HIV/AIDS Programme

MEETING REPORT ON

ASSESSMENT OF WORLD HEALTH ORGANIZATION HIV DRUG RESISTANCE EARLY WARNING INDICATORS

Report of the Early Warning Indicator Advisory Panel Meeting

11–12 AUGUST 2011 GENEVA, SWITZERLAND

World Health Organization

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EXECUTIVE SUMMARY

Early warning indicators (EWIs) of HIV drug resistance (HIVDR) are a key component of the World Health Organization (WHO) public health strategy to minimize and assess HIVDR in countries scaling up antiretroviral therapy (ART). EWIs are quality of care indicators which specifically assess factors at individual antiretroviral therapy clinics associated with emergence of HIVDR. Where widely implemented, EWIs provide the necessary programmatic context to interpret results of surveys of transmitted and acquired HIVDR.

As of mid-2011, 52 countries had implemented 102 rounds of EWI monitoring which assessed over 16,000 patients. The implementation of EWI monitoring has progressively increased over time supported by a simple standardized data abstraction tool. HIVDR EWIs and targets were originally chosen in 2006 based on a review of the available medical literature and expert opinion.

In August 2011, an advisory panel review meeting was held in Geneva to consider revisions of the existing EWIs and associated targets. After a critical review of available medical literature using the GRADE methodology, recommendations were developed to simplify EWI definitions, account for implementation challenges, harmonize with other routinely reported indicators and adjust EWI definitions and targets based on new evidence. The revised recommended set of indicators which is designed to be implemented as a package includes a total of five indicators, one of which (viral load suppression at 12 months), is considered conditional and is designed to be implemented only at clinics where routine viral load monitoring is performed for all patients 12 months after ART initiation.

When possible, indicator definitions were harmonized with UNGASS or PEPFAR indicators and a target appropriate to HIVDR was established. The revised set of indicators is anticipated to require substantially less data abstraction with the abstraction and reporting function performed by the ART clinic rather than by data abstractors sent from the national programme level. Suggested modifications to EWI definitions and abstraction procedures are anticipated to substantially facilitate wider uptake, reporting, and sustainability.

INTRODUCTION

- As of December 2010, 6.6 million people living with HIV in low and middle income countries (LMICs) were receiving ART.

- The emergence and transmission of HIV drug resistance (HIVDR) is an unavoidable consequence of ART, even when appropriate drugs are prescribed and adherence is maximally supported. Nonetheless, efforts must be undertaken to limit HIVDR emergence especially because significant population-level HIVDR may necessitate switch from non-nucleoside reverse transcriptase (NNRTI) based first-line regimens to more expensive and less well tolerated boosted protease inhibitor-based second-line regimens.

- Individual HIVDR testing is not available, nor recommended, in most LMICs. Therefore, routine population-level laboratory based surveillance of HIVDR and assessments of how well ART programmes and clinics function to minimize emergence of HIVDR are required.

- WHO in collaboration with WHO/HIVResNet[1] developed a global strategy for the prevention and assessment of HIVDR. The strategy includes surveillance of transmitted HIVDR in recently infected populations, surveillance of acquired HIVDR in populations failing ART, and the monitoring of site and programme factors associated with emergence of HIVDR.

- HIVDR Early Warning Indicators (EWIs) are quality of care indicators which specifically assess factors at individual clinics associated with HIVDR emergence. EWIs form the foundation of WHO's HIVDR prevention and assessment strategy, and where widely implemented, provide the necessary programmatic context to interpret results of surveys of transmitted and acquired HIVDR. HIVDR EWIs and targets were originally chosen in 2006 based on a review of the available medical literature and expert opinion. Current WHO-recommended HIVDR EWIs and their corresponding targets are listed in **Table 1.** 2010 WHO HIVDR EWI guidance is available at: http://www.who.int/hiv/topics/drugresistance/hiv_dr_early_warning_indicators.pdf

1 WHO/HIVResNet is an advisory group of over 50 institutions.

HIVDR EWI OVERVIEW

- The purpose of implementing HIVDR EWI monitoring is to assess the extent to which ART programmes function to optimize the prevention of HIVDR. EWIs measure ART site factors known to be associated with good programmatic functioning and the prevention of HIVDR.

