Background Brief on the Prevention Benefits of HIV Treatment

Introduction
The advent in 1996 of potent combination antiretroviral therapy (ART), sometimes called HAART (highly active antiretroviral therapy) or cART (effective combination antiretroviral therapy), changed the course of the HIV epidemic [1]. These “cocktails” of three or more antiretroviral drugs used in combination gave patients and scientists new hope for fighting the epidemic [2] and have significantly improved life expectancy—to decades rather than months [1,3].

For many years, scientists believed that treating HIV-infected persons also significantly reduced their risk of transmitting the infection to sexual and drug-using partners who did not have the virus. The circumstantial evidence was substantial, but no one had conducted a randomized clinical trial—the gold standard for proving an intervention works. That changed in 2011 with the publication of findings from the HIV Prevention Trials Network (HPTN) 052 study, a randomized clinical trial designed in part to evaluate whether the early initiation of ART can prevent the sexual transmission of HIV among heterosexual couples in which one partner is HIV-infected and the other is not. This landmark study validated that early HIV treatment has a profound prevention benefit: results showed that the risk of transmitting HIV to an uninfected partner was reduced by 96% [4].

As a concept and a strategy, treating HIV-infected persons to improve their health and to reduce the risk of onward transmission—sometimes called treatment as prevention—refers to the personal and public health benefits of using ART to continuously suppress HIV viral load in the blood and genital fluids, which decreases the risk of transmitting the virus to others. The practice has been used since the mid-1990s to prevent mother-to-child, or perinatal, transmission of the virus. Research published in 1994 showed that zidovudine, more commonly known as AZT, when given to HIV-infected pregnant women and to their newborns reduced the risk of perinatal transmission from about 25% to 8% [5]. Since then, routinely testing pregnant women and treating infected mothers with ART during pregnancy, delivery, and while breastfeeding, when practiced according to recommendations, has reduced the mother’s risk of transmitting HIV to her child by 90% [6]. In one study, women who received at least 14 days of ART reduced the risk of transmitting HIV to their babies to less than 1% [7].

Putting Treatment as Prevention in Perspective
Treatment by itself is not going to solve the global HIV epidemic. On the domestic front, controlling and ultimately ending the epidemic will require a combination of scientifically proven HIV prevention tools as highlighted in the National HIV/AIDS Strategy (http://www.aids.gov/federal-resources/national-hiv-aids-strategy/overview/), including

- Focusing on science-based HIV prevention efforts by supporting and expanding targeted use of high-impact HIV prevention approaches.
- Making better investments by intensifying HIV prevention in the communities where HIV is most heavily concentrated.
- Increasing access to HIV screening and medical care, including through
  - boosting federal investments for AIDS Drug Assistance Programs (ADAPs) to expand access to life-saving medications, and
  - implementing the Affordable Care Act, which will increase health coverage for thousands of Americans living with HIV.
- Sustaining a shared response to the domestic epidemic through the support of HIV prevention efforts across all levels of society, including federal, state, and local governments, faith-based communities, and the private sector.

Providing treatment to people living with HIV infection to improve their health must always be the first priority. Getting an HIV test is the first step to identifying persons with HIV infection and the pivotal entry point into the medical care system for both treatment and prevention. More than 1.1 million persons in the United States are living with HIV, and almost 1 in 5 (18.1%) do not know they are infected [8]. By lowering the level of virus in the body, early ART helps people with HIV live longer, healthier lives and also lowers their chances of transmitting HIV to others. Although observational data had suggested that ART significantly reduces viral load and the risk of sexual transmission of HIV in heterosexual couples where one partner is infected and the other is not [9,10], it was the HPTN 052 study that definitively showed that early treatment of HIV-infected persons dramatically cuts the rate of new infections. Studies of communities with high concentrations of injection drug users (IDUs) and men who have sex with men (MSM) have shown that as ART use increased within the community, the community’s viral load declined, as did rates of new HIV diagnoses [11,12]. However, it is critical to remember that the prevention benefit of treatment is not 100%, and there has been at least one report of HIV transmission from a person with suppressed viral load to an uninfected sexual partner [13].

For persons living with or at risk for HIV infection, emphasizing these fundamental safeguards will continue to be crucial:
• Knowing their HIV status through routine testing.
• Getting into care soon after HIV diagnosis and starting antiretroviral treatment.
• Remaining in care and staying on HIV treatment.
• Modifying behaviors that reduce the probability of getting or spreading HIV—such as using condoms properly and consistently, reducing numbers of partners, and avoiding sharing needles and syringes.

Test and Treat
The ability of antiretroviral drugs to prevent secondary transmission of HIV from an infected person to an uninfected sexual or drug-using partner has led to several proposed “test-and-treat” strategies. Test-and-treat programs are based on the premise that the rate of new HIV infections will be maximally reduced by using aggressive methods to test and diagnose all people living with HIV infection, treat them with ART regardless of CD4 cell count or viral load at diagnosis, and link them to care. In one study, mathematical modeling suggested that a universal test-and-treat strategy in which all adults aged 15 years or older are tested annually could control the South African epidemic, reducing both HIV incidence and mortality to less than 1 case per 1,000 people per year within 10 years of full implementation of the strategy—and reducing prevalence of HIV infection to less than 1% within 50 years [14]. Other investigators have not been as optimistic about the ultimate benefits of this strategy. Only 50% of persons in the United States with HIV remain in care [15,16], and about 18% do not know they are infected; these persons may contribute to the onward transmission of HIV. In addition to expanding testing and treating HIV infection earlier, overcoming the challenges of undiagnosed infection and poor engagement in care will result in better care of HIV-infected populations and reduced numbers of new HIV infections [17,18].

