WHO HIV Drug Resistance Prevention and Assessment Strategy

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The HIV epidemic in ESA

- Estimated 14.9 million persons living with HIV in Eastern & Southern Africa (ESA)

- Southern Africa has 32% of all HIV infections in the world

- Generalized epidemic in most countries & a prevalence >15% (for Botswana, Lesotho, Mozambique, Namibia, South Africa, Swaziland, & Zimbabwe)

- Concentrated epidemics in the Island Countries
  - mainly in MARPs - IDUs, MSM, sex workers

- In general HIV epidemic stabilising in the region except for Mozambique
HIV Prevalence in ESA by country

Prevalence (%)
ART Scale up in Eastern & Southern Africa by Dec 2008

<table>
<thead>
<tr>
<th>Year</th>
<th>ART In Need of ART</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003</td>
<td>0.1</td>
</tr>
<tr>
<td>2004</td>
<td>0.3</td>
</tr>
<tr>
<td>2005</td>
<td>0.7</td>
</tr>
<tr>
<td>2006</td>
<td>1.1</td>
</tr>
<tr>
<td>2007</td>
<td>1.7</td>
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<tr>
<td>2008</td>
<td>2.4</td>
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</table>
Proportion of Patients on 1st and 2nd Line ART in ESA

<table>
<thead>
<tr>
<th>Country</th>
<th>1st Line ART</th>
<th>2nd Line ART</th>
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</thead>
<tbody>
<tr>
<td>Zambia</td>
<td>100%</td>
<td>0%</td>
</tr>
<tr>
<td>Uganda</td>
<td>100%</td>
<td>0%</td>
</tr>
<tr>
<td>South Africa</td>
<td>100%</td>
<td>0%</td>
</tr>
<tr>
<td>Namibia</td>
<td>100%</td>
<td>0%</td>
</tr>
<tr>
<td>Kenya</td>
<td>100%</td>
<td>0%</td>
</tr>
<tr>
<td>Swaziland</td>
<td>100%</td>
<td>0%</td>
</tr>
<tr>
<td>Ethiopia</td>
<td>100%</td>
<td>0%</td>
</tr>
<tr>
<td>Zimbabwe</td>
<td>100%</td>
<td>0%</td>
</tr>
<tr>
<td>Lesotho</td>
<td>100%</td>
<td>0%</td>
</tr>
<tr>
<td>Malawi</td>
<td>100%</td>
<td>0%</td>
</tr>
<tr>
<td>TOTAL</td>
<td>100%</td>
<td>0%</td>
</tr>
</tbody>
</table>
Impact of Scaling up

- While there is still a large unmet need for ART in the region
  - Cohort monitoring is critical for successful programme management

- Quality of health services likely to affect programme outcomes
  - Scale up efforts need to be accompanied by other infrastructure improvement e.g. human resources

- Emergence of drug resistance is inevitable
  - Advocacy & support in systematically implementing the global HIVDR Strategy important
A public health approach to HIVDR

- WHO recommends that countries develop a public health strategy
  - To assess and optimize ART programme performance related to HIVDR prevention
  - To assess emergence and transmission of HIVDR
  - To use results to minimize emergence & transmission of HIVDR
  - To provide useful information for policy makers at national, regional and global level

- Strategy should only be implemented if results will lead to programmatic action
  - Address systemic problems ➔ prevent the "preventable" HIVDR
Objectives of the WHO HIVDR Prevention & Assessment Strategy

National:
To provide data to inform ART programme to:
1. minimize the preventable emergence of HIVDR
2. maintain patients successfully on first-line ART as long as possible

National and Global:
1. To provide data to guide population-based selection of ART regimens
2. To provide data on programmatic factors related to HIVDR emergence and best practices to minimize it
WHO HIVDR Prevention and Assessment Strategy

