Treatment as Prevention

Introduction

The development of effective, well-tolerated antiretroviral therapies has not only revolutionized the medical treatment of people living with HIV, it has also begun to transform the world of HIV prevention. Research has demonstrated that antiretroviral therapies can often prevent HIV transmission, although questions about cost and long-term effectiveness across populations remain. This issue of Perspectives examines some of this evidence, as well as some of the controversies that are associated with treatment as prevention strategies. It also highlights the goals of treatment as prevention, and explores how HIV test counselors can facilitate these goals.

Most often the term “treatment as prevention” refers specifically to the fact that when an HIV-positive person is on an effective antiretroviral regimen, they are less likely to transmit the virus to other, HIV-negative people, and that subject is the focus of this issue. Strategies such as PEP (post-exposure prophylaxis) and more recently, PrEP (pre-exposure prophylaxis), involve HIV-negative people using antiretroviral medications to help them stay negative. These strategies have been discussed in earlier issues of Perspectives.

History

Effective antiretroviral treatment reduces the amount of virus in the body, sometimes to a level that is too low to be detected on a viral load test (which is a measurement of the amount of HIV genetic material [RNA] in plasma). Scientists had long suspected that people with lower viral loads would be less likely to pass HIV on to others. In fact, “treatment as prevention” has been used for almost 20 years to help prevent HIV-positive mothers from passing the virus to their children. Without the benefit of antiretroviral treatment, the odds of a mother passing HIV on to her child are 1 in 4. With treatment, those odds drop dramatically to less than 1 in 50.

In 2000, a Rakai, Uganda, study of 415 mixed-HIV status couples (one partner was HIV-positive, and one partner was HIV-negative) offered evidence that viral load suppression meant less sexual transmission of HIV as well. During the 30 months the couples were followed, 90 of the initially HIV-negative partners did contract HIV (seroconverted)—but there were no seroconversions among the 51 couples where the HIV-positive partner’s viral load was less than 1,500 copies per milliliter in their blood. Even among cou-
In 2008, the Swiss Federal AIDS Commission released a statement declaring that HIV-positive people “cannot pass on the virus through sexual contact” if they meet three conditions: they get their viral load checked regularly; their viral load has been undetectable (there are fewer than 40 copies of the virus per milliliter of blood) for at least six months; and no other STDs are present. Although the “Swiss Statement” had great impact on sexual decision making by mixed-status partners around the world, its authors later said that it was originally meant as guidance for Swiss physicians working with stable couples.

In 2011, researchers published results of the HIV Prevention Trials (HPTN) 052 study, which under-scored the importance of early HIV treatment and viral suppression in preventing HIV transmission. This study was groundbreaking because it was a randomized controlled trial, the strongest kind of experimental research design. Across nine countries in Africa, Asia, and the Americas, researchers enrolled 1,763 serodiscordant couples, 97 percent of whom were heterosexual. In each couple, the HIV-positive member had a CD4 cell count between 350 and 550. Half the participants were randomly assigned to receive “early” therapy (immediate antiretroviral treatment), and half were assigned to receive “delayed” therapy (after a drop in CD4 count or the start of HIV-related symptoms, which was the standard of care). Condom use was encouraged for all couples. In the first three years, there were 29 HIV transmissions between the couples enrolled in the study—and all but one of these occurred in the “delayed” therapy group, providing powerful support for the practice of preventing transmission through early treatment intervention.

In 2012, the Department of Health and Human Services revised its guidelines for the use of antiretrovirals, stating: “Antiretroviral therapy (ART) is recommended for all HIV-infected individuals” both “to reduce the risk of disease progression,” and “for the prevention of transmission of HIV.”

Lowering “Community Viral Load” to Prevent HIV

At the same time HPTN 052 researchers studied the biological effects of treatment on rates of transmission between individuals in mixed status couples, Danish researchers studied the effects of treatment on “community viral load.” Community viral load is the number you get when you add up the viral loads of all the members of a community and then divide the total by the number of HIV-positive people in that group. Crunching 1994 to 2009 data from the Danish national health survey, the researchers found something strange: although more men who have sex with men were having unprotected anal sex, the incidence of new HIV infections among them remained stable. At the 2010 International AIDS Conference in Vienna, presenter Susan Cowan suggested that HIV transmission rates had declined because of high rates of antiretroviral therapy use in the population, which had led to a reduction in “community viral load.”

