Preventing HIV Transmission in Persons with HIV

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Module 5: Prevention of HIV
Lesson 2: Preventing HIV Transmission in Persons with HIV

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Background

The availability of widespread effective antiretroviral therapy has transformed HIV from a fatal infection to a manageable chronic disease. Despite major advances in antiretroviral therapy, the incidence of new HIV infections in the United States continues to occur with more than 30,000 annual new HIV infections (Figure 1).[1] For persons living with HIV, antiretroviral therapy can dramatically reduce HIV transmission to others.[2,3,4,5] All health professionals involved with HIV care should have knowledge and awareness of effective strategies that can play a role in reducing HIV transmission. The use of antiretroviral therapy in people with HIV has emerged as a highly impactful means to prevent HIV transmission and this approach is referred to as treatment as prevention.[6] This topic review will focus on the biomedical, behavioral, and structural measures related to preventing transmission from persons with HIV, with an emphasis on treatment as prevention. The discussion of preventing HIV acquisition among individuals who do not have HIV is discussed in detail in the lesson HIV Preexposure Prophylaxis.

Antiretroviral Treatment as Prevention

HIV RNA Level and Risk of HIV Transmission

A sentinel study in Rakai, Uganda, first reported HIV RNA levels tightly correlated with the risk of heterosexual HIV transmission.[7] This study involved 415 serodifferent heterosexual couples not taking antiretroviral therapy.[7] The main finding was that mean serum HIV RNA was significantly higher in subjects whose partners seroconverted than in subjects whose partners remained HIV negative, and HIV transmission was considered rare among persons who had an HIV RNA level less than 1,500 copies/mL (Figure 2).[7] This study played a major role in spurring on studies that would examine the impact that lowering HIV RNA levels with antiretroviral therapy would have on sexual transmission of HIV.

Antiretroviral Therapy in HIV Serodifferent Couples

Convincing data from several studies have shown that antiretroviral treatment taken by individuals with HIV dramatically reduces HIV transmission to their sex partners.[3,4,8,9]

- **HPTN-052**: The concept of treating persons with HIV to prevent transmission to others, often referred to as treatment as prevention, garnered major support following the release of data from the landmark HPTN-052 trial.[3,4] The HPTN-052 trial was a randomized, controlled study that enrolled 1,763 HIV serodifferent, predominantly heterosexual couples from 9 countries. All persons with HIV had a CD4 count of 350 to 550 cells/mm^3 at enrollment, and none had HIV-related symptoms. The trial demonstrated that early initiation of antiretroviral therapy (started at the time of enrollment) reduced rates of sexual transmission of HIV to the partner without HIV by 96%, when compared with deferral of antiretroviral therapy (started when the CD4 count decreased to less than 250 cells/mm^3 or at the onset of an AIDS-related event) (Figure 3).[3,4]
- **PARTNER-1 Study**: In the first phase of the European PARTNER (Partners of People on ART—A New Evaluation of the Risks) study, investigators at 75 sites in 14 European countries evaluated the impact of antiretroviral therapy on HIV transmission risk in 888 HIV-serodifferent couples engaging in condomless sex, including 548 heterosexual couples and 340 gay male couples.[2] Enrollment eligibility required the partner with HIV to be taking antiretroviral therapy and have an HIV RNA level less than 200 copies/mL.[2] Enrollment took place from September 2010 through May 2014, and during this time, there were zero phylogenetically linked HIV transmissions that occurred in these couples, with an estimated 58,000 condomless sex acts (22,000 in gay male couples and 36,000 in heterosexual couples).[2] There were 11 new HIV infections during the study period, but none of these were phylogenetically linked.
- **PARTNER-2 Study**: In the second phase of the European PARTNER study, investigators at the same 75 sites in 14 European countries continued the PARTNER study, but additional enrollment was only for serodifferent gay men.[10] The enrollment period analyzed for PARTNER-2 was September 2010 through July 31, 2017, and included a total of 972 HIV serodifferent gay male couples.[10] As with PARTNER-1, enrollment eligibility required the partner with HIV to be taking antiretroviral therapy and have an HIV RNA level less than 200 copies/mL. During the study, the serodifferent gay male couples reported condomless anal sex a total of 76,088 times, and there were zero phylogenetically linked transmissions.[10] There were, however, 15 new HIV infections during the study period, but none of these were phylogenetically linked.[10]
- **Opposites Attract**: The Opposites Attract trial was conducted from 2012 through 2016 and enrolled 358 HIV-serodifferent gay male couples in Thailand, Brazil, and Australia.[11] Of the 358 couples that enrolled, 343 had at least one follow-up visit, and 258 of 343 (75%) of the partners with HIV had an HIV RNA level less than 200 copies/mL.[11] There were zero phylogenetically linked cases of HIV transmission from among 12,447 sex acts that involved (1) condomless anal intercourse, (2) partners with HIV taking antiretroviral therapy (and with an HIV RNA less than 200 copies/mL), and (3) partners without HIV not taking HIV preexposure prophylaxis (PrEP).[11] There were three new HIV infections during the study period, but none were phylogenetically linked.[11]

Undetectable Equals Untransmittable

Extensive data from multiple studies strongly support the concept that persons with HIV who consistently take antiretroviral therapy and maintain undetectable HIV RNA levels do not transmit HIV sexually to others, even with condomless sex.[2,10,11] This concept is commonly referred to as undetectable equals untransmittable.[5] The undetectable equals untransmittable concept is an extremely important message that is now widely endorsed by prominent scientists, clinicians, organizations, and societies.[5] The findings from the studies listed above serve as the foundation for the undetectable equals untransmittable concept, and these studies underscore the tremendous impact that antiretroviral treatment can have in preventing transmission of HIV from persons with HIV.[2,10,11] These findings also emphasize the benefit of routine HIV testing and prompt initiation of antiretroviral therapy for persons who acquire HIV. For persons with HIV who are having condomless sex, it is important to perform regular screening for sexually transmitted infections, since antiretroviral therapy does not protect against common sexually transmitted infections, such as chlamydia, gonorrhea, and syphilis.

