

Treatment as

The idea of treating people with HIV across the board to reduce transmission of HIV. *Relay* asked two of Canada's foremost



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Dr. Mark Tyndall says treatment to prevent transmission is an important way forward

Efforts to prevent HIV have two goals: stopping uninfected people from contracting HIV and protecting the rights and freedoms of those who are already infected. Increasing the number of people receiving HIV treatment in order to reduce transmission is a strategy that meets both of these goals.

Treatment reduces transmission

There is strong evidence that reduced HIV plasma **viral loads** are associated with reduced HIV transmission. Studies of couples where one partner has HIV and the other doesn't (serodiscordant couples), studies of mother to child transmission, and larger country-based studies all illustrate the effect of reduced viral load on HIV transmission. Further, the biological process through which suppressed circulating HIV virus reduces transmission is scientifically well supported. Although the evidence for reduced

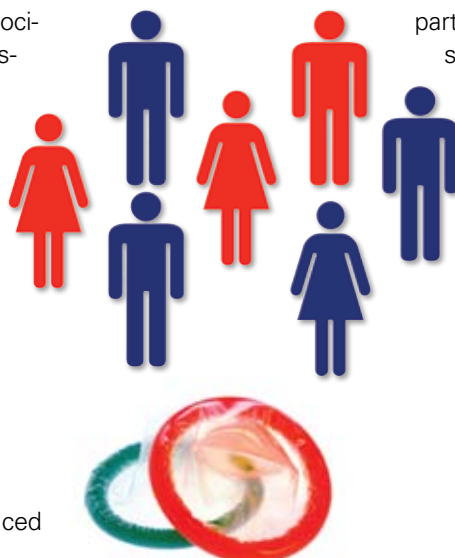
HIV transmission hasn't been demonstrated among injection drug users with very low viral loads, the same principles should apply.

Combined prevention approaches are needed

Traditional HIV prevention programs have had a tremendous impact on HIV transmission rates. Increased condom use, changes in sexual practices, a reduction in the number of concurrent partners, and other HIV prevention strategies have been effective in reducing the sexual transmission of HIV. However, these efforts have limitations and there are growing concerns that some of these messages are losing impact, especially in younger people.

One of the most contentious issues around using treatment to prevent transmission is that it would send the wrong message to both

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WARNING! This article presents the scientific opinion of two very prominent researchers, not the legal aspects of disclosure. As it stands now, the law states that if you're HIV positive you must declare your status to your sex partner even if you're effectively treated and engaging in safer sex. ARVs are not currently indicated for the prevention of the transmission of HIV.

prevention

viral loads has gained support as a way to prevent experts to describe the pros and cons of this approach.

Dr. Mark Wainberg thinks treatment to prevent transmission will have harmful consequences

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Although the idea of using widespread early treatment as a means of reducing HIV transmissions is appealing, the concept isn't without problems and may never be practical.

It might de-emphasize safe sex practices

We know that people whose HIV is well managed with antiretroviral (ARV) therapy are less infectious to others. However, this doesn't make it advisable for those who have achieved **undetectable viral loads** to abandon safe sex practices. A recent statement to this effect by a group of Swiss experts was met with considerable opposition, for several reasons.

One concern is that if people stop insisting on condom usage and become less preoccupied with safer sex, their number of sexual partners may increase. That would increase the transmission of sexually-transmitted diseases other than HIV.

Viral load control isn't constant

Not all people who are treated will necessarily maintain undetectable viral loads over long periods of time. A lapse in adherence to ARV regimens and/or the emergence of drug resistance might lead to higher viral loads, making some people newly capable of HIV transmission. In such cases, there's a

higher risk that the viruses being transmitted might contain one or more mutations associated with drug resistance.

Newly infected partners still pose risk

Sexual relations with an HIV-infected partner whose viral load is well suppressed may be safer than having relations with a newly infected person who doesn't know that he/she is HIV-infected. That person may not yet have developed an antibody response against HIV and would therefore still test seronegative. Newly infected people are known to have very high viral loads, often in the millions of copies of viral RNA per ml of blood. For that reason, it may in fact be safer to have sexual relations with someone who knows they have HIV and whose viral load is well suppressed through treatment, than to have relations with someone at high risk of acquiring HIV who doesn't know they're HIV positive.

Newly infected people play an important part in HIV transmission. According to recent studies, as many as half of all new HIV transmissions can be attributed to people who have themselves been infected for less than six months. This group would make any program using treatment as prevention much less



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people with HIV and those who may be at risk of infection: that other prevention strategies are no longer so important. This could potentially undermine traditional HIV prevention programs, leading to increased risky behaviours and a rise in new infections.

I believe that even though prevention messages should emphasize that the risk of transmission isn't completely eliminated with effective treatment, we're doing the community a disservice by understating the importance of HIV viral load in transmission risk. There's no reason that the traditional messages of HIV prevention can't be combined with a treatment-as-prevention message that can help further reduce transmission. This information needs to be available to people who are at risk for HIV infection and should be presented in clear and accessible ways.

