Top Questions in ID: Pre-exposure Prophylaxis for HIV

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HIV pre-exposure prophylaxis (PrEP) is highly efficacious at preventing HIV acquisition. This review discusses ways to identify candidates for PrEP, recommended PrEP regimens, baseline and follow-up evaluations, applications of PrEP for HIV-serodiscordant couples, resources to address financial barriers, investigational strategies for PrEP, and educational resources for clinicians and patients.

Keywords. HIV; prevention; pre-exposure prophylaxis.

WHO ARE THE BEST CANDIDATES FOR PrEP?

Pre-exposure prophylaxis (PrEP) is a highly efficacious strategy for the prevention of HIV acquisition [1–8]. Daily coformulated tenofovir disoproxil fumarate and emtricitabine (TDF/FTC; Truvada) was US Food and Drug Administration (FDA) approved for the prevention of HIV in adults in 2012, and the US Centers for Disease Control and Prevention (CDC) released guidelines for its use in 2014 [9]. PrEP is recommended for those at elevated risk for HIV infection, including men who have sex with men (MSM), heterosexual active men and women, and people who inject drugs (PWID). For MSM, indications for PrEP include having an HIV-infected sexual partner, a recent bacterial sexually transmitted infection (STI), multiple sex partners, or engaging in condomless anal sex and/or transactional sex. For heterosexual men and women, indications include having an HIV-infected sexual partner or engaging in transactional and/or condomless sex with partners who are at substantial risk of HIV infection [9]. For PWID, indications include having an HIV-infected injecting partner, sharing injection equipment, and recent drug treatment (but currently injecting) [9]. The CDC estimates that 1.2 million Americans have indications for using PrEP [10], though only about 100 000 persons have been prescribed PrEP [11].

Taking a sexual history and asking about sexual and drug using behaviors in an open-ended and nonjudgmental manner is a critical first step for identifying PrEP candidates in health care settings, but this history is often not obtained [12]. In addition, many people who may benefit from PrEP do not recognize themselves as at risk for HIV infection [13, 14].

There are courses available through the National Network of STD Prevention Training Centers to increase providers’ knowledge to better address their patients’ sexual health (http://nnptc.org/resourceTags/sexual-history/), and there are several online tools for assessing an individual’s risk that can be used by clients or providers (eg, https://wwwn.cdc.gov/hivrisk/estimator.html#, http://www.mysexpro.org/en/home/).

While these guidelines and tools are helpful, individual-level risk is not the only determinant of HIV risk, and criteria for PrEP in the USPHS guidelines will miss some MSM and other patients who may benefit from using PrEP. It is important to consider local epidemiology and HIV prevalence in sexual and drug using networks. For instance, black MSM are disproportionately impacted by HIV and STIs, despite having equivalent or lower individual-level risks [15, 16]. Despite this, uptake of PrEP among MSM of color is lower than that for whites [17–19]. PrEP uptake is also low among women [20], in part due to limited awareness of PrEP among women [21] and their providers [22]. It is critical for providers to consider demographic factors and address health disparities. In addition, some patients may feel uncomfortable disclosing HIV risk behaviors, and it is therefore reasonable to prescribe PrEP to patients who request it, regardless of self-reported risk.

WHAT IS THE BASELINE EVALUATION?

After assessing the risk of HIV acquisition, the provider should assess the patient’s knowledge and interest in PrEP and describe how PrEP works, including the small but statistically significant risks of renal and bone toxicity [1, 3] and the possibility of a transient “start-up” syndrome characterized by mild gastrointestinal symptoms that typically resolve after several weeks [3]. Confirming that the patient is HIV-uninfected is a critical element of the baseline evaluation (Table 1). The provider should determine when the patient’s last potential exposure to HIV occurred and should assess for signs or symptoms of acute HIV infection.
Clinicians should document a negative HIV antibody test result within the week before initiating PrEP, ideally with a combination HIV Ag/Ab test. Oral rapid tests should not be used to screen for HIV infection before PrEP use because of lower sensitivity than blood tests. Some PrEP providers also obtain a plasma HIV RNA test at PrEP initiation, particularly in patients who might have very recent exposures and/or symptoms suggestive of acute HIV infection [9, 17, 23]. If there is a high clinical suspicion for acute HIV, PrEP should be deferred until HIV RNA test results are known to lead to the development of antiretroviral resistance mutations [1, 3].