Recommendations for Antiretroviral Treatment as Prevention

The Adult and Adolescent ARV Guidelines cite prevention of sexual transmission of HIV as one of the main reasons to recommend antiretroviral therapy for all persons with HIV (Treatment as Prevention).[6,12] Further, all people with HIV should be informed that maintaining a plasma HIV RNA level less than 200 copies/mL with antiretroviral therapy will prevent sexual transmission of HIV.[12] Note, these recommendations do not address use of antiretroviral treatment to prevent HIV transmission among persons who inject drugs, but theoretically, use of antiretroviral therapy with achievement of undetectable plasma HIV RNA levels should decrease bloodborne transmission of HIV. The table below summarizes recommendations regarding the use of antiretroviral therapy to prevent sexual transmission of HIV (Table 1).[6]

Knowledge of HIV Status

The proportion of persons who are aware of their HIV has steadily increased from an estimated 75% in 2003 to 87% in 2022.[1,13,14] Several HIV transmission modeling studies for the United States have concluded that persons unaware of their HIV diagnosis account for a disproportionately higher number of transmitted HIV infections than persons aware of their HIV diagnosis.[15,16,17] In the 2016 CDC Progression and Transmission of HIV (PATH 2.0) model, investigators estimated that among all persons with HIV in the United States in 2016, the 14.5% of persons with undiagnosed HIV accounted for 37.5% of new HIV transmissions that year (Figure 4).[17] Knowledge of HIV serostatus is the first step toward linking persons to HIV medical care, whereby they can receive antiretroviral therapy. Individuals with HIV who are unaware of their status are not taking antiretroviral therapy and thus are missing out on this critical element of HIV prevention. In the Ending HIV Epidemic—A Plan for the United States, diagnosing all individuals with HIV as early as possible after infection is one of the main pillars in the strategic initiative.[18]

Behavioral Prevention Interventions

Risk Reduction Counseling

Counseling to reduce activities that can increase the risk of HIV transmission to others is inadequate as a primary strategy for reducing HIV transmission. For persons with HIV, the impact of consistently taking antiretroviral therapy and maintaining undetectable HIV RNA levels far exceeds the impact of prevention strategies that rely on behavioral interventions. Nevertheless, risk reduction counseling for persons with known HIV remains a complementary piece of a comprehensive prevention strategy.[19] The CDC has identified evidence-based risk reduction counseling strategies for people with HIV.[20] Moreover, older studies that examined the impact of behavioral interventions for people with HIV showed a reduction in self-reported condomless sex as well as a decline in the incidence of sexually transmitted infections in persons who received behavioral interventions.[21]

HIV Status Disclosure and Partner Testing

Public Health Services, such as partner counseling and referral, help people with HIV disclose their HIV status to current or former sex or injection drug partners. The public health system provides a trained counselor who can work with the person newly diagnosed with HIV to support disclosure to partners, as well as to provide partner notification directly in cases where the person with newly diagnosed HIV is not able to disclose their HIV status. Partner notification and testing are important because of the high yield in HIV case finding.[22,23] In two national studies, partner counseling and referral services that included partner notification and HIV testing, effectively identified a substantial number of partners with a new HIV diagnosis.[24,25] In these studies, 8% of the partners of persons newly diagnosed with HIV tested positive for HIV, and these results were consistent across a 10-year period.[24,25]

Condom Use

Multiple studies have shown that persons with HIV who are taking antiretroviral therapy and maintain HIV RNA levels consistently less than 200 copies/mL do not transmit HIV sexually to others, even with condomless sex.[2,5,10,11] Accordingly, efforts emphasizing condom use as the primary method for HIV prevention have markedly diminished in recent years. Nevertheless, condoms still have a role for persons with HIV, especially in persons newly starting on antiretroviral therapy and for persons who do not have consistently suppressed HIV RNA levels. In addition, condoms play a key role in preventing the transmission and acquisition of other sexually transmitted infections. Consistent, correct condom use decreases HIV transmission by 70 to 80% among HIV-serodifferent heterosexual couples when compared with non-condom users.[26,27,28] In a separate analysis of the protective effect of condom use among HIV-serodifferent male couples who have anal sex, consistent condom use reduced the risk of HIV transmission by approximately 70%.[29]

Serosorting and Seropositioning

Serosorting and seropositioning practices are self-selected behaviors intended to reduce HIV transmission risk and are referred to as seroadaptive strategies.[30,31] Serosorting describes the practice of choosing sex partners based on concordant HIV status, typically with the practice of selectively using condoms only when sex occurs with persons of a serodifferent HIV status. Data on the impact of serosorting have been mixed.[32,33,34] Seropositioning refers to choosing a different sexual position or practice based on the HIV serostatus of one’s partner. For men utilizing seropositioning, the person with HIV typically takes the receptive role during unprotected anal sex when the partner with HIV has the insertive role. There are no guidelines in the United States that recommend serosorting or seropositioning as an impactful prevention measure. In addition, the interest in serosorting and seropositioning as an HIV prevention measure has markedly decreased with the emphasis on HIV treatment as prevention and HIV preexposure prophylaxis (PrEP).