Over the past few years, researchers and public health officials have paid increasing attention to community viral load as a measure of the “HIV burden” on a population and a predictor of transmission rates. Researchers Gregorio Millett and Ronald Stall have suggested, for example, that the high prevalence of untreated HIV infection may help explain why infection rates among Black men who have sex with men continue to be disproportionately high, despite no greater behavioral risks.

Researchers in Vancouver studied a large community of injection drug users for 11 years, and

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found that there was a significant correlation between the median community viral load and the incidence of new HIV cases. In British Columbia, researchers found a strong association between greater ART coverage of the population between 1996 and 2009 and decreased viral load, as well as decreased HIV incidence. In 2010, San Francisco Department of Public Health Director of HIV Research Moupali Das and her colleagues at the DPH found that reductions in community viral load in San Francisco were associated with a decrease in HIV infections between 2004 and 2008. And in 2013, researchers in rural KwaZulu-Natal, South Africa, found that a person’s chances of becoming infected were significantly (38 percent) lower in a community where 30 to 40 percent of the population was being treated than in a community where less than 10 percent of HIV-positive people were being treated.

Test and Treat

As the benefits of antiretroviral therapy continue to be identified, promotion of “test and treat” has increased. This strategy involves initiating antiretroviral therapy earlier in the course of infection, thereby suppressing the virus more effectively. Viral suppression has strong potential health benefits at the interpersonal and community levels, which are described above. At the individual level, suppressing the virus earlier seems to reduce the inflammatory processes and immune deactivation that people living with HIV often experience, and helps to prevent disease, since HIV replication in the body can be associated with cognitive impairment and heart, kidney, and liver disease. In the HPTN 052 study cited above, participants in the early therapy group had fewer HIV-related medical problems than those on delayed treatment, “indicating both personal and public health benefits from such therapy.”

The HPTN 065 study, which has been conducted in the Bronx, N.Y., and Washington, D.C., since 2010, is exploring how best to implement this strategy in the United States. Also called “TLC-Plus” (for Test, Link to Care, Plus treat), involves expanded hospital testing efforts, media targeting of men who have sex with men to encourage testing, and financial incentives to stay linked to care.

Currently, in San Francisco Department of Public Health community health clinics, every person who is diagnosed with HIV is promptly medically evaluated, and provider and client together decide whether to initiate antiretroviral treatment. This “test and treat” strategy is designed to take advantage of the benefits of early antiretroviral treatment for HIV-positive people, their negative partners, and the populations to which they belong.

Challenges

Despite the potential that universal early treatment holds, many challenges remain. These challenges are not arguments against treatment as prevention, but they do suggest the need for more research, as well as the complexity involved with scaling up this approach, and educating the public about the limitations of the protection that treatment as prevention provides. Some of these challenges are:

Cost. Antiretrovirals are expensive. And although it is possible that earlier treatment could greatly reduce the number of new cases of HIV, it is not clear where the money would come from to put all people living with early HIV disease on medications. Currently, of the approximately 32 million people living with HIV, only 8 million people are on treatment, while 24 million are not. In 2011, the United Nations set a target of having 15 million of the people living with HIV on antiretrovirals by 2015. Since all of the people who are living with HIV will eventually need treatment, the financial argument for treating earlier rather than later is that costs of increased HIV incidence and illness will be avoided, but the upfront cost is still daunting.

Adherence Can Be Difficult.

Although current regimens are simpler and better tolerated than ever before, adherence remains a challenge. A study on the effectiveness of treatment as prevention in Los Angeles County, published in 2012, found that even though antiretroviral coverage rates were high, approximately 27 percent of those on treatment were not virally suppressed, leading the authors to conclude that interventions that support adherence are crucial. For people who lack basic necessities, or struggle with mental health concerns, adherence may be especially difficult. Keeping people engaged in care is crucial, and will likely demand additional social supports for an expanded population on treatment (peer advocacy, case management, supportive housing, mental health services, food, and transportation). Providing these vital services is another challenge in an era of shrinking resources.

