

what is the effect of HIV treatment on HIV prevention?

why HIV treatment and prevention?

Traditionally, HIV prevention efforts have focused on uninfected persons at risk, encouraging them to adopt and maintain safer sex and drug-using behavior that would keep them uninfected. Less attention was paid to prevention among persons who were already infected, where the priority was maintaining their health in the face of a devastating disease. Providers and programs for prevention and care were distinct and separate. While such a division was always short-sighted (naturally the behavior of both HIV+ and HIV- persons influence transmission), in today's era of more effective treatment for HIV, it is even more important that prevention and care be permanently linked.

More effective treatment, also known as highly active anti-retroviral therapy or HAART, can have differing effects on HIV prevention. On the one hand, HAART has dramatically improved the length of survival and the physical well-being of persons living with HIV/AIDS, and with it has increased the opportunities for transmission of the virus to others. On the other hand, treatment may decrease the opportunity for HIV transmission by lowering the amount of HIV virus shed through blood and genital secretions.

The availability and use of HAART also may have produced changes in attitudes that can help or hinder HIV prevention. Prevention efforts must therefore carefully weigh and address the potential positive and negative effects of HAART on HIV transmission.

can treatment benefit prevention?

There is a variety of evidence supporting HAART's beneficial effect on HIV prevention, both in the acquisition of infection among HIV- persons and in the transmission of infection from HIV+ persons to others.

First, the provision of anti-retroviral treatment to HIV+ women and their infants around the time of delivery has been shown to reduce mother-to-child transmission.¹ Treatment is thought to work by reducing the mother's infectiousness and/or by blocking the establishment of infection in the infant.

Second, follow-up of healthcare workers exposed to HIV through needlestick injuries or other accidental contact with body fluids found that persons taking anti-retroviral post-exposure prophylaxis (PEP) were less likely to become infected compared to those who did not.² The concept has been extended to the provision of PEP to prevent HIV infection resulting from episodes of unprotected sex or needle-sharing.³

A third argument is indirect. HAART can dramatically reduce the levels of virus in the blood, often to the point of becoming undetectable by current tests. Although not a one-to-one relation, lower blood levels of virus tend to correlate with lower genital fluid levels of virus.^{4,5} At least one study in Africa observed that low blood viral load translated to low likelihood of sexual transmission; no HIV transmissions were observed among discordant couples when the partner's blood viral load was under 1500 copies per ml.⁶ If treatment can reduce blood levels of virus to below this level, the reasoning goes, then it can prevent HIV transmission. This conclusion, while appealing, has not been proven.

Even in patients on HAART, virus remains in many tissues of the body, inside cells and in the blood despite being undetectable with tests.⁷ While it is probably true that a low viral load makes someone less infectious, viral loads fluctuate over time due to changes in adherence, the development of drug resistance or the natural history of infection. While the evidence suggests treatment can reduce infectiousness, it does not eliminate it at all points in time. Until the conditions when someone is not infectious are well-defined, it is safest to assume that an HIV+ person remains potentially infectious for life.

On a different level, HAART can help prevention by providing hope to persons affected by AIDS. There is greater incentive to seek HIV testing (and therefore risk reduction counseling) when effective HIV treatment is available and greater disincentive when it is not, especially where high stigma of HIV exists. Moreover, communities devastated by friends and families getting sick and dying may view HIV infection as inevitable and self care and prevention take low priority. A study in Baltimore, MD, found that informal caregivers were more likely to promote prevention messages in the community when their friends and family had access to HIV treatment, giving them hope for the future.⁸

Says who?

1. Mofenson LM. Technical Report: Perinatal Human Immunodeficiency Virus Testing and Prevention of Transmission. *Pediatrics*. 2000;106:E88.
2. Cardo DM, Culver DH, Ciesielski CA, et al. A case-control study of HIV seroconversion in health care workers after percutaneous exposure. *New England Journal of Medicine*. 1997;337: 1485-1490.
3. Kahn JO, Martin JN, Roland ME et al. Feasibility of postexposure prophylaxis (PEP) against human immunodeficiency virus infection after sexual or injecting drug use exposure: the San Francisco PEP study. *Journal of Infectious Diseases*. 2001;183: 707-714.
4. Barroso PF, Schechter M, Gupta P, et al. Adherence to anti-retroviral therapy and persistence of HIV RNA in semen. *Journal of Acquired Immune Deficiency Syndromes*. 2003;32:435-440.
5. Goulston C, McFarland W, Katzenstein D. Human immunodeficiency virus type 1 RNA shedding in the female genital tract. *Journal of Infectious Diseases*. 1998;177:1100-1103.
6. Quinn TC, Wawer MJ, Sewankambo N, et al. Viral load and risk of heterosexual transmission of HIV-1 among sexual partners. Presented at the Conference on Retroviruses and Opportunistic Infections. Jan 30-Feb 2, 2000. Abst# 193.
7. Zhu T, Wang N, Carr A, et al. Genetic characterization of human immunodeficiency virus type 1 in blood and genital secretions: evidence for viral compartmentalization and selection during sexual transmission. *Journal of Virology*. 1996;70:3098-3107.

can treatment harm prevention?