Importance of Diagnosing and Treating Acute HIV

At the time of early HIV infection (less than 6 months after HIV acquisition), patients usually have high HIV RNA levels and lack significant neutralizing antibodies and thus are considered highly infectious.[35,36,37] Studies have evaluated the relative likelihood of transmitting HIV during acute or early HIV infection, and estimate a significantly higher risk of transmission with acute (or early) HIV than with chronic HIV infection.[38,39,40,41] Indeed, using the 2016 CDC Progression and Transmission of HIV (PATH 2.0) model, the Centers for Disease Control and Prevention estimated the highest risk of HIV transmission along the HIV continuum of care occurred in persons with acute HIV who were unaware of their HIV diagnosis (Figure 5).[17] Accordingly, it is important to diagnose individuals with acute and recent (early) HIV whenever possible. To this end, the CDC HIV testing algorithm recommends the use of the HIV-1/2 antigen-antibody immunoassay for use as the initial HIV screening test in an effort to improve the diagnosis of persons with acute HIV.[42,43] In addition, all persons diagnosed with acute HIV should immediately start antiretroviral therapy to reduce the risk of HIV transmission, as well as to garner potential long-term immunologic benefit from early therapy.[44,45]

Screening and Treating Sexually Transmitted Infections

Sexually transmitted infections can facilitate transmission and acquisition of new HIV infection, especially when the individual with HIV is not taking suppressive antiretroviral therapy.[46] Rates of sexually transmitted infections, particularly syphilis, gonorrhea, and chlamydia, are disproportionately higher among men with HIV who have sex with men.[47] Non-injection drug use, particularly with methamphetamine, as well as recreational use of erectile-enhancing medications, among men with HIV who have sex with men has been implicated in transmission of sexually transmitted infections.[48,49] Available data on herpes simplex virus (HSV) have not shown a convincing reduction in HIV transmission risk with acyclovir suppressive therapy taken by persons with HIV.[50] Screening, diagnosis, and treatment of sexually transmitted infections in persons with HIV remain a priority, but in the current era, the impact of treatment of sexually transmitted infections on preventing HIV transmission is unclear, especially for persons taking fully suppressive antiretroviral therapy.

- **Screening Recommendations for Sexually Transmitted Infections**: The 2021 STI Treatment Guidelines recommend that all sexually active persons with HIV undergo routine screening for sexually transmitted infections at all exposed anatomic sites (e.g., pharynx, rectum, urethra) and that testing include serologic screening for syphilis.[51] Any identified sexually transmitted infection should be promptly treated along with treatment of the partner.[52]

Prevention Strategies in Persons with Substance Use

Substance use disorders among people are a recognized cofactor for HIV transmission.[53,54,55] Substance use can impact sexual activity and can potentially lower rates of antiretroviral therapy adherence.[56] Alcohol use is the most prevalent risk factor for poor HIV medication adherence and lower rates of viral suppression.[57,58] Methamphetamine and other amphetamine-type stimulant use can alter antiretroviral medication adherence and increase sexual activities associated with increased risk of HIV transmission.[59,60] In addition, injection of methamphetamine and/or opioids can enhance the risk of HIV transmission through sharing of injection equipment. Screening for substance use disorders in people with HIV can play a significant role in prevention, especially if persons identified with a substance use disorder can receive counseling, treatment, and prevention services.[61,62]

Harm Reduction Approach

Harm reduction is based on a set of practical strategies and ideas aimed at reducing negative consequences associated with drug use. In addition, harm reduction programs do not insist on abstinence, and these programs typically utilize a spectrum of services, including providing safe injection counseling, HIV prevention education, and opiate substitution therapy. Harm reduction programs ideally provide a comprehensive set of services, including HIV counseling and testing (for individuals with HIV and their needle-sharing partners) and referral to substance use treatment programs. It is extremely important to remember that persons who inject drugs can also acquire and transmit HIV via sexual contact and should be counseled about sexual risk reduction strategies.[63]

Summary Points

- In the United States, integrated, evidence-based biomedical, behavioral, and structural interventions can substantially reduce transmission of HIV from persons with HIV to others.
- Antiretroviral therapy is recommended for all persons with HIV to prevent HIV transmission to others. Persons with HIV who consistently take antiretroviral therapy and maintain undetectable HIV RNA levels do not sexually transmit HIV to others, even with condomless sex.
- Persons unaware of their HIV status account for a disproportionate number of new HIV infections in the United States.
- For persons newly diagnosed with HIV, partner notification and contact HIV testing provide effective HIV case finding and the opportunity to decrease exposure to others.
- Consistent and correct condom use decreases HIV transmission by approximately 80% among serodifferent heterosexual couples and reduces the per-contact risk of HIV infection by 78% among men who have sex with men who practice receptive anal intercourse.
- Persons with undiagnosed acute (early) HIV have the highest relative risk of HIV transmission to others. Diagnosis, counseling, and treatment of persons with acute HIV can substantially reduce new HIV infections.
- Screening and treatment of sexually transmitted infections is an important component of overall HIV prevention services.
- Screening for substance use can help providers identify individuals with HIV who could benefit from counseling and support for a substance use disorder.

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Figures

Figure 1 Estimated HIV Incidence in United States, 2018-2022

Source: Centers for Disease Control and Prevention. Estimated HIV Incidence and Prevalence in the United States, 2018–2022. HIV Surveillance Supplemental Report. 2024;29(No. 1):1-131. Published May 2024 (revised February 7, 2025).

