



Big differences in virological outcomes among people taking first-line HIV therapy in resource-limited settings

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Virological outcomes vary enormously among people taking antiretroviral therapy in different resource-limited settings, according to research published in *Clinical Infectious Diseases*. An international team of investigators monitored outcomes in patients in five African and two south-east Asian countries 12 and 24 months after starting HIV therapy. World Health Organization (WHO) approaches for the delivery and monitoring of antiretroviral therapy were used in all seven countries. Rates of virological failure differed significantly between settings, from a low of 3% to a high of 26%.

Access to antiretroviral therapy in resource-limited settings is expanding rapidly, partly because of WHO models for delivery and monitoring of treatment, which take into account limited financial resources of low- and middle-income countries and the logistical constraints of their health systems. WHO recommends viral load monitoring where possible, which is not feasible in most settings.

After the introduction of antiretroviral roll-out programmes in low- and middle-income countries patient outcomes were shown to be at least equal to those observed in wealthier countries. However, subsequent research has highlighted alarmingly high rates of virological failure accompanied by

the development of drug-resistant viruses. An international team of investigators analysed 12- and 24-month outcomes among patients who started HIV therapy in seven low- and middle-income countries in Africa (Burkina Faso, Cameroon, Ivory Coast, Senegal and Togo) and south-east Asia (Thailand and Vietnam).

Blood samples were taken at routine clinic visits and sent for viral load testing. A viral load above 1 000 copies/ml was the threshold for virological failure. Samples with a viral load above this figure were subjected to genotypic resistance testing.

Viral load for approximately 4 000 patients taking first-line therapy was sampled between October 2009 and December 2011. Women represented 70% of patients from African countries, whereas men were in the majority in south-east Asia. Data on 12-month outcomes were analysed for 2 060 patients and 24-month outcomes for 1 875 individuals. Treatment regimens included d4T (stavudine (Zerit)) or AZT (zidovudine (Retrovir)) with 3TC (lamivudine (Epivir)) and either efavirenz (Sustiva or Stocrin) or nevirapine (Viramune). A very small number of patients received tenofovir (Viread), but none was treated with a protease inhibitor.

Overall, 11% of patients experienced virological failure at month 12 and 12% at month 24. Detailed analysis, however, revealed that outcomes varied significantly between countries.

Very low rates of treatment failure at both month 12 and month 24 (3 - 5%) were observed in Burkina Faso (group A countries). The frequency of treatment failure after one or two years of treatment varied between 9% and 14% in Cameroon, Senegal and Vietnam (group B countries). In group C countries (Ivory Coast and Togo), between 18% and 20% of patients had a viral load above 1 000 copies/ml after 12 months of treatment. This increased to between 14% and 26% at month 24.

Between 10% and 50% of patients had a viral load of 1 000 - 5 000 copies/ml, which means that the WHO threshold for failure

at 5 000 copies/ml may lead to significant misclassification of treatment failure.

Almost three-quarters (71%) of patients experiencing failure at month 12 developed strains of drug-resistant virus, and there was an 86% prevalence of drug resistance among patients with virological failure after two years of therapy.

The proportion of patients with two or more resistance mutations varied between 7% and 24%. Most of the mutations concerned the drugs used in first-line therapy, but a few patients developed cross-resistance to similar drugs.

The investigators were encouraged by the low prevalence of resistance observed in group A countries, which they note was 'unexpected' and 'similar, if not better than those obtained from countries where patients obtain adequate treatment monitoring, including viral load assessment, generally industrialised countries or well monitored cohort studies'.

The authors stress that the differences in outcomes between countries cannot be explained by differences in study populations or HIV treatment regimens. The investigators call for 'better programme management and implementation of actions to improve factors such as patient adherence, drug stock-outs and lost to follow-up'.

The author of an accompanying editorial does not believe that the high failure rates observed in some countries can be ascribed to lack of routine viral load monitoring and stresses that the drug-resistance testing is not feasible in most resource-limited countries.

Aghokeng AF, et al. Extraordinary heterogeneity of virological outcomes in patients receiving HAART and monitored with World Health Organization public health approaches in sub-Saharan Africa and south-east Asia. *Clin Infect Dis* (online edition), 2013.

Katzenstein DA. HIV RNA and genotype in resource limited settings. Can we do better? *Clin Infect Dis* (in press).