HIV+ persons and HIV- persons have been having sex and/or injecting drugs since the beginning of the epidemic, before the advent of HAART. In the past few years, however, there have been increases in sexually transmitted diseases (STDs) and sexual risk behavior in the US and across the developed world.⁹⁻¹² These increases might be a sign of upcoming increases in HIV infection. It is difficult to determine if this is due to improved treatment or not.

Outbreaks of syphilis among men who have sex with men (MSM) have occurred in several cities across the US. Around half of the men in these outbreaks were HIV+, with many receiving treatment.⁹ In San Francisco, CA, acquiring an STD after AIDS diagnosis was associated with the use of HAART.¹⁰ STDs can promote HIV transmission by increasing HIV infectiousness in HIV+ persons and increasing susceptibility to HIV in HIV- persons.¹³

Internationally, increases in sexual risk behavior and STDs have been documented among both HIV- and HIV+ MSM in the last few years. In London, Manchester and Brighton, England, Amsterdam, the Netherlands and Sydney, Australia, high-risk sexual behavior increased since 1996, especially among MSM.¹²

These increases in sexual risk behavior in recent years have led to heated discussion on the role of "treatment optimism" in HIV transmission. Treatment optimism means that people are more likely to engage in sexual risk behavior because they believe treatment will make them or their partners less infectious or they believe that HIV is less serious a disease than before. In fact, a recent review of studies on treatment optimism in three continents found few gay men were optimistic overall and the association between optimism and sexual risk behavior was inconsistent.¹⁴ That is, treatment optimism may be causing an increase in sexual risk behavior among some communities or segments of communities of gay men, but not among others.

The trade-offs between the potential benefits of HAART in reducing the likelihood of HIV transmission and potential harm resulting from increased risk behavior have been included in many complex mathematical models of the epidemic. The models suggest that HIV transmission can increase in a community where greater than 50% of infected persons are on HAART if risk behavior increases on the order of 10% or more.¹⁵

what needs to be done?

HIV care programs provide opportunities for treatment and prevention to work together. Health care providers can take a greater role in HIV prevention, making prevention activities an expected part of medical care. Key prevention components can include regular risk reduction counseling and STD screening. Training and support are needed for HIV care providers unfamiliar with these roles.

Programs outside medical care settings are needed to help HIV+ and HIV- persons avoid transmission.¹⁶ These prevention programs should incorporate a variety of strategies, including counseling and training on when and how to disclose HIV status, how to maintain consistent condom use in the absence of disclosure, how to address HIV-related stigma, and how to keep intimacy in serodiscordant and seroconcordant relationships. This should be available for HIV+ and HIV- persons in the context of managing a healthy sex life. Communities impacted by HIV need better understanding of and access to research on when and how persons are infectious and how to best use HIV treatment to reduce the risk of transmission, so that they can make appropriate informed decisions.

Persons who know they are HIV-, know they are HIV+, or do not know their serostatus all need community-level prevention messages that address sexual and drug-related behavior. New HIV tests that are easier to use and give faster results should facilitate increased testing for those who do not know their status. HIV testing should be made more widely available through as many outlets as possible, including anonymous and confidential test sites and home collection kits.

The fight against the HIV/AIDS epidemic should not be divided into treatment for HIV+'s and prevention for HIV-'s. Treatment will not eliminate the epidemic in the absence of prevention programs for HIV- and HIV+ persons; prevention will not work unless relevant to those infected and uninfected.

PREPARED BY WILLI MCFARLAND* AND PAMELA DECARLO**
*SAN FRANCISCO DEPARTMENT OF PUBLIC HEALTH, **CAPS

8. Knowlton AR. Social network approaches to HIV prevention and care: theoretical and methodological considerations of intervention. Presented at the International AIDS Conference, Barcelona, Spain. 2002. ThOR1501.

9. Valdiserri RO. Preventing new HIV infections in the US: what can we hope to achieve? Presented at the 10th Conference on Retroviruses and Opportunistic Infections, Boston, MA. February 10-14, 2003.

10. Scheer S, Chu PL, Klausner JD, Katz MH, Schwarcz SK. Effect of highly active antiretroviral therapy on diagnoses of sexually transmitted diseases in people with AIDS. *Lancet* 2001 Feb 10;357(9254):432-5.

11. Katz MH, Schwarcz SK, Kellogg TA, et al. Impact of highly active antiretroviral treatment on HIV seroincidence among men who have sex with men in San Francisco. *American Journal of Public Health*. 2002;92:388-394.

12. Stolte IG, Coutinho RA. Risk behaviour and sexually transmitted diseases are on the rise in gay men, but what is happening with HIV? *Current Opinions in Infectious Diseases*. 2002;15:37-41.

13. Fleming DT, Wasserheit JN. From epidemiological synergy to public health policy and practice: the contribution of other sexually transmitted diseases to sexual transmission of HIV infection. *Sexually Transmitted Infections*. 1999;75:3-17.

14. Elford J, Bolding G, Sherr L. HIV optimism: fact or fiction? *FOCUS*. 2001;8:1-3.

15. Blower S, Schwartz EJ, Mills J. Forecasting the future of HIV epidemics: the impact of antiretroviral therapies and imperfect vaccines. *AIDS Reviews*. 2003;5:113-125.

16. Collins C, Morin SF, Shriver MD, et al. Designing Primary Prevention for People Living with HIV. Monograph published by the AIDS Policy Research Center & Center for AIDS Prevention Studies. March, 2000. www.caps.ucsf.edu/publications/pozmono.pdf