

Treatment as prevention

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A large randomised study of treatment as prevention has closed more than three years early after interim analysis of the data showed that antiretroviral treatment reduced the risk of HIV transmission from treated partner to uninfected partner by 96%.

The magnitude of the reduction in risk is almost the same as that observed in multiple cohort studies in sub-Saharan Africa, and is the strongest effect seen in any trial that has used an antiretroviral-based prevention method.

This large, international study randomised 1 736 male-female couples, in which one partner was HIV positive, either to begin antiretroviral therapy immediately or to wait until treatment was clinically indicated (at a CD4 count of 250 cells/mm³).

The study began enrolling participants in 2005 in Botswana, Brazil, India, Kenya, Malawi, South Africa and Zimbabwe, and recruited couples in which the HIV-positive partner had a CD4 cell count between 350 and 550 cells/mm³. The median CD4 count at the time of joining the study was 436 cells/mm³. This level is higher than the threshold at which World Health Organization guidelines currently recommend starting treatment.

The study was due to run until 2015.

The study was halted after an interim review by the Data and Safety Monitoring Board, which found that 39 infections had occurred. Twenty-eight could be genetically linked to the HIV-positive partner, and of these 27 occurred in couples where the HIV-positive partner did not begin antiretroviral therapy immediately. This translates into a 96% reduction in the risk of transmission. This result was highly statistically significant ($p < 0.0001$).

All participants received regular counselling on safer sex, free condoms and treatment for sexually transmitted infections.

The results of the study show that treatment of people with relatively high CD4 cell counts results in a very substantial reduction in the risk of HIV transmission.

The study also found a statistically significant reduction in the risk of extrapulmonary tuberculosis in the early treatment arm: 17 cases occurred in the deferred treatment arm, compared with 3 cases in the early treatment arm ($p = 0.0013$).

There was not a significant difference in the death rate; however, 13 deaths occurred in

the deferred treatment arm and 10 in the immediate treatment arm. There were 105 morbidity and mortality events – 65 events in the delayed treatment arm and 40 in the immediate treatment arm.

Implications

Coming just ahead of the UN General Assembly Special Session on AIDS in New York, these results are likely to give a powerful boost to messages that greater investment in HIV treatment could have a significant impact on the growth of the epidemic.

‘This breakthrough is a serious game changer and will drive the prevention revolution forward. It makes HIV treatment a new priority prevention option,’ said Michel Sidibé, Executive Director of the Joint United Nations Programme on HIV/AIDS (UNAIDS). ‘Now we need to make sure that couples have the option to choose treatment for prevention and have access to it. People living with HIV can now, with dignity and confidence, take additional steps to protect their loved ones from HIV,’ said Mr Sidibé.

‘The upcoming UN High Level Meeting on AIDS should set treatment and prevention targets that take [the study] results into account,’ said Mitchell Warren of AVAC, an organisation which advocates new HIV prevention technologies. ‘We need to start critical discussions and come to quick decisions about where and how to deploy treatment as prevention in the short-term. Government and international normative agencies now have a critical mass of data to publish guidelines for appropriate implementation of treatment as prevention in concert with other prevention methods.’

The results are also likely to give further impetus to studies that are planning to look at the effect of offering early treatment at the population level. These trials will investigate what happens when HIV testing and treatment are offered as widely as possible in a community. The studies will also look at the impact on HIV infections over time and at factors that could impede the success of treatment as a prevention tool. These include factors such as adherence to treatment, stigma and discrimination, development of drug resistance and changes in sexual behaviour as a result of the availability of treatment.

‘Today’s result should be viewed in light of other recent findings from trials using ARVs for prevention,’ said Mitchell Warren of AVAC. ‘The recent results from the iPrEx trial showed that PrEP is effective in gay men and transgender women, while the CAPRISA 004 microbicide trial showed that 1% tenofovir gel is effective at reducing HIV risk for women.’



‘Together, these results allow us to imagine a world in which men and women seek HIV testing with the knowledge and confidence that they will receive a range of highly effective options for staying healthy and protecting themselves and their partners – whatever the test result,’ Warren added. ‘The results of the study require us to rethink how we structure the delivery and funding of HIV services overall.’

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