Clinicians should determine renal function and test for infection with hepatitis B virus (HBV) and hepatitis C virus (Table 1). Patients with a creatinine clearance <60 mL/min should not start PrEP. Hepatitis B is not a contraindication to PrEP use; however, because both TDF and FTC are active against HBV, it is important to be cognizant of the patient's hepatitis B status and to ensure that liver function is closely monitored if PrEP is stopped because reactivated HBV infection can result in hepatic damage [24]. Providers should assess for risk factors for renal disease and screen patients for syphilis, gonorrhea (GC), and chlamydia (CT), including at extragenital sites, as the majority of extragenital infections are asymptomatic [25]. Women initiating PrEP should have a pregnancy test, and all patients should be counseled about the importance of adherence and counseled on how to optimize it [9]. Lastly, patients should be offered immunizations for vaccine-preventable STIs if they are eligible (Table 1).
WHAT IS THE RECOMMENDED REGIMEN?

The only recommended, FDA-approved regimen for PrEP is daily TDF/FTC. With daily adherence, this regimen is >95% effective for the prevention of HIV infection in MSM [5, 8, 26, 27]. Efficacy may be slightly lower in women [1, 28, 29], given that oral TDF achieves lower concentrations of tenofovir in the female genital tract than in colorectal tissues [30], and in PWID [2]. MSM are also likely to gain high levels of protection with at least 4 doses per week of TDF/FTC [26], whereas pharmacologic models suggest that women need to take at least 6 doses per week to gain protective benefits [30]. While 1 study found that event-driven PrEP (ie, PrEP taken only before and after possible sexual exposures to HIV) may be effective for MSM [7], this regimen is not FDA approved in the United States (nor recommended by the CDC) given concern about a lack of data for MSM as studies have not tested the efficacy of this regimen for MSM [9].

WHAT IS THE RECOMMENDED FOLLOW-UP?

Individuals using PrEP should be screened for HIV at least every 3 months, and sooner if there is suspicion of acute HIV infection (Table 1). To support adherence to quarterly HIV testing, it is recommended that providers prescribe no more than a 90-day supply of PrEP at each visit. As some patients will face challenges with adherence and persistence with PrEP [33], clinicians should also assess and counsel about adherence at follow-up visits [9]. PrEP should be discontinued if the patient tests positive, and the patient should be linked promptly to HIV care and started on a therapeutic HIV regimen. PrEP users should also be screened regularly for STIs and should have renal function checked at least every 6 months. Those with risk factors for renal disease, for example, age >40 years, lower baseline creatinine clearance, and/or predisposing conditions (eg, diabetes mellitus, hypertension), should have creatinine checked more frequently [34, 35]. Women should be counseled about contraception and tested for pregnancy if indicated.

WHAT DO YOU DO IF YOUR PATIENT CAN’T TAKE TDF/FTC?

If a patient cannot use TDF/FTC because of contraindications to using TDF, such as renal insufficiency or osteoporosis [9], there are currently no evidence-based alternative regimens available. In this situation, clinicians should counsel patients that condom use and/or safer sex [32] for sexual exposures and use of sterile syringes for injection drug use exposures are effective options until additional PrEP modalities become available (see the “Investigational Strategies” section below), or until patients no longer have contraindications to using TDF (eg, if their renal and bone parameters improve). In the unusual case that a patient cannot use TDF/FTC because of a contraindication to using FTC, then TDF monotherapy could be used as an alternative PrEP regimen for heterosexual partners of HIV-infected people and for PWID as there are data showing that mono-prophylaxis was effective in these populations [1, 2, 4]. The CDC does not recommend TDF monotherapy for MSM as studies have not tested the efficacy of this regimen for MSM [9].
HOW OFTEN DO YOU MONITOR PATIENTS FOR SEXUALLY TRANSMITTED INFECTIONS?

