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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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Introduction and 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 at a significant number, with about 32,000 to 36,000 persons newly acquiring HIV in recent years (Figure 1).[1] For persons living with HIV, antiretroviral therapy can dramatically reduce HIV transmission to others.[2,3,4,5] All clinicians providing HIV services should have knowledge and awareness of effective strategies that can play a role in reducing the risk of HIV transmission from persons with HIV. This topic review will focus on biomedical, behavioral, and structural measures related to preventing transmission from persons with HIV, a concept often referred to as Treatment as Prevention (TasP).[6]

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]
- **Observational Trials**: Several observational studies with serodifferent heterosexual couples have similarly demonstrated that antiretroviral treatment of a partner with HIV is a potent intervention for preventing sexual transmission of HIV.[10] Further, data from a meta-analysis of 5,021 heterosexual serodifferent couples reinforces this finding; no HIV transmissions were reported from persons with HIV who were treated with antiretroviral therapy if the person with HIV had an HIV RNA level below 400 copies/mL.[9]
- **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] The eligibility for enrollment 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 (Partners of People on ART—A New Evaluation of the Risks) study, investigators at the same 75 sites in 14 European countries continued the PARTNER study, but additional enrollment was only for serodifferent gay men.[11] The enrollment period analyzed for PARTNER-2 was September 2010 through July 31, 2017, and included a total of 972 serodifferent gay male couples.[11] The design to include only serodifferent gay male couples was to account for some of the imbalance of the predominantly heterosexual serodifferent couples enrolled in the PARTNER-1 trial. As with PARTNER-1, the eligibility for enrollment 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.[11] There were, however, 15 new HIV infections during the study period, but none of these were phylogenetically linked.[11]

- **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.[12] Of the 358 couples that enrolled, 343 had at least one follow-up visit, and 75% (258 of 343) of the partners with HIV had an HIV RNA level less than 200 copies/mL.[12] 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).[12] There were three new HIV infections during the study period, but none were phylogenetically linked.[12]

Undetectable Equals Untransmittable (U=U)

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.[2,11,12] This concept is commonly referred to as Undetectable equals Untransmittable or U=U.[5] The U=U concept is an extremely important message that is now widely endorsed by prominent scientists, clinicians, organizations, and societies.[5] The findings from the studies that serve as the foundation for the U=U concept underscore the tremendous impact that antiretroviral treatment can have in preventing transmission of HIV from persons with HIV. 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 provide protection against common sexually transmitted infections, such as chlamydia, gonorrhea, and syphilis.

Recommendations for Antiretroviral Treatment as Prevention

The Adult and Adolescent ART Guidelines cite prevention of sexual transmission of HIV as one of the main reasons to recommend antiretroviral therapy for all persons with HIV.[13] This recommendation to use antiretroviral treatment as prevention is now supported by multiple studies that persons who consistently maintain plasma HIV RNA levels less than 200 copies/mL do not transmit HIV to sex partners.[9,11,12,14] The Adult and Adolescent ART Guidelines also provide specific recommendations for the use of antiretroviral therapy to prevent sexual transmission of HIV (Treatment as Prevention); these recommendations clarify that persons with HIV who are starting antiretroviral therapy should use another form of HIV prevention with sex partners (e.g., condoms, preexposure prophylaxis for the HIV-negative sex partner, sexual abstinence) for at least the first 6 months of treatment and until they have achieved an HIV RNA level less than 200 copies/mL.[6] 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 the Adult and Adolescent ART Guidelines recommendations for the use of antiretroviral therapy to prevent sexual transmission of HIV.[6]

Table 1. **Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV**

Use of Antiretroviral Therapy to Prevent Sexual Transmission of HIV	
• All persons 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 to their partners. Patients may recognize this concept as Undetectable = Untransmittable or U=U **(AII)**. • Persons with HIV who are starting	

ART should use another form of prevention with sexual partners (e.g. condoms, pre-exposure prophylaxis [PrEP] for the HIV-negative sexual partner, sexual abstinence) for at least the first 6 months of treatment 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, additional methods are needed to prevent transmission of HIV to sexual partners until resuppression to <200 copies/mL has been confirmed **(AIII)**.
- Persons 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 patients regarding the importance of ART to 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 sexually active persons with HIV for STIs, both for their own health and to prevent transmission of STIs to others **(AIII)**.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized 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). December 18, 2019. [HIV.gov]

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Community Viral Load and Treatment Impact at Population Level

Several groups have shown that a reduction in community viral load is associated with decreased numbers of new HIV infections in that community, supporting the hypothesis that wide-scale use of antiretroviral therapy in persons with HIV could significantly reduce HIV transmission at the population level. For example, in British Columbia, the scale-up of antiretroviral therapy from 1996 through 2009 led to a 52% decline in new HIV infections.[15] A separate study performed in San Francisco found that reductions in mean and total community viral load from 2004 through 2008 were associated with a decrease in new HIV diagnoses.[16] Furthermore, mapping of mean and total community viral load can identify disparities. For example, a community viral load study in Washington, D.C. revealed the highest viral loads in low-income areas with low education rates;[17] a similar study in New York City showed that low-income neighborhoods had the highest community viral loads, HIV prevalence, and HIV-related death rates.[18] Mathematical modeling also shows that expanded utilization of antiretroviral therapy is cost-effective due to the number of new infections averted.[19]

Knowledge of HIV Status

The proportion of persons with undiagnosed HIV has steadily decreased from an estimated 25% in 2003 to 12.7% in 2021.[1,20,21] 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.[22,23,24] 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).[24] Knowledge of HIV serostatus is the first step toward linking persons to HIV medical care whereby they can receive antiretroviral therapy. 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.[25] Older studies have shown that persons with a known diagnosis of HIV reduce sexual activities associated with an increased risk of HIV transmission, but these data may not be applicable to the current era.[26,27]

Behavioral Prevention Interventions for Persons with HIV

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.[28] The CDC has identified evidence-based risk reduction counseling strategies for people with HIV.[29] 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.[30] In the current era, however, medical providers often do not see risk reduction counseling as a high priority as they prioritize comprehensive HIV care.[31] Overall, the impact of risk reduction counseling in preventing HIV transmission from persons with HIV is minor compared with the impact of taking antiretroviral therapy and maintaining undetectable HIV RNA levels.

