

AIDS brief

Monitor patients before treatment to improve survival in HIV

Acquired immunodeficiency syndrome (AIDS) has killed more than 25 million people since the first case in 1981, and about 33 million people are currently infected with the human immunodeficiency virus (HIV), which causes AIDS. HIV destroys immune system cells (including CD4 cells, a type of lymphocyte), leaving infected individuals susceptible to other infections. Early in the AIDS epidemic, most HIV-positive individuals died within 10 years, but in 1996 combination antiretroviral therapy (ART), a mixture of powerful but expensive antiretroviral drugs, was developed. For HIV-positive people living in affluent, developed countries who could

afford ART, AIDS then became a chronic disease, but for those living in low- and middle-income countries it remained a death sentence – ART was too expensive. In 2003, this lack of access to ART was declared a global health emergency and governments, international organisations, and funding bodies began to implement plans to increase ART coverage in developing countries.

The roll-out of ART in developing countries has concentrated so far on finding HIV-positive people who currently need treatment. In developing countries, these are often individuals who have AIDS-related symptoms such as recurrent severe bacterial infections. But healthy people are also being diagnosed as HIV positive during voluntary testing and at antenatal clinics. How should

these HIV-positive but symptom-free individuals be managed? Should regular health-monitoring appointments be scheduled for them and when should ART be initiated? Management decisions like these will determine how well patients do when they eventually start ART, as well as the demand for ART and other health-care services. The full range of alternative patient management strategies cannot be tested in clinical trials – it would be unethical – but public-health officials need an idea of their relative effectiveness in order to use limited resources wisely. In this study, therefore, the researchers use mathematical modelling to investigate the impact of alternative patient management and ART initiation strategies on the impact of ART programmes in resource-poor settings.

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The researchers' mathematical model, which includes data on disease progression collected in Africa, simulates disease progression in a group (cohort) of 1 000 HIV-infected adults. It tracks these individuals from infection, through diagnosis and clinical monitoring, into treatment, and predicts how many will receive ART and their length of survival under different management scenarios and ART initiation rules. The model predicts that if HIV-positive individuals receive ART only when they have AIDS-related symptoms, only a quarter of them will ever start ART and the average life-years saved per person treated will be 6 years (that is, they will live 6 years longer than they would have done without treatment). If individuals are recruited to ART programmes when they are healthy and are frequently monitored using CD4

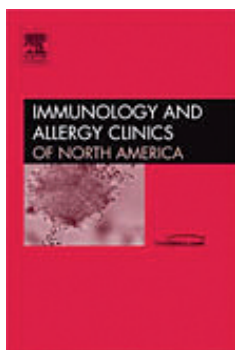
cell counts to decide when to start ART, three-quarters of the cohort will be treated and 15 life-years will be saved per person treated. The impact of ART programmes will be increased further, the model predicts, by preferentially monitoring people who are more than 35 years old and the most immunosuppressed individuals. Finally, strategies that measure CD4 cells frequently will save more life-years because ART is more likely to be started before the immune system is irreversibly damaged. Importantly for resource-poor settings, these strategies also save more life-years per year on ART.

As with all mathematical models, the accuracy of these predictions depends on the assumptions built into the model and the reliability of the data fed into it. Also, this model does not estimate the costs of the various management options,

something that will need to be done to ensure effective allocation of limited resources. Nevertheless, these findings provide several general clues about how ART programmes should be implemented in poor countries to maximise their effects. Early diagnosis of infections, regular monitoring of patients, and using CD4 cell counts to decide when to initiate ART should all help to improve the number of life-years saved by ART. In other words, the researchers conclude, effectively managing individuals at all stages of HIV infection is essential to maximise the impact of ART.

Hallett TB, Gregson S, Dube S, Garnett GP. The impact of monitoring HIV-infected patients prior to treatment in resource-poor settings: Insights from mathematical modelling. *PLoS Med* 2008; 5(3): e53.

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