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HIV DRUG RESISTANCE

MEETING REPORT

IMPLEMENTATION & SUSTAINABILITY OF HIV DRUG RESISTANCE SURVEILLANCE IN AFRICA ADDIS ABABA, ETHIOPIA

25–27 JUNE 2013

World Health Organization

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1. INTRODUCTION

In 2004, WHO and the United States Centers for Disease Control and Prevention (US-CDC), in collaboration with HIVResNet, developed a global strategy for the assessment and prevention of HIVDR. To date, one or more element of the strategy has been implemented in over 50 countries. However, lessons learned from implementation and the evolution of ART programmes suggested that parts of the strategy required updating. In order to maximize country input throughout the revision process and ensure a transparent and collaborative effort, a series of regional consultations were organized between February and July 2013 in Beijing (China), Brasilia (Brazil), Montpellier (France, for francophone African countries), Addis Ababa (Ethiopia) and Cape Town (South Africa) involving country programme managers, technical experts and local and international partners.

It is expected that revised methods should facilitate survey implementation and the timely and accurate collection of HIVDR data. New population-based HIVDR surveys should generate nationally representative data to better detect trends over time and improve programme planning and decision making.

This report concerns the regional consultation held in Addis Ababa. This consultation was organised with logistics support from the Ethiopian Public Health Association and from the African Society for Laboratory Medicine, whose support WHO would like to gratefully acknowledge.

2. MEETING OBJECTIVES

The meeting had four main objectives:

i. Provide a platform for countries to share their experiences in implementing HIVDR surveillance activities,
ii. Introduce draft revised methods for the surveillance of transmitted, pre-treatment and acquired HIV Drug Resistance and obtain country and partner feedback,
iii. Assist countries in the development of draft national HIVDR surveillance plans using available country-specific data, and
iv. Identify technical support needs that WHO will need to provide in the short term to assist with implementation.

3. PARTICIPANTS

ART programme managers, WHO-AFRO office, WHO-HQ, African Society for Laboratory Medicine (ASLM), PharmAccess African Studies to Evaluate Resistance (PASER), United States Centers for Disease Control and Prevention (US-CDC) and regional experts in HIVDR surveillance (list of participants can be found in Annex 1).

4. MEETING OVERVIEW

The meeting was held between June 25 and June 27 2013 and discussions were arranged so as to provide an opportunity for countries to present their experiences in implementing HIVDR surveys using old survey methods, followed by presentations of proposed new draft survey approaches and the development of country plans for the period of 2013-2017.

Day 1: (i) presentation of key results from WHO's Global HIVDR Report 2012, (ii) early warning indicators (EWI), (iii) transmitted drug resistance (TDR), and (iv) Pre-treatment HIVDR (PDR).

Day 2: (i) acquired drug resistance (ADR) and (ii) HIVDR in children.

Day 3: provided an opportunity for countries to develop, with the support of WHO, country plans for the implementation of HIVDR surveys using proposed new survey methods during the period 2013-2017.

The full meeting agenda can be found in Annex 2.

Session 1: Overview of HIV Drug Resistance (HIVDR) at the global level and WHO's response

A brief summary of the WHO HIV Drug Resistance Report 2012 was presented. An overview the WHO Early Warning indicators (EWI) of HIVDR, which underwent revision and simplification in 2012 was presented. Additionally, overviews of draft revisions to the four assessment elements of the global strategy requiring HIVDR genotyping were presented:

i. Transmitted drug resistance (TDR) surveys
ii. Pre-treatment drug resistance (PDR) surveys in ARV-naive and ARV-exposed individuals
iii. Acquired drug resistance (ADR) surveys
iv. Surveys of HIVDR in infants < 18 months of age (paediatric)
v. Finally, it was stated that the Global Fund for AIDS Tuberculosis and Malaria has encouraged countries for funding of HIVDR surveillance activities.