HIV Status Disclosure and Partner Testing

Partner counseling and referral services is a public health service that helps 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 is important because of the high yield in HIV case finding.[32,33] In two national studies, partner counseling and referral services, including partner notification and HIV testing, effectively identified a substantial number of partners with a new HIV diagnosis; 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.[34,35]

Condom Use

Extensive data has 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.[2,5,11,12] 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 prevent the 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.[36,37,38] 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%.[39] Correlates of condom failure include improper or inconsistent use of appropriate lubricants, amphetamine use, heavy alcohol use, and lower socioeconomic status; proper use of condom-compatible lubricants improves condom effectiveness by lessening the risk of condom breakage and by reducing rectal or vaginal trauma.[40] Unfortunately, negotiating condom use can be problematic in some situations.[28,41,42]

Serosorting and Seropositioning

The practice of serosorting and seropositioning (strategic positioning) and condom serosorting are self-selected behaviors intended to reduce HIV transmission risk and are referred to as seroadaptive strategies.[43,44] 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. Strict serosorting for gay men usually refers to men having sex only with other men

who have the same HIV status as themselves. Position serosorting (also called strategic positioning or seropositioning) refers to choosing a different sexual position or practice based on the HIV serostatus of one's partner—the person with HIV typically taking the receptive role during unprotected anal sex when their partner does not have HIV. Data on the impact of serosorting have been mixed.[44,45,46,47] There are no guidelines in the United States that recommend serosorting as an impactful prevention measure.

Importance of Diagnosing and Treating Acute HIV Infection

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.[48,49,50] 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.[51,52,53,54] 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 6).[24] Accordingly, it is important to diagnose individuals with acute and recent (early) HIV whenever possible. To this end, the 2014 CDC HIV testing guidelines recommend 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.[55,56] In addition, all persons diagnosed with acute HIV should immediately start antiretroviral therapy to prevent forward transmission of HIV infection, as well as to garner potential long-term immunologic benefit from early therapy.[3,57,58,59]

Screening and Treatment of 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.[60] Trends of increasing sexually transmitted infections, particularly syphilis, gonorrhea, and chlamydia, have been reported among men with HIV who have sex with men.[61] Non-injection drug use, particularly with methamphetamines, 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.[62,63] Available data on herpes simplex virus (HSV) has not shown a convincing reduction in HIV transmission risk with acyclovir suppressive therapy taken by persons with HIV.[64] 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 (Table 2).[65] Despite these recommendations, several studies suggest there have been low rates of screening at rectal and pharyngeal sites in persons with HIV.[66,67] Any identified sexually transmitted infection should be promptly treated along with treatment of the partner.[68]

Circumcision

Male circumcision studies related to HIV prevention have involved men without HIV (as a means to prevent HIV acquisition) and men with HIV (as a means to prevent HIV transmission to others). Given the extremely high impact of HIV antiretroviral therapy and HIV preexposure prophylaxis in preventing HIV transmission and acquisition, the current utility and impact of male circumcision is not known.

- **Male Circumcision in Males without HIV**: Three studies conducted in Africa from 2002 through 2006 evaluated more than 10,000 African heterosexual couples and addressed the impact of male circumcision on HIV acquisition among men from their female sex partners; overall, there was a 51 to 60% reduction in HIV incidence among men who were circumcised compared to men who were uncircumcised (Figure 5).[69,70,71,72] Studies have also shown that lack of circumcision increases the risk of genital ulcer diseases, which in turn can increase the risk of HIV acquisition.[73,74] A meta-analysis that examined the impact of circumcision on HIV acquisition among men who have sex with men concluded insufficient evidence exists that male circumcision protects against HIV acquisition in this group.[75]
- **Male Circumcision in Males with HIV**: In contrast to the benefit of circumcision in heterosexual men without HIV, there is no evidence that performing circumcision on males with HIV will reduce HIV transmission to their heterosexual or same-sex partners. In a large study in Rakai District, Uganda, that enrolled 922 uncircumcised heterosexual men with HIV who had a CD4 count of at least 350 cells/mm^3, investigators randomized the men to receive immediate circumcision or delayed circumcision (24 months later), and circumcision did not reduce HIV transmission to female partners; the investigators stopped the trial early due to futility (Figure 7).[76] In the United States, there are no recommendations for using circumcision as an HIV prevention measure.

Prevention Strategies in Persons with Substance Use

Alcohol and illicit drug use are common among people with HIV and are recognized cofactors for HIV transmission.[77,78,79] In addition, substance use among persons with HIV is associated with higher rates of HIV transmission risk behaviors and lower rates of antiretroviral therapy adherence.[80] Alcohol use is the most prevalent risk factor for poor HIV medication adherence and lower rates of viral suppression.[81,82] Methamphetamine and other amphetamine-type stimulant use can be an important factor in HIV transmission.[83,84] Injection of methamphetamine plays a dual role in HIV transmission—through sharing injection equipment and by altering antiretroviral medication adherence and sexual behavior while high on methamphetamine. Screening for alcohol use disorder, methamphetamine use, and opioid use can play an important role in prevention, especially if persons identified with a substance use disorder can receive counseling, treatment, and prevention services, including use of syringe services programs for individuals who are injecting drugs. Prevention efforts, including implementation of syringe services programs, have led to a major decline in HIV transmission among persons who inject drugs.[85,86]

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 equipment, HIV prevention education, and opiate substitution therapy. In harm reduction programs, syringe services often provide a comprehensive set of services beyond basic needle exchange, including HIV counseling and testing, screening for sexually transmitted infections, screening for tuberculosis, vaccination services, 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.[87]

Syringe Services

In the United States, an estimated 10 to 15% of people living with HIV acquired HIV through injection drug use.[1] Thus, persons who inject drugs represent a significant source of potential HIV transmission in the United States. The use of sterile needles and clean injection equipment with each fix is an effective way for persons who inject drugs to limit their risk of acquiring and transmitting HIV and hepatitis C virus (HCV).[88] Opponents of syringe services argue that these programs condone and even encourage drug use, especially among youth; an early cohort study showed that a needle exchange program in Montreal was associated with a higher rate of HIV seroconversion, likely due to new social networks formed through the exchange, and this negative view has persisted.[89] In contrast, multiple studies and reviews have concluded that providing sterile equipment to persons who inject drugs reduces injecting risk behaviors, lowers the risk of HIV and/or HCV infection, and facilitates entry into drug treatment.[60,90,91,92]