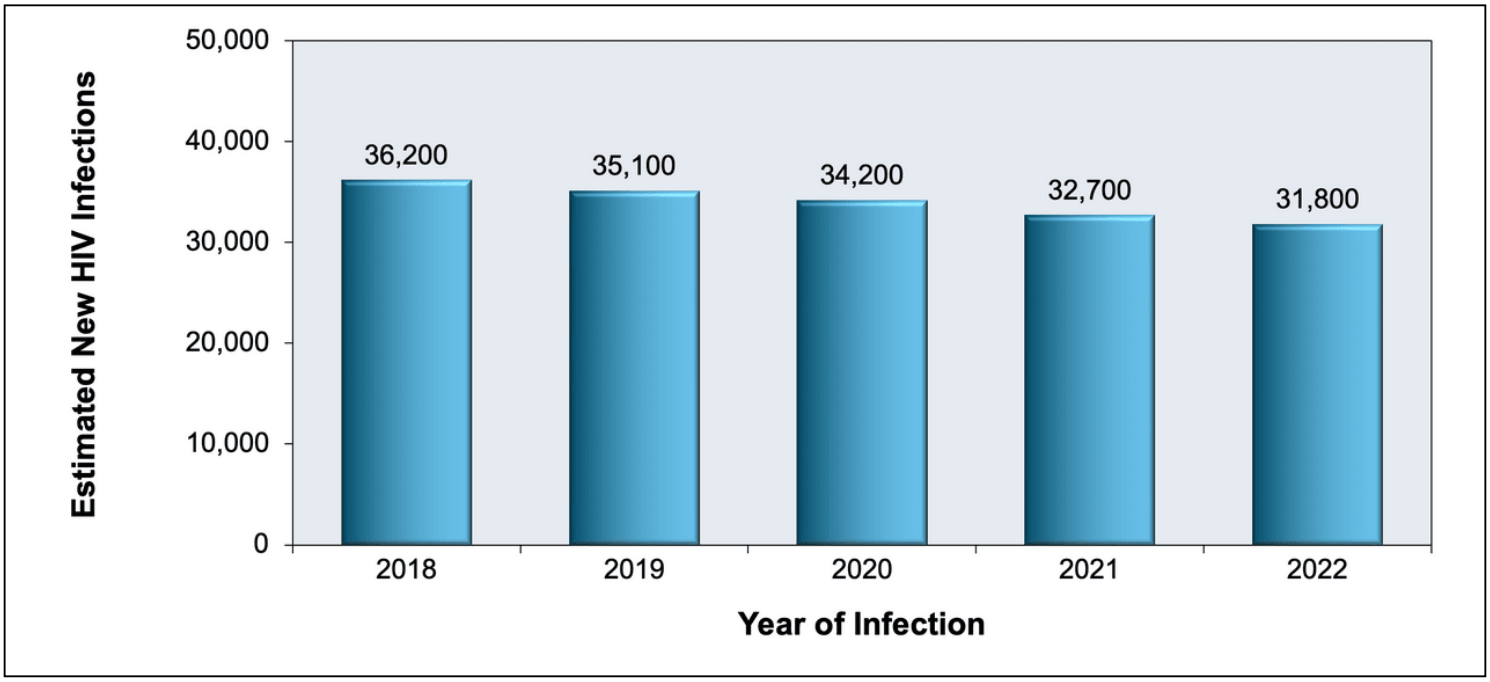


Figure 2 Adjusted Rate Ratio of Heterosexual Transmission of HIV-1 According to Serum HIV-1 RNA Level of the HIV-1 Positive Partner

This graphic illustrates the correlation of risk of HIV transmission and serum HIV-1 levels in the person infected with HIV. No HIV transmissions occurred from persons with HIV who had serum HIV RNA-1 levels less than 1,500 copies/mL.

Source: Quinn TC, Wawer MJ, Sewankambo N, et al. Viral load and heterosexual transmission of human immunodeficiency virus type 1. Rakai Project Study Group. N Engl J Med. 2000;342:921-9.