STIs are commonly diagnosed in PrEP users [5–8]. Although the CDC PrEP guidelines recommend STI screening at least every 6 months, data from 1 MSM cohort suggest that screening every 6 months as opposed to quarterly will cause a delay in treatment for more than one-third of GC, CT, and syphilis infections [36]. In addition, more than 75% of CT and GC infections are missed if extragenital sites are not screened [36]. A recent modeling study supports the importance of regular STI screening for PrEP users and shows that quarterly STI screening could eventually reduce STI incidence among MSM at the population level [37].

WILL PATIENTS INCREASE THEIR SEXUAL RISK BEHAVIORS WHILE USING PrEP?

In randomized studies of PrEP, participants did not report increased HIV risk behaviors and did not have increased rates of STIs while using PrEP, suggesting that they did not engage in risk compensation (ie, increase their risk behaviors while using PrEP) [1, 2, 6, 26]. However, in a survey of patients receiving PrEP during clinical care, 41% of patients reported decreased condom use while using PrEP [5], underscoring the need for clinicians to engage in comprehensive risk reduction counseling with patients using PrEP. Even if patients increase their risk behaviors while using PrEP, this intervention is likely to provide substantial protective benefits against HIV acquisition when taken with high adherence [5], so patient reports of ongoing or increased risk taking are not reasons for clinicians to discontinue PrEP. Rates of STIs have increased among MSM and other priority populations in recent years [38], but these increases began prior to the availability of PrEP, so they are likely multifactorial in nature.

WHAT DO YOU DO IF YOUR PrEP CANDIDATE IS IN A MONOGAMOUS, HIV-SERODISCORDANT RELATIONSHIP?

HIV-infected persons who use antiretroviral treatment (ART) and achieve stable virologic suppression are at extremely low risk of transmitting HIV to their sexual partners [39–41]. Therefore, if HIV-infected partners in monogamous, serodiscordant relationships have achieved virologic suppression, the additional protection of PrEP for HIV-uninfected partners is minimal. However, HIV-uninfected persons could derive substantial protective benefits from using PrEP if their HIV-infected partners have not initiated ART or have not yet achieved durable virologic suppression from ART and/or have suboptimal treatment adherence. Additionally, nonmonogamous HIV-uninfected partners in serodiscordant relationships could benefit from PrEP.

WHAT IS THE ROLE OF PrEP IN CONCEPTION FOR HIV-UNINFECTED WOMEN? FOR HIV-UNINFECTED MEN?

HIV-uninfected women who wish to conceive children with HIV-infected male partners can use PrEP as part of a multicomponent strategy to reduce their risk of HIV acquisition. Additional components may include virologic suppression for their male partners, limiting condomless sex to peak fertility, screening and treatment of STIs, and intrauterine insemination after sperm washing to remove HIV from a male partner’s semen [42–44]. For HIV-uninfected males, intrauterine insemination of their sperm into a female partner without intercourse can be used to achieve conception without risk of HIV transmission [42, 43]. Being circumcised will also decrease their risk of HIV acquisition. Prioritization of approaches to safer conception will depend on economic, structural, and personal factors, such as insurance status, access to assisted reproduction technologies, which may not be accessible to many individuals with socioeconomic challenges, and personal preferences.

WHAT DO YOU DO IF PATIENTS FACE CHALLENGES WITH PAYING FOR PrEP?

Patients with health care insurance may face substantial out-of-pocket costs for PrEP because of varying insurance coverage determinations for PrEP-related care and medications and/or because of high co-pays or deductibles. Insurance barriers may result in discontinuations of PrEP use, which have been associated with HIV seroconversion [45, 46]. Several resources are available to help cover the cost of PrEP medications and follow-up care (eg, clinical visits, laboratory tests) (Table 2). Of note, even though PrEP is costly, with TDF/FTC priced at over $10,000 annually, numerous modeling studies suggest that PrEP is cost-effective when used in subgroups with high rates of new HIV infections (eg, MSM engaging in high-risk behaviors). However, PrEP may not be cost-effective at current drug prices when used in other subgroups (eg, PWID, MSM with low-risk behaviors) [47–50].