Use of Federal Funds for Syringe Services Programs

The use of federal funds for needle exchange programs in the United States has been a highly controversial issue.[93] In 1988, opponents of needle exchange programs passed a law that explicitly banned federal funding for any needle exchange programs.[93] The funding ban was in existence until late 2015, except for a brief lift in the ban during 2010 and 2011. In December 2015, the Consolidation Appropriations Act was signed into law, and it modified then existing restrictions on the use of federal funds for programs that distribute sterile needles or syringes. Although the new law continues to prohibit federal funding to purchase sterile needles or syringes, it does allow use of federal funds for other elements of a syringe service program if it is deemed appropriate by a relevant State or local health department (in consultation with the Centers for Disease Control and Prevention). In 2016, the Department of Health and Human Services issued guidance for state, local, tribal, and territorial health departments in requesting and implementing federal funds to support syringe service programs.[94] In June 2022, the Legislative Analysis and Public Policy Association published a

document that provided detailed information regarding state-specific syringe services policies; this document is titled Syringe Services Programs: Summary of State Laws.[95]

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.
- Most persons aware of their HIV status have a substantial reduction in activities associated with increased risk of HIV transmission to others.
- For persons newly diagnosed with HIV, partner notification and contact HIV testing provides 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.
- Circumcision reduces the risk of acquiring HIV in heterosexual men, but there is no evidence that performing circumcision on males with HIV will reduce HIV transmission to their heterosexual partners who do not have HIV. The benefit of circumcision in preventing HIV acquisition or transmission in men who have sex with men is unclear.
- Screening for substance use can help providers identify individuals with HIV who could benefit from support to decrease or stop alcohol and illicit drug use. Providing counseling and treatment of substance use, including syringe services programs and opiate substitution therapy when indicated, can reduce injecting and sexual risk behaviors, and promote adherence to antiretroviral therapy.

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Figures

Figure 1 Estimated HIV Incidence in United States, 2017-2021

Note: Data for the year 2020 should be interpreted with caution due to the impact of the COVID-19 pandemic on access to HIV testing, care-related services, and case surveillance activities in state/local jurisdictions.

Source: Centers for Disease Control and Prevention. Estimated HIV Incidence and Prevalence in the United States, 2017–2021. HIV Surveillance Supplemental Report. 2023;28(3). Published May 2023.

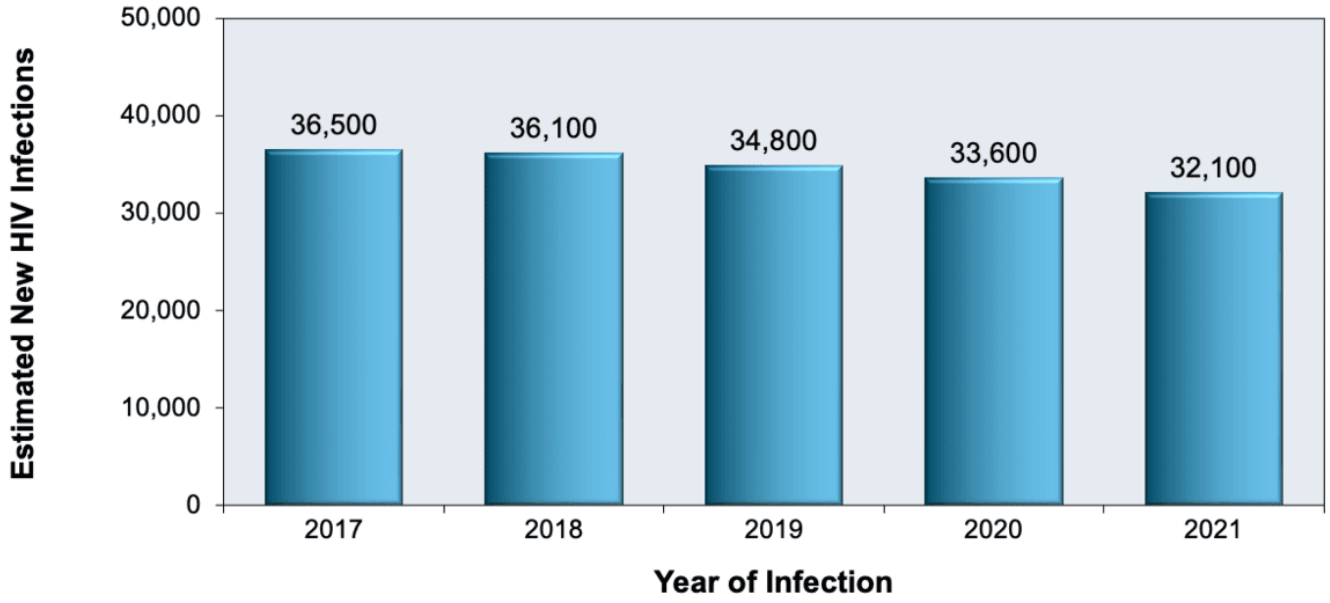

Figure 2 Adjusted Rate Ratio of Heterosexual Transmission of HIV-1 According to Serum HIV-1 RNA Level of the HIV-1 Positive Partner

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.