Possible Drug Resistance. If
people are not able to be adherent to medications, for whatever reason, the possibility of drug resistance (a mutation of the virus so that the medication being used to fight it is no longer effective against it) increases.25 Whether earlier antiretroviral treatment will lead to increased drug resistance is controversial. Some data suggest that drug resistance is actually reduced when people begin antiretroviral treatment earlier in the course of the disease.26 Others warn that the substantial benefits of test and treat could be offset by increases in multi-drug-resistant strains of HIV, and so rates of drug-resistant virus should be monitored. A mathematical model developed by researchers at the University of Southern California and published in 2013 projects that “test and treat” for men who have sex with men in Los Angeles County would lead to a 34 percent reduction in new infections and a 19 percent reduction in deaths by 2023. The model also projects that cases of multi-drug-resistant virus would nearly double (from 4.79 percent to 9.06 percent).27

**Increased Drug Toxicity.** Although many regimens may not increase drug toxicity when they are introduced at earlier CD4 levels, or taken for longer periods of time, some do. Physicians must evaluate which antiretrovirals are likely to be most effective with the least toxicity for a given patient.28

**Blood Isn’t Semen.** Even if virus is suppressed in blood, it may not be suppressed in the genital tract. A 2012 Boston University study of 101 men (97 percent of whom were men who have sex with men) at the Fenway Health Center in Boston revealed that even though 83 participants had undetectable HIV in their blood plasma samples, 25 percent of these men had HIV detectable in their semen, in amounts ranging from 80 to 2,560 copies per milliliter. Sexually transmitted infections, and genital inflammation were associated with HIV detection in the semen of otherwise virally suppressed men.29 This raises the concern that mixed-status couples who relied solely on an undetectable (blood) viral load test to prevent transmission might not be as protected as they believe.

**When Was That Viral Load Test?** The amount of virus in a person’s body changes over time. Sometimes there is a “breakthrough” or “blip” in viral load replication, even when someone has been successfully treated for some time.30 As Das stated, “Somebody who had a totally suppressed viral load in May may not in September,” so frequent, consistent monitoring of the viral load is crucial.31

**Risk Compensation.** Some experts are concerned that people might increase risk behavior because they believe that suppressed community viral load is enough to eliminate their personal HIV risk, or because the HIV-positive partner in a couple is on treatment. The degree to which such “risk compensation” occurs is unknown, although a 2010 study of PrEP among men who have sex with men suggests that it may not occur often enough to significantly increase the number of HIV transmissions.32

**Will It Work as Well for Men Who Have Sex with Men (MSM)?** Most studies of treatment as prevention, including the Rakai study, the 052 study, and the studies cited by the authors of the “Swiss Statement” have relied on data regarding transmission within heterosexual couples. And the U.S. Department of Health and Human Services has stated that the evidence for treatment as prevention is stronger for perinatal and heterosexual transmission than for other transmission modes.33 As a recent review of the evidence concludes, “The benefits of TaP [treatment as prevention] for MSM are highly plausible, but not certain.” The authors add that “some biological and epidemiological evidence suggests that” treatment as prevention may be less effective in protecting against HIV transmission during anal intercourse than it is during vaginal intercourse.34

Because of these and other challenges, most proponents of treatment as prevention have advocated for a combination of HIV-prevention interventions, including both antiretroviral treatment and behavioral prevention strategies.

**The Need for Combination Interventions**

Behavioral interventions and other supports for medication adherence are crucial to the success of treatment as prevention strategies. According to Myron Cohen, the principal investigator on the HPTN 052 study cited above, states, “The protection provided from ART is not absolute and not absolutely predictable.”35 So even if treatment as prevention is an extremely effective way of reducing rates of new HIV infections, there will still be some HIV transmissions between people who have unprotected sex or share needles. Reduced risk improves many individuals’ chances of staying HIV-negative, but does not guarantee protection against HIV
transmission for any one person.

