

# Early treatment for HIV slows damage to immune system and reduces risk of transmission

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A 48-week course of antiretroviral medication taken in the early stages of HIV infection slows the damage to the immune system and delays the need for long term treatment, according to research published today in the *New England Journal of Medicine* (1). However, the delay was only marginally longer than the time already spent on treatment.

The study, the largest clinical trial ever undertaken looking at treating people with recent HIV infection, also suggests that the [treatment](#) lowers the amount of virus in the blood for up to sixty weeks after it is stopped, which potentially reduces the risk of onward transmission.

SPARTAC (Short Pulse Anti-Retroviral Therapy at HIV Seroconversion), a [randomised controlled trial](#), took place over five years and involved 366 adults – mainly heterosexual women and gay men – from Australia, Brazil, Ireland, Italy, South Africa, Spain, Uganda and the UK. It was funded by the Wellcome Trust and coordinated by researchers from Imperial College London and the Medical Research Council's Clinical Trials Unit, with immunology research conducted by the University of Oxford.

Unless regularly tested, most people will be unaware that they are HIV-positive during the first few years after they have become infected. Initial symptoms can be similar to flu or other [viral infections](#), and for most people, there follows a period of many years when they carry the

virus but are not sick. However, the [immune system](#) never successfully clears HIV; instead, the virus hides away, slowly weakening the body's defences and destroying [CD4 T-cells](#), which play a key part in the [immune response](#).

Without treatment, the immune system steadily becomes more compromised, leaving the individual at increased risk of developing other life-threatening infections. To stop this from happening, when the number of remaining CD4 T-cells reaches a certain level – 350 cells per cubic millimetre – international treatment guidelines recommend that an individual begins life-long treatment with antiretroviral drugs. These drugs not only prevent further damage to the immune system, but also allow it to recover.

Several observational studies have suggested that treatment at the time HIV infection occurs could delay the amount and speed of immune damage and so delay the need to start lifelong antiretroviral medication. SPARTAC is the first large randomised study to test this hypothesis.

All volunteers in the SPARTAC trial were identified within six months of becoming infected with HIV and were randomly allocated to receive antiretrovirals for 48 weeks, 12 weeks or to receive no medication (the standard practice in HIV management at this stage of infection). The researchers then measured the time until each volunteer's CD4 T-cell count fell below 350 cells per cubic millimetre and/or they began a lifelong course of antiretroviral medication.

The researchers found that on average, participants who had received no medication needed to begin taking a lifelong course of treatment 157 weeks after infection. Those in the group receiving antiretrovirals for 12 weeks began their lifelong course of treatment on average 184 weeks after infection (a delay of 27 weeks, but not considered by the researchers to be a significant effect).

However, those volunteers who received antiretrovirals for 48 weeks took an average of 222 weeks before beginning long term treatment – a delay of 65 weeks. This represents an important delay compared with no treatment or 12 weeks of medication, but overall was not significantly longer than the time those participants had already spent on treatment.

In addition, over the whole time in the study, participants on the 48 week course had higher CD4 T-cell counts than those in the other two treatment groups, potentially reducing their risk of developing secondary infections such as tuberculosis. They also had lower levels of HIV in the blood for over a year after stopping treatment compared to the other volunteers, which could play a role in reducing the risk of passing on the virus to sexual partners.

The researchers found no evidence that treatment within the first six months of infection led to the virus becoming resistant to the drugs or that coming off the course led to unexpected deaths, or damage to the immune system.

A separate analysis of the results suggested that the 48-week treatment was more beneficial the closer it was started to the time of infection. Participants who were enrolled closer to the time of HIV infection tended to have faster declines in the number of CD4 cells if they did not receive treatment, indicating greater damage to their immune systems. It was amongst this group that the 48-week treatment appeared to have the biggest benefit. However, it is unclear why these people were coming to see a clinician so early after infection; the researchers believe it may be that they had felt unwell. More research focusing on people in the very early stages of infection, a challenging group to identify, needs to be done to confirm this observation.

Dr Sarah Fidler from Imperial College London, who led the study, says: "These results are promising and suggest that a year-long course of

treatment for people recently infected with HIV may have some benefit on both the immune system as well as helping control the virus. The treatment also reduces the amount of virus in the body for some time after the patient has stopped taking the medication. This could be very important for helping reduce the risk of passing on the virus to a sexual partner."

Professor Jonathan Weber, the chief study investigator, says that the study reinforces the importance of frequent testing for HIV, particularly amongst high risk groups: "Early testing and diagnosis are incredibly important. When a person first contracts HIV, they are at their most infectious. But they are also often unaware that they have contracted the disease and hence are more likely to spread the infection. The sooner they can be diagnosed, the better our chances of limiting the spread of the virus and the sooner they can be offered appropriate guidance and counselling.

"If, as our study suggests, they can then be treated in such a way as to slow the progression of the disease and reduce their risk of secondary infections from potentially deadly diseases such as TB, then this offers a win-win situation."

Professor Gita Ramjee, Director of the South African Medical Research Council's HIV Prevention Research Unit, who led from the South African sites, adds: "We now need to weigh up whether the benefits offered by early intervention are outweighed by the strategic and financial challenges such a change in policy would incur, particularly in resource-poor settings such as Africa, although this may be where the most benefits are seen in terms of TB rates."

In the same edition of the [New England Journal of Medicine](#) a large observational study (2) of immune function amongst individuals with recent infection shows that early initiation of antiretroviral therapy –

within four months of infection – is accompanied by an enhanced recovery of the immune system that is not seen to the same extent if treatment is started in later stages of infection. These findings support the main trial result of the SPARTAC study. In an accompanying editorial addressing both these studies, Walker and Hirsch comment that there is now increasing evidence of the value of early treatment to the individual and inferred benefit at a population level of reducing infectiousness.

Combating infectious diseases is one of the strategic priorities of the Wellcome Trust, which funded the SPARTAC study. Commenting on the research, Dr Jimmy Whitworth, Head of International Activities at the Wellcome Trust, said: "This study adds to increasing evidence that early initiation of HIV treatment is of benefit to the individual in preventing severe disease and in reducing infectiousness to his or her partners. Questions remain about whether a longer course at an early stage could be more beneficial or whether early treatment should be continued for life."

**More information:** 1. SPARTAC Trial Investigators. The effect of short-course antiretroviral therapy in primary HIV infection: final results from SPARTAC, an international randomized controlled trial. *NEJM*; 17 Jan 2013.

2. T Le et al. Enhanced CD4+ T-Cell Recovery with Earlier HIV-1 Antiretroviral Therapy. *NEJM*; 17 Jan 2013

Provided by Wellcome Trust

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