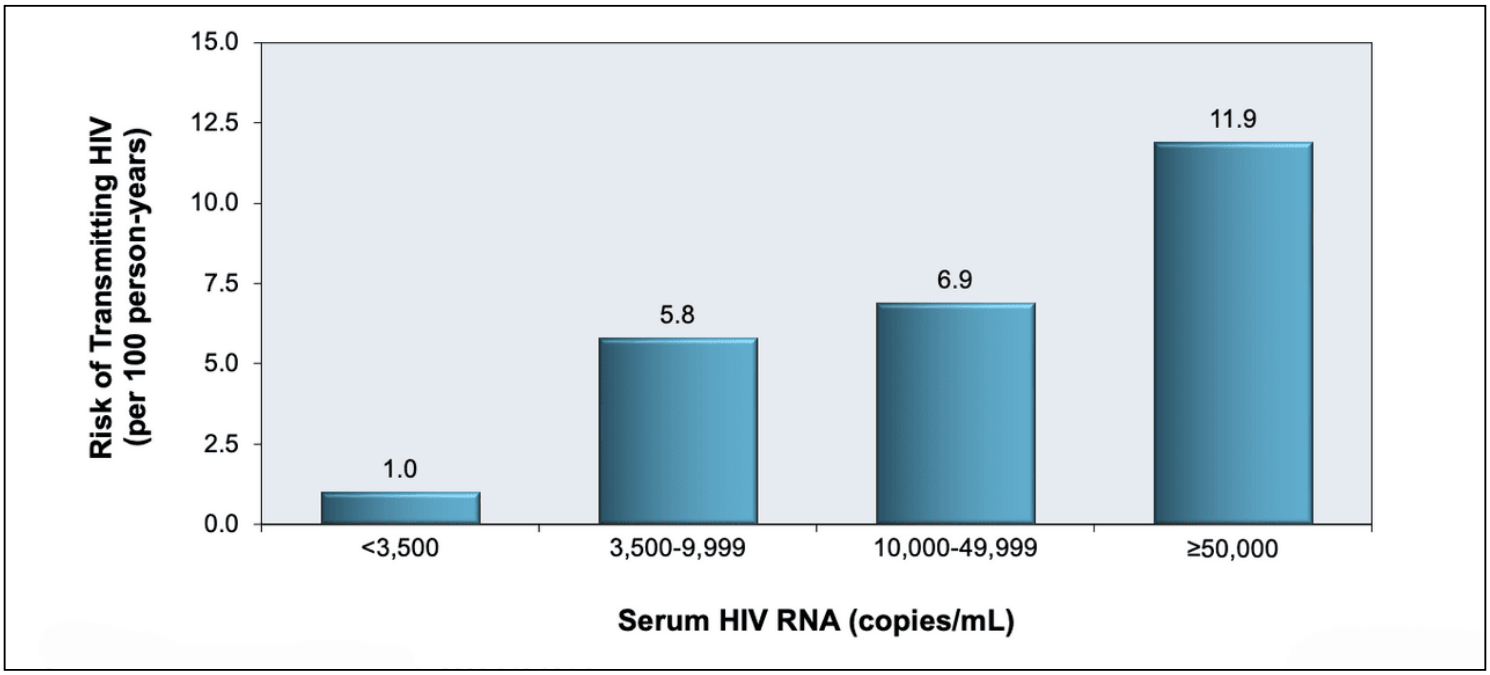

Figure 3 (Image Series) - HPTN 052 and Antiretroviral Therapy for the Prevention of HIV-1 (Image Series) - Figure 3 (Image Series) - HPTN 052 and Antiretroviral Therapy for the Prevention of HIV-1
Image 3A: HPTN 052 Patient Population

The HPTN 052 trial enrolled 1,763 HIV serodifferent couples and 97% of the couples were heterosexual.

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.

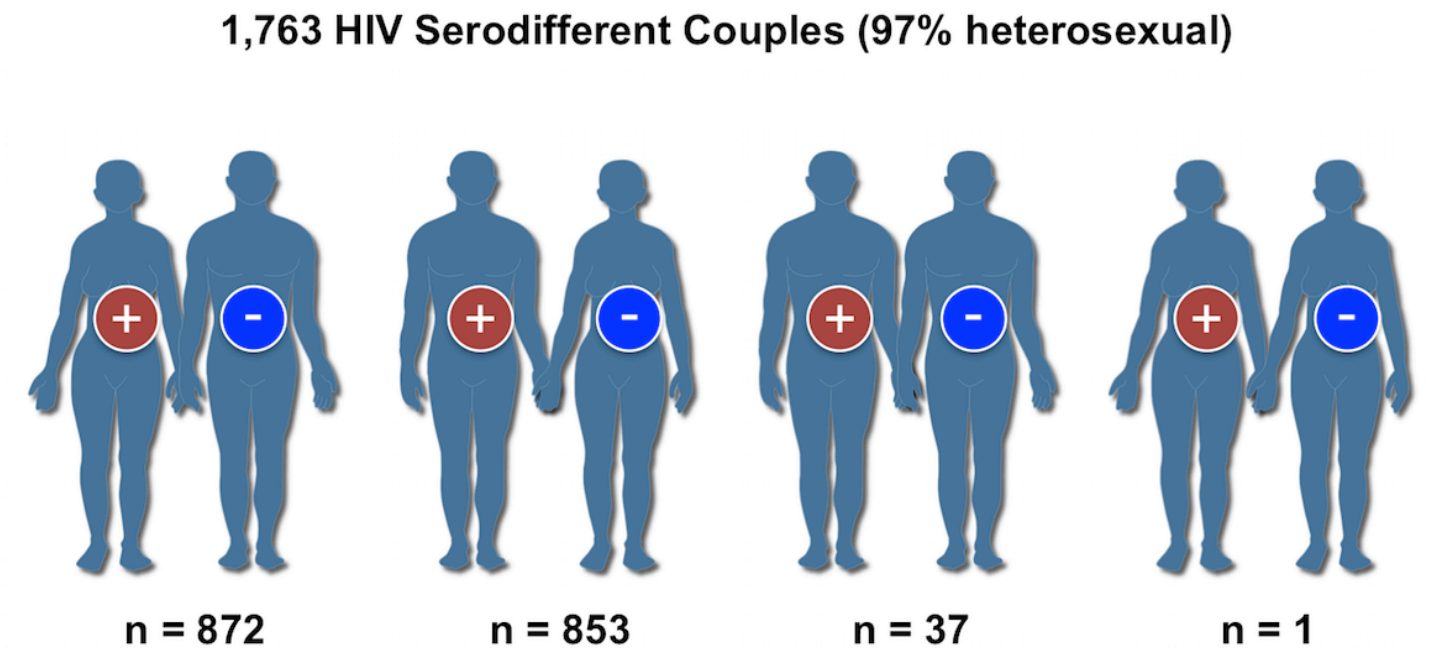

Figure 3 (Image Series) - HPTN 052 and Antiretroviral Therapy for the Prevention of HIV-1
Image 3B: HPTN 052 Study Design

The HIV-positive participants in the early therapy arm received combination antiretroviral therapy and those in the deferred therapy arm started 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.

