WHO HIV drug resistance (HIVDR) early warning indicators

WHO HIV Drug Resistance Team

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WHO-recommended national HIVDR prevention and assessment strategy elements for countries scaling up antiretroviral treatment (ART)

A. Development of a national HIVDR strategy working group, three-to-five year plan and budget
B. Regular assessment of HIVDR "early warning" indicators (EWIs) from all ART sites (or representative sites)
C. Surveys to monitor HIVDR prevention and associated factors in sentinel ART sites
D. HIVDR transmission threshold surveys in geographic areas where ART has been widespread for ≥ 3 years
E. HIVDR database development
F. Designation of an in-country or regional WHO-accredited HIVDR genotyping laboratory
G. Review of and support for HIVDR prevention activities
H. Preparation of annual HIVDR report and recommendations; use of data for ART and prevention planning

Introduction to HIVDR EWIs (1)

- Specific ART programme factors are known to be associated with the emergence of HIVDR during ART
- Action to minimize preventable HIVDR requires monitoring of indicators on ART programme functioning at ART sites
- WHO recommends the monitoring of a feasible set of HIVDR EWIs from all ART sites, or a nationally representative subset of sites

Helpful Prerequisites

- **Standard "HIV care/ART card" or electronic medical record (EMR)**
- **Minimum national list of data items collected for all patients on ART**
- **Population-based and site-based ART monitoring systems**

Introduction to HIVDR EWIs(2)

- Unlike most other national indicators, the HIVDR EWIs are reported on a site-by-site basis
- WHO recommends minimum targets for each indicator; but countries may select more stringent targets
- HIVDR EWI monitoring should start even before national HIVDR surveys that include genotyping are implemented

> Genotyping surveys indicating the emergence of resistance are of limited use without ART programme information on which to base public health action to limit resistance

- The national HIVDR working group produces an annual summary of EWI information and plan for HIVDR prevention action

WHO-recommended HIVDR EWIs (1)

1. Prescribing practices

   - % of patients initiating ART who are prescribed an appropriate first-line regimen over a specified time period; *or*

   -% of patients picking up an ART prescription during a specified time period who pick up appropriate regimen

   Suggested target: 100%

2. % lost to follow-up during the first 12 months of ART

   % lost to follow-up 12 months after initiating ART during a specified time period

   Suggested 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

   Suggested target: ≥ 70%

National definitions for key concepts (e.g., "appropriate ART regimen") should be specified before EWI monitoring begins

WHO-recommended HIVDR EWIs (2)

4. On-time ARV drug pick up

   % of ART patients picking up prescribed ARV drugs on time (before previous drugs run out)

   Suggested target: ≥ 90%

5. ART appointment-keeping

   % of ART patients attending all clinic appointments on-time (within 7 days of scheduled appointment)

   Suggested target: ≥ 80%

6. Drug supply continuity

   – ART stops, substitutions, and switches due to ARV shortages during a specified time period

   Suggested target: 0%

   – % of months during a year with no antiretroviral drug stock outages

   Suggested target: 100%

Two optional indicators: 7.pill count/adherence and 8. viral load suppression at 12 months (only countries where pill counts/standardized adherence measures and/or viral loads are performed and recorded routinely for all patients should consider monitoring these EWIs)

National selection of HIVDR EWIs

- Countries evaluate which EWI can be captured from current HIV care/ART patient medical records (manual or electronic) or pharmacy records
- Countries should collect only those EWIs that can be extracted from existing routine patient /pharmacy information systems
- 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

HIVDR EWI denominator time period

For each indicator selected for the national EWI monitoring strategy, a specific **denominator time period** should be identified (likely to be different for each indicator)

- For *cohort* EWIs, the denominator time period is a designated period during which patients initiate ART; the numerator evaluates the specific outcome of the initial cohort 12 months later
- For *cross-sectional* EWIs: the denominator time period is a designated time period during which specific outcomes are evaluated as cross-sectional

In countries with many ART sites with small numbers of ART patients a maximum of two denominator time periods for each EWI may be identified to be used in "small" and "large" ART sites respectively

Selection of ART sites for HIVDR EWI monitoring

EWI should be monitored in a selection of ART sites during the pilot phase in the first year. Selection of pilot sites may be based on feasibility in terms of travel time and data collection, but should not be limited to sites known to record data well.