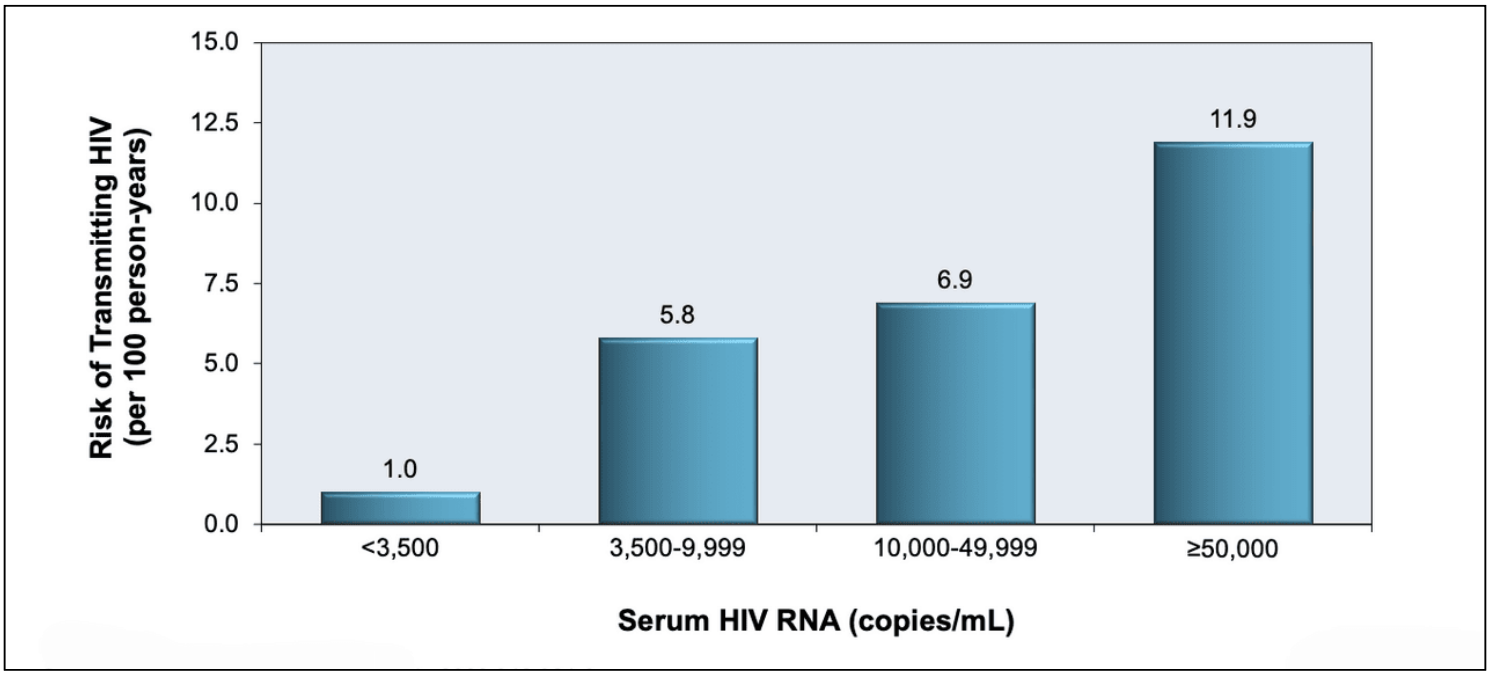


Figure 3 (Image Series) - HPTN 052 and Antiretroviral Therapy for the Prevention of HIV-1 (Image Series) - Figure 3 (Image Series) - HPTN 052 and Antiretroviral Therapy for the Prevention of HIV-1
Image 3A: HPTN 052 Patient Population

The HPTN 052 trial enrolled 1,763 HIV serodifferent couples, and 97% identified as heterosexual couples.

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

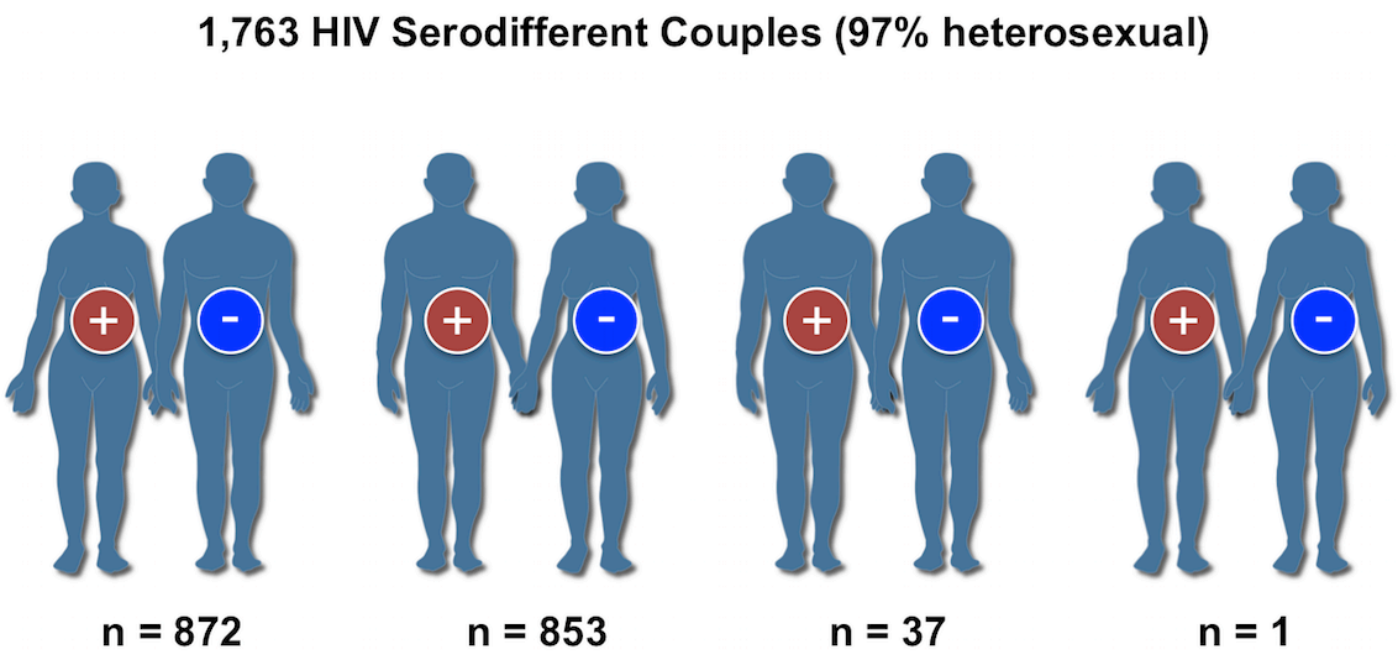


Figure 3 (Image Series) - HPTN 052 and Antiretroviral Therapy for the Prevention of HIV-1
Image 3B: HPTN 052 Study Design

Adults with HIV in the early therapy arm received combination antiretroviral therapy, and those in the deferred therapy arm started antiretroviral therapy when their CD4 decreased to less than 250 cells/mm^3, or they had an AIDS-related event.