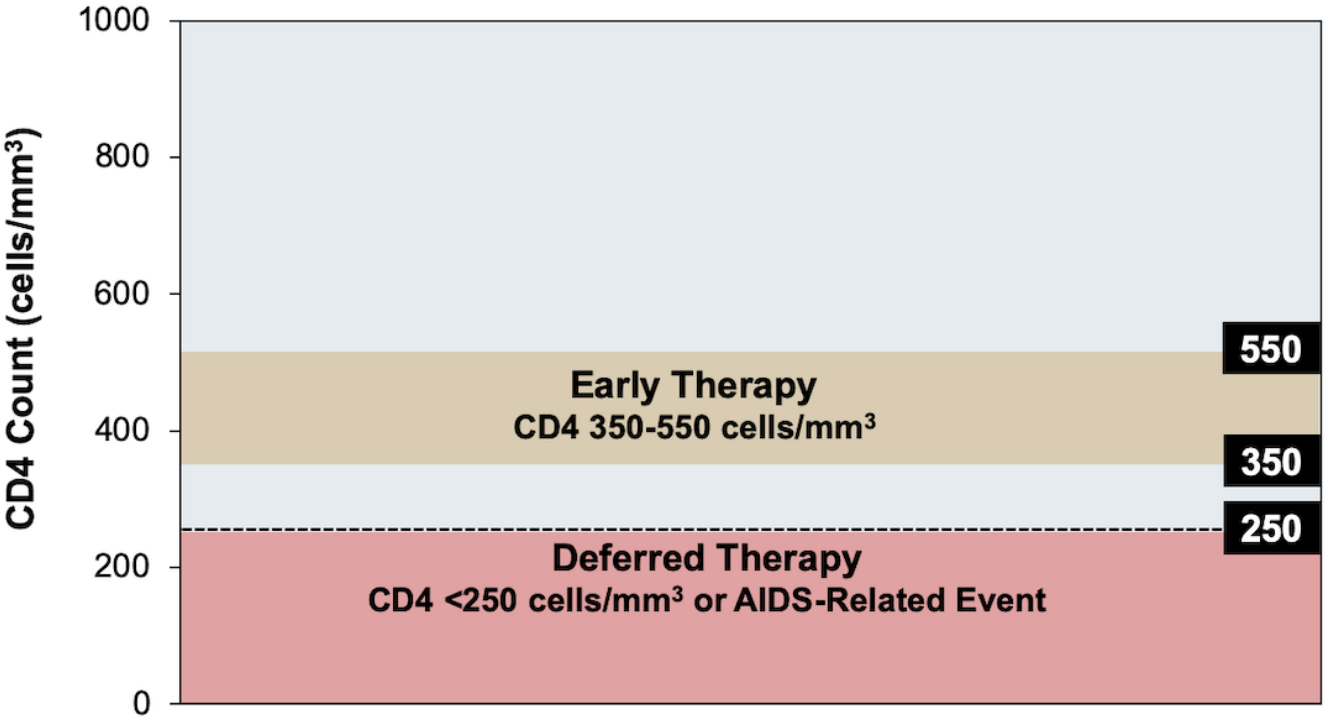

Figure 3 (Image Series) - HPTN 052 and Antiretroviral Therapy for the Prevention of HIV-1
Image 3C: HPTN 052 Results

This graphic shows linked transmissions in the two study groups. 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.

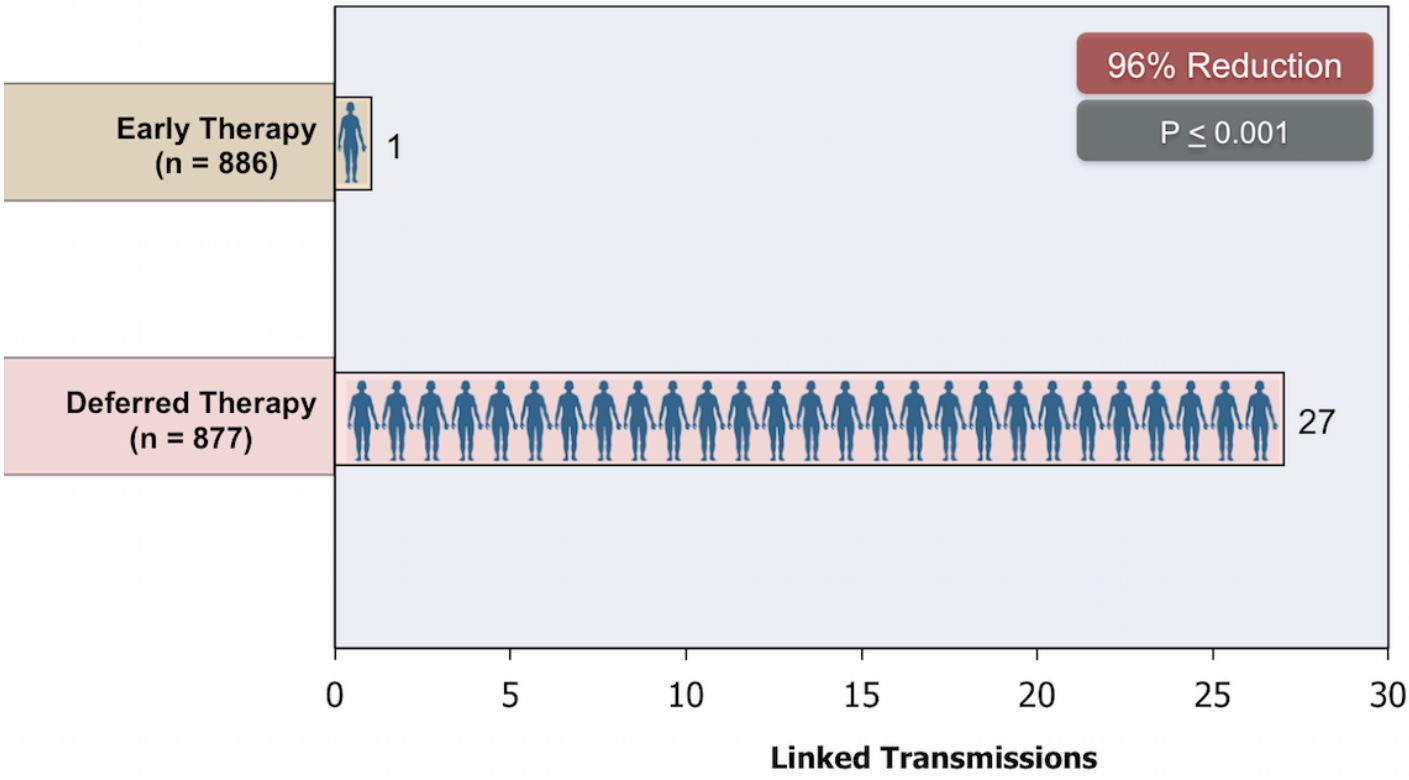

Figure 4 Transmission of HIV and Awareness of HIV Status

This graph shows the estimated percentage of HIV transmissions based on awareness of HIV diagnosis. These estimates were based on the 2016 Center 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.

