# HIV treatment strategies that can weather future challenges

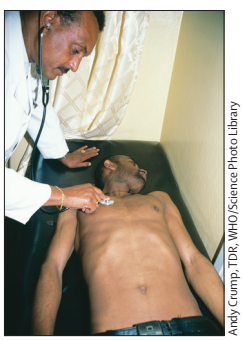
Early initiation of antiretroviral therapy not only prevents AIDS and extends survival of people with HIV, but also significantly reduces new HIV infections.[1] At the core of the treatment-as-prevention strategy is the goal of using safer, simpler, and better tolerated antiretroviral regimens to sustain suppression of viral replication and maintain an undetectable plasma viral load. The goal of treatment as prevention is to achieve immune reconstitution and disease-free survival; as the viral load becomes undetectable in biological fluids (eg, semen, vaginal fluids, blood) the risk of HIV transmission decreases by more than 95%.[2]

The 2013 WHO guidelines[3] recommend that lifetime antiretroviral therapy be offered to HIV-positive individuals with CD4 counts of 500 cells per μL or less, to HIV-positive people irrespective of CD4 cell counts if they have active tuberculosis or liver disease caused by hepatitis B infection, to HIV-positive partners in serodiscordant couples, to HIV-positive pregnant and breastfeeding women, and to children younger than 5 years with HIV. The guidelines increased the number of people eligible for treatment from about 15 million to 29 million, of the 35 million people living with HIV in low-resource and middle-resource countries.[4] WHO estimates[5] that implementation of the 2013 guidelines would avert 3 million deaths and 4 million new HIV infections in these countries by 2025. Furthermore, UNAIDS estimates that optimum implementation of the new guidelines would decrease new HIV infections by 90% in low-resource and middle-resource countries within 40 years. The new guidelines are broadly aligned with those produced by the International AIDS Society–USA in 2010[6] and the US Department of Health and Human Services in 2011.[7]

In *The Lancet Infectious Diseases*, Sayoki Mfinanga and colleagues[8] report results of a clinical trial involving 1538 African patients. The researchers show that among HIV-positive men and women with tuberculosis, initiation of antiretroviral therapy within 2 weeks of starting tuberculosis treatment when the CD4 count is greater than 220 cells per μL was not associated with a significant decrease in mortality. Of patients with a CD4 count of 220–349 cells per μL, 26 (8%) of 331 patients who started antiretroviral treatment early reached the composite endpoint compared with 33 (10%) of 342 who had delayed treatment (RR 0·80, 95% CI 0·46–1·39; p=0·6). For those with CD4 counts of 350 cells per μL or more, 39 (9%) of 436 versus 38 (9%) of 429 reached the primary endpoint (RR 1·01, 95% CI 0·63–1·62; p=0·4). On the basis of these results, the investigators suggest that present WHO recommendations might need revision to allow deferral of antiretroviral therapy in these patients until after tuberculosis treatment is completed.[9]

By contrast, we propose that deferral of antiretroviral therapy should be strongly discouraged, even in patients with tuberculosis. On one hand, the results of the present study show no deleterious effect of early initiation of antiretroviral therapy for patients being treated for tuberculosis. On the other hand, the effect of immediate initiation of antiretroviral therapy on overall morbidity, mortality, and HIV transmission is abundantly documented. Indeed, if there was an attempt to revise the present guidelines, we would propose that a simplified test-and-treat approach would be a more reasonable way forward. At present, the 2013 WHO guidelines are challenging and programmatically complex. More than 80% of people with HIV are in need of antiretroviral therapy, according to the 2013 guidelines and the remaining 20% will need antiretroviral therapy within a few months to a few years. Furthermore, patents who remain on treatment can expect to have an almost normal quality of life for about 50 years.[10] From a practical standpoint, the strategy outlined in the 2013 guidelines spends valuable resources deferring treatment for a few people with HIV for a short period of time with potentially devastating consequences. There are concerns that treatment deferral could negatively affect subsequent adherence to antiretroviral therapy, but equally important, deferral might compromise the patient's response to treatment (eg, more side-effects, poorer CD4 cell count recovery) and promote ongoing HIV transmission.

The wild card in all scenarios is climate change. UNAIDS and UN Education Programme emphasise the need to consider the effects of climate change on HIV and to actively prevent and mitigate the effects of climate-related food insecurity, infectious diseases, and population displacement as part of a comprehensive HIV strategy.[11–13] Food insecurity has been associated with



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delayed access to antiretroviral therapy, compromised pharmacokinetic efficacy, suboptimum adherence to and poor virological and immunological responses to treatment, and reduced survival.[14] The potential for mass migration—especially in regions hardest hit by HIV—poses numerous challenges to adherence and the continuum of care. Most displaced people will be women and children, who have a high biological and behavioural risk of HIV infection and are likely to concentrate in urban areas with high prevalence of HIV infection and transmission risk.[5,12]

The goal of zero new HIV infections, AIDS-related deaths, and discrimination over the coming decades requires ongoing evidence-based clinical and public health strategies and coordination across sectors. We therefore must urgently and optimally deploy the 2013 WHO guidelines and continue to work to expand free access to HIV testing and care services as well as immediately offering free antiretroviral therapy to all people with HIV worldwide.

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