The financial cost of rolling out a program of increased HIV drug treatment is high, but the cost of allowing current HIV transmission rates to continue is many times higher, not only in terms of drug costs but also in human suffering



More treatment costs less than more infections

The promotion of a treatment-as-prevention strategy isn't without challenges. The financial cost of rolling out a program of increased HIV drug treatment is high, but the cost of allowing current HIV transmission rates to continue is many times higher, not only in terms of drug costs but also in human suffering. Having people with HIV start antiretroviral drugs (ARVs) when they're not at risk of HIV-related infections poses other problems. However, the past decade has seen major progress in reducing drug toxicity and increasing the convenience and choice of ARVs. This progress will continue to make treatment a much more attractive option for people with higher CD4 levels.

Even low viral loads have health impact if untreated

We're also now seeing evidence that untreated HIV infection, even in those who maintain reasonable CD4 counts, may have negative health consequences. These factors have recently led to a revision of the HIV treatment guidelines. Treatment should now be recommended to people with CD4 counts below 350 copies/mm³. The fact that HIV infected individuals become less infectious to their own sexual partners is just an added benefit of taking HIV medications.

Many researchers expect that increasing the number of people receiving ARVs will also increase the appearance of resistant virus. This effect will need to be monitored.

Conclusion

It's the evolution of HIV treatment over the past decade that's made it even possible to treat large numbers of people. Perhaps the most encouraging story for HIV/AIDS in recent years has been the rollout of antiretroviral drugs in poorer countries. These programs have shown that HIV treatment is possible even in regions where resources are scarce.

Like any HIV prevention program, a treatment-as-prevention strategy will need to be carefully evaluated to see how it affects outcomes as treatment is increased. HIV prevention advocates should enthusiastically embrace the message that effective HIV treatment greatly reduces viral transmission. After all, reducing HIV transmission is the ultimate goal of prevention. **R**

A further complication is the difficulty of identifying newly infected people in the first place. HIV diagnostic testing is an imperfect process

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effective at reducing transmission rates. How can we possibly provide ARVs to people who don't yet know they're infected?

Individual rights vs societal benefits

Today, many people who test positive for HIV choose to delay starting treatment as long as they maintain high CD4 counts, and won't necessarily benefit from treatment in terms of personal health. Enough side effects and inconvenience are still associated with treatment to make this a perfectly sensible decision. Adopting a treatment-as-prevention approach could create an ethical conflict between individual rights to delay treatment and potential benefits to society as a whole, if HIV-infected persons were treated aggressively from the time they tested positive to render them non-infectious.

A further complication is the difficulty of identifying newly infected people in the first place. HIV diagnostic testing is an imperfect process. People who haven't yet developed antibodies won't be detected by conventional diagnostic tests, despite potentially high viral loads. We know that other diagnostic tests such as polymerase chain reaction (PCR) or detuned p24 Ag are far better than antibody testing at detecting HIV soon after transmission, but these tests aren't in common use.

Transmission of resistant virus

At least 10% of all new HIV infections in developed countries involve the transmission of viruses that contain at least one **mutation** associated with drug **resistance**. In some people, however, certain mutations may only be present at very low levels in viral samples. This is true of mutations associated with resistance to first generation non-nucleoside reverse transcriptase inhibitors (NNRTIs) and has led to treatment failure in some people taking NNRTIs such as nevirapine (Viramune®) and efavirenz (Sustiva®).

Unless ultrasensitive methods are used to check for the presence of mutations in plasma viral samples, these resistant strains could

present a serious obstacle for treatment as prevention efforts.

Widespread early treatment would increase the number of people on ARVs who aren't highly motivated to adhere to therapy, which would increase the prevalence of resistant viral strains that could then be sexually transmitted.

Developing countries

The use of treatment as prevention could have the greatest impact in developing countries where ARVs are not widely available for therapy.

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However, the ARVs used in developing countries are often more toxic than drugs used in richer countries, and lead to more problems with adherence and greater development of drug resistance. As an example, recent studies in Malawi have shown that the use of treatment regimens that include ddI/d4T (Videx®/ Zerit®) can easily produce drug resistant strains that contain the multi-nucleoside resistance K65R mutation. The K65R mutation renders the virus resistant to abacavir (Ziagen®), tenofovir (Viread®) and emtricitabine (Emtriva®). Resistant viruses will in all likelihood be sexually transmitted.

Conclusion

The basic idea behind using treatment as prevention is appealing, but in practice, it would face many obstacles and potentially create new problems. Not least of these would be the identification of people in need of treatment and the development and transmission of drug resistance. Studies in limited settings to see whether widespread treatment can reduce transmission should be accompanied by careful monitoring of HIV drug resistance. **R**

If my viral load is undetectable, can I infect my partner or not?

Dr. Wainberg: If your viral load is undetectable you might still be able to infect your partner and therefore should use a condom during sexual relations. You should also recognize that your viral load may have been undetectable when last measured but may not be negligible today.

Dr. Tyndall: It's very clear that the risk of HIV transmission is closely related to the level of virus in the blood. People who have undetectable viral loads through anti-retroviral treatment have a greatly reduced risk of transmitting HIV to their sexual partners. However, reduced risk isn't the same as no risk and safer sexual practices remain advisable.