WHICH TYPES OF CLINICIANS SHOULD PRESCRIBE PrEP?

Ideally, any clinician who provides health care to individuals at risk for HIV infection would be trained and prepared to prescribe PrEP. Infectious diseases physicians who provide care to persons living with HIV infection have an opportunity to provide PrEP to the sexual partners of their HIV-infected patients when appropriate; these physicians may also receive patient referrals from generalist colleagues with less experience prescribing antiretroviral medications. However, there are insufficient numbers of infectious diseases physicians to meet the demand for PrEP nationally, so it is important to engage and support additional clinicians to prescribe PrEP, including primary care clinicians (as part of routine preventive health care), providers at sexual health or family planning clinics, and others.

WHAT INVESTIGATIONAL STRATEGIES ARE UNDER STUDY FOR PrEP?

TDF/FTC is “PrEP 1.0”; that is, new regimens are being evaluated [51], with the goal of offering at-risk persons a range of
options, analogous to hormonal contraception. Tenofvir alafenamide (TAF) has been shown to cause less renal and bone toxicity than TDF [52], and TAF/FTC PrEP is under study in a randomized controlled trial, comparing it with TDF/FTC. Cabotegravir, an integrase strand transfer inhibitor that may be able to be administered as infrequently as every 8 weeks, is also being evaluated as PrEP [39]. Studies of immunoprophylaxis using parenterally administered monoclonal antibodies are also underway [37]. Each approach may offer some unique advantages—for example, less frequent dosing, fewer specific toxicities—but none of them are currently available, so optimization of adherence to daily TDF/FTC is the best way to ensure chemoprophylactic efficacy at present.

WHAT ARE ADDITIONAL EDUCATIONAL RESOURCES FOR CLINICIANS WHO PROVIDE PReP CARE? ADDITIONAL RESOURCES FOR PATIENTS?

Numerous educational resources about PrEP are available for clinicians and for patients, including comprehensive clinical practice guidelines from normative bodies (eg, US Public Health Services [9]) and informational materials in diverse modalities (eg, videos, webinars, downloadable brochures) from various advocacy organizations devoted to HIV care and prevention (Table 2).