Session 2: WHO Early Warning Indicators (EWIs) of HIV Drug Resistance

This session discussed key lessons from the field in implementing the first generation of EWIs, and provided an overview of the simplifications introduced in 2012 to the recommended set of EWI and their respective targets. Revised guidance recommends that four indicators should be collected and abstracted by all clinics as part of routine monitoring and evaluation:

i. On-time pill pickup
ii. Retention in care at 12 months
iii. Pharmacy stock-outs
iv. Dispensing practices

A fifth indicator, viral load (VL) suppression at 12 months, is conditional and should only be monitored in clinics where routine viral load measurement is performed on all patients 12 month after ART initiation. WHO currently provides a target for clinic level viral load suppression for the 12 month time point. Because WHO 2013 treatment guidelines recommend viral load testing 6 months after ART initiation and annually thereafter, new viral load suppression targets for 6 and 18 months will be developed.

Early warning indicators should be monitored at all sites dispensing ART. It was emphasized that this can be accomplished progressively through inclusion of larger and larger numbers of sites (ideally sampled in a representative way until all sites in a country are reporting EWI annually). When a representative sample of ART clinics is used, data may be aggregated to estimate each indicator at the national level. EWI alert programme managers and signal the need for additional investigation.

In 2012, EWI underwent a simplification process and attempts were made to harmonize definitions with other internationally reported indicators. Specifically, the EWI LTFU was dropped from the set of indicators and the retention indicator which was kept and the definition changed to be identical to the UNGASS 12-month retention indicator.

EWI: Topics discussed during question and answer period

- How can EWI data abstraction move from a centralized to a decentralized procedure whilst preserving the quality of the data?
- How can EWI be best integrated in the ART programs?
- What kind of data quality monitoring exists in countries and what kind of guidelines should WHO provide in this matter?
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- What kind of data quality monitoring exists in countries and what kind of guidelines should WHO provide in this matter?

Session 3: Surveillance of transmitted HIV Drug Resistance (TDR) in recently infected individuals

A draft WHO concept note on the surveillance of transmitted HIV Drug Resistance in recently infected populations was presented for feedback and discussion. The main goal of TDR surveillance is to inform optimal regimen selection for pre- or post-exposure prophylaxis. For economic and feasibility reasons, WHO recommends that countries integrate TDR surveillance into pre-existing HIV surveillance systems or routine diagnostic testing activities, if the reporting system is centralized and reporting rate is >90%. Thus, survey duration and survey sites should be the same used for HIV surveillance. Patient inclusion criteria remain unchanged from previous WHO TDR survey guidance. To maximize the inclusion of individuals with recent infection (i.e. in last 3 years), epidemiological markers (e.g., age <25 year) or laboratory criterion (i.e., CD4>500 cells/mm^3) should be used. In addition, to minimize inclusion of individuals with prior ARV exposure, women with previous pregnancies should be excluded.

Unlike the old TDR survey, the draft concept note presents a method that permits a national estimate of TDR. The national prevalence estimate has advantages over the previous method which only permitted classifications in defined geographic areas.

In the draft TDR concept note, the sample size will decisively influence the survey confidence interval. If the estimated sample size is N < 50, the result will be a point prevalence estimate with a very wide confidence interval, thus rendering it inappropriate for programme decision

applied if available. Age and parity remain the main eligibility criteria for TDR surveys.
- Recruitment period be extended to increase the sample size.
- The group also discussed whether eligibility criteria based on laboratory assay should be recommended, given the trade-offs between accuracy and the feasibility of recruiting enough eligible patients. Overall, it was felt that laboratory assays were too restrictive for the purposes of TDR surveillance as they greatly reduce the sample size limiting TDR survey implementation without providing any advantage.

Session 4: Surveillance of HIV Drug Resistance in populations initiating ART; i.e. PDR

The WHO draft concept note for surveillance of resistance in populations initiating ART was presented for feedback and discussion. In 2006, WHO developed a prospective survey method to assess HIVDR by following a cohort of ART initiators and assessing HIVDR at start of treatment initiation (baseline) and 12 months thereafter. This original prospective method has been revised and split into two stand-alone cross-sectional surveys: the first, surveillance of HIVDR among patients initiating first-line ART and the second, surveillance of acquired HIVDR in populations experiencing virological failure while on first-line ART. The recommended duration of patient enrolment is 6 months to ensure timely availability of results for decision making. Separate assessments should be performed in populations (i) initiating ART without prior ARV exposure and (ii) initiating ART with prior ARV exposure, but countries should decide, based on their own needs, whether to do only surveillance in populations without prior exposure or in populations without and with prior exposure. The main goal of performing PDR surveillance is to inform the selection of optimal first-line regimens.