

## Early-warning indicators for drug resistance in resourcelimited settings piloted in Namibia

## **KELLY SAFREED-HARMON**

A pilot project using 'early-warning indicators' (EWIs) to minimise antiretroviral resistance in Namibia has provided further evidence of the potential value of this strategy in settings where routine viral load monitoring is not feasible.

The World Health Organization (WHO) has encouraged resource-limited countries to integrate EWIs into their monitoring activities. EWIs measure how well antiretroviral programmes are performing in terms of factors associated with the emergence of drug resistance, such as clinic appointment-keeping and loss to follow-up.

With more than 4 million people in the developing world now receiving antiretroviral therapy, but few of those people able to access the relatively costly laboratory tests that are a standard component of HIV medical care in wealthy countries, there is ongoing concern that high rates of undetected treatment failure could cause widespread drug resistance.

In Namibia, which has an 18% adult HIV prevalence rate, antiretroviral treatment is free of charge at public-sector clinics. Namibia has one of the highest antiretroviral coverage rates in sub-Saharan Africa, with treatment being provided to 88% of people for whom treatment is indicated. That figure represents 40 000 public-sector patients and 12 000 private-sector patients.

Public health planners in Namibia implemented the EWI approach using data from a sample of 3 240 patients attending nine public-sector HIV treatment centres. Their analysis, presented as an advance online publication of the *Journal of Acquired Immune Deficiency Syndromes*, highlighted strengths and weaknesses of the national antiretroviral treatment programme. It also called attention to data gaps that hampered programme monitoring.

Data were available for three EWIs chosen for the pilot project: antiretroviral prescribing practices; patient loss to follow-up at 12 months; and patient retention on first-line antiretroviral treatment at 12 months.

All patients in the study sample were found to have received one of the first-line antiretroviral regimens named in Namibia's national guidelines. Thus, all nine study sites achieved the WHO-proposed target of 100% appropriate prescribing practices.

Eight sites reported losing no more than 20% of patients to follow-up within 12 months of antiretroviral initiation, another WHO target. Six sites met the WHO target of not having any patients switch to a second-line antiretroviral regimen within 12 months of the initiation of therapy.

The pilot project called attention to the fact that it was not possible to measure a fourth EWI of interest: the percentage of antiretroviral patients who filled their prescriptions on schedule. Efforts to collect these data revealed that few of the study sites' pharmacies followed the recommended practice of counting leftover pills when patients came for refills.

Another EWI measuring the extent to which stock-outs limited the availability of prescribed drugs also needed to be dropped because of data limitations.

The authors of the journal article note that the study sites' appropriate antiretroviral prescribing and low levels of loss to followup represent success at minimising two important causes of antiretroviral resistance.

At the same time, the monitoring exercise called attention to a worrisome treatment interruption trend. More than 20% of patients had gone for periods of time without documented use of antiretrovirals during the first year on treatment. The median length of treatment interruption was 2.3 months.

The article reports that Namibia's Ministry of Health and Social Services (MoHSS) believes the treatment interruptions to be reflective of seasonal migration to other areas of the country. It is possible that some patients who migrate continue receiving antiretroviral treatment at other treatment sites, but such behaviour cannot be documented because records are not linked.

'As a result of this pilot,' the authors note, 'the MoHSS has planned an intensification of existing ART defaulter tracing mechanisms through improvements in (electronic record-keeping), the establishment of a national patient database with unique patient identifiers, and increased mobilization ... of human resources.'

Similarly, changes are planned to improve pharmacy reporting on pill counts when patients present for refills and to track the occurrence of stock-outs of antiretroviral drugs. Based on the overall outcomes of the pilot project, the Namibian government intends to scale up EWI monitoring at all public-sector antiretroviral treatment sites nationally and to integrate EWIs into its established HIV monitoring and evaluation system. There is also interest in collaborating with privatesector partners to use insurance company data to assess EWIs in Namibia's large population of private health care patients.

WHO describes the use of EWIs as a key element in the global HIV drug resistance strategy it introduced in 2008.

WHO has selected six core EWIs and two optional EWIs partly on the basis of how feasible it is thought to be for countries to use existing electronic and paper-based records for monitoring: see the agency's recently updated *HIV Drug Resistance Early Warning Indicators* for more information. As Namibia's experience suggests, operational research may be required to determine how to promote the collection of the desired information in standardised form.

Hong SY *et al.* Population-based monitoring of HIV drug resistance in Namibia with early warning indicators. *J Acquir Immune Defic Syndr*, advance online publication, 10 September 2010.

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A study on seasonal success rates of IVF, presented at the World Congress on Fertility and Sterility in Munich recently, suggests that levels of oestadiol are significantly higher in spring.

A team, led by Daniela Braga of the Assisted Fertilisation Centre in Sao Paulo, Brazil, measured hormone levels in 1 932 women undergoing IVF treatment. They found that levels of oestradiol were significantly higher in spring and correlated with a 45% higher fertilisation rate during this season.

Another survey presented at the conference, by the Internation Federation of Fertility Societies, highlighted the lack of consistent global safety standards for IVF. Ian Cooke of the IFFS, who co-authored the survey, is now developing an international code of practice.

New Scientist, 18 September 2010.