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References

1. Baeten JM, Donnell D, Ndase P, et al; Partners PrEp Study Team. Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. N Engl J Med 2012; 367:399–410.
2. Choopanya K, Martin M, Suntharasamai P, et al; Bangkok Tenofovir Study Group. 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; 381:2083–90.
3. Grant RM, Lama JR, Anderson PL, et al; iPrEx Study Team. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. N Engl J Med 2010; 363:2587–99.
4. Thiggen MC, Kebaabetswe PM, Paxton LA, et al; TDF2 Study Group. Antiretroviral preexposure prophylaxis for heterosexual HIV transmission in Botswana. N Engl J Med 2012; 367:423–34.
5. Volk JE, Marcus JL, Phengrasamy T, et al. New HIV infections with increasing use of HIV preexposure prophylaxis in a clinical practice setting. Clin Infect Dis 2015; 61:1601–9.
6. 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; 387:53–60.
7. Molina JM, Capitant C, Spire B, et al; ANRS IPERGAY Study Group. On-demand preexposure prophylaxis in men at high risk for HIV-1 infection. N Engl J Med 2015; 373:2237–46.
8. Liu AY, Cohen SE, Vittinghoff E, et al. Preexposure prophylaxis for HIV infection integrated with municipal- and community-based sexual health services. JAMA Intern Med 2016; 176:75–84.
9. US Public Health Service. Preexposure prophylaxis for the prevention of HIV infection in the United States—2014. A clinical practice guideline. Available at: https://www.cdc.gov/hiv/pdf/prepguidelines2014.pdf. Accessed 13 September 2017.
10. Smith DK, Van Handel M, Wolitski RJ, et al. Vital signs: estimated percentages and numbers of adults with indications for preexposure prophylaxis to prevent HIV acquisition—United States, 2015. MMWR Morb Mortal Wkly Rep 2015; 64:1291–5.
11. Merz R, McCallister S, Palmer B, et al. Truvada (TDF) for HIV pre-exposure prophylaxis (PrEP) utilization in the United States (2013–2015). Paper presented at: 21st International AIDS Conference; July 18–22, 2016, Durban, South Africa. Abstract TUA0051LB. Available at: http://programme.aids2016.org/Abstract/Abstract10159. Accessed 13 September 2017.
12. Bernstein KT, Liu KL, Begier EM, et al. 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; 168:1458–64.
13. Cohen SE, Vittinghoff E, Bacon O, et al. High interest in preexposure prophylaxis among men who have sex with men at risk for HIV infection: baseline data from the US PrEP demonstration project. J Acquir Immune Defic Syndr 2015; 68:439–48.
14. Chan PA, Glynn TR, Oldenburg CE, et al. Implementation of preexposure prophylaxis for human immunodeficiency virus prevention among men who have sex with men at a new england sexually transmitted diseases clinic. Sex Transm Dis 2016; 43:717–23.
15. Rosenberg ES, Millett GA, Sullivan PS, et al. Understanding the HIV disparities between black and white men who have sex with men in the USA using the HIV care continuum: a modeling study. Lancet HIV 2014; 1:e112–8.
16. Oster AM, Wiegand RE, Stonean C, et al. Understanding disparities in HIV infection between black and white MSM in the United States. AIDS 2011; 25:1103–12.
17. Marcus JL, Volk JE, Pinder J, et al. Successful implementation of HIV preexposure prophylaxis: lessons learned from three clinical settings. Curr HIV/AIDS Rep 2016; 13:116–24.
18. Cahill S, Taylor SW, Elesser SA, et al. Stigma, medical mistrust, and perceived racism may affect PrEP awareness and uptake in black compared to white gay and bisexual men in Jackson, Mississippi and Boston, Massachusetts. AIDS Care 2017; 1–8.
19. Kuhns LM, Hotton AL, Schneider J, et al. Use of pre-exposure prophylaxis (PrEP) in young men who have sex with men is associated with race, sexual risk behavior and peer network size. AIDS Behav 2017; 21:1376–82.
20. Bush S, Magnuson D, Rawlings K, et al. Racial characteristics of FTC/TDF for pre-exposure prophylaxis (PrEP) users in the US. Paper presented at: American Society for Microbiology (ASM) Microbe 2016; June 16–20, 2016, Boston, MA. Available at: http://www.abstractsonline.com/pp8/#!/4060/presentation/16214. Accessed 13 September 2017.
21. Auerbach JD, Emsky S, Brown G, Charles V. Knowledge, attitudes, and likelihood of pre-exposure prophylaxis: lessons learned from three clinical settings. Curr HIV/AIDS Rep 2016; 13:116–24.
women using tenofovir disoproxil fumarate with or without emtricitabine. J Infect Dis 2016; 214:55–64.
31. CDC statement on IPERGAY trial of pre-exposure prophylaxis (PrEP) for HIV prevention among men who have sex with men. Available at: https://www.cdc.gov/nchhstp/newsroom/2015/croi-media-statement.html. Accessed 27 June 2017.