A. Development of a national HIVDR Working Group
B. Regular assessment of HIVDR "early warning" indicators from ART sites
C. Surveys to monitor HIVDR prevention and associated factors
D. Surveillance of HIVDR transmission
E. HIVDR database
F. Designation of a WHO-accredited HIVDR genotyping laboratory
G. Review of and support for HIVDR prevention activities
H. Preparation of annual HIVDR report and recommendations
A. National HIVDR working group

- Formation of national HIVDR working group within the Ministry of Health
- WG is multidisciplinary (lab, clinical, epi)
- Integration of HIVDR strategy into country HIV prevention and care plan
- Collaborations with national and international partners at country level
- 5 year work plan and budget
Prospectively monitor HIVDR prevention/emergence and associated factors in **cohorts of patients starting first line ART**

- Patients followed for **12 months** or until lost to follow-up, stop, switch
- Genotyping at baseline and 12 months or switch endpoint
1. To improve ART programme functioning for HIVDR prevention, by identifying factors related to HIVDR prevention/emergence

2. To maximize the long term effectiveness of available regimens

3. To evaluate HIVDR patterns acquired with failing first-line ART to support optimal regimen selection
Surveillance of transmitted HIVDR

**Purposes**

*To evaluate levels of HIVDR to common first-line regimens in recently infected populations*

A high level of HIVDR in recently infected persons may require:

- Change of first line regimens used for ART, PMTCT or PEP (or PrEP) for majority of patients
- Investigations as to reasons for suspected HIVDR transmission
- Consideration of baseline HIVDR testing for specific groups/settings
Introduction to HIVDR Early Warning Indicators

- Specific ART programme factors can be associated with virological failure and emergence of HIVDR

- To minimize preventable HIVDR requires monitoring of indicators on ART program functioning
  - At all ART sites, or
  - At a representative subset of sites

- Excel abstraction and analysis tools developed by WHO for use in countries

- WHO recommends minimum targets for each indicator; but countries may select more stringent targets
Specific ART program factors are associated with the emergence of HIV drug resistance (HIVDR)

Action to minimize preventable HIVDR requires monitoring of indicators on ART program functioning at ART sites

WHO recommends the monitoring of HIVDR "early warning indicators" (EWI) from all ART sites

HIVDR EWI are reported on a site by site basis

WHO recommends minimum targets for each indicator; but countries may select more stringent targets

HIVDR working group produces an annual summary and plan for HIVDR prevention
WHO Recommended HIVDR EWIs

1. **Prescribing practices**
   - % of patients* starting ART prescribed an appropriate 1st-line regimen  
     **Target:** 100%

2. **% lost to follow-up during the first 12 months of ART**
   % of patients* lost to follow-up 12 months after initiating ART  
   **Target:** < 20%

3. **Patient retention on first-line ART**
   % of patients initiating ART* during a specified time period who are on an appropriate first-line ART regimen 12 months later  
   **Target:** > 70%
4. **On-time ARV Drug pick up**
   % of ART patients picking up prescribed ARV drugs on time
   Target: \( \geq 90\% \)

5. **ART appointment-keeping**
   % of ART patients attending all clinic appointments on-time
   Target: \( \geq 80\% \)

6. **Drug Supply Continuity**
   - % of months during a year with no antiretroviral drug stock outages
   Target: \( : 100\% \)
EWI Data Abstraction

- A set of instruments to be used for data abstraction at ART site level

- Tools available in two formats:
  - Paper or manual abstraction version
  - Electronic abstraction version

- EWI are assessed by abstracting a specific set of data from medical and/or pharmacy records at each ART site.