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

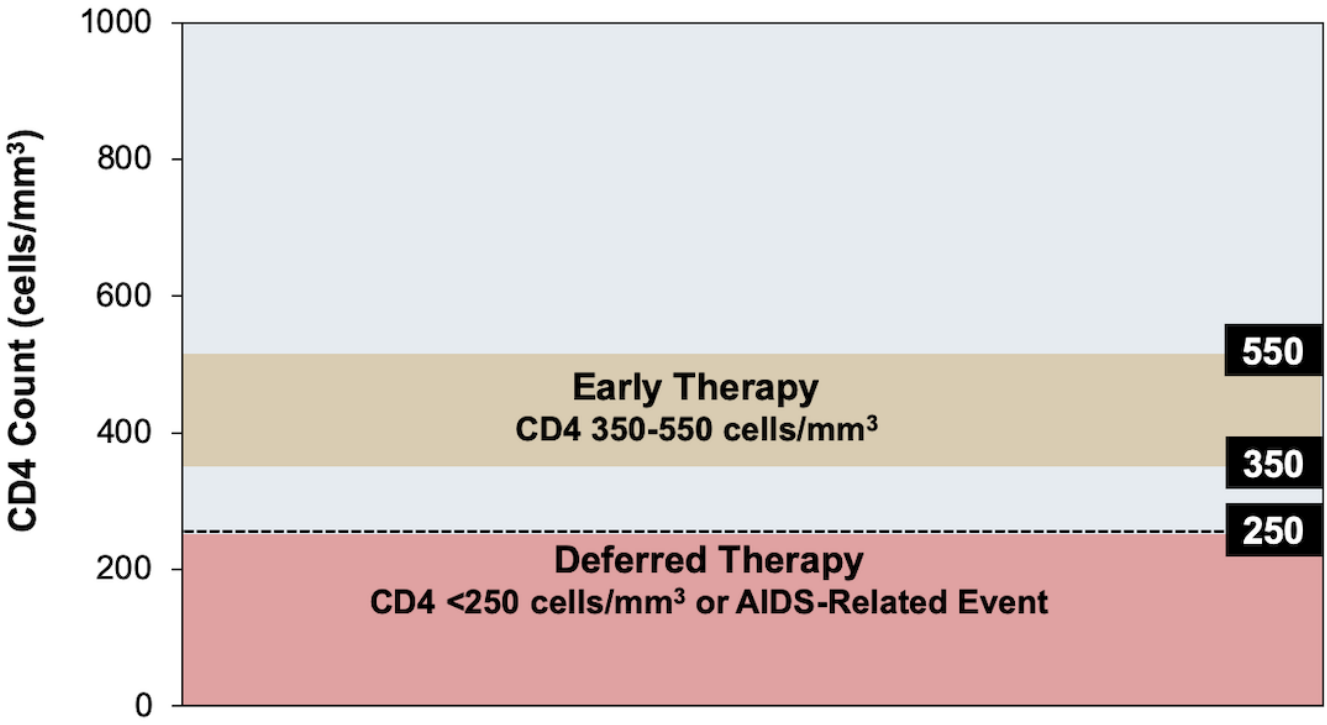


Figure 3 (Image Series) - HPTN 052 and Antiretroviral Therapy for the Prevention of HIV-1
Image 3C: HPTN 052 Results

This graphic shows linked transmissions. Couples in the early therapy arm had a 96% reduction in new HIV transmission events.