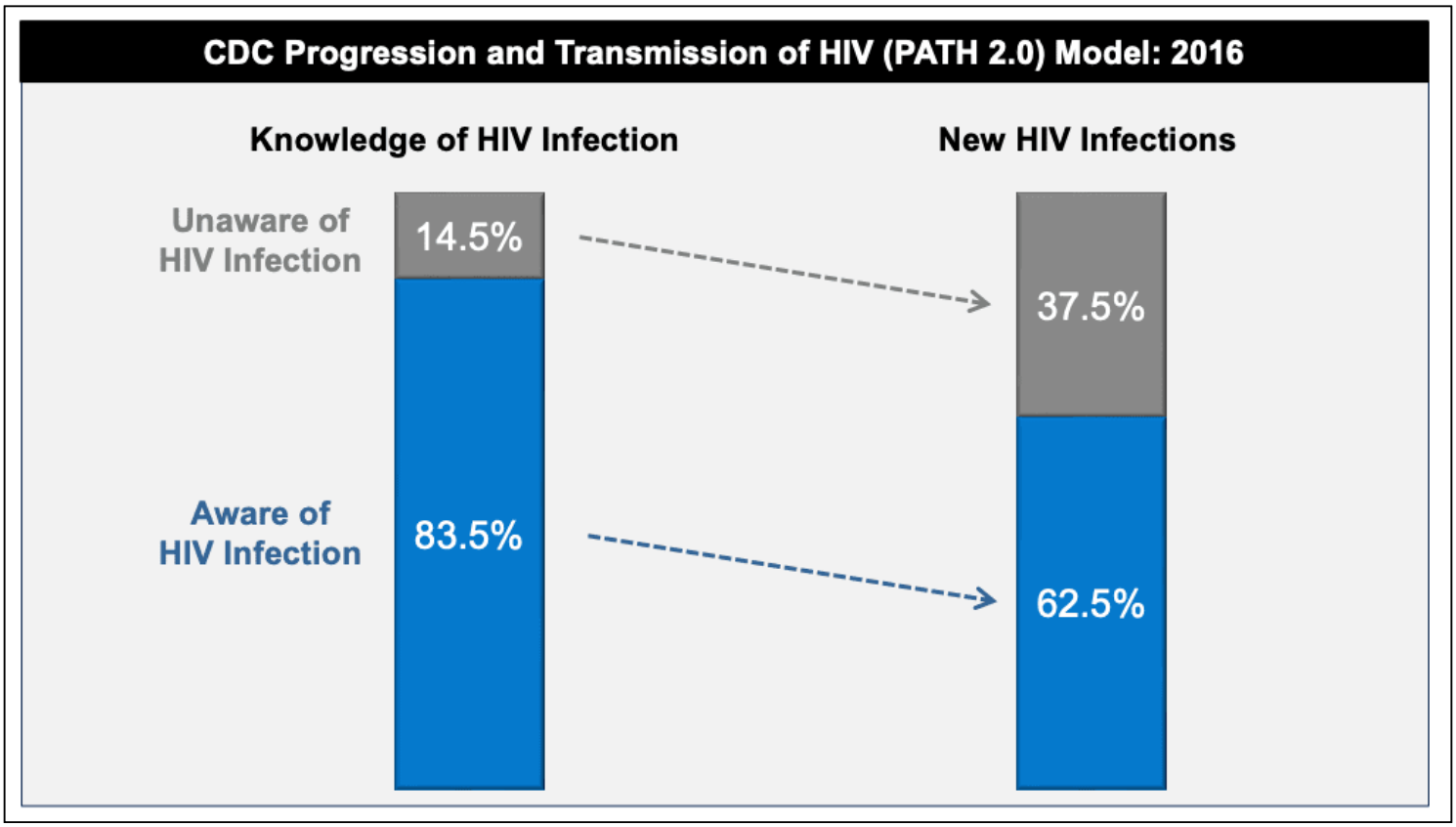

Figure 5 Risk of Heterosexual Male HIV Acquisition Based on Circumcision Status of Males Living in Africa

Abbreviation: RR = relative risk
These three studies conducted in Africa addressed the risk of heterosexual HIV acquisition in men based on their circumcision status. As shown, the risk of HIV acquisition was significantly lower in men who were circumcised when compared with those who were uncircumcised.

Source: (1) 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. / (2) Bailey RC, Moses S, Parker CB, et al. Male circumcision for HIV prevention in young men in Kisumu, Kenya: a randomised controlled trial. Lancet. 2007;369:643-56. / (3) Gray RH, Kigozi G, Serwadda D, et al. Male circumcision for HIV prevention in men in Rakai, Uganda: a randomised trial. Lancet. 2007;369:657-66.