Abstraction Instruction manual available
Data for EWI 1

- Abstraction eligibility date is pre-determined by WG
  - E.g. from 1 January 2009

- Sample size for each ART site is pre-determined by WG
## EWI Sampling strategy for each site

<table>
<thead>
<tr>
<th>Patients starting ART in the year/or receiving ART during the year</th>
<th>Number to be sampled</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-75</td>
<td>All</td>
</tr>
<tr>
<td>76-110</td>
<td>75</td>
</tr>
<tr>
<td>111-199</td>
<td>100</td>
</tr>
<tr>
<td>200-299</td>
<td>130</td>
</tr>
<tr>
<td>300-2500</td>
<td>180</td>
</tr>
<tr>
<td>&gt;2500</td>
<td>Consult WHO</td>
</tr>
</tbody>
</table>
What data to abstract from the records for EWI 1a

- **Records should provide these Variables**
  - Patient ID
    - ART Cohort Register
  - ART initiation date at the site
  - ART regimen initially prescribed/picked up
    - Patient ART Card/Pharmacy record
do not include patients if transferred in on ART
Numerator: number of patients initiating ART at the site who are prescribed, or who initially pick up from the pharmacy, an appropriate first-line ART regimen.

Denominator: number of patients initiating ART at the site (full sample size) on or after the abstraction eligibility date.
National selection of HIVDR EWI

- Monitor only EWI that can be extracted from existing routine patient/pharmacy information systems.

- Countries evaluate which EWI can be captured from current HIV care/ART patient medical records (manual or electronic) or pharmacy records.

- Planners should visit sites to observe which information is reliably recorded in site records, rather than assuming that all sites follow guidelines and training materials.

- Data abstractors should be trained to abstract the required information in a standard format from paper records.
Planning HIVDR EWI Data Abstraction

- Initially EWI abstraction may become a medical/pharmacy records quality assurance exercise.
  - Identifying problems and taking action to rectify them contributes indirectly to HIV drug resistance prevention.

- Paediatric and adult indicators are monitored separately

- ART site profile data supports interpretation of results
  - Also site profiles evaluate many HIVDR prevention factors at a site level

- Validation of abstraction and of data is crucial
Involve everyone
### Partial example: HIVDR EWI at representative ART sites, Country X

<table>
<thead>
<tr>
<th>Site</th>
<th>Months with no ARV drug stockouts Target = 12</th>
<th>% appropriate Initial ART Regimen Prescriptions Target = 100%</th>
<th>% lost to follow up at 12 months Target = &lt; 20%</th>
<th>%on ART keeping all clinical appointments on time Target = &gt; 80%</th>
<th>% on ART picking up all ART drugs on time Target = &gt; 90%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12</td>
<td>75/75 (100%)</td>
<td>3/75 (04%)</td>
<td>182/ 209 (87%)</td>
<td>184/ 192 (96%)</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>130/ 130 (100%)</td>
<td>16/130 (12%)</td>
<td>342/402 (85%)</td>
<td>176/ 220 (80%)</td>
</tr>
<tr>
<td>3</td>
<td>9</td>
<td>140/180 (78%)</td>
<td>58/180 (32%)</td>
<td>122/ 244 (50%)</td>
<td>144/ 206 (70%)</td>
</tr>
<tr>
<td>4</td>
<td>12</td>
<td>100/ 100 (100%)</td>
<td>10/ 100 (10%)</td>
<td>891/ 993 (90%)</td>
<td>483/ 508 (95%)</td>
</tr>
<tr>
<td>5</td>
<td>12</td>
<td>208/210 (99%)</td>
<td>45/210 (45%)</td>
<td>753/ 1506 (50%)</td>
<td>829/1202 (69%)</td>
</tr>
</tbody>
</table>
## HIVDR EWI Summary Report example

<table>
<thead>
<tr>
<th>Early Warning Indicator (EWI)</th>
<th>EWI Target for all sites (Time period)</th>
<th>number of sites meeting EWI target (% of sites meeting target)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Months with no ARV drug stock-outs</td>
<td>100%</td>
<td>165/175 (94.2 %)</td>
</tr>
<tr>
<td>% appropriate initial ART regimen prescriptions</td>
<td>100%</td>
<td>151/175 (86.2%)</td>
</tr>
<tr>
<td>% starting first line ART lost to follow up at 12 months of ART</td>
<td>≤ 20%</td>
<td>145/175 (82.8 %)</td>
</tr>
<tr>
<td>% on ART attending all clinical consultations within 7 days of scheduled appointment</td>
<td>≥ 80%</td>
<td>165/175 (94.1 %)</td>
</tr>
<tr>
<td>% on ART picking up all ART drugs before previously dispensed drugs ran out</td>
<td>≥ 90%</td>
<td>108/175 (61.7%)</td>
</tr>
</tbody>
</table>
ART Site profiles assist in interpretation of EWI results

