HIV/AIDS Programme

MEETING REPORT ON

WHO RESNET ANNUAL MEETING

4 MARCH 2012 BILL AND MELINDA GATES FOUNDATION, SEATTLE, USA

World Health Organization

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BACKGROUND

The World Health Organization's Global Network HIVResNet, which benefits from technical support of HIVDR experts worldwide, was formed to address concerns regarding HIV drug resistance (HIVDR) emergence and to develop strategies to monitor and prevent HIVDR. In 2005, under ResNet endorsement, the World Health Organization (WHO) developed a public health strategy to minimize and assess HIVDR in countries scaling up antiretroviral therapy (ART) with a special focus on resource-limited settings (RLS).

Since 2005, standardized methods to inform population-based selection of first- and second-line ART regimens and support national programs to optimize patient care and minimize the emergence and transmission of HIVDR have been developed. Through the implementation of WHO recommended protocols, a considerable amount of data on transmitted and acquired HIV drug resistance has been produced.

The objectives of this ResNet consultation was to provide an update on the ongoing activities in HIV ResNet, obtain ResNet endorsement for newly developed components in the global HIV drug resistance surveillance and monitoring strategy, and discuss the scenarios to strengthen implementation and the strategy in the future.

SUMMARY PRESENTATIONS

SESSION A

IMPLEMENTATION, RESULTS AND INTERPRETATION OF HIVDR WHO RECOMMENDED SURVEYS

WHO HIVDR data from HIVDR Early Warning Indicators and Surveillance of acquired and transmitted HIVDR were presented.

1. MONITORING OF HIVDR "EARLY WARNING INDICATORS" (EWI) FROM ART CLINICS

HIVDR EWIs assess factors at individual clinics which are known to be associated with emergence of HIVDR. Results provide an alert for corrective action to improve ART clinic performance and programme functioning.

As of 2011, 124 rounds of EWI monitoring in 58 countries in >2000 clinics were reported.

The implementation of EWI monitoring has progressively increased over time with 144 performed cumulatively since inception. EWIs 1, 2, 3 and 5 (see table 1) were those most frequently reported, particularly in Africa and Asia. To facilitate EWI monitoring, WHO developed an EXCEL based tool which has proven to be simple to use and which supports standardization.

TABLE 1 EARLY WARNING INDICATORS

EWI	EWI Target
1. Prescribing practices	100%
2. Lost to follow-up at 12 months	≤20%
3. Retention on first-line ART at 12 months	≥70%
4. On-time drug pick up	≥90%
5. On-time appointment keeping	≥80%
6. Drug supply continuity	100%
8. Viral load <1000 copies/ml at 12 months	≥70%

In August 2011, an expert panel meeting review meeting was held in Geneva to consider revisions to currently recommended EWIs and targets. After a critical review of available medical literature using the GRADE methodology, panel made several recommendations to WHO. Specifically recommendations were made to simplify EWI definitions, account for implementation challenges, harmonize with other routinely reported indicators and adjust based on new evidence. The suggested revised set of indicators

which is designed to be implemented as a package is presented in Table 2. Notably, the total number of indicators was reduced from seven to four. The fifth indicator (viral load suppression at 12 months), is considered conditional and is designed to be implemented only at sites where routine viral load monitoring is performed for all patients 12 months after ART initiation.

TABLE 2. REVISED EWI 2011

HIV Drug Resistance Early Warning Indicator Score Card		
Early Warning Indicator	**Status**	**Target**
1. On-time pill pick-up		• Red <80% adherence in ≥90% of patients • Amber 80–95% adherence in ≥90% of patients • Green >95% adherence in ≥90% of patients
2. Retention in care		• Red <75% retained after 12 months ART • Amber, 75–85% retained after 12 months ART • Green >85% retained after 12 months ART
3. Pharmacy stock-outs		• Red <100% of a 12 month period with no stock-outs • Green 100% of a 12 month period with no stock-outs
4. Prescribing practices		• Red >0% dispensing of mono or dual therapy • Green 0% dispensing of mono or dual therapy
5. Virological suppression#		• Red <70% viral load suppression after 12 months of ART • Amber 70–85% viral load suppression after 12 months of ART • Green >85% viral load suppression after 12 months of ART

Notes:
Red (poor performance, below desired level)
Amber (fair performance, not yet at desired level but progressing towards desired level)
Green (excellent performance, achieving desired level)
Grey (data not available)
Targets for virological suppression in children <2 years old
Red <60% viral load suppression after 12 months of ART
Amber 60–70% viral load suppression after 12 months of ART
Green >70% viral load suppression after 12 months of ART

The revised set of indicators is anticipated to require substantially less data abstraction and whenever possible indicator definitions were harmonized with UNGASS or PEPFAR indicators and a target appropriate to HIVDR was established.

To further stimulate widespread uptake of EWIs, sustainability and ownership, data abstraction and reporting responsibilities will be delegated to ART clinics.

2. SURVEILLANCE OF ACQUIRED HIVDR

Thirty-four monitoring surveys were conducted at 34 ART clinics in 10 countries (Burundi, India, Malawi, Mozambique, Nigeria, Zimbabwe, Cameroon, Swaziland, Indonesia, and Namibia) for a total of 4251 patients surveyed between 2006 and 2011. In a combined analysis of all available data, approximately 6% (N=3604 from the 15 surveys with available data) of patients initiating ART at the clinics (naïve and ARV exposed) had detected HIVDR at time of ART initiation. The proportion of patients with virological suppression (<1,000 copies/ml) at 12 months (N=2150) was 90% for patients retained in care and alive and 70% when LTFU and ART stops are included and classified virological failure.

Approximately 35% of those with virological failure at 12 month had wild type suggesting that adherence counselling should be strengthened. At 12 months, in patients failing ART (N=128) the prevalence of thymidine analogue mutations (TAMs) remained limited (4.7% ≥3 TAMs). 67% had NNRTI resistance including 52% with 184I/V and 6.3% with K65R.

Surveys proved useful as they provided site-specific assessments of viral load suppression, especially in sites where viral load monitoring was not routinely performed. However, survey results cannot be used to inform on the appropriate composition of second line regimens beyond 12-15 months as the number of specimens from patients was too small to allow generalisation and in many RLS patient may remain on failing regimens for long durations and subsequently accrue additional HIVDR.

During the discussion it was highlighted how measuring viral load is critical to minimize HIVDR by detecting early failure, thus preventing accrual of additional HIVDR, and that individual HIVDR testing is not critical to inform switch to second-line as resistance to protease inhibitors is not observed and drug options are limited. Drawbacks of current methodologies are addressed in a new cross-sectional survey of acquired HIVDR which is presented as part of the new global strategy in section C.

3. SURVEILLANCE OF TRANSMITTED HIVDR

Ninety-four surveys (54 surveys with available data from 22 countries) were conducted between 2002-2011, mostly between 2005-2009.

Overall, 81% of surveys showed low TDR (<5%), suggesting that TDR was low in the areas and populations assessed at the time the surveys were conducted. 19% of surveys showed moderate TDR