Reports on the pilot phase should discuss limitations of monitoring EWI in unrepresentative sites

The national EWI strategic plan should include expansion in the year following the pilot to a representative system:

1. monitoring of EWI from all ART sites in the country; *or*
2. representative ART sites

Either a stratified hierarchical cluster sampling, or a manual process categorizing ART sites in the country on the important characteristics to be represented and selecting appropriate numbers representing those characteristics, should be used

Planning HIVDR EWI data abstraction

- Evaluate available records systems and data entered into the systems to identify the data that can be feasibly abstracted, and which information fields in each system should be used

If electronic record-keeping systems are in use at EWI sites:

- program electronic systems appropriately to download the required sets of data to monitor EWI at each site

If paper based record-keeping systems are in use at EWI sites, or if download of data from electronic system is not feasible:

- data abstractors should be trained to abstract the required information in a standard format from paper records

WHO EWI data abstraction tools, both electronic and paper-based printable versions, are available for data abstraction

Example:
HIVDR EWI 1: ART prescribing practices (country X)

ART prescribing practices – EWI 1 version a1

% of patients initiating ART at the site during a selected time period who are initially prescribed, or who initially pick up from the pharmacy, an appropriate first-line ART regimen.

Country X target: 100%

Denominator time period: 1st quarter (January–March)

- Denominator: number of patients initiating ART at each site during the first quarter (Jan–Mar) of the relevant year
- Numerator: number of patients initiating ART at each site who are prescribed, or who initially pick up from the pharmacy, an appropriate first-line ART regimen during the first quarter (Jan-Mar) of the relevant year

Abstractors record only patient and regimen information. At the central level, analysts decide whether each regimen recorded meets the country definition of "appropriate".

Data abstraction for EWI 1 in country X

Data abstractors record the following for each patient initiating ART during January-March 2008:

