HIV treatment as prevention—it works

Last week any doubts around treatment as an approach to halt the spread of the HIV epidemic were allayed. An international study showed that antiretroviral treatment can prevent the sexual transmission of HIV among heterosexual couples in whom one partner is HIV-infected and the other is not. UNAIDS described the result as a "serious game changer" for HIV prevention.

The phase 3 clinical trial, HPTN 052, was done by the HIV Prevention Trials Network and funded by the US National Institutes of Health. It was due to run until 2015, but compelling interim results led the international data and safety monitoring board to recommend the results be publicly released as soon as possible. Although the results are unsurprising given the extensive ecological data supporting the prevention benefits of treatment, this is the first large randomised trial to provide a true impact evaluation. The study showed a 96% reduction in risk of HIV transmission—the primary outcome.

The trial began in 2005 and enrolled 1763 HIV serodiscordant couples across 13 sites in nine countries in Asia, Africa, and the USA. At enrolment, the HIV-positive partner was required to have a CD4 cell count between 350 and 550 cells per μL. The median CD4 count at enrolment was 436 cells per μL. This level is higher than WHO's recommendation to start treatment, which is at 350 cells per μL or less. This difference is important because the HIV-positive individuals were asymptomatic, did not require treatment, and certainly would not have been eligible for treatment, according to most national guidelines. Couples were randomised so that the HIV-positive partner received antiretrovirals immediately, or delayed treatment until their CD4 counts fell below 250 cells per μL, or had an AIDS-related event such as pneumocystis pneumonia. Throughout the study both groups received the same amount of HIV-related care and counselling.

Among the 877 couples in the delayed group, 27 HIV transmissions occurred compared with one transmission in the immediate group. This difference was highly statistically significant ($p<0·0001$). Furthermore, the new infections were confirmed as being genetically linked to the HIV-positive partners, though there were a cluster of unlinked cases, raising the issue of concurrency. The study also found a statistically significant reduction in extrapulmonary tuberculosis with 17 cases in the delayed group versus three cases in the immediate group. Study participants and investigators have been informed of the results and all participants offered the appropriate care. All study participants will be followed for at least 1 more year.

Clearly, treating sooner rather than later results in both a clinical benefit for the individual and has a potentially enormous public health benefit in slowing the spread of infection. These results are likely to provide a new level of dialogue between physician and patient. Besides emphasising the benefit of medication adherence to the patient, clinicians could stress how it has the potential to benefit others alongside other altruistic practices such as condom use. Indeed, one of the most interesting observations was that most patients adhered to treatment and 95% had viral load suppressed at all times, which is a rare outcome for an HIV clinical trial. Treatment as prevention should decrease stigma and improve uptake of testing because there is more of an incentive for people to know their status with the reassurance of knowing that if treated early they are unlikely to infect others.

Many interesting research questions now lie ahead. But most urgent will be the assessment of the practical impact of these findings and their public health importance in generalised epidemics. Another immediate issue will be to reflect these findings in ongoing and future prevention trials. Certainly in discordant couples it will be unethical not to offer treatment to infected people.

Findings now need to be translated into policy and action. Agencies such as President's Emergency Plan For AIDS Relief and the Global Fund to Fight AIDS, Tuberculosis and Malaria need to reassess their prevention portfolios and consider diverting funds from programmes with poor evidence (such as behavioural change communication) to treatment for prevention. There is now an ethical imperative for guidelines to be revised to start treatment much earlier than recommended. But, with 6 million people on treatment and another 9 million needing treatment, how to fund and sustain such an endeavour with functioning health systems and a sufficient workforce will be a huge challenge.

One needs to take this data yet to be peer reviewed and published with caution. But if true, these findings present an opportunity to make a big difference in the epidemic over the next few years. ■ *The Lancet*

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For the **National Institutes of Health news release on the HPTN 052 trial** see http://www.niaid.nih.gov/news/newsreleases/2011/Pages/HPTN052.aspx

For more on the **HPTN 052 trial** see http://www.hptn.org/web%20documents/PressReleases/HPTN052PressReleaseFINAL5_12_118am.pdf