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

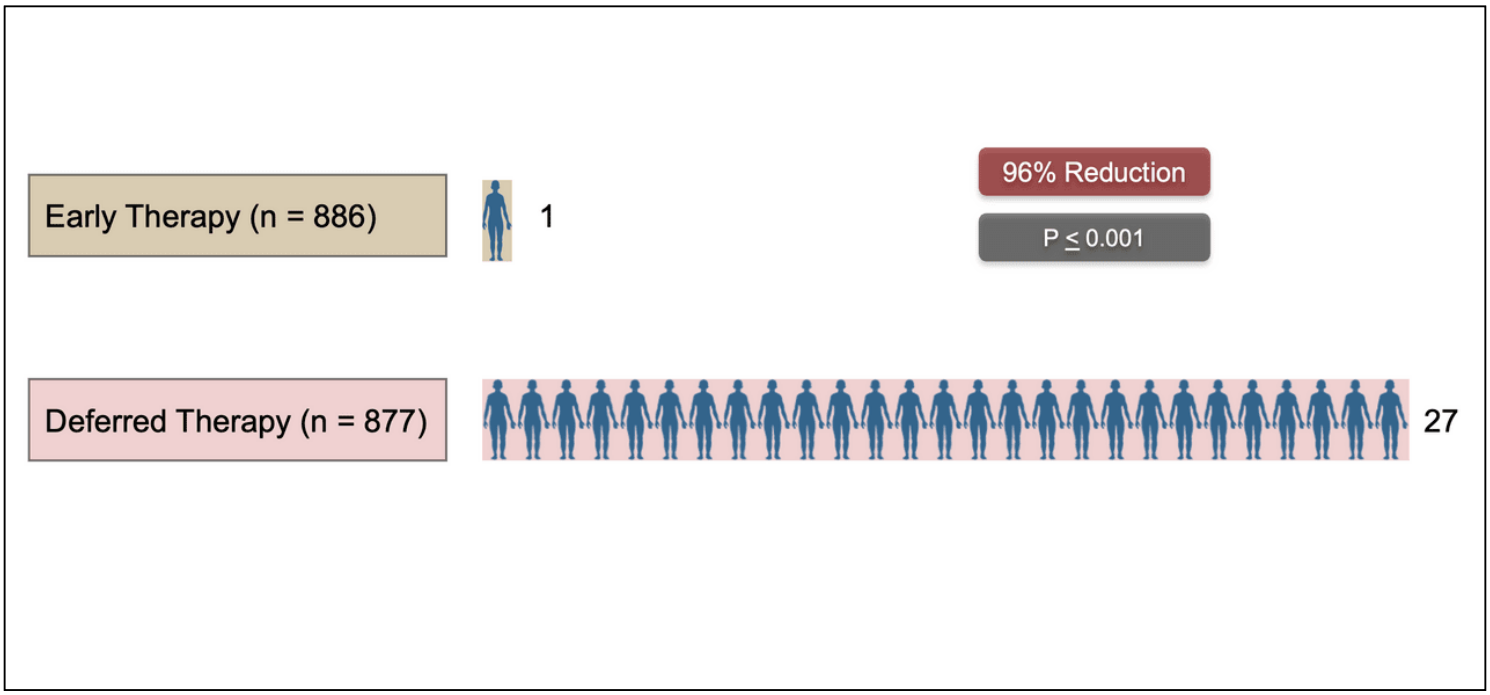


Figure 4 Transmission of HIV and Awareness of HIV Status

This graph shows the estimated percentage of HIV transmissions based on awareness of HIV diagnosis. These estimates were based on the 2016 Centers for Disease Control and Prevention (CDC) Progression and Transmission of HIV (PATH 2.0) model.

Source: Li Z, Purcell DW, Sansom SL, Hayes D, Hall HI. Vital Signs: HIV transmission along the continuum of care - United States, 2016. MMWR Morb Mortal Wkly Rep. 2019;68:267-72.

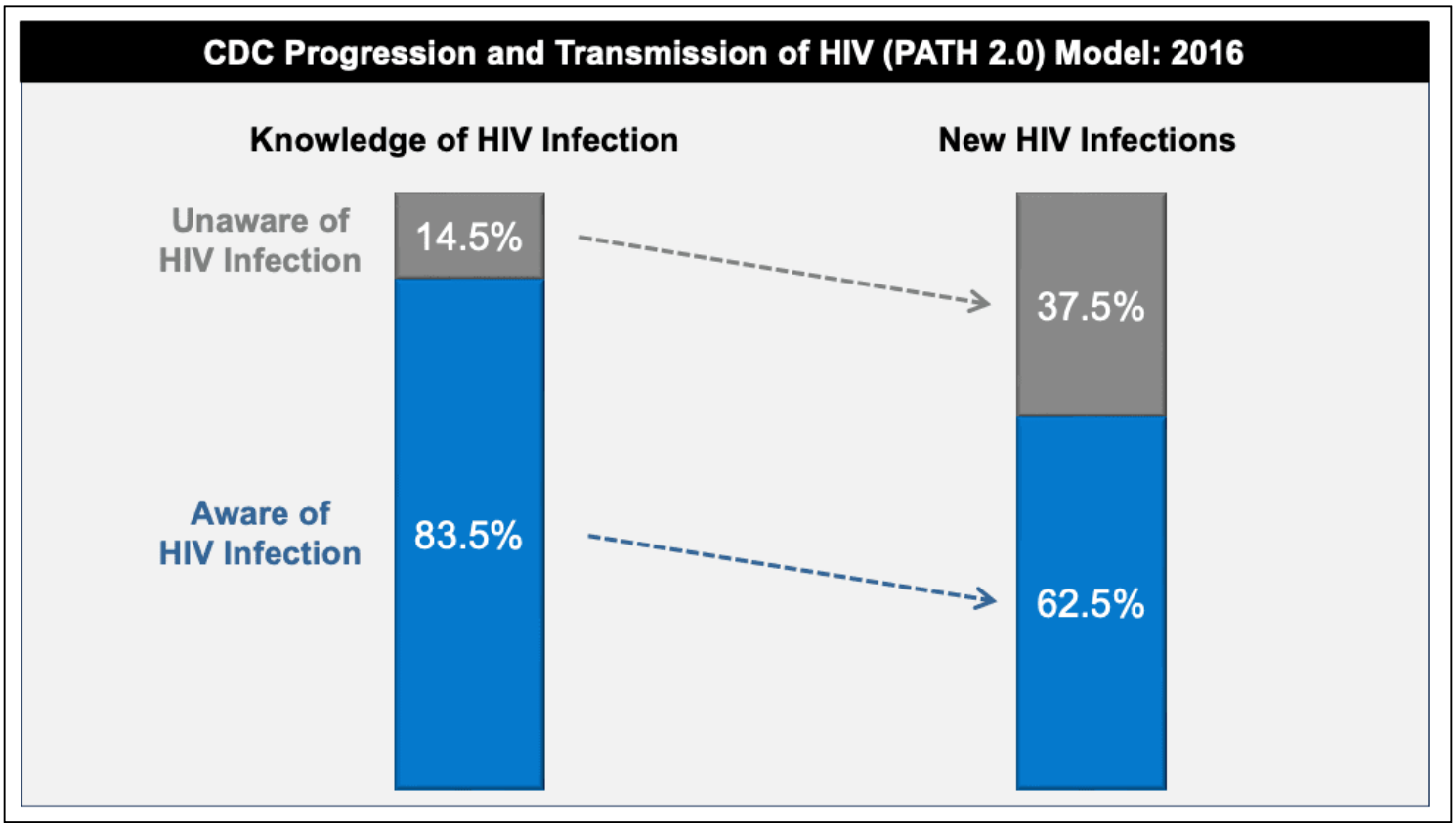


Figure 5 Relative Risk of HIV Transmission Along the HIV Care Continuum

This graph shows the estimated transmission rate based on transmissions per 100,000 person-years. These estimates were based on the 2016 Centers for Disease Control and Prevention (CDC) Progression and Transmission of HIV (PATH 2.0) model.