Challenges and the Future of HIV Prevention
The landmark HPTN 052 clinical trial was conducted almost solely among heterosexual couples who, as part of the study, received frequent counseling related to HIV, sexually transmitted diseases (STDs), and family planning. Results of a recent observational study of more than 38,000 serodiscordant heterosexual couples across China showed that treating the HIV-infected partner reduced the risk of transmitting HIV to the uninfected partner by 26%—a much more modest effect than that found in the HPTN 052 study couples. Unlike the couples enrolled in HPTN 052, the couples in China were not part of an intensive study, and data were not available on sexual risk factors, adherence to antiretroviral treatment, or virological treatment outcome measures [19]. Additional data are needed to estimate the prevention benefit of treatment for other populations, such as MSM, IDUs, and persons with acute or primary HIV infection [20], and in other settings such as North America and during routine clinical care.

As HIV treatment has evolved from a complicated regimen of numerous pills taken several times a day with severe side effects to a now once-daily pill with few side effects, some persons living with HIV may have become complacent about maintaining safer sex and safer injection use practices. Since HIV treatment became widely available in developed countries, several studies have shown a resurgence of HIV infections and increases in STDs, in particular syphilis, and especially among MSM [21]. Some studies have cautioned that the prevention benefits of effective ART would be offset by risk compensation, meaning that increases in risky sexual and injection-drug-use behavior might be observed as effective ART is widely disseminated [22-24]. However, results of one meta-analysis demonstrated that HIV-positive persons receiving ART, compared with those not receiving ART, did not show increased sexual risk behavior, even when therapy resulted in an undetectable viral load [25]. Yet, persons with HIV who believe that using ART or having a suppressed viral load protects them against transmitting HIV may be more likely to engage in unprotected sex or other risky behaviors. These behaviors might be amenable to change through prevention messages and other effective approaches [25-28]. Making sure that preventive behaviors are sustained in communities facing higher risk of HIV infection is crucial [29].

The future of HIV prevention will be shaped by operational and implementation research on the efficacy of combination prevention strategies, of which treatment may be one component [30-32]. Providing treatment to all HIV-infected persons will be an important step—a recommendation that is included in the current Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents [33]. The Department of Health and Human Services panel based its recommendations primarily on mounting evidence showing the harmful impact of ongoing HIV replication on AIDS and non-AIDS disease progression. In addition, the updated recommendations reflect emerging data showing the benefit of effective ART in preventing secondary transmission of HIV. Although the panel agrees that this public health benefit of ART is significant, its recommendations on when to begin ART are based primarily on the benefit of treatment to the HIV-infected individual [33]. If treatment is to achieve its full prevention potential, current gaps in the HIV prevention, treatment, and care continuum must be narrowed or closed. Considerable changes in the US health care delivery system will be required to accommodate the increased demand for services that expanded testing, treatment, and linkage and retention in care will bring [34].

Now that early ART of HIV-infected persons has been shown to be very effective at preventing secondary transmission of HIV among individuals, the current goal is to determine the extent to which ART can be used broadly and effectively to reduce the spread of HIV within a population. At least two community randomized trials that use ART as their basis are planned [35], and the results could determine the conclusive benefit of this successful intervention [36].

Still, resource constraints, logistical hurdles, emergence of drug-resistant viral strains, adherence to therapy regimens,
and risk compensation remain concerns that scientists, health care providers, policy makers, and communities must confront if the individual and public health benefits of treatment are to be fully realized [37].

**What CDC Is Doing**

Much of CDC’s funding supports and expands prevention services for persons living with HIV, including

- Linkage to care and treatment, and interventions to improve retention in and re-engagement to care, prevention, and treatment for people living with HIV.
- Referral to other medical and social services, such as substance abuse and mental health services.
- Behavioral interventions and other risk-reduction services for HIV-positive persons and their sexual or needle-sharing partners to reduce the likelihood of HIV transmission.

Three evidence-based interventions have proved effective in treatment settings and can be delivered by providers as brief messages during clinic visits: **Partnership for Health** (http://www.effectiveinterventions.org/en/HighImpactPrevention/Interventions/PfH.aspx), **Options** (http://www.cdc.gov/hiv/topics/research/prs/resources/factsheets/options.htm), and **Positive Choice** (http://www.cdc.gov/hiv/topics/research/prs/resources/factsheets/positive-choice.htm).

CDC’s **Prevention IS Care** (http://www.cdc.gov/actagainstaids/) campaign also emphasizes ongoing, brief prevention counseling to help health care providers integrate into routine care simple approaches to prevent transmission by persons living with HIV. Medical visits provide a vital opportunity to reinforce HIV prevention messages, discuss sexual and drug-related risk behaviors, diagnose and treat other STDs, review the importance of medication adherence, and foster open communication between provider and patient.

Expanded HIV testing efforts will help more people know their status so that they can get life-saving treatment and will strengthen the impact of efforts to increase adherence to treatment, particularly in areas where large numbers of persons remain undiagnosed.

Additionally, CDC and the Health Resources and Services Administration have supported studies that suggest several promising opportunities to improve retention in care, including collaborating with other service providers to identify persons poorly retained in care, enhancing outreach programs, and addressing unmet psychosocial needs [38,39].

**Summary**

To realize the full prevention benefit of treating HIV infection, we should keep in mind four overarching tenets:

- HIV testing is the foundation for both prevention and care efforts.
- Early identification of infection empowers individuals to take action that benefits both their own health and the public health.
- Early treatment of infected persons substantially reduces their risk of transmitting HIV to others.
- The prevention benefit of treatment can only be realized with effective treatment, which requires linkage to and retention in care, and adherence to antiretroviral therapy.

**References**