Condom use during vaginal and anal sex remains an excellent way of preventing HIV transmission between partners, but not everyone uses condoms every time they have sex with a person of different or unknown status. Behavioral interventions that encourage condom use, as well as other harm reduction measures, together with biomedical interventions such as “test and treat,” which reduce community viral load, are thought by many to be the best approach.

How Test Counseling Fits into the Treatment Cascade

The treatment cascade (see the graphic on Page 5) illustrates the steps necessary for HIV-positive people to achieve an undetectable viral load that can lead to better health outcomes, as well as reducing the possibility of transmission. It also highlights the places where people can be lost to the successful treatment that is necessary to achieve an undetectable viral load. There are many ways in which effective HIV test counseling works together with treatment as prevention to help close the gaps in the treatment cascade. HIV test counseling reduces transmission by increasing the number of people with HIV who know their status, giving people the information that they need to protect their own and their partners’ health. But the test counseling role goes further in supporting clients by linking newly diagnosed people to care, which, it is hoped, will lead to viral suppression. When counselors offer the client a good testing experience it is more likely that those who test negative will return to test again, and those who test positive accept referrals. It is important that counselors actively link clients to care (and to providers who can facilitate successful entry into care) since working with an HIV specialist helps maintain optimum health. This means offering assistance to clients in making medical appointments, not just suggesting that the client consider medical care at a later date. A study published in 2011 by the University of California, San Diego and the California Department of Public Health exploring barriers to care among 215 HIV-positive Californians found that people who had never been in care were significantly less likely to say that they had been offered help in setting up an appointment for HIV-related medical care than people who were currently receiving HIV care.36

When they link clients to Partner Services, counselors help the clients’ partners to know they may have been exposed to HIV, to test and know their status, and to enter care themselves if needed.

Finally, by linking clients to services that support a stable environment, such as housing, benefits, and other social services, HIV test counselors help draw on resources that can support HIV-negative clients in staying negative, and help HIV-positive clients stay healthy and in treatment. By helping newly diagnosed clients connect with medical care, counselors make it less likely that people will delay treatment because of poverty, stigma, or other barriers. In this way, counselors fulfill the goals of the National HIV/AIDS Strategy of reducing HIV-related health disparities, increasing access to care and optimizing health outcomes, and reducing the incidence of new HIV infections.37

An Active, Yet Limited Role

Although the test counseling role is a critical one, with ripples throughout the treatment cascade, it is also limited. Referrals are one way that counselors can help their clients overcome some of the barriers to care, without stepping outside this role. Even when counselors have personal or professional expertise, it is generally not part of the test counseling role to give specific medical advice to a particular client. It is, however, always
appropriate to encourage clients who test positive to seek HIV-related medical care, and to help them follow through on it. A counselor might say, “Many people are living long, healthy lives with HIV—and for many of them, the key to doing that is regular medical care.” Or, “A doctor can tell you more about how your health is right now, and can also help you to maintain your best health.” If a client asks, “Does this mean I should be on meds right now?” rather than giving medical advice, again emphasize the importance of getting linked to HIV-specific medical care. “An HIV doctor can tell you about what treatments, if any, are right for you right now. Can I help you make an appointment, so that you can get some of these questions answered?”

**Harm Reduction Counseling Messages**

Client-centered HIV test counseling uses a harm reduction approach. This means that as counselors, we understand that it is possible for people to make choices that greatly reduce their chances of getting HIV without eliminating all activities that could possibly transmit HIV. Viral suppression is a powerful harm reduction tool. But it does not completely eliminate the risk of getting HIV or passing it to others. Viral suppression is more likely to prevent transmission if clients have accurate information about it and can communicate effectively with their partners about it.