- EWIs evaluate factors associated with HIVDR prevention without requiring laboratory testing for drug resistance.

- Strengthening specific aspects of ART programme delivery at the site level will minimize preventable HIVDR and promote the long-term efficacy and durability of available first- and second-line regimens. EWI monitoring provides the evidence base for programmatic change and/or public health action to prevent and address HIVDR.

- Information collected as part of EWI monitoring includes: ART prescribing practices; loss to follow-up 12 months after initiation of ART; retention on appropriate first-line therapy at 12 months; on-time patient appointment keeping and antiretroviral (ARV) drug pick-ups; ARV drug supply continuity, patient adherence to ART through standardized measures (for example pill count), and rates of HIV viral load suppression rates at 12 months.

- The WHO recommends indicator-specific targets that clinics should reach to minimize emergence of HIVDR in ART patients. Currently recommended EWI definitions and targets were established based on a review of the published medical literature and consensus of international experts in 2006.

TABLE 1 WHO HIVDR EWIs (2010 GUIDANCE)

EWI	EWI target (%)
1. Prescribing practices (% of initail ART prescripitions congruent with national/WHO guidelines)	100
2. Loss to follow-up (% of patients lost to follow-up at 12 months)	≤20
3. Retention on first-line ART (% of patients retained on first-line ART at 12 months)	≥70
4. On-time pill pickup (% of patients with 100% on-time drug pickups during the first 12 months of ART, or during a specified time period)	≥90
5. On-time clinic appointment keeping (% of patients who attended all appointments on time during the first 12 months of ART, or during a specified time period)	≥80
6. Drug supply continuity (% of clinics with antiretroviral drug supply continuity during a 12-month period)	100
7. Adherence as measured by pill count (% patient adherence to antiretroviral therapy by pill count or other standardized measure)	≥90
8. Viral load suppression 12 months after ART initiation (% of patients with viral load <1000 copies/mL at 12 months)	≥70

ART = antiretroviral therapy; EWI = early warning indicator; HIV = human immunodeficiency virus; WHO = World Health Organization.

- Monitoring EWIs alerts national ART programme managers to clinic factors that need increased support to reduce the potential for significant population-level virological failure and emergence of preventable HIVDR. Routine EWI monitoring alerts clinic and district managers to specific areas which require attention and supports overall optimization of patient care.

- EWI results form the basis of recommendations for action either at the site level or, if many sites do not achieve targets, at the national ART programme level. Recommendations may include increased training and resources for specific aspects of care, provision of targeted support for adherence, or help with drug supply chain management and reduction of barriers to continuous access to ARVs. Additional assessment, including operational research to clarify the source of problems and the support required to address them, may also be recommended.

- 2010 EWI guidance recommends that EWIs be monitored at all ART sites within a country or a large number of representative sites. The sites where EWI are monitored are referred to as the primary sample. 2010 guidance does not describe how primary sampling should be performed to achieve results which are likely to be representative of overall ART programme functioning. However, guidance for sampling at an individual site (secondary sampling) for each EWI is provided to achieve a result that can be generalized to the site's entire clinic population. Secondary sampling is based on the total number of patients in care or receiving ART at the time EWI monitoring is performed. A full description of current primary and secondary sampling guidance, including a sample size look-up table is included in the 2010 EWI guidance available at: http://www.who.int/hiv/topics/drugresistance/hiv_dr_early_warning_indicators.pdf

- As of mid-2011, 52 countries had implemented 102 rounds of EWI monitoring (largely pilot experiences) which assessed over 16,000 patients receiving ART worldwide. EWIs have been monitored at >2,000 clinics and have formed the basis for public health action in many settings.

HIVDR EWI MEETING GOALS

- Between 2006 and 2011, important lessons were learnt regarding HIVDR EWIs. Although EWI monitoring provided countries with valuable and actionable programmatic information, and the HIVDR EWI data abstraction tool developed by WHO was simple to use, functional