.

Conclusion: It is feasible to provide nPEP and oPEP in resource-constrained settings. Lack of HIV testing, delayed presentation, ARV discontinuation, and loss to follow-up are challenges in Western Kenya. Centralization of PEP services may improve coordination and supervision.

Authors, year: Tissot et al, 2010[48]

Type of study: Retrospective medical record abstraction of nPEP administrations during 1998–2007

Location: Lausanne, Switzerland

Sample size: n=1,233 consultations for potential HIV exposure; n=910 exposures among 867 persons included in final analysis; n=830 individuals requested nPEP at least once; n=710 initiated nPEP; 64% male, median age 30 years (range, 14–87 years)

Risk: 58%=heterosexual; 15%=homosexual; 6%=sexual assault; 20%=nonsexual (mainly CA-NSI or sharing of injection drug equipment)

Intervention: 3-drug regimen

Drug regimen: Mainly ZDV + 3TC + NFV (n=548, 77%) or ZDV + 3TC + LPV/r (n=108, 15%)

Time from exposure to nPEP: 60% sought care ≤24 hours after exposure and 82% sought care ≤48 hours

Completion of nPEP: 423/710 (60%) completed 28-day course; 396/620 (64%) for which data were available, reported side effects (mainly gastrointestinal disturbance and fatigue)

HIV seroconversions: 2 seroconversions occurred during follow-up, not attributable to nPEP failures

Conclusion: HIV testing in source persons avoided nPEP in 31% of exposures.

Authors, year: Tosini et al, 2010[49]

Type of study: Multi-site prospective study to evaluate the tolerability of nPEP with TDF/FTC +LPV/r

Location: France

Sample size: n=249 men and women; mean age 31.5 years; n=166 completed 28 days of PEP (tolerability good in 58%)

Risk: Nonoccupational exposures: sexual intercourse n=204 (82%), other n=5 (2%); occupational exposures (n=40)

Intervention: One 3-drug regimen; 2-pill burden

Drug regimen: TDF + FTC + LPV/r vs. historical controls taking ZDV containing regimens or TDF + ATV

Time from exposure to nPEP: ≤48 hours

Completion of nPEP: 166/188 (88%)

HIV seroconversions: No HIV seroconversions were recorded during the study

Conclusion: The TDF/FTC + LPV/r regimen proved easy to use, well-tolerated, and had less participants to discontinue medications secondary to adverse effects when compared with historical controls. The authors recommend this regimen as standard of care for HIV nPEP. Among those with ≥1 side effect, 78% diarrhea, 78% asthenia, 59% nausea and/or vomiting.

Authors, year: Wong et al, 2010[50]

Type of study: Observational study of nPEP use following nPEP protocol and guidelines development in one Canada province

Location: Alberta, Canada

Sample size: n=174 persons received nPEP (135 females, 39 males); median age 24 years (range 4–69 years)

Risk: Sexual assault (68%, n=118), percutaneous (21%, n=36), consensual sex (7%, n=12), mucosal (3%, n=5), other (0.6%, n=1), not documented (1%, n=2)

Intervention: Primarily 2 and 3-drug regimens, one 4-drug regimen

Drug regimen: Not explicitly reported; most regimens included ZDV

Time from exposure to nPEP: 86% of cases ≤48 hours

Completion of nPEP: 86/174 (49%)

HIV seroconversions: 0 of 143

Conclusion: The majority of nPEP cases were sexual assaults in young women. No seroconversions were observed, however, lack of follow-up and early discontinuation of medication were problematic. NPEP programs need to better address adherence and follow-up.