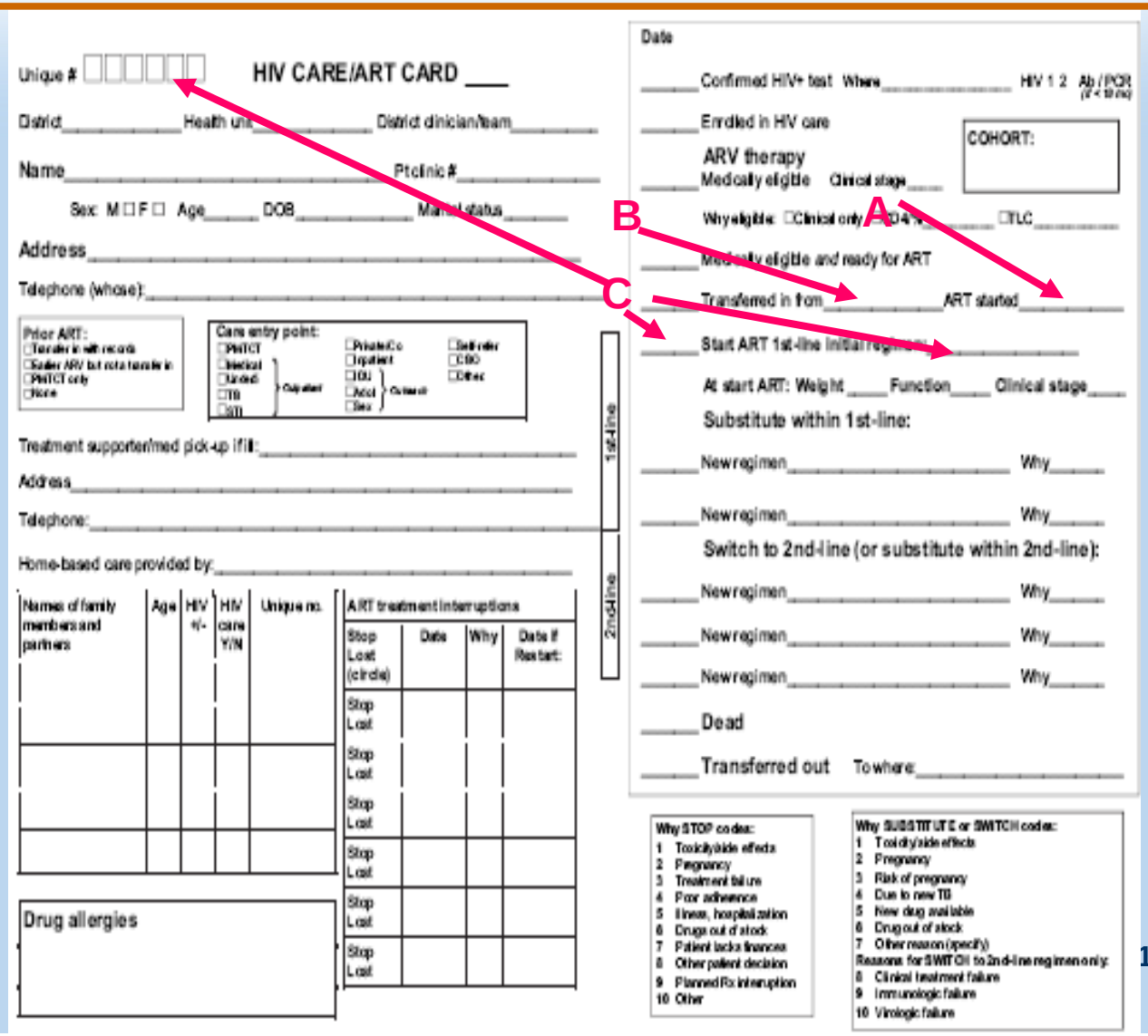
- a patient identifier;
- the date of ART initiation at the site (either as ART prescription or ARV drug pick-up) during the selected time period;
- the ART regimen initially prescribed (or ARV drugs initially picked up).

Codes may be abstracted for regimens, but if there is a code for "other", the data abstractor must list the ARV drugs in the regimen coded "other".

Example: prescribing practices for a cohort of patients. Starting ART using patient ART cards

A. Select all cards with ART start date during the relevant period
B. Exclude cards of those who transferred in
C. Record patient ID, date, initial regimen

Data extractors should record regimens; they should not make the decision on whether or not a regimen is appropriate



HIVDR EWI site-based report example

Site	Months with no ARV drug stockouts 2007 Target = 12	% appropriate Initial ART Regimen Prescriptions (1–3/ 2008) Target = 100%	% starting first line ART (6-8/2006) lost to follow up at 12 months Target = ≤ 20%	%on ART keeping all clinical appointments on time (first 2 appointments after 6/ 2007) Target = ≥ 80%	% on ART picking up all ART drugs on time (first 2 pick-ups after 7/ 2007) Target = ≥ 90%
1	12	94/ 94 (100%)	4/ 96 (04%)	182/ 209 (87%)	184/ 192 (96%)
2	10	81/ 81 (100%)	9/ 74 (12%)	342/402 (85%)	176/ 220 (80%)
3	9	31/ 40 (78%)	12/ 37 (32%)	122/ 244 (50%)	144/ 206 (70%)
4	12	104/ 104 (100%)	10/ 99 (10%)	891/ 993 (90%)	483/ 508 (95%)
5	12	112/ 112(100%)	13/ 105 (12%)	262/ 305 (85%)	184/ 202 (91%)
6	11	98/1 01 (97%)	2/ 90 (02%)	416/ 442 (95%)	254/ 359 (71%)
7	12	98/ 98 (100%)	9/ 88 (10%)	602/ 683 (88%)	369/ 402 (95%)
8	12	203/ 203 (100%)	43 /195 (22%)	292/356 (82%)	254/ 284 (86%)
9	12	304/ 305 (99.7%)	117/ 260 (45%)	753/ 1506 (50%)	829/1202 (69%)
10...	12	94/ 94 (100%)	12/ 90 (13%)	271/305 (89%)	269/ 290 (93%)
152	12	33/ 33(100%)	4/ 31 (13%)	147/ 180 (82%)	143/ 159 (90%)
153	10	26/ 34 (76%)	7/ 35 (20%)	148/ 224 (66%)	129/ 182 (71%)
154	12	73/ 73(100%)	9/ 69 (16%)	178/203 (87%)	146/154 (95%)