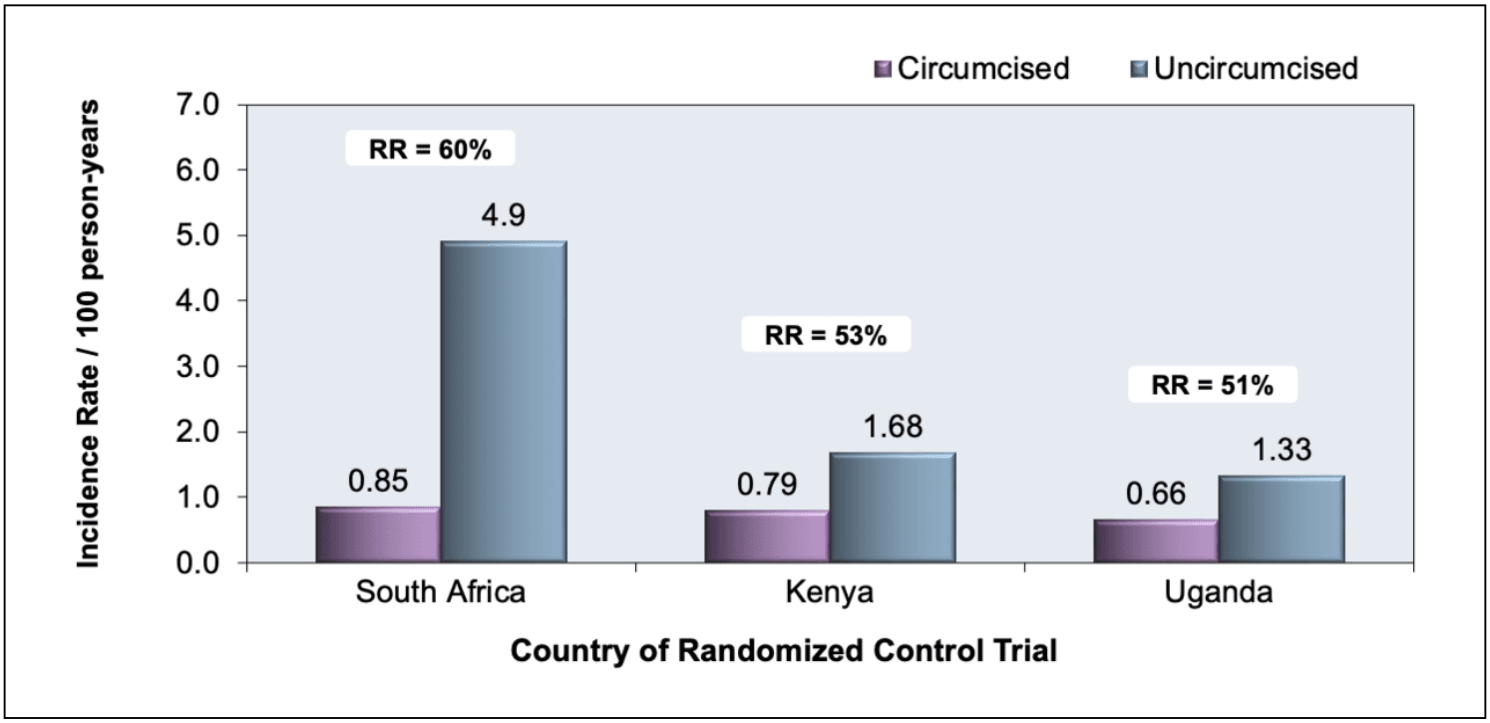

Figure 6 Relative Risk of HIV Transmission Along the HIV Care Continuum

This graph shows the estimated transmission rate based on transmissions per 100,000 person-years. These estimates were based on the 2016 Center 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.

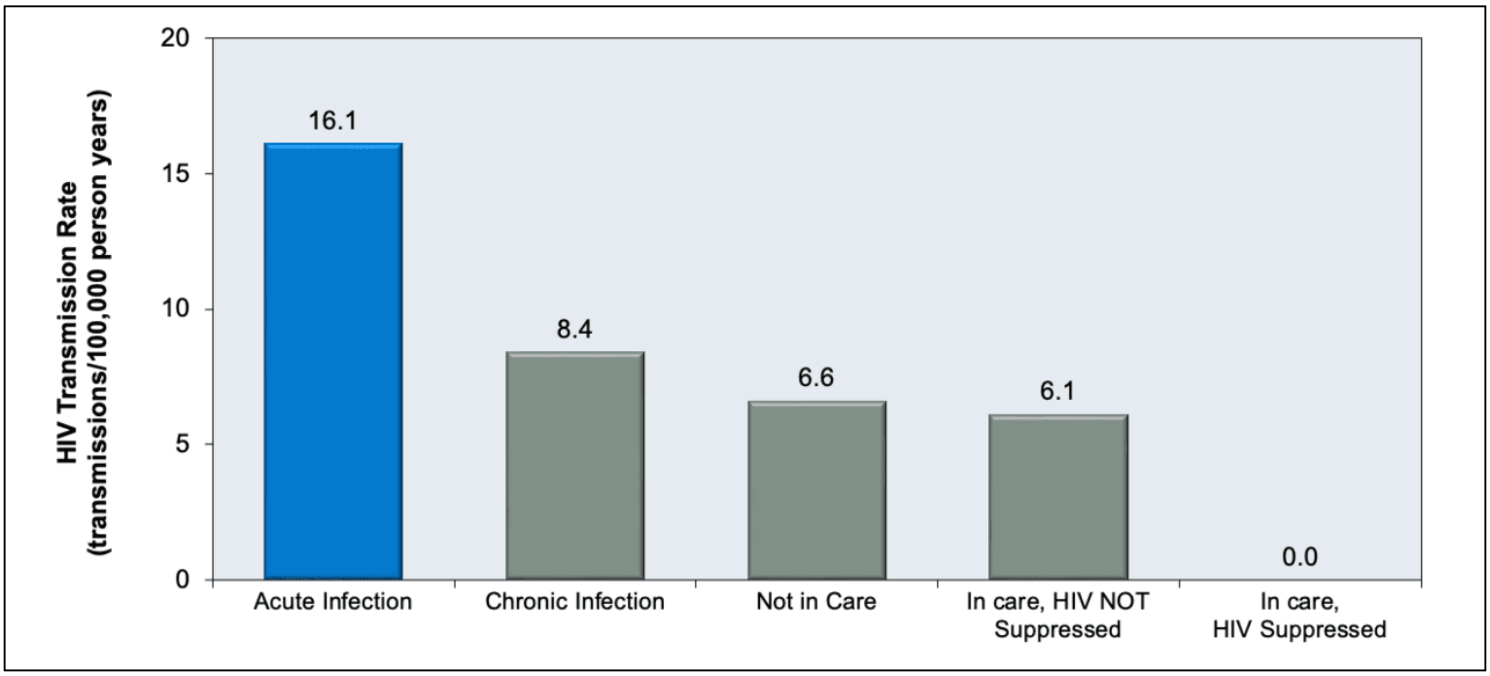

Figure 7 Risk of Heterosexual Female HIV Acquisition Based on Circumcision Status of Male Sex Partner

In this study, investigators in Rakai, Uganda enrolled 922 uncircumcised males with HIV infection who were randomized to undergo immediate circumcision (intervention group) or have circumcision delayed for 24 months (control group). The trial was stopped early because of futility and there was no reduction in risk of female HIV acquisition from their male partners who had been circumcised.

Source: Wawer MJ, Makumbi F, Kigozi G, et al. Circumcision in HIV-infected men and its effect on HIV transmission to female partners in Rakai, Uganda: a randomised controlled trial. Lancet. 2009;374:229-37.