Blood Transfusion Study

Authors, year: Al-Hajjar et al, 2014[71]

Type of study: Case report of nPEP use following inadvertent HIV-infected blood transfusion

Location: Riyadh, Saudi Arabia

Sample size: One 12 year old girl with sickle cell disease

Risk: Child was inadvertently transfused with large volume of HIV-infected packed red blood cells

Intervention: 4-drug regimen

Drug regimen: TDF, FTC, DRV/r and RAL (DRV/r subsequently changed to LPV)

Time from exposure to nPEP: At 24 hours after transfusion

Completion of nPEP: Completed 13 weeks of ARV PEP

HIV seroconversions: Patient did not seroconvert (negative for HIV-1 DNA and plasma HIV-1 RNA by PCR through 8 months following exposure)

Conclusion: Authors report successful use of combination ART nPEP after a large volume transfusion of HIV-contaminated blood despite detection initially of HIV antibodies immediately after the transfusion. The fact that antibodies disappeared after nPEP initiation cautions against not starting or stopping nPEP in patients with detectable antibodies immediately after a contaminated blood transfusion.

Abbreviations

3TC, lamivudine; ATV, atazanavir; AZT, zidovudine; CA-NSI, community-acquired needlestick injury; d4T, stavudine; DRV/r, darunavir + ritonavir; ED, emergency department; ELISA, enzyme-linked immunosorbent assay; EFV, efavirenz; FTC, emtricitabine; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; IDV, indinavir; LPV, lopinavir; LPV/r, lopinavir/ritonavir; MSM, men who have sex with men; NFV, nelfinavir; nPEP, nonoccupational postexposure prophylaxis; NVP, nevirapine; oPEP, occupational postexposure prophylaxis; PEP, postexposure prophylaxis; PI, protease inhibitor; PrEP, preexposure prophylaxis; RAL, raltegravir; RNA PCR, ribonucleic acid polymerase chain reaction; RPV, rilpivirine; SD, standard deviation; TDF, tenofovir disoproxil fumarate; ZDV, zidovudine.

Trade-named Drug Compositions

Combivir, ZDV+3TC; Kaletra, LPV/r (lopinavir + ritonavir); Truvada, TDF + FTC.

Appendix 4

Consideration of Other Alternative HIV nPEP Antiretroviral Regimens[a]

Create a combination regimen alternative to those in Table 5: May combine 1 drug or drug pair from Column A with 1 pair of nucleoside/nucleotide reverse transcriptase inhibitors from Column B.

Or

Use an existing fixed-dose combination alternative to those in Table 5.

Prescribers unfamiliar with these medications should consult physicians familiar with the agents and their toxicities.

Column A	Column B
Raltegravir Darunavir + ritonavir Etravirine Rilpivirine Atazanavir + ritonavir Lopinavir/ritonavir Dolutegravir	Tenofovir DF+ emtricitabine Tenofovir DF + lamivudine Zidovudine + lamivudine Zidovudine + emtricitabine

Fixed-dose combinations

The fixed-dose combinations Stribild (elvitegravir, cobicistat, tenofovir DF, emtricitabine) and Complera (rilpivirine, tenofovir DF, and emtricitabine) are complete regimens and no additional antiretrovirals are needed.

ALTERNATIVE ANTIRETROVIRAL MEDICATIONS FOR USE AS nPEP ONLY WITH EXPERT CONSULTATION

Efavirenz
Enfuvirtide
Fosamprenavir
Maraviroc
Saquinavir
Stavudine

ANTIRETROVIRAL MEDICATIONS GENERALLY NOT RECOMMENDED FOR USE AS nPEP

Didanosine
Nelfinavir
Tipranavir
Abacavir

ANTIRETROVIRAL MEDICATIONS CONTRAINDICATED AS nPEP

Nevirapine
Efavirenz (not for pregnant women)
Tenofovir (not for persons with eCrCl < 60 ml/min)

Abbreviations: DF, disoproxil fumarate; eCrCl, estimated creatinine clearance; nPEP, nonoccupational postexposure prophylaxis; TM, trademark.

[a] These antiretrovirals can be considered for use in regimens alternative to those in Table 5. For detailed information on each drug, please refer to individual drug package inserts available at: AIDSInfo Drugs Database at: http://aidsinfo.nih.gov/drugs. For consultation or assistance with HIV nPEP, contact PEPline (telephone 888-448-4911; internet site: http://www.nccc.ucsf.edu/about_nccc/pepline/).