HIVDR EWI summary report example

EWI	EWI target for all sites (time period)	number of sites meeting EWI target (% of sites meeting target) N=154 ART sites
Months with no ARV drug stock-outs	100% (2007)	149/154 (96.7 %)
% appropriate initial ART regimen prescriptions	100% (Jan–March 2008)	146/154 (94.8 %)
% starting first line ART lost to follow up at 12 months of ART	≤ 20% (Jun–Aug 2006)	151/154 (98 %)
% on ART keeping all clinical appointments on time	≥ 80% (2 appointments after June 2007)	145/154 (94.1 %)
% on ART picking up all ART drugs on time	≥ 90% (2 appointments after July 2007)	95/154 (61.7%)

ART site profiles assist in interpretation of EWI results (1)

- Catchment area and population groups served; services provided at clinic
- Number of patients started on ART in the past 12 months
- Number of patients planned to be started on ART in the next 12 months
- List of first-line ARV drugs and second-line drugs routinely prescribed at site
- Method of determining patient eligibility for ART
- Provider/patient ratio
- Training level and ongoing training for persons who start patients on ART
- Training level and ongoing training for persons who provide routine care during ART
- Role of staff who dispense ARV drugs (physician, nurse, pharmacist, other (specify)
- Location of ARV drug pick-ups (pharmacy in clinic, pharmacy off-site, treatment room in clinic, other (specify)
- Role of staff who dispense ARV drugs (physician, nurse, pharmacist, other (specify)
- 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)
- "Prevention for positives" programme (describe programme and staffing)

ART site profiles (2)

- Costs of care to patient (record 0 if no cost)
  - Cost of initial registration at clinic
  - Cost of each appointment
  - Cost of first-line ARV drugs and/or pharmacy pick-up charge
  - Cost of each routine laboratory test used in ART
  - Cost of special laboratory tests used in ART
- Maximum, minimum, and mean distance traveled by patients to clinic; brief description of most common means of transport
- Longest, shortest, and mean waiting times for routine ART appointment at clinic
- Longest, shortest, and mean waiting times for ART drug pick-ups
- Days of the week: clinic opening and closing times for ART clinical appointments
- Days of the week: pharmacy opening and closing times for ARV drug pick-ups
- Needs identified by site personnel for better care delivery
- Other relevant information (HIVDR working groups specify)

Examples of recommendations based on EWIs

Sites not meeting a specific EWI target:

assess similarities among sites: rural sites, small sites, etc?

- < 100% appropriate prescriptions: assess drug supply continuity, assess need for additional training
- > 20% lost to follow-up: increase resources for patient follow-up
- < 90% on-time drug pick-up: targeted surveys to assess programmatic factors that could be addressed (transport, pharmacy hours, pharmacy waiting time, need for community outreach resources, need for less frequent appointments, increased support for adherence)
- <80% appointment keeping (see previous indicator)

Examples of recommendations based on EWIs

Sites meeting all targets

- What are operational lessons that can be applied to other sites?

EWI results should be critically evaluated to identify sites that have problems meeting targets for several indicators, and indicators for which many sites do not meet the target. EWI results may be used to support evidence-based recommendations for in-depth surveys, programmatic changes or requests for additional support both at ART site and ART programme level.