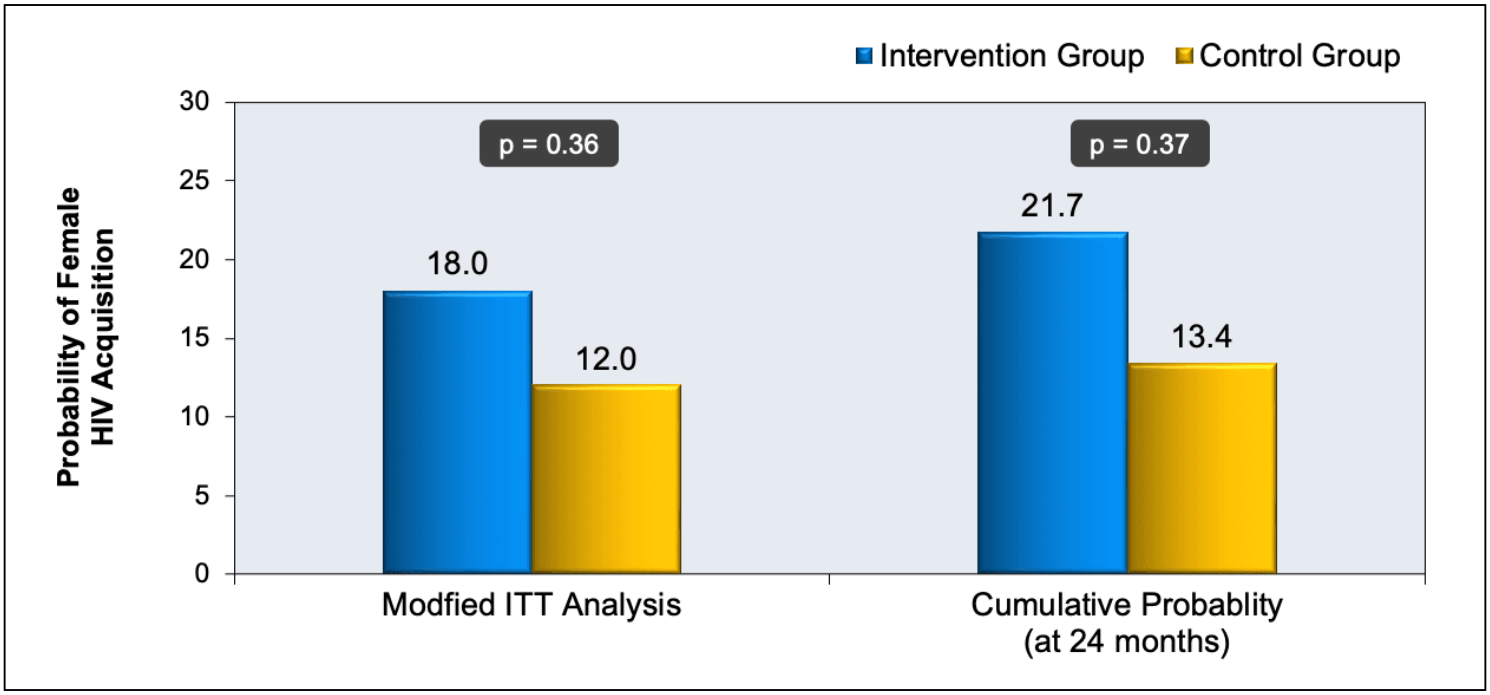

Table 1. **Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV**

Use of Antiretroviral Therapy to Prevent Sexual Transmission of HIV
• All persons 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 to their partners. Patients may recognize this concept as Undetectable = Untransmittable or U=U **(AII)**. • Persons with HIV who are starting ART should use another form of prevention with sexual partners (e.g. condoms, pre-exposure prophylaxis [PrEP] for the HIV-negative sexual partner, sexual abstinence) for at least the first 6 months of treatment 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, additional methods are needed to prevent transmission of HIV to sexual partners until resuppression to <200 copies/mL has been confirmed **(AIII)**. • Persons 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 patients regarding the importance of ART to 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 sexually active persons with HIV for STIs, both for their own health and to prevent transmission of STIs to others **(AIII)**.
Rating of Recommendations: A = Strong; B = Moderate; C = Optional Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

Source:

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Table 2.

STI Screening Recommendations in Persons with HIV

STI	Screening Indications and Frequency
Chlamydia	• For sexually active individuals, screen at first HIV evaluation, and at least annually thereafter • More frequent screening might be appropriate depending on individual risk behaviors and the local epidemiology
Gonorrhea	• For sexually active individuals, screen at first HIV evaluation, and at least annually thereafter • More frequent screening might be appropriate depending on individual risk behaviors and the local epidemiology
Syphilis	• For sexually active individuals, screen at first HIV evaluation, and at least annually thereafter • More frequent screening might be appropriate depending on individual risk behaviors and the local epidemiology
Herpes	• Type-specific herpes simplex virus (HSV) serologic screening for HSV-2 should be considered for persons presenting for an STI evaluation (especially for those persons with multiple sex partners)
Trichomoniasis	• Recommended for sexually active women at entry to care and at least annually thereafter
HPV, Cervical Cancer	• Sexually active women with HIV who are at least 21 years of age should undergo cervical cancer screening at initial entry to HIV care and again 12 months later. • Annual Pap testing is recommended in women with HIV younger than 30 years of age, but if 3 consecutive annual screens are normal, Pap tests can be performed every 3 years. • Women with HIV who are 30 years of age and older should have either (1) cervical cancer screening by Pap testing alone or (2) Pap testing plus simultaneous HPV co-testing. If Pap testing alone is used, it should be performed at baseline and every 12 months; if the results of 3 consecutive Pap tests are normal, then follow-up testing can occur every 3 years. If Pap and HPV co-testing is performed and both are negative, follow-up screening can be performed in 3 years. • Cervical cancer screening should continue throughout the life in women with HIV.
Anal Cancer	• Digital anorectal rectal exam • Screen men who have sex with men with HIV

STI	Screening Indications and Frequency
	who are 35 years of age and older and screen all others with HIV who are 45 years of age and older. Specific screening recommendations depend on availability of high resolution anoscopy (HRA).
Hepatitis B Screening	• At the initial evaluation, test for hepatitis B surface antigen (HBsAg), antibody to hepatitis B core (anti-HBc), and hepatitis B surface antibody (anti-HBs)
Hepatitis C Screening	• At the initial evaluation, perform serologic testing for antibody to HCV (anti-HCV), with reflex to HCV RNA for all positive anti-HCV tests • Annual HCV serologic testing in men who have sex with men • For persons with prior spontaneous or treatment clearance of HCV, screening should be conducted with HCV RNA
NOTE: This table is modified from recommendations in the Centers for Disease Control 2021 Sexually Transmitted Infections Treatment Guidelines and the Panel on Opportunistic Infections in Adults and Adolescents with HIV Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV.	

Source:

- Panel on Opportunistic Infections in Adults and Adolescents with HIV. Guidelines for the prevention and treatment of opportunistic infections in adults and adolescents with HIV: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Human papillomavirus disease. July 9, 2024. [HIV.gov]
- Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. Screening Recommendations and Considerations Referenced in Treatment Guidelines and Original Sources. MMWR Recomm Rep. 2021;70(No. RR-4):1-187. [2021 STI Treatment Guidelines]