32. US Centers for Disease Control and Prevention. Safer sex 101 for HIV. Available at: https://www.cdc.gov/hiv/pdf/library/factsheets/cdc-hiv-safer-sex-101.pdf. Accessed 4 July 2017.
33. Chan PA, Mena L, Patel R, et al. Retention in care outcomes for HIV pre-exposure prophylaxis implementation programmes among men who have sex with men in three US cities. J Int AIDS Soc 2016; 19:20903.
34. Gandhi M, Glidden DV, Mayer K, et al. Association of age, baseline kidney function, and medication exposure with declines in creatinine clearance on pre-exposure prophylaxis: an observational cohort study. Lancet HIV 2016; 3:e521–8.
35. Gandhi M, Bacchetti P, Koss CA, et al. Older age associated with both adherence and renal decline in the PrEP Demo Project. Paper presented at: 2017 Conference on Retroviruses and Opportunistic Infections; February 13–16, 2017; Seattle, WA. Abstract 978. Available at: http://www.croiconference.org/sessions/older-age-associated-both-adherence-and-renal-decline-prep-demo-project. Accessed 13 September 2017.
36. Cohen SE, Vittinghoff E, Philip SS, et al. Quarterly screening optimizes STI detection among PrEP users in the Demo Project. Paper presented at: 2016 Conference on Retroviruses and Opportunistic Infections; February 22–25, 2016; Boston, MA. Abstract 870. Available at: http://www.croiconference.org/sessions/quarterly-sti-screening-optimizes-sti-detection-among-prep-users-demo-project-0. Accessed 13 September 2017.
37. Jenness SM, Weiss KM, Goodreau SM, et al. Incidence of gonorrhea and chlamydia following HIV preexposure prophylaxis among men who have sex with men: a modeling study. Clin Infect Dis 2017; doi: 10.1093/cid/cix439.
38. US Centers for Disease Control and Prevention. 2015 sexually transmitted diseases surveillance. Available at: https://www.cdc.gov/std/stats15/toc.htm Accessed 11 August 2017.
39. Cohen MS, Chen YQ, McCauley M, et al; HPTN 052 Study Team. Antiretroviral therapy for the prevention of HIV-1 transmission. N Engl J Med 2016; 375: 830–9.
40. Cohen MS, Chen YQ, McCauley M, et al; HPTN 052 Study Team. Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med 2011; 365:493–505.
41. 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.
42. 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 Morb Mortal Wkly Rep 2017; 66:554–7.
43. Matthews LT, Beyeza-Kashesya J, Cooke I, et al. Consensus statement: supporting safer conception and pregnancy for men and women living with and affected by HIV. AIDS Behav 2017; doi: 10.1007/s10461-017-1777-7.
44. Whetham I, Taylor S, Charlwood L, et al. Pre-exposure prophylaxis for conception (PrEP-C) as a risk reduction strategy in HIV-positive men and HIV-negative women in the UK. AIDS Care 2014; 26:332–6.
45. Marcus JL, Hurley LB, Hare CB, et al. Preexposure prophylaxis for HIV prevention in a large integrated health care system: adherence, renal safety, and discontinuation. J Acquir Immune Defic Syndr 2016; 73:540–6.
46. Krakower D, Maloney K, Levine K, et al. Unplanned discontinuation of HIV pre-exposure prophylaxis during clinical care. Paper presented at: HIVR4P Conference; October 17–21, 2016; Chicago, IL. Available at: http://hivr4p.org/images/HIVR4P_2016_Abstract_Book.pdf. Accessed 13 September 2017.
47. Bernard CL, Brandeau ML, Humphreys K, et al. Cost-effectiveness of HIV preexposure prophylaxis for people who inject drugs in the United States. Ann Intern Med 2016; doi: 10.7326/M15-2634.
48. Jacobsen MM, Walensky RP. Modeling and cost-effectiveness in HIV prevention. Curr HIV/AIDS Rep 2016; 13:64–75.
49. Juusola JL, Brandeau ML, Owens DK, Bendavid E. The cost-effectiveness of pre-exposure prophylaxis for HIV prevention in the United States in men who have sex with men. Ann Intern Med 2012; 156:541–50.
50. Kessler J, Myers JE, Nucifora KA, et al. Evaluating the impact of prioritization of antiretroviral pre-exposure prophylaxis in New York. AIDS 2014; 28:2683–91.
51. AVAC. The years ahead in biomedical HIV prevention research. Available at: http://www.avac.org/infographic/years-ahead-hiv-prevention-research Accessed 1 July 2017.
52. Sax PE, Wohl D, Yin MT, et al; GS-US-292-0104/0111 Study Team. Tenofovir alafenamide versus tenofovir disoproxil fumarate, coformulated with elvitegravir, cobicistat, and emtricitabine, for initial treatment of HIV-1 infection: two randomised, double-blind, phase 3, non-inferiority trials. Lancet 2015; 385:2606–15.
53. 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:e1002132.