World Health Organization

TECHNICAL UPDATE

HIV DRUG RESISTANCE

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ACRONYMS AND ABBREVIATIONS

ADR	Acquired HIV drug resistance
ART	Antiretroviral therapy
DBS	Dried blood spot
EID	Early infant diagnosis
EWI	Early warning indicators
HIVDR	HIV drug resistance
PDR	Pre-treatment HIV drug resistance
WHO	World Health Organization

INTRODUCTION

Unprecedented scale-up of antiretroviral therapy (ART) has been observed over the past decade: at the end of 2015, 16 million people were receiving ART in low- and middle-income countries. However, the emergence of HIV drug resistance (HIVDR) can compromise the effectiveness of antiretroviral drugs, thereby jeopardizing the efficacy of ART to further reduce HIV incidence and HIV-associated morbidity and mortality.

HIVDR emerges when HIV replicates in the presence of antiretroviral drugs. If HIVDR becomes widespread, the drugs used to treat HIV infection may become ineffective. To date, levels of HIVDR in countries scaling up ART remain manageable; however, they are slowly increasing. For example, in East Africa, resistance rates to non-nucleoside drugs (such as nevirapine and efavirenz) have recently been reported as above 10%.

Although new ART recommendations ("treat all") and the scale-up of pre-exposure prophylaxis using antiretroviral drugs are likely to further increase levels of HIVDR, concerns about resistant virus should not preclude adoption of a treat-all approach.

To minimize the emergence and spread of HIVDR, the World Health Organization (WHO) recommends HIV treatment scale-up be accompanied by measures to monitor and improve the quality of ART delivery and surveillance of HIVDR[1,2].

At country level, the strategy endorses:

1. country ownership through
   a. formation of a national HIVDR working group;
   b. integration of the national HIVDR strategy into the National Strategic HIV Plan; and
   c. integration of HVDR activities into routine Monitoring and Evaluation function.
2. HIVDR assessments including
   a. surveillance of HIVDR; and
   b. annual monitoring of early warning indicators (EWI) of HIVDR
3. leveraging of enablers
   a. use of WHO-designated laboratory for HIVDR testing; and
   b. identification and allocation of resources
4. use of all available information to minimize the emergence and transmission of drug-resistant HIV; and
5. timely dissemination of information

Recommendations include the following priority assessment activities:

1. monitoring EWI of HIVDR;
2. surveillance of pre-treatment HIV drug resistance (PDR) in populations initiating ART; and
3. surveillance of acquired HIV drug resistance (ADR) in populations receiving ART[3].

Due to greater operational complexity, WHO no longer recommends the routine implementation of surveys of transmitted HIVDR among recently infected populations. However, in limited circumstances, if the results will influence a planned public health intervention, surveys of transmitted HIVDR may add value by documenting transmission of drug-resistant virus in specific populations or geographic areas. Countries considering surveillance of transmitted HIVDR are encouraged to contact WHO to discuss its relevance and proposed methodology.

This update provides an overview of the essential elements that programme managers should include in programme planning to prevent and monitor the emergence of HIVDR. It also describes programmatic relevance and use of data.

1 Consolidated strategic information guidelines for HIV in the health sector. World Health Organization. World Health Organization, Geneva, Switzerland. 2015. Available at: http://who.int/hiv/pub/guidelines/strategic-information-guidelines/en/

2 Global Health Sector Strategy on HIV, 2016–2021. World Health Organization. World Health Organization, Geneva, Switzerland. 2016. Available at: http://www.who.int/hiv/strategy2016-2021/en/

3 When countries reach optimal coverage of VL testing for routine patient monitoring, remnant VL specimens can be used to inform HIVDR surveillance, if specimens are accessible for genotyping and no major biases are identified.

MAIN COMPONENTS

1. EWI of HIVDR

The first and most important step is to assess whether ART programmes deliver services with the quality required to minimize the emergence of HIVDR. This assessment is achieved through the use of a set of indicators known as "EWI of HIVDR". These indicators should be integrated into the routine monitoring and evaluation systems of ART programmes. Results should be used to identify gaps in service delivery, for which corrective actions may be taken at the ART clinic or programme level to optimize overall programme performance.

EWI monitoring assesses retention on ART, drug supply continuity, adherence to prescribed ART, viral load suppression, and coverage of viral load testing.

Standardized definitions and performance targets have been developed for each EWI, along with a colour-based scorecard system, in which "red" signals situations that require corrective action and "green" signals satisfactory performance.

It is recommended that EWI be monitored annually at all treatment sites. If this is not feasible, EWI may be monitored through a nationally representative sample of clinics, with the goal to progressively add more clinics in subsequent years until all of them are included. This approach will generate a reliable overview of a national programme's performance.

EWI monitoring should be integrated into routine monitoring and evaluation systems, to minimize costs and strengthen existing data collection and reporting processes.[1]

If EWI data are not routinely available, the following costs should be taken into account when planning for their abstraction:

1. sensitization of staff at treatment sites to the relevance of measuring performance against a series of standardized indicators, and how these can be used to improve service delivery;
2. organization of data abstraction and data entry (i.e. training and salaries for data abstraction and data entry to ensure high-quality data are obtained);
3. supervisory costs related to data quality assurance (e.g. travel to sites, per diem costs, etc.);
4. data analysis (e.g. data manager, statistician, etc.); and
5. report writing and dissemination, and use of data for clinic and programme optimization.

Responsibility for data abstraction can be assigned to existing clinic staff or, alternatively, new staff may be recruited for this task for a limited time. Abstraction costs depend on the number and location of sites, the size of the patient population, whether records are paper- or electronic-based, and ultimately whether abstraction is integrated with other routine monitoring activities.

Past experience monitoring EWI suggests that data abstraction in sites working exclusively with paper records

Table 1: Recommended high-priority activities for the surveillance of HIVDR

Type of survey	Population of interest	Outcome measure	Programmatic relevance	Recommended periodicity
PDR	Individuals initiating ART	Nationally representative estimate of HIVDR among	Presence of resistance prior to ART initiation can compromise both the therapeutic and prevention benefits	Priority element. To be repeated