Some of the factors that determine how effective viral suppression is as a tool include how often the HIV-positive person has his or her viral load tested; how sensitive those tests are; how closely the amount of virus in the body fluid being tested corresponds to the amount of virus in the body fluid being exchanged; and how adherent the person has been to antiretrovirals since his or her last viral load test. Relying on viral suppression to prevent transmission also requires accurate, current information, and communication with partners. If a client who tests negative says that he “only has sex with guys who are undetectable,” it’s helpful to explore how he gets information about his partners. One client might decide that a partner’s viral load is undetectable after a conversation in which some of the factors listed above are discussed. Another might decide his partner is undetectable based on seeing antiretrovirals in the medicine cabinet while using the partner’s bathroom, or based on the fact that the partner was openly HIV-positive in his online profile, “so he must be on meds.”

The key is neither to dismiss viral suppression as a useless strategy because it isn’t perfect, nor to promise clients that a suppressed viral load offers 100% protection against HIV transmission. Instead, our goal is to talk with clients about their own risk tolerance—the level of risk they feel comfortable taking—and how viral load suppression fits in with that tolerance. Some clients may decide to use condoms (or use their own injection needles) even when they or their opposite-status partners are virally suppressed, whereas others may decide that they are willing to have unprotected sex (or share needles) if the virus is undetectable.

**Conclusion**

In 2009, World Health Organization medical officer Reuben Granich and his colleagues suggested that heterosexually acquired HIV could be nearly eliminated in 50 years through universal voluntary counseling and testing, coupled with immediate antiretroviral treatment. And indeed treatment as prevention for HIV disease is an exciting development that has the potential for dramatic impact on reduced HIV transmission over time. Although some concerns, including cost, continue to challenge scale-up efforts, “test and treat” promises to be a powerful tool in helping end the HIV/AIDS epidemic. For HIV test counselors, the advent of treatment as prevention means that our role in linking HIV-positive clients to HIV-specific medical care as soon as possible, and making referrals to resources that can help support their ability to stay in treatment, is more important than ever.
References


Review Questions
1. “Treatment as Prevention” has been used for more than 20 years to help prevent HIV transmission within what population(s)? a) Men who have sex with men; b) Pregnant women to prevent transmission to their children; c) Heterosexual couples; d) Injection drug users and their sexual and needle-sharing partners.

2. In the Rakai study mentioned in the article, what did the researchers conclude was the chief predictor of risk of HIV transmission among heterosexual couples? a) The viral load of the HIV-positive partner; b) The strain of virus the positive partner was living with; c) The viral load of the community the couple belongs to; d) All of the above.

3. True or False: The “Swiss Statement” declared that if an HIV-positive person has had at least one undetectable viral load test within the past year, they cannot pass HIV on to uninfected partners through sex.

4. Which of the following studies on treatment as prevention was a randomized controlled trial? a) The Rakai study; b) The HPTN 052 study; c) The Danish National Health Survey; d) None of the above.

5. True or False: “Community viral load” may help explain why HIV infection rates among Black MSM are disproportionately high.

6. What is the HIV test counselor’s role in treatment as prevention? a) To refer an HIV-positive client to a doctor and offer the client detailed medical advice about the treatment the client should take; b) To tell the client that medical treatment is something they might want to consider at a later date; c) To share with the client that many people with HIV are living long, healthy lives, and to actively attempt to link the client to medical treatment; d) Not to mention treatment because the client is probably too overwhelmed by the HIV-positive result.

7. True or False: “Test and Treat” only benefits the community, not HIV-positive individuals and their partners.

Discussion Questions
1. What is your agency’s protocol for linkage to care? What role do you play in that process?
2. What do you think are the key factors that lead HIV-positive people in your community to be lost to medical treatment?
3. What referral resources do you offer clients who test HIV-positive, and how do these resources help clients get closer to the goal of an undetectable viral load?
4. When a client tests HIV-positive, how can the counselor mention the importance of avoiding transmitting the virus to others in a way that does not make the client feel stigmatized?

Answers
1. b.
2. a.
3. False. The “Swiss Statement” said that a person would have to have their viral load checked regularly, and have had an undetectable viral load (less than 40 copies/milliliter) for at least 6 months.
4. b.
5. True.
6. c.
7. False. “Test and Treat” has individual, interpersonal, and community benefits.