Source: Li Z, Purcell DW, Sansom SL, Hayes D, Hall HI. Vital Signs: HIV transmission along the continuum of care - United States, 2016. MMWR Morb Mortal Wkly Rep. 2019;68:267-72.

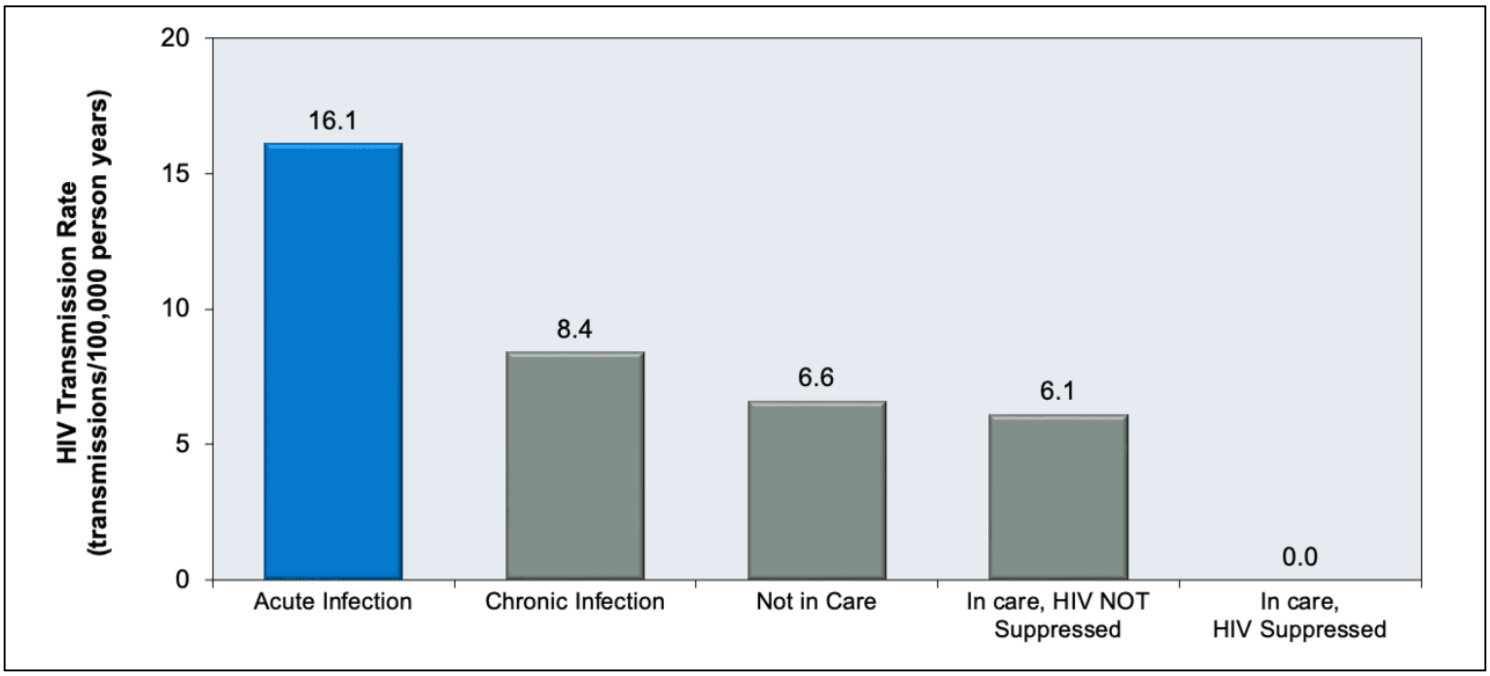


Table 1. Antiretroviral Therapy to Prevent Sexual Transmission of HIV: *Adult and Adolescent ARV Guidelines*

Recommendations
• All people with HIV should be informed that maintaining a plasma HIV RNA (viral load) of <200 copies/mL, including any measurable value below this threshold value, with antiretroviral therapy (ART) prevents sexual transmission of HIV. This concept may be recognized as Undetectable = Untransmittable **(AII)**
• People with HIV who are starting ART should use another form of prevention with sexual partners (e.g., condoms, pre-exposure prophylaxis [PrEP] for the sexual partner who is HIV-negative) for at least the first 6 months of ART and until a viral load of <200 copies/mL has been documented **(AII)**. Many experts would recommend confirming sustained suppression before assuming that there is no further risk of sexual HIV transmission **(AIII)**.
• When the viral load is ≥200 copies/mL, at least one additional HIV prevention method (e.g., condoms, sexual abstinence, or HIV PrEP for the HIV-negative partner) is recommended to prevent sexual HIV transmission until resuppression to <200 copies/mL is confirmed **(AIII)**.
• People with HIV who intend to rely upon ART for prevention need to maintain high levels of ART adherence **(AIII)**. They should be informed that transmission is possible during periods of poor adherence or treatment interruption **(AIII)**.
• At each visit for HIV care, clinicians should assess adherence to ART and counsel people with HIV on the importance of ART for their own health as well as its role in preventing sexual HIV transmission **(AIII)**.
• Providers should inform patients that maintaining a viral load of <200 copies/mL does not prevent acquisition or transmission of other sexually transmitted infections (STIs) **(AII)**.
• Providers should also routinely screen all people with HIV who are sexually active for STIs, both for their own health and to prevent transmission of STIs to others **(AIII)**.
Rating of strength of recommendation for the statement: A = Strong; B = Moderate; C = Weak *Quality of evidence for the recommendation: I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, non-randomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Source:

- Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in adults and adolescents living with HIV. Department of Health and Human Services. Antiretroviral therapy to prevent sexual transmission of HIV (treatment as prevention). September 25, 2025 [HIV.gov]