- Catchment area and population groups served; services provided at clinic
- Number of patients started on ART in the past 12 months
- List of first-line ARV drugs and second-line drugs routinely prescribed at site
- Provider/patient ratio
- Training level and ongoing training for persons who start patients on ART
- Procedures for monitoring, reporting, and acting on drug shortages
- Procedures for following up patients who do not return to clinic for ART appointments (write "None" if no procedures)
- Type of adherence support provided (describe type of support, staffing)
General Discussion of EWI Results (examples)

- EWI results should be first of all evaluated to assess quality of medical/pharmacy records.

- EWI results should be critically evaluated to identify sites that have problems meeting targets for indicators,
  - Similarities among sites should be explored and evaluated for example.

- Barriers to continuity of care should be explored for each ART sites (costs, transport, clinic and pharmacy hours).
General Discussion of EWI Results (examples)

- EWI results may be used to support evidence-based recommendations for in-depth surveys, programmatic changes or requests for additional support at ART site and/or ART programme level

- Were there justifiable reasons for "inappropriate" prescriptions? (From medical record search or site interviews)
Review of and support for HIVDR prevention activities

- Standard prescribing practices, guidelines for ART and PMTCT, appropriate ART eligibility definitions in place, training for clinicians
- Support for and monitoring of adherence
- Removal of barriers to continuous access to care
- Resources and personnel for follow-up of ART patients
- Adequate and continuous drug supplies; monitoring at site and regional levels of drug supply shortages
- Ongoing quality assurance for drugs (not only initial QA)
- Standard ART patient records to facilitate ART patient and cohort monitoring
- Prevention programs to reduce HIV transmission from persons in treatment
EWI Progress

- 12 countries implementing at least 2 elements of the HIVDR strategy

- Partners include CDC/PEFPAR, UN Agencies,

- Main Sources of funding:
  - Gates Foundation
  - GFTAM
  - Spanish Government
  - MoHs
<table>
<thead>
<tr>
<th>Country</th>
<th>HIVDR WG</th>
<th>EWI</th>
<th>Prevention surveys</th>
<th>HIVDR-Threshold surveys</th>
</tr>
</thead>
<tbody>
<tr>
<td>Botswana</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Ethiopia</td>
<td>✓</td>
<td>✓</td>
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<td>✓</td>
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<td>Kenya</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
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<td>Malawi</td>
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<td>Mozambique</td>
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<td>✓</td>
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<td>✓</td>
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<td>Namibia</td>
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<td>Tanzania</td>
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<td>✓</td>
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<tr>
<td>Zimbabwe</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
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Challenges

- Multiple ART record systems in different countries require different abstraction plans, different training
  - More progress (Malawi, Zambia, Ethiopia) in persuading donors and NGOs to adopt national record system
- ART medical records often incomplete or inadequate
- Abstraction validation not always performed correctly
- ART program managers at the centre are frequently convinced that medical records are complete and accurate
- Despite emphasis on evaluation of reasons for not meeting targets and provision of additional support, some WG still censure sites not meeting targets
National HIVDR report

- Summary of HIVDR strategy elements implemented in the country
- Reviewing the data annually to draw lessons, make recommendations to improve public health practice
Conclusions

- Need to explore Areas of synergies

- Need to catalyze coordination of the EWIs and HIVQual initiatives to ensure linkages & efficient use of resources

- Both EWI & QI programmes have the goal of programme performance improvement

- Both EWI & QI are a minimum resource strategy

Use of routinely available systems
Thank You